Fundamentals of Pediatric Neuroanesthesia

Girija Prasad Rath
Editor

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Affectionately dedicated to my father
Sh. Bhagirathi Rath

Foreword

The relative importance of medical care can be appreciated by assessing its efficacy in terms of life-years gained—the simple notion that successful treatment of a 70-year-old may extend life by 7 years, while successful treatment of a 7-year-old might extend life by 70 years. From that perspective, pediatric neurosurgery gains particular salience. And, as every neurosurgeon knows, excellent anesthetic management complements excellent surgical technique—and both require extraordinary understanding supplemented by continuing medical education (CME).

Pursuant to highly specialized medical education, Professor Girija Rath has assembled a volume that serves the purpose of both a textbook and a handbook. He has accomplished that by sandwiching chapters on the anesthetic management of most specific neurosurgical procedures between chapters that convey overarching concepts and considerations that apply to pediatric neurosurgical patients generally. Accordingly, *Fundamentals of Pediatric Neuroanesthesia* can be a valuable resource for anesthesiologists working in general hospitals as well as hospitals that specialize in neurosurgery.

English is the primary language of science, including medical science, and India is second only to the United States in the number of English speakers. If one accepts the proposition that any phonetic language is more efficient than any pictographic language when it comes to written communication, it follows that *Fundamentals of Pediatric Neuroanesthesia* should be welcomed as a global asset.

Brooklyn, NY, USA

James E. Cottrell
John Hartung

Preface

The blooming growth of neuroanesthesia as a superspecialty was in tandem with tremendous technological advancements in neurosurgery during the last 50 years. Similarly, the subspecialty of pediatric neuroanesthesia was a felt necessity when children, a large chunk of the neurosurgical patient population, required definitive management. Perioperative care of such pediatric neurosurgical patients should be considered separately owing to inherent problems of anesthesia for children apart from their associated neurological conditions. There are many specific issues prevalent among these children, surgical and anesthetic management of which require advanced clinical training and practice with direct bearing on the perioperative outcome.

This book aims to provide a thorough review of most of the clinical aspects of neuroanesthesia in children, including neurosurgeries during the fetal stage to neonatal, infancy, toddler, and school-going age groups. It also covers the diagnosis, imaging, surgical, and anesthetic management of all the neurosurgical problems encountered in children. To provide optimal anesthetic care in children undergoing neurosurgery, the anesthesiologist must have adequate knowledge of the developing brain and spinal cord, the effect of anesthetics on the neuronal tissues, and the inherent issues of the child's neurologic lesions. In this context, the chapters in this book are broadly covered in three sections: the first part includes general considerations which start with the evolution of the subspecialty from a historical perspective, basic neurophysiology, and general concerns during neurosurgery in children such as fluid management, blood transfusion, and temperature regulation. The subsequent section on specific problems describes a wide range of topics such as anesthesia for brain tumor surgery, hydrocephalus, neural tube defects, cerebrovascular surgeries (e.g., intracranial aneurysms, arteriovenous malformations, moyamoya disease, and vein of Galen malformation), functional neurosurgery, neuroendoscopy, craniovertebral junction anomalies, spinal surgeries, neurotrauma, endovascular surgery, brain abscess, and congenital heart diseases. There are descriptions of contentious issues such as neuroanesthesia in remote locations, regional anesthesia for neurosurgery, and anesthesia in children with neuromuscular diseases. It includes advanced anesthesia techniques employed during awake craniotomy and epilepsy surgery. Technically, challenging issues of anesthesia for fetal neurosurgery and craniopagus separation surgery have also been described in detail. The postoperative intensive care management for each problem has been described at the end of the respective chapters. Moreover, in the final section on

postoperative care, the common critical care issues are elaborated that includes recovery and care immediately after surgery, management of pain, respiratory complications, ventilatory strategies, brain death, and organ donation in children. This section also covers a couple of miscellaneous practical considerations such as anesthesia for radiation therapy for neurologic ailments and the neurological perspectives in cardiac surgery.

As a teaching faculty, I am privileged to be part of the Department of Neuroanesthesiology and Critical Care at the Neurosciences Center of All India Institute of Medical Sciences (AIIMS), New Delhi. My neuroanesthesia journey started approximately two decades ago, and I have been able to satisfy numerous academic quests during all these years. Over a period of time, I realized that my main area of interest is pediatric neuroanesthesia. *Fundamentals of Pediatric Neuroanesthesia* is a memorable journey for me because it was my first book project, but it also taught me some of the painful lessons of my life. This book was conceptualized long back (2013–14) as I felt there were many things about children undergoing neuroanesthesia that are not compiled appropriately inside a single cover. However, the project witnessed multiple emotional as well as practical hurdles from close quarters when the actual work was started during the year 2015. I often thought of winding up the project before completion for different reasons, such as nonadherence to the editorial expectations in some of the chapters and lack of time owing to my engagement in academic leadership roles. Finally, I bowed to the wishes of my students, who are the primary motivation behind compiling this book; some of them turned out to be contributors as well.

I am reasonably sure that *Fundamentals of Pediatric Neuroanesthesia* would be a reference treatise for neuroanesthesiologists, pediatric anesthesiologists, anesthesia/neuroanesthesia residents and fellows, practicing anesthesiologists, pediatric neurointensivists, nurse anesthetists, and neurosurgeons/pediatric neurosurgeons. It would also serve as a reference book for the DM (Neuroanesthesiology), DrNB-SS (Neuroanesthesiology), and MD (Anesthesiology) curriculums apart from anesthesia residency and pediatric anesthesia/neurosurgery fellowship programs offered at various institutions globally. Despite our best efforts, there must be shortcomings in editing this book; I shall appreciate it if the readers could provide us their feedback.

New Delhi, Delhi, India Girija Prasad Rath

Acknowledgments

Despite initial hiccups during the preparatory phase of this book, the final editing of the chapters was quite enjoyable for me. I convey my heartfelt gratitude to all the contributors who came up with meaningful information on their respective chapters. I am thankful to the Director of All India Institute of Medical Sciences (AIIMS), New Delhi, Prof. Randeep Guleria, for providing the institutional permission to prepare the *Fundamentals of Pediatric Neuroanesthesia*. I take this opportunity to thank my beloved teachers, Prof. Harihar Dash and Prof. Parmod K Bithal, for being the constant sources of encouragement during my personal and professional journey. I offer my sincere gratitude to our departmental chair, Prof. Arvind Chaturvedi, faculty, residents, technicians, and nurses of the Department of Neuroanaesthesiology and Critical Care for providing me a favorable atmosphere to pursue the academic and clinical practice of pediatric neuroanesthesia; this book is the culmination of all their support. I am extremely thankful to my colleagues, Drs. Vanitha Rajagopalan, Sameera Vattipalli, and Jayanth R Seshan from AIIMS, New Delhi; Kiran Jangra of PGIMER, Chandigarh; Sidharth Chavali of AIG Hospitals, Hyderabad; and Ritesh Lamsal of Tribhuvan University Teaching Hospital, Kathmandu, for providing me the readers' perspective on different chapters whenever I required them. Special thanks to Dr. Naren Agrawal, Ms. Jagjeet Saini, and Mr. Ejaz Ahmad of Springer-Nature publications for guiding me to give a final shape of this book. I acknowledge the constant motivation of my father, elder brother, and in-laws for writing scientific literature. I thank my wife and critic, Dr. Sarita Mohapatra, and son Naman Rath, for their unlimited support and coping with my busy academic journey. Last but not least, I am grateful to Prof. James E Cottrell and Prof. John Hartung of SUNY Downstate Medical Sciences University, New York, United States, for writing the foreword of *Fundamentals of Pediatric Neuroanesthesia*.

Girija Prasad Rath, MD, DM

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About the Editor

Girija Prasad Rath is a professor of neuroanesthesiology and critical care at Neurosciences Centre of All India Institute of Medical Sciences (AIIMS), New Delhi, India. Dr. Rath has received three years of exclusive training in neuroanesthesia at AIIMS and is among the first batch of anesthesiologists in India to hold a superspecialty degree, i.e., Doctorate of Medicine (DM) in neuroanesthesiology. He has been involved in educational and clinical research activities in neuroanesthesia and neurocritical care with a special interest in pediatric neuroanesthesia. To his credit, he has more than 230 scientific articles published in peer-reviewed journals, edited a book on Trigeminal Neuralgia, and is on the editorial board of four peer-reviewed journals, including *Neurology India (NI)* and *Indian Journal of Anaesthesia (IJA*). Since its inception, Dr. Rath is also the executive editor of the *Journal of Neuroanaesthesiology and Critical Care (JNACC)*. He has mentored several residents and fellows of neuroanesthesia and neurocritical care at AIIMS. Dr. Rath is a past treasurer of the *Indian Society of Neuroanaesthesiology and Critical Care (ISNACC*) and an active member of many international scientific bodies. He is an executive council member of *Asian Society of Neuroanesthesia and Critical Care (ASNACC)*, director-at-large for *Society for Neuroscience in Anesthesiology and Critical Care (SNACC)* board of directors, the chair for *SNACC Global Outreach Sub-Committee*, and also a reviewer for *the International Council on Perioperative Neuroscience Training (ICPNT).* He is an invited speaker in the scientific meetings of various anesthesia societies that include the *Indian Society of Anaesthesiologists (ISA)*, *ISNACC, ASNACC, EURONEURO, Bangladesh Neuroanesthesia Conference, Neuroanaesthesia Symposium (NAS) of Malaysia*, and *World Congress of Anaesthesiologists (WCA)*. Dr. Rath was involved in the first successful separation surgery of conjoined craniopagus twins in India. He is a recipient of the ICMR International Fellowship (ICMR-IF) and is a Fellow of the Indian College of Anaesthesiologists (FICA).

Part I

General Considerations

1 Pediatric Neuroanesthesia: Evolution of a New Subspeciality

Girija Prasad Rath, Jayanth R Seshan, and Ashok Kumar Mahapatra

Key Points

- Modern neurosurgery and neuroanesthesia have existed and developed concurrently, largely due to significant contributions by pioneers to both specialties.
- Rapidly evolving diagnostic and surgical modalities have facilitated the possibility of safe and effective complex neurosurgeries in children.
- The development of pediatric neuroanesthesia as a separate subspecialty is essential considering the unique anatomical and physiological features, the requirement of special skill sets and experience with invasive procedures, and effective management of the child in the perioperative period.
- Currently, the setting up of advanced training programs in pediatric neuroanesthesia and neurointensive care is in its nascent stage.
- Future prospects in the field of pediatric neuroanesthesia include meaningful research in the management of significant comorbid neurological diseases, including cerebral palsy, epilepsy, and traumatic brain injury.

1.1 Introduction

A better understanding of human pathophysiology as well as technological advances has encouraged every specialty of medical science to focus on specialized care instead of generalized approaches. During the last 100 years, a lot of development has been witnessed in the anesthesia practice as a specialty of medicine. Several subspecialties have come up intending to approach a particular set of patients to ensure better care and provide clinical scientists with research opportunities. Cardiac anesthesia, neuroanesthesia, obstetric anesthesia, pediatric anesthesia, pain medicine, palliative care, and critical care medicine are well-established, currently, with a distinct identity.

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1.2 Development of Neuroanesthesia Along with Neurosurgery

Neuroanesthesia, as a specialty, should be discussed in the context of the evolution of neurosurgery. Although trephination or trepanning used to be carried out during the primitive civilizational period and continued until the early twentieth century [1] for different beliefs, the beginning of neurosurgery and neuroanesthesia must be viewed from the late part of the eighteenth and early nineteenth centuries [2]. The significant discoveries of anesthesia during the nineteenth century gave shape to the development of modern neurosurgery. Carbon dioxide, hydrogen, and nitrogen were discovered during the end of the eighteenth century; their role in anesthesia was explored, along with other agents such as oxygen and nitrous oxide [3]. Sir Humphry Davy (1798) suggested that the use of nitrous oxide (laughing gas) could relieve pain during surgery, and it was used quite often in dental extraction procedures for analgesia. However, its popularity was reduced with ether's introduction to remove a neck tumor by Dr. Crawford Long in 1842 [2]; unfortunately, it remained unpublished until 1849 [4]. After the first successful public demonstration of ether use at Massachusetts General Hospital by William Thomas Green Morton on 16 October 1846, there was a quick spread of news worldwide, and it led to a revolution in the field of surgery and anesthesia. Subsequently, Sir James Young Simpson introduced chloroform (1847) which further overshadowed nitrous oxide. While chloroform was mainly used in Europe and South America, ether was used in England and North America [2]. Therefore, the use of chloroform and ether became routine for modern anesthesia. However, the implementation of anesthetics in neurosurgery took a decade to develop [3]. The pioneer neurosurgeons then stepped in and utilized these agents for brain surgery to establish the specialty of neurosurgery. The contributions of Sir William Macewen (1848–1924; Glasgow), a precursory neurosurgeon and pioneer anesthetist, marked the dawn of neuroanesthesia; he was a general surgeon with interest in neurosurgery. In 1879, he performed the first-ever successful brain tumor removal at the Glasgow Royal Infirmary. The procedure was carried out under endotracheal anesthesia and not with a tracheotomy which was the convention till then [2]. He developed metallic tubes which could be introduced into the trachea and, later on, the red rubber tubes. A decade later, Sir Ivan Magill and Stanley Rowbotham popularized the technique of endotracheal anesthesia, which is still in use in the current-day practice [5]. Victor Horsley, a contemporary of Macewen and a general surgeon with a special interest in neurosurgery, carried out animal experiments and investigated the effects of ether, chloroform, and morphine on intracranial contents. He recommended using chloroform rather than ether; although relatively safe, ether caused an increase in blood pressure and, hence, is considered to have a potential for hemorrhage. He described anesthesia for brain surgery in *British Medical Journal* in 1888. The use of morphine was excluded from his anesthesia regimen due to its respiratory depressant effects. Because of his interest in anesthesia, he became part of the "Special Chloroform Committee," which recommended that the use of chloroform in a concentration of more than 2% was unsafe. Horsley believed a dose of less than 0.5% after bone removal during the craniotomy is safe [6]. He also described the role of local anesthesia in the form of cocaine infiltration over the dura, especially in patients with cardiac dysfunction, where chloroform is contraindicated [7]. An interesting fact about the early days of neurosurgery is the time taken for the procedures, which is described in the literature as lasting up to 1.5 h (usually 30 min!) which reduced the anesthetic needs. This was mentioned by Dr. Zebulon Mennell, the first British neuroanesthetist (who worked with Victor Horsley), that an ambidextrous Horsley seldom took more than half an hour for his cranial cases [8]. Compare this to modern-day neurosurgery practice with advanced operating techniques that have prolonged the procedure's duration and require ever-modifying anesthetic needs.

Harvey Cushing, another contemporary pioneer of neurosurgery and anesthetics, suggested using ether anesthesia while restricting chloroform use in children. He was the first to introduce the concept of induction of anesthesia [3].

His initial anesthesia experience as a medical student was terrible. He was a stand-in anesthetist, and the patient died of aspiration of vomitus. Along with Codman, he utilized his experiences to develop an anesthesia record (ether record). He recommended continuous monitoring of pulse rate, respiration, and temperature every 5 min. He later added blood pressure charting after a visit to Italy (1900), where he was introduced to Riva-Rocci cuffs [9]. Due credit must be given to Cushing to realize the need for a full-time anesthetist, and he employed Dr. Griffith Davis, with whom he reported performing over 300 cranial surgeries. He mentions that an expert and fully devoted anesthetist is essential in neurosurgeries to deal with major issues like the positioning of the patient, level of narcosis, and continuous monitoring of cardiac and respiratory rhythm by auscultation [10].

Deliberate hypotension was described in neurosurgery by Fedor Krause (1857–1937), a German neurosurgeon. He used increasing concentrations of chloroform to cause hypotension and, hence, reduce bleeding. Induced hypotension using non-anesthetic drugs was described by Janice Peeler in Australia for the first time in scoliosis correction surgeries (Harrington rods) using sodium nitroprusside for reducing bleeding [11]. Krause also introduced the surgical treatment of epilepsy in Germany and was an early practitioner of the intraoperative electrostimulation of the cerebral cortex. He also emphasized the importance of a light plane of anesthesia during brain surgery as the brain was insensitive to pain [7].

The contributions of Albert Faulconer (Mayo Clinic) through publications on the electroencephalogram (EEG) responses to anesthetics and the development of an EEG-based device to monitor the anesthetic depth (1949) are considered significant to the beginning of modern neuroanesthesiology [12, 13]. This was later (1969) followed by further such demonstrations by John D. Michenfelder, which were majorly responsible for the spread of Neuroanesthesia as a sub-specialty. It is for this reason that Michenfelder is considered the Father of Modern Neuroanesthesiology [14, 15]. Robert J. White, the first neurosurgeon to perform a successful "cephalic exchange" in monkeys (1971), is also credited with a significant contribution to neuroanesthesia. Teaming up with Maurice S. Albin, a neuroanesthesiologist, he conducted significant research on hypothermia for neuroprotection after spinal cord injury. He demonstrated total hemispherectomy in monkeys and paved the way for the procedure to be adapted for the treatment of intractable epilepsy and resection of large tumors in humans [16, 17]. Our understanding of intracranial dynamics is based on two significant contributions in the form of Monro-Kellie doctrine, which explains the relationship between the components of the intracranial compartment and the description of intracranial pressure (ICP) waveforms by Lundberg [18–20]. These two basic principles still influence neuroanesthesia and intensive care practice, and to date, research is on to identify the ideal intracranial dynamics using various monitoring modalities. This is even more significant in children as the cerebral hemodynamics are fluctuating with increasing age.

Many important landmarks in anesthesia were achieved by people who did pioneering work in neurosurgery, thanks to their continued efforts in striving for the best possible care of their patients. Their work was greatly enabled by the discovery of the germ theory of disease and the advent of the concept of aseptic precautions. Apart from their innovations in surgical procedures and their meticulous techniques, these pioneers also contributed immensely to anesthesia by describing different anesthetic agents used, their administration techniques, and monitoring these patients. Because of due realization, dedicated anesthesiologists were appointed for intraoperative care, resulting in a much better understanding of neurophysiological requirements during surgery.

1.3 Development of Pediatric Neurosurgery as a Subspecialty

Surgery of the brain and spinal cord among children constitutes a significant proportion of neurosurgical procedures. Starting from prehistoric times until the Harvey Cushing era, neurosurgery was sporadically practiced on children. Pediatric neurosurgery, as a subspecialty, was in a devel-

oping stage when the pioneering neurosurgeons such as Harvey Cushing, Walter Dandy, Norman Dott, and Kenneth McKenzie operated in various countries on children with hydrocephalus or brain tumors. However, the formal development and teaching of the specialty were started by *Franc Ingraham* under the directions of Harvey Cushing (***father of neurosurgery***) at the Boston Children's Hospital when he established the first center for treatment of neurosurgical diseases in children. By the early 1950s, the role of pediatric neurosurgery was already being defined in the major cities worldwide, Boston, Chicago, London, Paris, and Toronto, to name a few. Ingraham is credited with describing methods for the treatment of conditions like craniosynostosis, diastematomyelia, hydrocephalus, spina bifida, and subdural hematomas. He is credited with the training of many surgeons in pediatric neurosurgery and, hence, is also considered the ***father of pediatric neurosurgery*** [21]. Ingraham and his protégé, Donald Matson, published *Neurosurgery of Infancy and Childhood* in 1954, the first textbook on pediatric neurosurgery. Matson was a brilliant technical surgeon and used to resect craniopharyngiomas before the introduction of surgical microscopes [22].

The notable contributions of Cushing in pediatric neurosurgery include the description of a lumbo-peritoneal shunt and an article highlighting his experiences in the management of cerebellar astrocytomas [23]. Hydrocephalus is a condition associated more commonly with the pediatric population and several innovations for the drainage of cerebrospinal fluid (CSF) starting from Cushing's lumbo-peritoneal shunt to Torkildsen (1939) describing a ventriculocisternal shunt and Matson's lumbo-ureteral (1949) and ventriculo-ureteral (1951) shunts. Valve-based shunts were first described by Holter, which led to the first reported CSF drainage into the jugular vein in 1952 [24, 25]. Since then, numerous improvements have been made in the materials and techniques used, including endoscopy and image guidance.

The first instance of the description of epilepsy surgery was by Horsley (1886) of a 22-year-old man who had been suffering from seizures since 15 years of age. A craniotomy was performed for the removal of a focus of irritation (proposed by Jackson in 1870) [26].

Craniectomy for craniosynostosis was first described in a 9-month-old infant by Lane in 1892. He mentions the use of ACE (alcohol, chloroform, and ether) mixture for anesthesia. Ironically, the child died 14 h postoperatively, and the cause of death was attributed to the effect of anesthesia [27, 28].

Moyamoya disease was first recognized in 1957 in Japan by Takeuchi and Shimizu, and the characteristic angiographic appearance of a "puff of smoke" was described by Takaku in 1969. The earliest described surgery for moyamoya disease was cervical carotid sympathectomy and superior cervical perivascular ganglionectomy by Suzuki [29, 30].

The first edition of the *Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents* was published in 2003 [31]. Although the entity was recognized much earlier, significant research went into developing these guidelines by the *Brain Trauma Foundation*, which is being updated periodically. The first pediatric neurosurgical society, the European Society for Pediatric Neurosurgery (ESPN), was founded when the first such scientific meeting was held in Vienna, Austria, in 1967 [21]. In 1971, Jacques Rougerie held a meeting in Paris just before the second meeting of ESPN; it was decided to found an international society which was formally established in the subsequent year (1972) as the International Society for Pediatric Neurosurgery (ISPN). During the second meeting of ISPN, the creation of their official journal 'Child's Brain' was announced, which was later rechristened (1985) as 'Child's Nervous System.' The American Society of Pediatric Neurosurgeons (ASPN) was formed in 1978; similar professional bodies were formed in Japan (1973), Mexico (1999), and Australia (2002).

Training in pediatric neurosurgery is addressed with fellowship programs all over the world. To begin with, in 1953, there was a so-called fellowship at Boston Children's Hospital, with "supernumerary residency." By 1978 the

programs were sustained at five places: Boston, Toronto, Philadelphia, Chicago, and Los Angeles [32]. Currently, many places offer such fellowships. A 1-year clinical fellowship following the completion of a general neurosurgical residency is usually recommended [21, 33]. There is a paucity of such advanced training to meet the growing disease burden in low- and middle-income countries (LMIC). Expertise in the management of hydrocephalus and spina bifida, the two of the most common pediatric neurosurgical conditions, offers better outcomes in terms of reduced morbidity and mortality. The CURE Hydrocephalus and Spina Bifida (CHSB) fellowship offers advanced subspecialty training to equip surgeons from LMIC with optimum surgical skills and equipment to manage effectively such common childhood neurosurgical conditions [34]. All India Institute of Medical Sciences (AIIMS), New Delhi, and Park Clinic, Kolkata in India, offer pediatric neurosurgery fellowships. A repository of information concerning pediatric neurosurgery fellowships worldwide is available on the ISPN website (https://www.ispneurosurgery.org/international-fellowships/).

1.3.1 Neurosurgery: *An Indian Perspective*

Although Dr. Ram Ginde's survey of neurosurgery in India between 1926 and 1953 gives an idea of what was then being done at most large teaching hospitals in the country, it is well known that prior to 1949, neurosurgery was being practiced by general surgeons [35]. Meanwhile, Professor Jacob Chandy of Christian Medical College (CMC), Vellore, received his neurosurgical training at the Montreal Neurological Institute (MNI) with Wilder Penfield and in Chicago with Theodore Rasmussen [36]. It can be said that his return to CMC marked the beginning of modern neurosurgery in India. Chandy established the first neurosurgery department in South Asia at CMC and initiated the neurosurgical training and neurological services in 1957–1958. Several of his trainees pioneered neurosurgical departments all over India. He was one of the four founder members of the Neurological Society of India (NSI) in 1951 and was also the founder president (1952) [36, 37]. His tremendous contributions place him as the ***father of neurosciences/neurosurgery in India***. Meanwhile, B. Ramamurthi, another pioneer neurosurgeon, after his training under Rowbotham of Newcastle, UK, started the Department of Neurosurgery in the Government General Hospital, Madras, in 1950 (Madras Institute of Neurology, MIN); V. Rajagopalan underwent training in neuroanesthesia in the UK and joined MIN in 1953 [38].

Significant contributions to neurosurgical literature from India were in the 1960s when Wadia described his pioneering work on congenital atlantoaxial dislocations [39]. Subsequently, P N Tandon, a pioneering neurosurgeon, an MNI alumnus, and founder of the Department of Neurosurgery at AIIMS, New Delhi, published a series of 30 cases of anterior encephalocele in children [40]. Upadhyay, a pediatric surgeon, created an indigenous shunt for hydrocephalic children [41]. The development of modern pediatric neurosurgery in India began with holding the 17th Annual Conference of ISPN at Mumbai (1989). Dr. S. N. Bhagwati of Bombay Hospital hosted a satellite meeting of the International Society for Pediatric Neurosurgery (ISPN) in Mumbai just before the World Congress [42]. Enthused with the success of the meeting, he formed a special interest group (SIG) on pediatric neurosurgery in India, which was later formalized as the Indian Society for Pediatric Neurosurgery (IndSPN) in 1990 with himself as the founder president. He became the President of the International Society for Pediatric Neurosurgery (ISPN) in 1994–1995, being the first Indian to be nominated to that position. IndSPN is responsible for organizing regular meetings and continuing medical education (CME) programs in cooperation with the ISPN. Bhagwati was supported by a group of dedicated neurosurgeons from different parts of India. Notable among them are A. K. Banerji of AIIMS, New Delhi, a pioneer neurosurgeon of Northern India; S. Kalyanaraman; V. K. Kak; D. K. Chhabra of King George's Medical College, Lucknow; Chandrasekhar Deopujari of Bombay Hospital; and Ashok Kumar Mahapatra

of AIIMS, New Delhi; they all succeeded him as presidents of IndSPN [43]. Among them, Prof. Mahapatra continued to work as a dedicated pediatric neurosurgeon throughout his career and contributed several scientific publications on pediatric neurosurgery, apart from editing two books—*Tenets of Craniosynostosis* and *Split Cord Malformations*. He was instrumental in carrying out the rare yet first successful craniopagus separation surgery in India (2017). The *Journal of Pediatric Neurosciences*, the official publication of the IndSPN, was launched in 2006 and continues to excel as an international journal on pediatric neurosurgery.

1.4 Pediatric Neuroanesthesia: *Not Just "Anesthesia" or "Neuroanesthesia"*

Pediatric neuroanesthesia is an evolving subspecialty in anesthesia that deals with the perioperative care of children during neurosurgery. As of now, pediatric neurosurgery is a well-established neurosurgical specialty to deal with the special challenges and considerations that a child with central nervous system (CNS) disease poses. Concurrently, the need for well-trained and skilled pediatric neuroanesthesiologists has also risen in recent times, focusing on dedicated care of such children. Pediatric neuroanesthesia owes most of its routines, techniques, and instrumentation to anesthetics for children in general. Perioperative anesthetic care of children requires catering to and adapting to the differences in children's anatomy and physiology from adults. Performing invasive maneuvers and procedures like dealing with airway, vascular cannulation, and positioning for surgery is always a challenge for the anesthesiologist. The response of neonates and infants to stress (bradycardia) is markedly different from older children and adults; they have poor metabolic control and are more prone to hypothermia. Combined with the general physiological differences, the neuroanesthesiologists have a better understanding of the neurological pathology and concerns relating to ICP; they play a major role in the optimal management of such children, greatly influencing the outcome.

Certain neurological conditions are specific to children, which can be attributed in part to their association with genetic abnormalities. Several syndromes with CNS and multi-system manifestations have been described, and the attending anesthesiologist needs to be aware of the problem at hand. Intracranial tumors, intractable epilepsy syndromes, craniofacial abnormalities (craniosynostosis and craniopagus twins), neurotrauma, hydrocephalus, spinal and cranial dysraphisms (neural tube defects), craniovertebral junction abnormalities (Chiari malformations), neurovascular diseases, moyamoya disease, the vein of Galen aneurysmal malformations, and kyphoscoliosis are some of the pathological conditions the anesthesiologist needs to have a thorough understanding of.

The perioperative anesthetic and neuro-intensive care management of pediatric traumatic brain injury is also significantly unique and is still a research topic. Although not restricted to pediatric neuroanesthesia specialty, research on the toxicity of anesthetic drugs on the developing brain could be a significant game-changer for the evolution of this specialty. The earliest descriptions regarding fetal neurosurgical diseases were from Charpentier (1887), who described fetal hydrocephalus in 200 cases, one of the major causes of maternal deaths [44]. The first description of a fetal neurosurgical procedure was by Barke et al. (1966), who described the use of gas ventriculography to confirm the diagnosis of hydrocephalus [45]. Cephalocentesis and ventriculo-amniotic shunting were followed in the 1980s [46, 47]. The first in utero endoscopic repair of neural tube defects (meningomyelocele) was done in 1994, which was deemed unsatisfactory and replaced by hysterotomy [48, 49]. Advancements in fetal neurosurgery started to begin after observing that open fetal MMC repair resulted in the reversal of Chiari II malformation [50]. Prospective studies have established superior outcomes with the prenatal treatment of hydrocephalus and neural tube defects [51].

The most common abnormality of intracranial circulation in children is arteriovenous malforma-

tion (AVM). Their high risk of intracranial hemorrhage mandates early management. Several advancements have been made in the treatment options ranging from open surgeries to endovascular techniques [52].

The performance of pediatric awake craniotomy is precluded by patient cooperation. Though neurosurgeries were performed even much before the pre-anesthetic era, Pasquet described the first awake craniotomy with combined local and general anesthesia [53]. In children, awake brain surgeries have been carried out for epilepsy and tumors in the eloquent cortex.

Deep brain stimulation (DBS), traditionally for the management of Parkinson's disease, has also been used to treat generalized dystonias [54]. In children, pallidotomy has been a surgical management option since the 1960s but with limited long-term efficacy data [55]. Deep brain stimulation for dystonia in an 8-year-old child was first described in 1996, with lasting efficacy noted at 20 years. Since then, several such surgeries have been carried out [56, 57].

Management of TBI in children has special considerations due to the neurophysiological differences (cerebral autoregulation) and differences in patterns of injury. Data pertaining to this topic is available since the early part of this century and evolving continuously [58–60]. Anesthetic neurotoxicity is one of the most intriguing topics of research in the conduct of pediatric surgeries, and certain features like longer duration of exposure and the prospect of multiple exposures with regards to neurosurgeries give more relevance to its consideration in the field of pediatric neuroanesthesia. Michenfelder is credited with early reports of nitrous oxide toxicity during anesthesia exposure in children [61]. Since then, literature is being updated periodically on this topic and has been covered in this textbook elsewhere. Although neuroanesthesiologists or pediatric anesthesiologists have been attending to pediatric neurosurgeries routinely in their practice by virtue of their clinical experience and advanced exposure, it is wise to believe that full-time pediatric neuroanesthesiologists, as a separate group, will create new dimensions to the perioperative and intensive care management of such children. This optimism is similar to the recommendation of the "Children's Surgical Forum," which views the children's welfare could be better served by a degree of sub-specialization [62]. The surgeries are recommended to be undertaken by appropriately trained designated surgeons with a workload sufficient to maintain competence. The task force for the Society of British Neurological Surgeons (SBNS) in 1998 defined the "Safe Pediatric Neurosurgery" objectives to ensure children's care to be of the highest quality and delivered by recognized pediatric neurosurgeons supported by staffs and facilities [63]. However, structured training programs on pediatric neuroanesthesia similar to pediatric neurosurgery are rare. In most places, pediatric anesthesiologists with exposure to neuroanesthesia manage the perioperative care of such patients. However, with increasing fellowship programs on neuroanesthesia, more neuroanesthesiologists with pediatric anesthesia experience manage the care. Cincinnati Children's Hospital Medical Center, USA, offers advanced pediatric neuroanesthesia fellowship (18 months' duration) for internationally trained candidates under the core fellowship program of pediatric anesthesia. In other universities of the USA, the experience of pediatric neurosurgical procedures for the neurosurgical anesthesia fellowship is offered as a part of rotational policy in conjunction with pediatric anesthesiology, which is the case in most parts of the world as well. In the Indian subcontinent, neuroanesthesiologists with advanced pediatric neurosurgery experience are the foremost practitioners of pediatric neuroanesthesia.

Specific literature in relation to pediatric neuroanesthesia was first published during the late 1960s and 1970s [64–70]. During the fifth Italian-French meeting on neuroanesthesia and resuscitation, a symposium on pediatric anesthesia was organized at Turin, Italy, probably for the first time [71]. The necessary presence of a skilled neuroanesthesiologist familiar with the physiologic and psychological needs of the children undergoing epilepsy surgery was highlighted for the first time [39]. Sulpicio Soriano and colleagues from Boston Children's Hospital continued emphasizing the role of pediatric neu-

roanesthesiologists for children undergoing neurosurgery in different scientific meetings and publications [72–75]. There is increased awareness of this specialty which has been reflected in terms of further publications during the last 20 years, and more such publications were added to the literature with a special issue on pediatric neuroanesthesia in the journal *Pediatric Anesthesia* [76–79].

The first textbook on Neuroanesthesia was published in 1964 by Andrew Hunter, Manchester [80]. James Edward Cottrell, the founder-editor of JNA, is credited with being the author of immensely popular textbooks in neuroanesthesia, from 'Anesthesia and Neurosurgery' (1980) [81] until the recent edition of 'Neuroanesthesia' (Cottrell and Patel) (2016) with a reasonably informative chapter on pediatric neuroanesthesia [82]. The JNA is affiliated with the Society of Neuroscience in Anesthesiology and Critical Care (SNACC). The formation of an organizational structure for neuroanesthesia began with the Neuroanesthesia Travelling Club of Great Britain and Ireland (1965), co-founded by Allan Brown and Andrew Hunter. The precursor for SNACC, the Neurosurgical Anesthesia Society (NAS) was formed in 1973 with John Michenfelder as its first president. The NAS has undergone title changes such as the Society of Neurosurgical Anesthesia and Neurological Supportive Care (SNANSC) in 1973 to the Society of Neurosurgical Anesthesiology and Critical Care in 1986, and a revised nomenclature of Society of Neuroscience in Anesthesiology and Critical Care, since 2009 [83].

In India, perioperative care for pediatric neurosurgery was provided by pediatric anesthetists, to begin with. After training in neuroanesthesia started at different institutions, it became a routine for trained neuroanesthesiologists to be involved in these children's care. Prof. SS Saini was the first designated faculty (assistant professor, 1979) of neuroanesthesia in India and became professor in 1987. He founded a dedicated Department of Neuroanesthesia at Neurosciences Center of AIIMS, New Delhi (1986–1987), and was supported by his mentees and colleagues, Harihar Dash and Parmod Bithal. Dash took over the departmental reins from Saini and, in 2001, registered the *Indian Society of Neuroanaesthesiology and Critical Care* as its founder president. In the subsequent year (2002), he initiated the first structured neuroanesthesia doctorate training program (3-year DM in Neuroanaesthesiology) in Asia/India; it included advanced pediatric neuroanesthesia. It was followed by several other institutions such as Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum; the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore; Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh; Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry; CMC, Vellore; and AIIMS-like institutions initiating the DM courses. It is probably the reason why most of the neuroanesthesia- or pediatric neuroanesthesia-related scientific articles from India are published after 2002. The practice of pediatric neuroanesthesia, however, is not restricted to these hospitals. The training continued to be provided earlier by renowned neuroanesthesiologists such as G. Parameswara and GS Umamaheswara Rao (NIMHANS, Bangalore), Grace Korula (CMC, Vellore), V Padmanabha Iyer and Annapurna Rout (SCTIMST, Trivandrum), Amna Goswami and Bibhukalyani Das (Bangur Institute of Neurosciences, Kolkata), and Vinod Grover (PGIMER, Chandigarh), to name a few. Mumbai neuroanesthesiologists also played an active role in this regard; prominent were Vasumathi Divekar (KEM Hospital) and Vikram Datar (Bombay Hospital).

1.5 Future Prospects as a Subspeciality

Neurosurgery as a specialty is rapidly evolving with the advent of newer diagnostic modalities such as functional magnetic resonance imaging (*f*MRI); surgical techniques, microneurosurgery, endoscopy, and stereotactic and robotic surgeries; and endovascular techniques. Many of these techniques are being increasingly employed in pediatric neurosurgery as well. It is essential that

the neuroanesthesiologist or pediatric anesthesiologists need to be abreast of the latest developments to provide appropriate perioperative care among these children undergoing neurosurgery. In this regard, it is essential for the recognition of pediatric neuroanesthesia as a separate subspecialty. Currently, the focus of pediatric neurosurgery and neuroanesthesia appears to be restricted to the management of hydrocephalus, neural tube defect, and tumors. There are other common CNS issues in children like vascular problems, epilepsy, cerebral palsy, and traumatic brain injury. Pediatric neuroanesthesiologists and neurointensive care specialists should be involved in a multidisciplinary team that, hopefully, engages in research in the perioperative care of these children. In the present world of evidence-based medicine, literature on these topics appears to be limited as far as prospective randomized controlled trials are concerned. There is hope that with the evolution of this subspeciality, more meaningful research will be carried out and the spectrum of evidence regarding management widens.

The advanced training on pediatric neuroanesthesia can be imparted in the tertiary care centers where significant loads of pediatric neurosurgical patients are managed. It is only a matter of time that pediatric neuroanesthesia societies or special interest groups (SIGs) are formed. "Paediatric Neuroanaesthesia Network (PNAN)" is an active SIG for the cause which is part of "Neuro Anaesthesia & Critical Care Society (NACCS) of Great Britain and Ireland." Regular meetings/conferences showcasing the progress in this field and sharing knowledge across various platforms are expected to occur in the foreseeable future.

1.6 Conclusion

Neuroanesthesia has seen rapid evolutionary changes over the past century with significant pioneering contributions of physicians and surgeons alike. It can be ascertained with a reasonable level of confidence that pediatric neuroanesthesia, one of the newest entrants in the category of medical "subspecialties," offers much scope in clinical and research work for the anesthesiologist. Combining adequate knowledge and skill of pediatric anesthesia, neurosurgical anesthesia, and intensive care is essential to ensure that pediatric neuroanesthesia flourishes. This calls for establishing training programs to develop an appropriate curriculum taking into account the depths of the broad specialties involved. It is not unreasonable to expect significant contributions from this subspecialty in clinical management and research in the coming future.

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2 Developmental Anatomy and Physiology of the Central Nervous System in Children

Vanitha Rajagopalan and Ramamani Mariappan

Key Points

- The central nervous system (CNS) is incompletely developed at birth, and its growth and maturation continue until the end of the second year of life.
- The CNS anatomy and physiology of neonates and infants are profoundly distinct from that of older children; hence, the pediatric population should not be treated as a homogenous group.
- The brain is supplied by the bilateral internal carotid, vertebral arteries, and venous drainage via the cerebral veins and dural venous sinuses that drain into the internal jugular veins.
- The cerebral blood flow is approximately 40–50% of cardiac output in children between 1 and 3 years of age, making them vulnerable to cerebral ischemia following systemic hypotension.
- The cerebral autoregulation and CO_2 reactivity are preserved in preterm and term neonates.
- The immature neurons are more vulnerable to adverse influences of toxic substances, and hence, neuroprotective strategies and treatment are warranted.

2.1 Introduction

The pediatric age group ranges from neonates, infant to adolescent. Neonates are termed as preterm, term, and post-term according to their postconceptional age. Based on their postnatal age and birth weight, children are classified further with different terminologies (Table 2.1). Each age group has a unique physiology to understand. Children should not be handled as a homogenous group, especially between birth and 8 years of life, due to the differences in anatomy, physiology, pharmacokinetics, dynamics, and pathological conditions. The central nervous system (CNS) is immature at birth and keeps growing until the end of the second year of postnatal life. The CNS of neonates and infants is profoundly distinct from that of older children and an adult. Therefore, the neuroanesthesiologists must have a comprehensive understanding of the intracranial compartment, cerebrovascular physiology, and the developmental oddities of the nervous system, including the pathologies in children and their difference from adults. This chapter discusses clinically pertinent aspects of the CNS development and function in children and their application to pediatric neuroanesthesiology.

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Table 2.1 Terms used according to the post-gestational and postnatal age

Age	Terminologies
According to the gestational age	
<37 weeks	Preterm
32–37 weeks	Mild preterm
28–31 weeks	Moderate preterm
<28 weeks	Extreme preterm
37–42 weeks	Term
>42 weeks	Post-term
According to the postnatal age	
Neonates	First 28 days of postnatal life
Early	First 7 days
Late	8–28 days
Infants	29th day to first year
Smaller children	1–6 years
Bigger children	7–12 years
Adolescents	13–16 years
According to the birth weight	
2500 g to 4200 gm	Normal birth weight
<2500 gm	Low birth weight
<1500 gm	Very low birth weight
<1000 gm	Extreme low birth weight

This knowledge is essential as it allows for the established and safe care for pediatric neurosurgical patients across the entire spectrum of age and disease.

2.2 Development of the Central and Autonomic Nervous Systems

2.2.1 Intrauterine Development

Intrauterine development starts from conception and continues to grow till birth. This prenatal period consists of three stages, which include the germinal, embryonic, and fetal stage. The germinal stage starts with conception, implantation of the embryo into the uterine wall, and the formation of the placenta, which lasts about 2 weeks. The second, embryonic stage, where there are intense cell proliferation, migration, and differentiation leading to the establishment of major organs, happens. This second stage lasts from the third to eighth week. During the fetal stage, there is a functional differentiation of organs formed during the embryonic stage, which lasts from the ninth week to the end of pregnancy. The development of the CNS and autonomic nervous system (ANS) is discussed in detail below.

2.2.2 Development of the Brain

A human embryo consists of a three-layered disc—ectoderm, mesoderm, and endoderm [1–3]. From this embryo, on the 12th day, the notochord develops as a cellular rod along the midline axis around which the vertebral bodies are organized. The following three steps are observed in the CNS embryogenesis process: (a) neurulation, (b) canalization, and (c) retrogressive differentiation.

(a) ***Neurulation:*** The embryonic ectoderm which lies in the midline, on the dorsal aspect of the embryonic disc, over the developing notochord, thickens to form a neural plate by about 18 days. The neural plate gets depressed along the midline and forms the neural groove, and the lateral part of the neural plate gets elevated and forms neural folds. The neural groove progressively gets deeper, and the neural folds continue to elevate and fuse in the midline and form the neural tube. This process of neural tube formation (Fig. 2.1) from the 15th to 28th day of post-conceptional age, during which the brain and the spinal cord through L2–4 develop, is called neurulation.

Development of the Brain: The fusion of neural folds originates in the cervical region and advances in a cephalocaudal direction. The neural tube is open cranially and caudally until the fusion is completed, and these openings are called the anterior and posterior neuropores, respectively. The two edges of the neural plate also fuse along cranio-caudally. The cranial part of the neural tube gets enlarged and forms the brain, and the tubular caudal part forms the spinal cord.

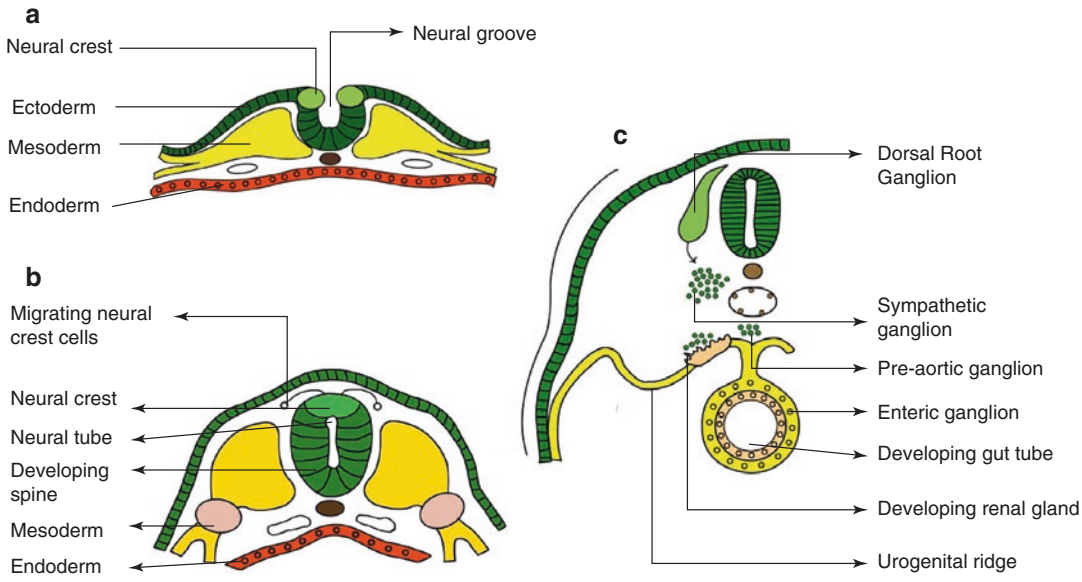


Fig. 2.1 Formation of neural groove (**a**), neural tube (**b**), and neural crest (**c**). Cells of the neural crest migrate and develop into cranial and spinal sensory ganglia

By the third week of gestation, the cranial part of the neural tube demonstrates three dilations (three primary brain vesicles), which form the three main subdivisions: the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon). Simultaneously, two flexures form: one at the confluence of the hindbrain and the spinal cord called cervical flexure and the second one forming at the midbrain region (Fig. 2.2). By the end of 5 weeks, the three vesicles become five vesicles. The prosencephalon divides further into telencephalon and diencephalon; the mesencephalon remains the same. The rhombencephalon becomes metencephalon and myelencephalon. Figure 2.2 shows the development of the brain from the cranial part of the neural tube. Simultaneously, two flexures form; one is the rhombencephalic isthmus, which separates the mesencephalon and the metencephalon, and the other is pontine flexure, which separates the metencephalon and myelencephalon. The five secondary vesicles form the different parts of the brain. The cavity of the neural tube at each portion of the brain becomes the ventricle or foramen connecting the ventricles. Figure 2.3a, b shows the development of various parts of the brain.

(b) ***Canalization:*** The second process of CNS embryogenesis is canalization, which lasts between 30 and 52 days of post-gestational age. During this process, the sacrococcygeal segments of the spinal cord are formed by the fusion of the notochord and the neural epithelium with caudal cell mass.

(c) ***Retrogressive differentiation:*** The third process of CNS embryogenesis is retrogressive differentiation, which starts on the 46th day of post-gestational age and continues to develop till birth. During this process, the excessive cells formed during recanalization undergo necrosis leaving the cauda equina and filum terminale.

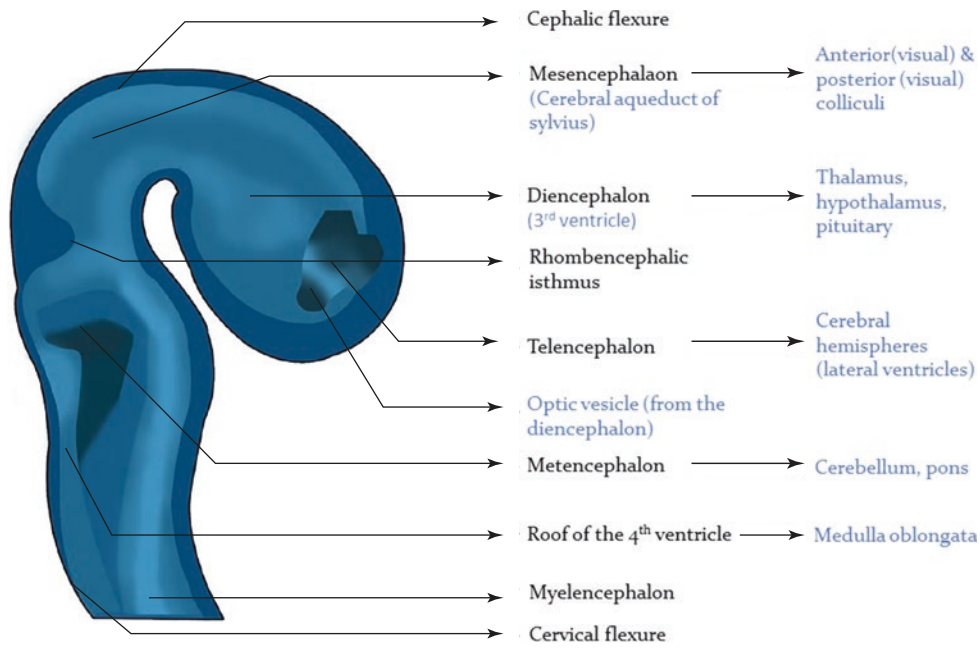


Fig. 2.2 Development of the brain from the cranial part of the neural tube

***Neural Crest Formation*:** Around the time of formation of the neural tube, the neural crest, which lies on the dorsolateral aspect of the neural tube and develops from the cells at the junction of the neural tube and the rest of the ectoderm on either side, it transforms into specialized cells and gets separated from the rest of the ectoderm (Fig. 2.1c). Later, these cells lose its adhesiveness and migrate freely to different parts of the body tissue and form essential structures such as dorsal root ganglia, all sympathetic and parasympathetic ganglia, preaortic ganglia, Schwann cells, enteric neuronal plexus, the pia mater, and the arachnoid mater, adrenal medulla, melanocytes, odontoblasts, parafollicular cells (calcitonin-producing C cells), and aorticopulmonary septum.

2.2.3 Development of the Spinal Cord

The caudal part of the neural tube forms the spinal cord (Fig. 2.4). Neuroepithelial cells lining the neural tube undergo rapid proliferation once the neural tube closure occurs, forming the inner layer, which lines the central canal. The outer layer of neuroepithelial cells transforms and produces another cell type (with a large round nucleus, pale nucleoplasm, and dark staining nucleolus) called primitive nerve cells or neuroblasts. This neuroblast forms the *mantle layer*, which later forms the *gray matter of the spinal cord*. Nerve fibers are arising from the neuroblast pass through the *outermost layer or marginal layer*. The myelination of this nerve fiber gives a white appearance; hence, the name of this layer is *white matter of the spinal cord*.

Continuous proliferation of neuroblasts in the mantle layer forms ventral and dorsal thickening. *Ventral thickening*, otherwise called a *basal plate*, *contains ventral motor horn cells* and transforms into a motor area. The *dorsal thickening*, otherwise called the *alar plate*, forms the sensory area. *Sulcus limitans*, a longitudinal groove, separates the ventral and dorsal thickening. *Intermediolateral horn*, which lies between the ventral and dorsal horn, contains the cell bodies of the sympathetic nervous system at the thoracic (T1–12) and lumbar (L1–L2) levels of the spinal cord (Fig. 2.4). The midline portion of the neural

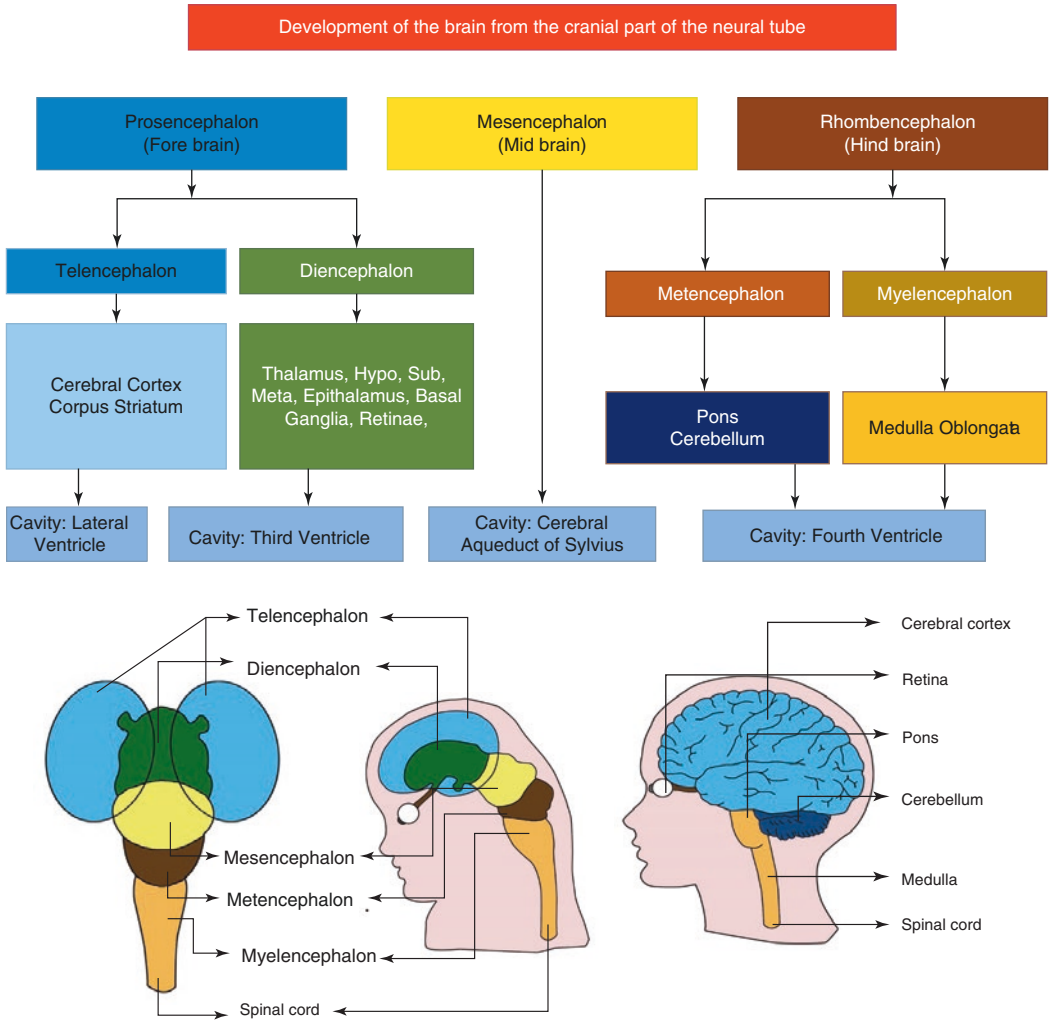


Fig. 2.3 Line diagram (**a**) and schematic embryological development of various parts of the brain (**b**)

tube on the dorsal and ventral aspect is called a roof and floor plate, where the nerve fibers cross from one side to another side.

The spinal cord fills the spinal canal during embryonic life. Later, the growth of osseous structures exceeds that of neural structures during the fetal period. Hence, the cord and dural sac terminate at higher levels compared to the vertebral level. The spinal cord ends at the L3 intervertebral level at birth and reaches the adult level (L1–L2) by 8 years of age. The dural sac ends at S3 vertebral level at birth and reaches the adult level (S2) by 1 year of age. Biomechanical maturation of the spine is a progressive process; the pediatric spine resembles the adult spine only after 8–9 years. Since the termination of the spinal cord and dura happens at the lower level, it is better to approach the epidural and subarachnoid spaces at a lower intervertebral level to avoid any inadvertent damage to the neural structure.

2.2.4 Autonomic Nervous System (ANS)

ANS consists of both sympathetic and parasympathetic system (Fig. 2.5). *The sympathetic system* (Fig. 2.5a) originates from the

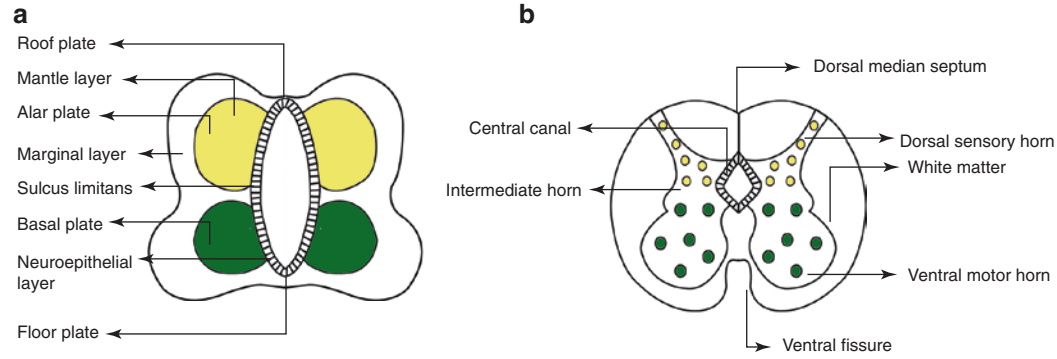


Fig. 2.4 Development of the spinal cord: (**a**) stage of formation of basal, alar, roof, and floor plates; (**b**) formation of ventral motor horn, dorsal sensory horn, and intermediate column

intermediolateral horn of the spinal cord from segments T1 to L2, where the preganglionic nerve cell body lies. The first-order neuron (preganglionic fiber) starts from there and enters the ventral nerve root, ventral primary rami, and white rami communicantes. It synapses at the sympathetic ganglia or, without synapsing at the sympathetic ganglia, passes through it as abdominopelvic splanchnic nerves and synapses at the prevertebral ganglia. Postganglionic fibers arise from sympathetic trunk/para-aortic ganglia and innervate the organs.

The parasympathetic system (Fig. 2.5b) has a craniosacral outflow with preganglionic cell bodies arise from brain stem cranial nerve nuclei III, VII, IX, and X and the sacral spinal cord segments S2–4. The first-order neuron travels through the corresponding cranial nerves and synapses at the ciliary ganglion (CN III), pterygopalatine (CN VII), and otic ganglia. Vagus nerve (CN X) synapses at the ganglia, which lies close to the visceral organ. Preganglionic fibers from sacral segments leave the ventral primary rami of spinal nerves S2–4 as pelvic splanchnic nerves and innervate the gastrointestinal tract, from the distal two-thirds of the transverse colon to the rectum. Both sympathetic and parasympathetic ganglia are derived from neural crest cells.

The ANS is fairly mature in the newborn. The parasympathetic effects on the cardiovascular system are totally operative after birth, and reflex apnea, bradycardia, or laryngospasm may result due to activation of the laryngeal reflex by the excitement of receptors located on the face, nose, and upper airways of the newborn. The sympathetic effects are seen only at 4–6 months of age. Baroreflexes involving the medullary vasomotor centers (pressor and depressor areas) to maintain the blood pressure and heart rate are functional in awake newborns since birth but diminished in the anesthetized newborn.

2.2.5 Neuronal and Cellular Proliferation

Neuroblast multiplies between 10 and 18 weeks of gestational age resulting in brain growth, and this is the phase when the CNS is extremely sensitive to the extrinsic noxious impact of viral infections, drugs, toxins, and X-rays [4]. Neurons, astrocytes, oligodendrocytes, and glial cells continue to differentiate, and they are in continuous formation and remodeling of axons and synaptic connections. Neuronal cells increase from about one-fourth at birth to two-thirds of intracranial volume by 6 months, and their complete growth

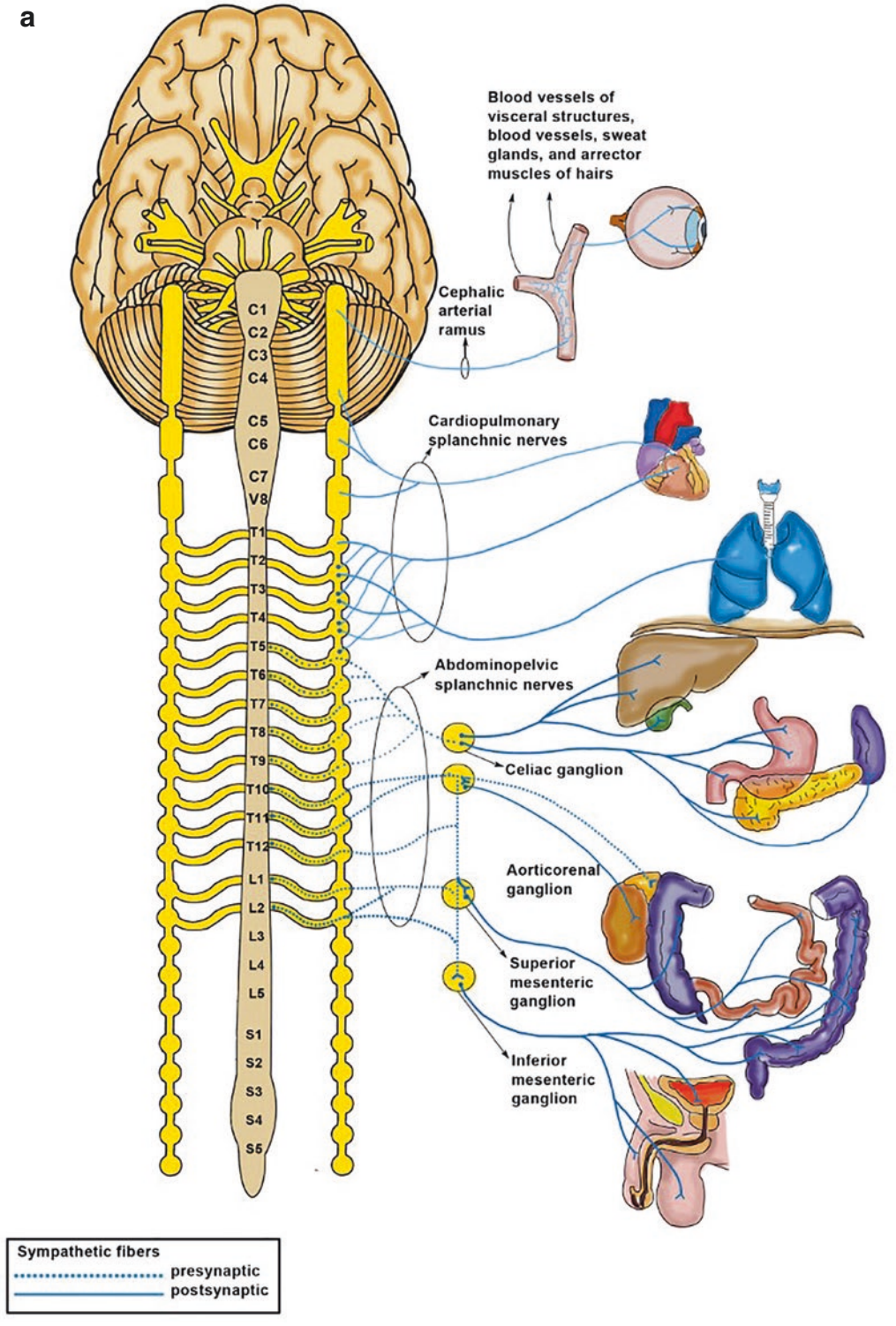


Fig. 2.5 Autonomic nervous system: sympathetic nervous system (**a**) and parasympathetic nervous system (**b**)

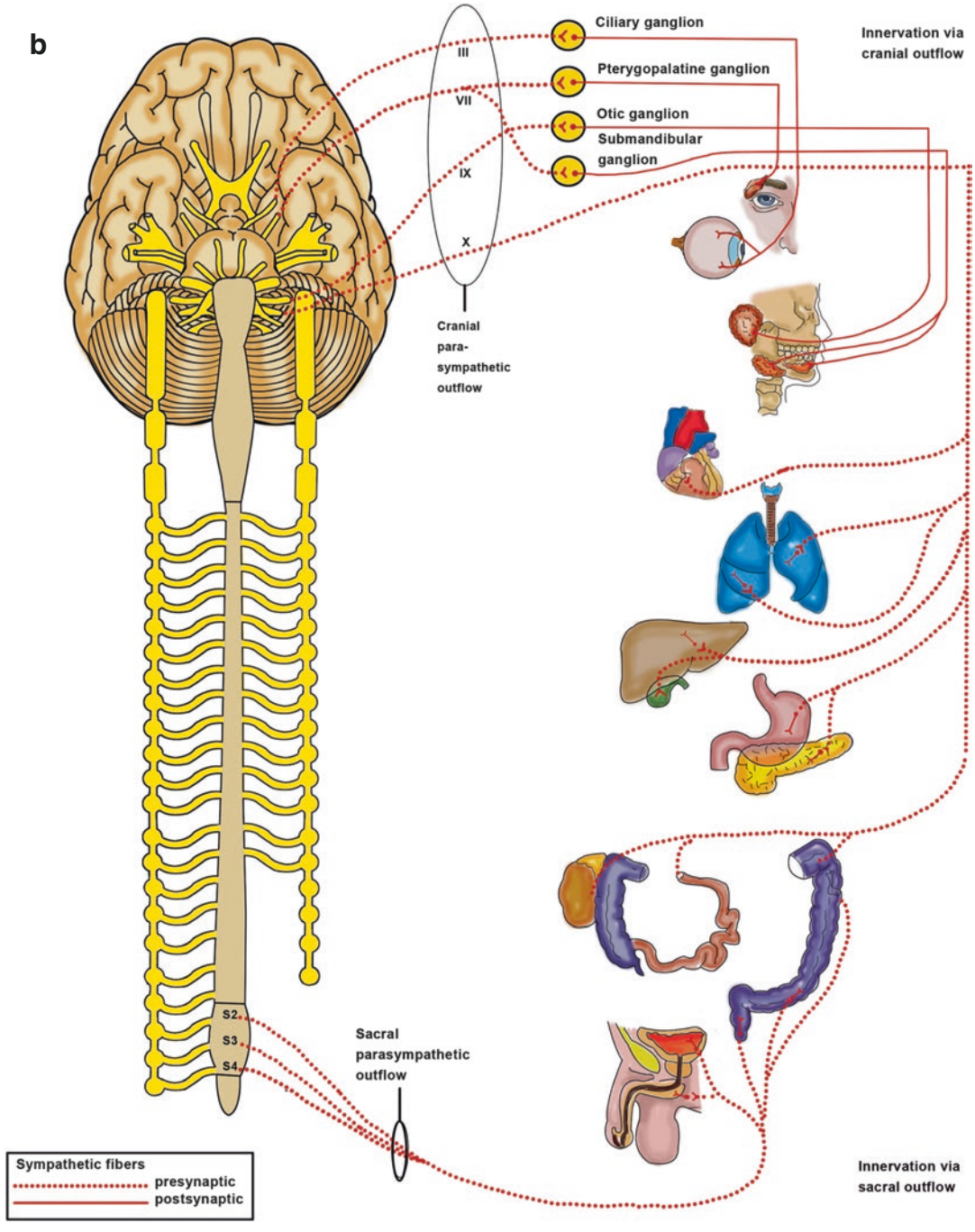


Fig. 2.5 (continued)

is achieved during the second year of life. Differential growth rates occur in different areas: the cerebellum, which is underdeveloped at birth, becomes fully developed in the first year of life ahead of the cortex and brain stem development. Neurons relocate to form the cortical layers by the eighth week of gestation, and this migration is completed by the sixth month. Cerebrospinal fluid (CSF) production starts between 6 and 8 weeks.

2.2.6 Myelination

Myelinization and amplification of dendritic processes start at the third trimester and continues till the second year of postnatal age. Myelination starts at the cervical neuromeres and extends both cranially and caudally and gets completed by 12 years of age. The primitive reflexes, the Moro and grasp reflexes in the neonate, occur due to incomplete myelinization and help to assess neurodevelopment.

The reduced size of nerve fibers due to lack of myelin and shorter distance between successive nodes of Ranvier favor local anesthetics penetration and hasten nerve blockade even with the use of dilute solutions. Nutrition is a critical factor for full cerebral development, and deficient cerebral lipid and protein content that results from malnutrition results in a reduction in the number of cells and dendritic connections. The brain weighs approximately 335 gm at birth, which is about 10–15% of body weight (1/10 of body weight compared with 1/50 of body weight in the adult). Brain weight doubles by 6 months to about 900 gm at 1 year and 1000 gm at 2 years, reaching the final adult weight of 1200–1400 gm by about 12 years of age.

2.3 Relevant Anatomy

2.3.1 Head Size, Suture, and Fontanelle

Growth in children is assessed by changes in weight, length, and head circumference (HC). Percentile charts of variables mentioned above help in tracking the child's growth and development. Deviations from the past percentile are more significant than any single measurement of growth. The head (with respect to body and trunk) is relatively larger in children compared to adults. At birth, the HC measures about 35 cm (Table 2.2). The HC increases by 10 cm during the first year. Then, it slowly expands and reaches the adult level by 6 years of age.

Head size contributes about 1/5 (19%) of total body surface area (BSA) till infancy and gradually decreases and reaches by 11% by 14 years of age (Table 2.3). It matches the adult value of 7% by 25 years of age. HC increases further in children with intracranial pathology causing separation of the sutures and widening of fontanelles.

Skull has two main parts – (i) calvaria or the brain box which encloses the brain consisting of 14 bones which include 3 paired ear ossicles and (ii) the facial skeleton consisting of 14 bones, including the mandible, with 28 bones altogether. Calvarial bones are thin and connected by fibrous structures called sutures. The sutures allow the bones to enlarge evenly as the skull expands to accommodate the growing brain. There are four major sutures of the skull. *Metopic suture* joins the two frontal bones in the midline and extends from the vertex down the center of the forehead, toward the nose. It is the first suture to close

Table 2.2 An expected increase in head circumference at each stage of development

Age	Increase in head circumference
0–3 months	By 2 cm/month
3–6 months	By 1 cm/month
6–12 months	By 0.5 cm/month
1–3 years	0.25 cm/month
4–6 years	1 cm/year

Table 2.3 The ratio of head to the total body surface area (BSA) at various ages

Age	% of body surface area (BSA)
0–1 year	19
1–4 years	17
5–9 years	13
10–14 years	11
Adult	7

physiologically, starts at 3 months of age, and completely fuses at 8 months of age. *Coronal suture* connects the frontal bone with a parietal bone and extends from one ear to the other. *Sagittal suture* joins the two parietal bones in the midline and runs anteroposteriorly. *Lambdoid suture* joins each parietal bone with the occipital bone and extends across the back of the head.

The area between the bones of an infant's skull where the sutures intersect is called **fontanelles**. There are six fontanelles at birth: two major—anterior and posterior fontanelles—and four minor, anterior sphenoid (two on either side) and the posterior mastoid (two on either side), fontanelles, which are covered by durable membranes and protect the underlying soft tissues and brain. The *anterior fontanelle (AF)* is formed at the intersection of the metopic, coronal, and sagittal sutures and the junction of the two frontal and two parietal bones. It usually closes by about 9–18 months. By feeling the AF, the clinical assessment of dehydration (sunken AF), increased ICP (bulging AF) may be made. Ultrasound examination of the fontanelle can detect intracranial bleeding in neonates. AF allows noninvasively monitoring the intactness of the intracranial blood vessels and the status of the neonatal brain [5]. Trans-fontanelle ultrasound imaging can detect both intraventricular and cerebellar hemorrhage [6]. *Posterior fontanelle* is formed at the junction of the two parietal bones and the occipital bone and usually ossifies first, by about 2–3 months. The clinical implication of large heads in pediatric neurosurgical patients is that they are more prone to the difficult airway, increased blood loss, and difficulty with temperature control under anesthesia. The bony skull both protects and jeopardizes the integrity of the pediatric brain. When infants sustain a head injury, because of thin calvarial bone and large head size with the unfused sutures and fontanelles, there is deformation, with or without fracturing. The increased cerebral compliance in young children due to thin calvarial bone, open sutures, and fontanelles is limited only to a point. The slow expansion of the intracranial contents can mask the raised ICP and can be the reason for delayed presentation in children with slow-growing brain tumors. But a sudden acute rise in the intracranial volume (head injury or subarachnoid, intraventricular hemorrhage) results in an acute increase in ICP with resultant risks of herniation and stroke. Craniosynostosis is a condition in which there is a premature fusion of any of the sutures. There will be no growth in the area of the fused sutures and forcing the growth of the skull in another direction giving rise to abnormal head shape.

2.4 Cerebral Vascular Anatomy

2.4.1 Arterial Circulation

The arterial blood supply to the brain is from anterior and posterior circulation (Fig. 2.6a). *Anterior circulation* is formed by the internal carotid arteries (ICAs) on both sides, while the vertebrobasilar system forms the *Posterior circulation*.

Anterior circulation contributes to 80% of blood supply to the brain. ICA is a branch of the common carotid artery that arises from the brachiocephalic artery on the right side and directly from the aortic arch on the left side. The *ophthalmic, superior hypophyseal, posterior communicating, and anterior choroidal arteries arise from the ICA before it finally divides into two major end vessels—anterior and middle cerebral arteries (ACA, MCA)*. The two *anterior cerebral arteries* (A1) travel over the optic chiasm and communicate with each other through the *anterior communicating artery (ACOM)*. The paired A2 vessel arises from the Acom complex and travels posterosuperior over the corpus callosum. The A2 divides into pericallosal and callosomarginal arteries (A3). The terminal branch (A4) supplies the medial frontal lobe, which represents the lower limbs. MCA is divided into M1, M2, M3, and M4 segments. The *middle cerebral artery (MCA)* supplies the internal capsule through lenticulostriate branches (deep), while the terminal or cortical (superficial) supplies the lateral cortex. Vascular compromise produces dense hemiplegia, while the terminal branch occlusion results in brachiocephalic paralysis.

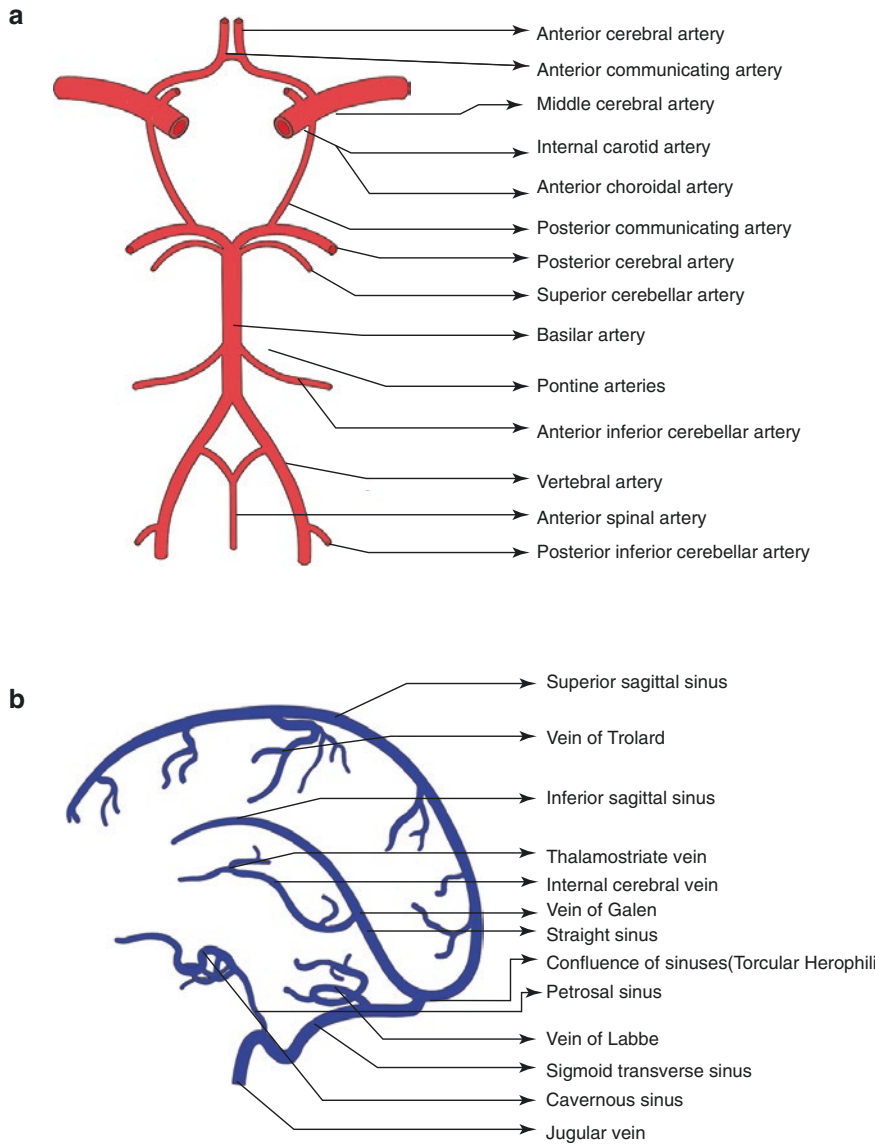


Fig. 2.6 Cerebral vascular anatomy: (**a**) blood supply of the brain, anterior, posterior circulation, and the "circle of Willis"; (**b**) venous drainage of brain

Ophthalmic artery (OA) supplies the globe, and the *superior hypophyseal artery* supplies the pituitary gland and stalk. *The posterior communicating (PCOM) artery* joins the posterior cerebral artery and divides the PCA into P1 and P2 segments. *The anterior choroidal artery* supplies the inner cortex and optic pathway and supplies the choroid plexus.

Posterior circulation contributes 20% of blood supply to the brain. The paired vertebral arteries (VA) arise from the second part of the subclavian artery. It travels cranially through the C6–C1 vertebral foramen. At the level of C1, it travels over the C1 posterior arch and enters the subarachnoid space at the level of the craniovertebral junction. It gives rise to a *posterior inferior cerebellar artery (PICA)* and travels cranially and joins to form the *basilar artery (BA)* at the pontomedullary junction. The BA gives rise to multiple *pontine branches*, *anterior*

inferior cerebellar (AICA) and *superior cerebellar arteries (SCA)*, and then terminates into paired posterior cerebral arteries. *The posterior cerebral artery (PCA)* supplies the occipital lobe. The BA gives rise to multiple perforators which supply the brain stem. AICA, PICA, and SCA supply the cerebellum.

The *"circle of Willis (CoW)"* is a circular vascular ring formed at the base of the brain. The anterior circulation communicates with the posterior circulation through the PCOM artery. It not only provides collateral flow in times of ischemia; it also reduces the pressure within the arterial system in times of high blood flow. Only about 42–52% of people have an intact CoW [7]. In children with incomplete CoW (a part of CoW is either absent or hypoplastic), collateral flow occurs through the distal leptomeningeal branches or the OA from the external carotid artery (retrograde flow) and supplies the surface of the brain and to the ICA, respectively.

2.4.2 Venous Drainage

The pial layer houses the cerebral veins, while the subarachnoid layer has the large collecting veins, which eventually run through the subdural space to drain into the cranial venous sinuses. The dural venous sinuses are the space between the endosteal and the meningeal layers of the dura. The cerebral venous system consists of the superficial and deep systems (Fig. 2.6b). The superior sagittal sinus drains into the transverse sinuses. The junction of superior sagittal, straight, and the two transverse sinuses is called "*torcular Herophili*." The transverse sinus continues with the sigmoid sinus and enters into the jugular foramen and drains into the internal jugular vein (IJV). The deep veins drain into the cavernous, superior, and inferior petrosal sinus. The paired thalamostriate veins, draining the deep structures of the brain, enter through the foramen of Monro and travel posteriorly in the roof of the third ventricle.

The *vein of Galen* is formed by the union of the two internal cerebral veins. The vein of Galen joins the basal vein of Rosenthal and the inferior sagittal sinus and forms the straight sinus. The straight sinus drains into the torcula. The ***vein of Trolard*** and the *vein of Labbe* are two important large veins draining the lateral cerebral cortex and temporal lobe, respectively. The cerebellum drains through the inferior cerebellar veins and into the occipital sinuses. Venous compromise can result in varying degrees of deficit and also can result in mortality. The superior sagittal sinus is particularly important to the anesthesiologist as it is superficial, and in the midline, the location puts it at risk during surgery. Most of the intracranial blood volume consists of blood in the venous sinuses and pial veins.

2.5 Cerebral Physiology

2.5.1 Cerebral Blood Flow (CBF)

There are no conclusive studies on CBF and autoregulation in the pediatric population, and similar mechanisms as in adults are reckoned. The CBF varies with age [8]; premature and the term newborn have lower CBF than adults, making them vulnerable to cerebral ischemia, while it is higher in infants and older children when compared to adults. The CBF peaks around 2 to 4 years of age and settles down at 12 years of age [9]. The normal average CBF values in the different age groups are enumerated in Table 2.4 [9]. The gray matter consisting of the cell bodies of the neurons and associated with the intricate functions receives a greater fraction of the arterial blood supply. The white matter is mostly composed of

Table 2.4 Normal cerebral blood flow (CBF) at various age groups

Age	Cerebral blood flow (ml/100gm/min)
Preterm neonates	12–20
Full-term neonates	23–40
Infants <6 months	40–42
6 months to 3 years	90
3 years to 12 years	100
Adults	50

axons, is involved with less complicated functions like transmission of impulses between the neurons, and needs a lesser amount of blood supply. This difference in CBF (compartmentalization) has been tested in sick neonates. Hence, the neonates are more prone to white matter ischemia in the presence of systemic hypotension. Premature neonates are more prone to hemorrhage in and around the ventricular area. The periventricular area is rich in germinal matrix, highly vascularized neuronal-glial precursor cells rich in frail blood vessels. These blood vessels are deficient in pericytes, have immature basal lamina, and lack glial fibrillary acidic protein (GFAP) in the encasing astrocytes' end feet, making them prone to hemorrhage.

2.5.1.1 Factors Affecting Cerebral Blood Flow

Many physiological and pathological factors affect the CBF; they are discussed in detail below (Fig. 2.7).

1. **Cerebral Perfusion Pressure (CPP)**: CBF depends upon the CPP, which in turn is related to mean arterial pressure (MAP) and the ICP. In most organs, the driving pressure depends upon the variation between the arterial and venous pressure. However, in the brain, the ICP is the downstream pressure and not the venous pressure. The brain lies within a confined cavity, and an increase in ICP results in a collapse of the bridging pial veins and venous sinuses, which act as Starling resistors. Hence, the CPP is the difference between the MAP and ICP [CPP = MAP – ICP]. In children MAP and ICP vary according to the age group. For calculating the normative BP, height, and birth weight, gestational age must be considered, but it is not considered in routine clinical practice. Even the definition of hypotension varies in neonates and infants. For defining hypotension in neonates and small children, systolic blood pressure (SBP) is often considered and not the MAP. Most pediatric anesthesiologists define hypotension as a threshold value for an SBP of 50 mmHg or assume a 20–30% decrease from baseline SBP value as clinically significant hypotension [10]. For calculating the CPP, measurement of MAP and

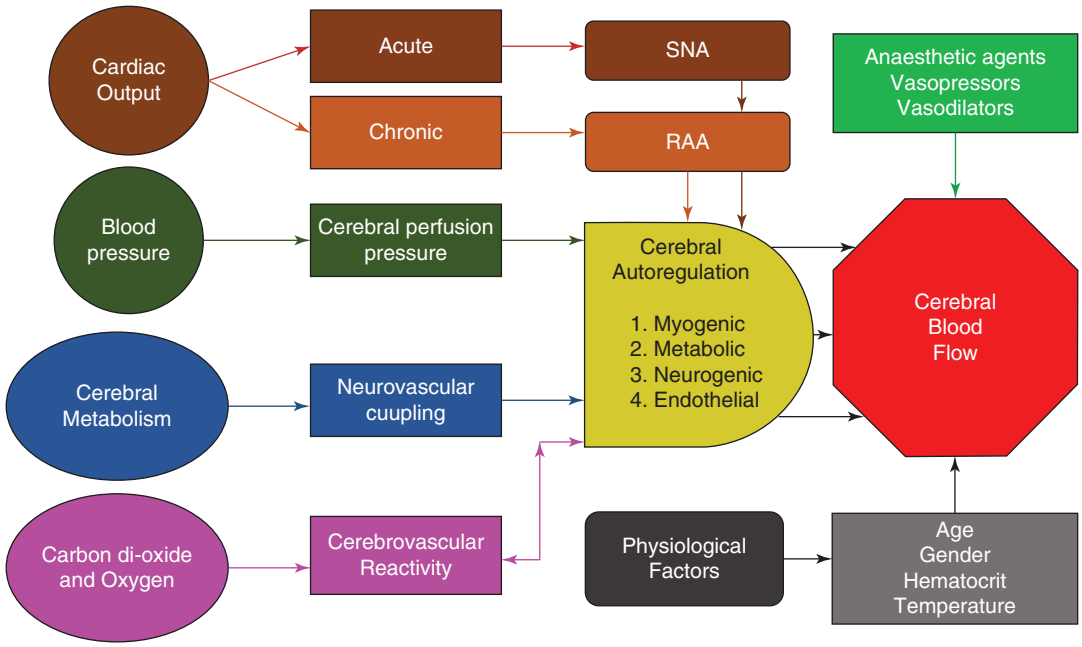


Fig. 2.7 Factors affecting the cerebral blood flow. *SNA* Sympathetic neuronal activity; *RAA* renin angiotensin aldosterone

the ICP are needed, and ICP varies with age. Neonatologists define hypotension as MAP less than or equal to the gestational age in weeks. One commonly used formula for estimating MAP in infants and small children is 1.5 X (age in years) + 40 (5th percentile at 50th height percentile) and 1.5 X (age in years) + 55 (50th percentile at 50th height percentile). Normal ICP varies between 1.5 and 6 mmHg in newborn and 3–7 mmHg in children. Measuring the ICP in children helps to maintain the optimal CPP. There are no recommendations regarding the age-dependent optimum CPP for children with raised ICP. The treatment guidelines for pediatric traumatic brain injury (TBI) recommend maintaining the ICP less than 20 mmHg and CPP greater than 40–50 mmHg (Level III evidence). The target CPP needs to be increased for older children and adolescents [11]. Studies have shown that children managed with BP recommended by the pediatric TBI group also had low brain oxygen [11]. Regarding the CPP, there are no age-based recommendations available for children with raised ICP. Future studies are recommended regarding the optimum CPP for each age group.

The increase in cerebrovascular resistance (CVR) impedes the CBF. The CBF is influenced primarily by the diameter of the vessels. During cerebral vasodilatation, the radius of the distal vessels increases, thereby decreasing the CVR and augmenting CBF. At the same time, vasoconstriction of the cerebral vasculature reduces CBF by increasing the CVR. The following relationship determines the CBF:

- CBF = CPP/CVR; CVR = $8\eta l/\pi$ r4, where l is the length of the vessel, η is the viscosity of blood, and r is the radius of the vessel.

2. **Arterial Carbon Dioxide Tension ($PaCO_2$):** CO_2 is the most important determinant of CBF. Cerebral blood vessels are susceptible to change in $PaCO_2$. CBF varies almost linearly with arterial carbon dioxide concentration between 18.5 and 60 mmHg (Fig. 2.8). Wyatt

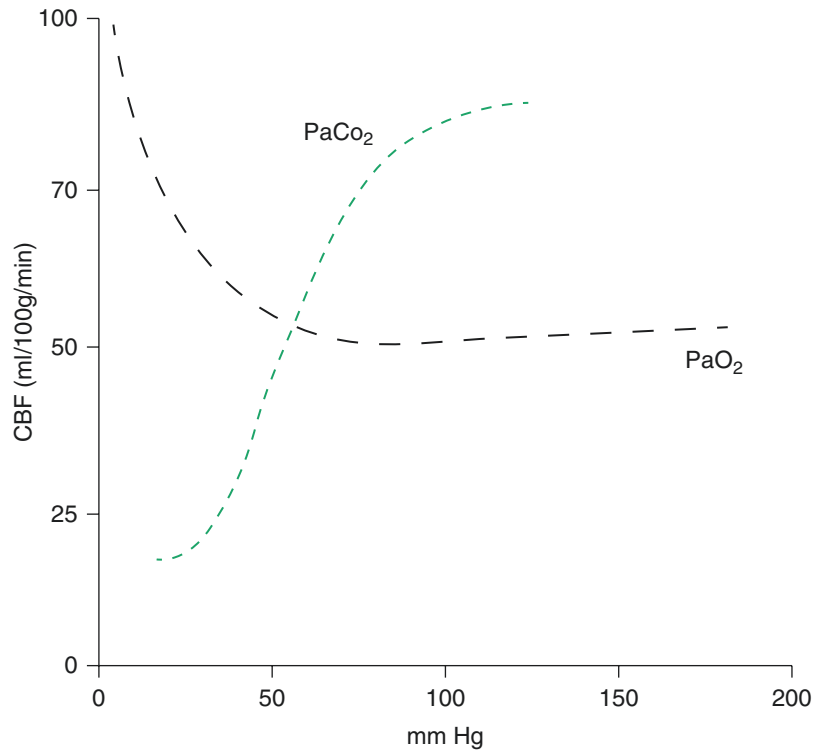


Fig. 2.8 The relationship of cerebral blood flow to arterial $PaCO_2$ and PaO_2

et al. [12], using near-infrared spectrophotometry in sick newborns, have illustrated that the $PaCO_2$-related changes in CBF are linear. Hyperventilation re-establishes autoregulation in the neonate as in adults [13]. The vasoreactivity response to a small change in $PaCO_2$ starts within seconds and reaches a steady state within 10 min [14], gradually returning toward baseline CVR over the next 3–6 h, corresponding with the time course of pH regulation through bicarbonate extrusion [15]. Persistent hypercapnia results in late hyperemia, and that does not return to normal even after normalization of serum bicarbonate.

Mechanism of Hypercarbia-Induced Increase in CBF in Neonates and Infants: Increase in arterial CO_2 easily diffuses into the brain through the BBB and combines with H_2O and forms the H_2CO_3 which dissociates to H^+ and $HCO3^-$. An increase in pH stimulates the K^+ ATPase channel and causes hyperpolarization and smooth muscle vasodilation. Activation of K^+ ATP channel, in turn, inhibits the Ca^{++} entry into the smooth muscle. An increase in H^+ also stimulates the cyclooxygenase enzyme in the capillary endothelium, which increases the prostaglandin through the CAMP pathway and causes cerebral vasodilation (Fig. 2.9).

Cerebrovascular Reactivity to Carbon Dioxide in Children

Changes in CVR and the CBF in response to changes in $PaCO_2$ are termed as *cerebrovascular reactivity* to carbon dioxide. It is expressed in terms of an absolute and relative term. Absolute CO_2 reactivity is defined as the change in CBF (ml/min) per unit change in $PaCO_2$ (mmHg). Relative CO_2 reactivity is defined as the percentage (%) change from the baseline value. The formula is expressed either in *ml/mmHg* (while using the direct method to measure the CBF) or *cm/sec/mmHg* if TCD is used to measure the CBF (Table 2.5).

The change in CBF occurs instantaneously after the $PaCO_2$ change, and complete equilibration takes about 2 min. Studies have shown that the cerebrovascular reactivity to CO_2 is preserved in the preterm, term, and small to bigger children. Intra- and inter-individual variability in CO_2 reactivity have been seen in preterm neonates during the first and second days. There is an

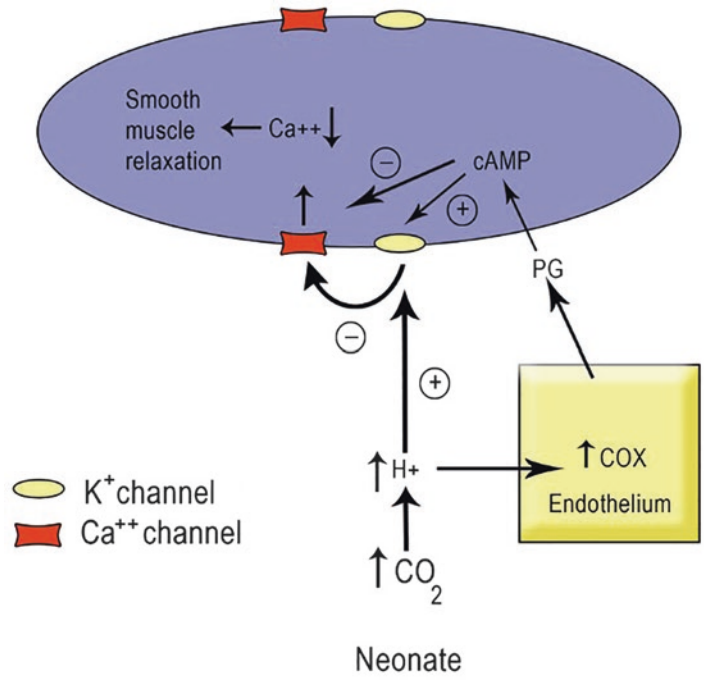


Fig. 2.9 The proposed mechanism of hypercapnic vasodilation in neonates

Table 2.5 Normal cerebrovascular reactivity to CO_2 in children in comparison to adult value

The formula for calculating CVR-CO_2	Normal value in adults	Normal values in awake children
Absolute CVRe = ΔCBF/Δ $PaCO_2$	*Using direct method:* 1–2 ml/100gm/min/mmHg ↑ or ↓ in CO_2 *Using indirect method (TCD):* 2–5 cm/sec/ mmHg ↑ or ↓ in CO_2	No studies available
Relative CVRe = Absolute CVRe/ baseline CBF) × 100	*Using direct method:* 2–4% change from baseline value in ml/mmHg *Using indirect method (TCD):* 2.5% to 6% change from baseline in cm/sec	No studies available

Δ *CBF* the difference in CBF between the baseline and after hyper- or hypocapnia, Δ*$PaCO_2$* the difference in $PaCO_2$ between the baseline and after hyper- or hypocapnia

increased incidence of intracranial hemorrhage in neonates who had absent CO_2 reactivity. Healthy children under propofol anesthesia [16] showed a 13.8% change in cerebral blood flow velocity (CBFV) per mmHg change in $EtCO_2$ while 10.3% change with inhalational agents (up to 1.0 minimum alveolar concentration, MAC); the reported values are much greater than the adult values [17–19]. This could be attributed to higher basal CBF in children. Hence, carbon dioxide is used as a drug to effect changes in CBF by pediatric anesthesiologists. Hyperventilation-induced decrease in CBV and CBF facilitates craniotomy in children with elevated ICP. Studies have shown that prophylactic hyperventilation in children with TBI caused cerebral ischemia. This led the Brain Trauma Foundation [20] to suggest that the prophylactic hyperventilation is contraindicated except when used transiently during surgery or to prevent impending herniation.

3. **Arterial Oxygen Tension (PaO_2):** The impact of the partial pressure of oxygen (PaO_2) on the cerebral circulation is of lower clinical significance than $PaCO_2$. PaO_2 between 50 and 300 mmHg does not substantially change the cerebrovascular tone (Fig. 2.8). CBF does not increase till the PaO_2 drops down to 50 mmHg and below which the CBF steeply increases. At 30 mmHg, the CBF doubles. When oxygen delivery hits a critical threshold, global hypoxic vasodilatation happens, and the cerebral autoregulatory mechanisms get disrupted. Once hypoxemia is established, the equilibration of CBF takes a longer time, around 6 min. The proposed mechanism is mediated by the release of metabolic by-products such as lactate, adenosine, and H^+-induced cerebral vasodilation. Also, hypoxia causes a decrease in ATP, which opens the K^+ ATP channel, leading to hyperpolarization of smooth muscle membrane and vasodilation. In the presence of hypoxia associated with hypocapnia, the rise in CBF is not significant. Hypoxia with hypercapnia causes a profound increase in CBF. Hyperoxia decreases the blood flow to 10–15% from the baseline. Hence, it is better to avoid hyperventilation during resuscitation after circulatory arrest. Figure 2.8 shows the relationship between $PaCO_2$ and PaO_2 on CBF.
4. **Hematocrit:** According to Hagen-Poiseuille's law, the CBF is indirectly proportional to blood viscosity. The hematocrit predominantly determines blood viscosity. A drop in hematocrit to less than 28% decreases the viscosity and improves CBF. It also decreases the oxygen-carrying capacity and can impair oxygen delivery and lead to vasodilation. Elevated hematocrit (polycythemia) of more than 44% increases blood viscosity and can reduce CBF. Optimal cerebral oxygen delivery usually occurs at a hematocrit of approximately 30%.
5. **Temperature:** Every 1-degree centigrade (1°C) increase or decrease in temperature

reduces the cerebral metabolic rate for oxygen ($CMRO_2$) by 6–7% from the baseline. Unlike anesthetic agents, which affect only the functional metabolism, hypothermia affects both basal and functional metabolism. Mild hypothermia preferentially suppresses basal metabolism [21, 22]. Deep hypothermia decreases both functional and basal metabolism. Q10 defines the metabolic rate reduction; Q10 denotes the ratio of metabolic rate associated with two temperatures that differ by 10°C. The Q10 between 37 and 27°C, 27 and 17°C, and 17 and 7°C is about 2.4, 5, and 2.3, respectively (Fig. 2.10). At 27°C, there is mild electroencephalography (EEG) suppression; as the temperature drops down to 17°C, there is a complete suppression of EEG, which accounts for the marked increase in Q10 between 27°C and 17°C. Global $CMRO_2$ at 17°C is lower than 10% of the normothermic control value. Deep hypothermic circulatory arrest for certain cardiac procedures (aortic arch replacement) and giant intracerebral aneurysms are performed at this temperature because of complete metabolic suppression at 17°C. As temperature rises, $CMRO_2$ increases and causes accumulation of metabolic by-products, which causes cerebral vasodilation and increases the CBF. Temperatures above 42°C produce a marked lowering in $CMRO_2$, perhaps due to neuronal injury and protein denaturation (Fig. 2.10).

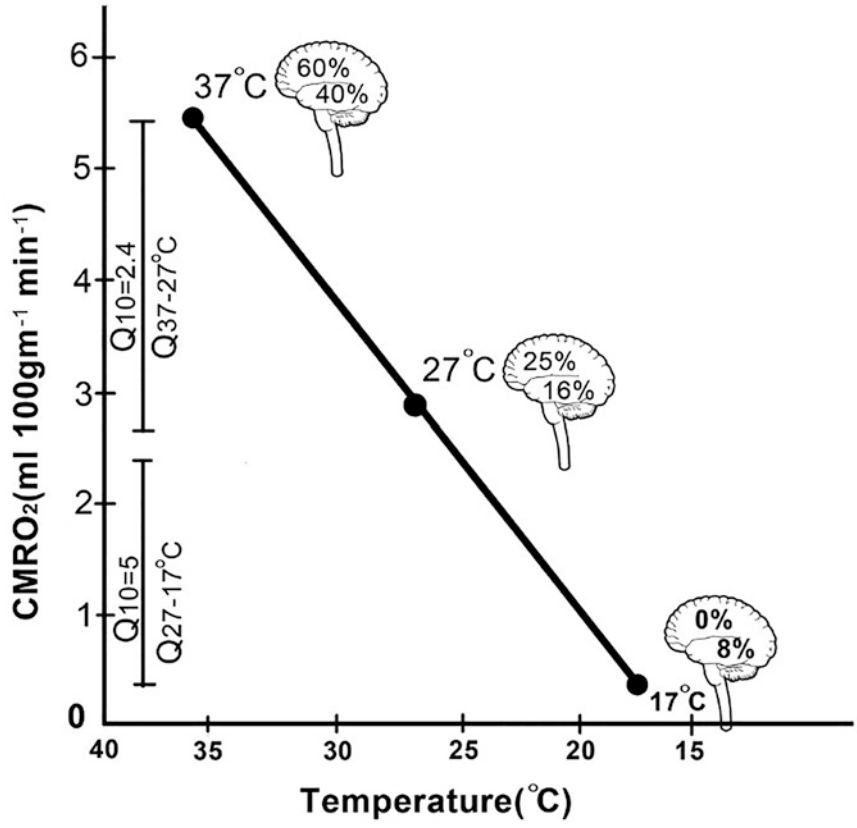


Fig. 2.10 The relationship between body temperature and cerebral metabolism

6. **Glucose:** The brain has limited glycogen reserves, and therefore, a constant supply of glucose is needed for its proper function. Akin to $CMRO_2$, the cerebral metabolic rate for glucose (CMRglu) is low in children at birth (13–25 μmol or 3.2 mg/100gm/min), increasing during childhood to highest values by 3–4 years (49–65 μmol or 5.3 mg/100gm/min), and remaining so until 9 years of age after which it decreases and reaches adult values (19–33 μmol/100gm/min). There is a direct linear relationship between the plasma and the brain glucose, even at very low plasma glucose levels. Glucose diffuses readily into neurons, even in the absence of insulin, unlike most other cells that require insulin for glucose transport from the serum to the intracellular space. CMRglu varies in different areas of the brain. Hypoglycemia induces cerebral vasodilation in specific brain regions rather than globally. Although exact glucose thresholds for cerebral vasodilation have not been defined in neonates and children, cerebral vasodilation occurs at serum glucose levels below 30 mg/dL in neonates without alterations in consciousness.
7. **Age:** CBF varies with age. Flow is least in preterm neonates to the maximum in children between 2 and 4 years of age. It reaches the adult value by 12 years of age. The normal CBF of children of various age groups is mentioned in Table 2.4.
8. **Gender:** CBF changes according to age are found to occur in both boys and girls. The anterior circulation flow velocities are higher than the posterior circulation in both genders. Gender-related differences in CBF were also noted in children. Girls aged 4–16 years have higher MCA and BA flow velocities compared to same-aged boys [23, 24]. These gender-related variations in blood viscosity can be explained by hematocrit or hormonal distinction, vessel size, cerebral metabolism, or cerebrovascular resistance (CVR) [24]. The abovementioned factors on CBF have not been proven yet except the effect of CVR on CBF. Young children have shown to have low CVR and a high CBFV [25].
9. **The Effect of Anesthetic Agents on CBF:** All inhalational agents in clinical use increase the CBF despite decreasing the cerebral metabolic rate (CMR) except nitrous oxide, which increases the CMR (luxury perfusion). All intravenous anesthetics reduce the CBF and CMR except ketamine, which increases both CMR and CBF. Increasing plasma concentrations of anesthetic agents cause increasing suppression of EEG activity with a concomitant reduction in CMR [26]. Elevating the plasma level of the agent beyond that needed to suppress the EEG results in no further decline in CMR.
10. **The Effect of Vasopressors on Cerebral Blood Flow:** The effects of vasopressors on CBF and CMR are variable with and without an intact BBB. Caution is needed while commencing epinephrine or low-dose dopamine to support the hemodynamics in children with moderate to severe TBI, which can increase the blood flow tremendously, thereby increasing the ICP. Table 2.6 shows

Table 2.6 The effect of vasopressor on CBF and $CMRO_2$

Pure agonist	Cerebral blood flow (CBF)	Cerebral metabolism ($CMRO_2$)
α1 agonist	0/–	0
α2 agonist	–	–
β—Agonist with intact BBB	+	+
β—Agonist with open BBB	+++	+++
Dopamine (low dose)	++	0
Dopamine (high dose)	–	0
Mixed drugs		
Norepinephrine with intact BBB	0/–	0/+
Norepinephrine with open BBB	+	+
Epinephrine with intact BBB	+	+
Epinephrine with open BBB	+++	+++

BBB blood-brain barrier; 0, +, ++, +++, showing relative effect 0 being no effect to +++ being maximum effect

the effect of commonly used vasopressors on CBF and the CMR.

11. **Functional State:** Cerebral metabolism (only 3% reduction from an awake state) and CBF decrease during non-rapid eye movement (REM) sleep and markedly increase during REM sleep. Sensory stimulation of the CNS, like arousal of any cause or mental tasks, during seizure activity, both, the CMR and the CBF increase significantly. The CMR and the CBF decrease in coma.

Measurement of CBF: CBF can be measured using various direct or indirect methods. The common methods of measuring the CBF in children are discussed here. The Kety-Schmidt technique is the gold standard for the measurement of global CBF [26]. The tailoring of this technique for children age 3–10 years showed that preteen children have a CBF nearly double that of adults [25]. The values of CBF at birth in healthy and in preterm infants without respiratory distress syndrome are seen to be roughly a third of adult measurements, which is very near to the ischemic threshold of 20 mL/100gm/min in most infants [27]. As the development progresses, shifts in regional blood flow have been demonstrated [28]. Regional cerebral blood flow can be measured by an invasive technique such as the xenon-133 clearance technique, xenon-computed tomography, single-photon emission computed tomography, positron emission tomography, perfusion computed tomography, and arterial spin labeling.

Transcranial Doppler (TCD) ultrasonography being noninvasive and easy to use, having no radiation risk, and with the ability to perform a repetitive examination at the bedside of critically ill patients, is frequently used to evaluate CBF and appreciate developmental cerebrovascular changes in healthy children. TCD ultrasonography, which measures CBFV of the basal cerebral arteries, is an indirect measure of CBF. Transcranial Doppler studies demonstrate that the CBFV is ~24 cm/s in healthy newborns and increases thereafter with age, peaking at 6–9 years (97 cm/s) [29]. It decreases approaching adult values [30, 31] of ~50 cm/s beyond 10 years of age [32, 33].

2.5.2 Cerebral Metabolic Rate (CMR)

The utilization of oxygen and other nutrients by the human brain is a complex process. The total energy requirement of the brain is utilized for two major processes (Fig. 2.11), namely, functional metabolism and basal metabolism. The functional metabolism expends almost 60% of the expenditure, and it is responsible for the excitatory synaptic activity. The remainder (40%) of energy requirement is utilized for the maintenance of cellular integrity. CMR varies directly with the neuronal activity. A surge in neuronal activity and CMR is concomitantly complemented by an increase in CBF [34, 35], a complex physiologic process known as *flow-metabolism coupling*, and is mediated by a combination of metabolic, glial, neural, and vascular factors. The metabolites (K^+, H^+, lactate, adenosine, and ATP) and increased production of nitric oxide (NO) alter the local blood flow by directly modulating vascular resistance. The CMR is the rate of utilization of metabolic substrates [e.g., oxygen ($CMRO_2$), glucose (CMRglu), or generation of by-products, e.g., lactate (CMRlact)] by the brain. In children, cerebral metabolism increases with advancing age because of progressive myelination and synaptogenesis. These changes cause a substantial increase in CBF, especially during the first 8 years of life. $CMRO_2$ is closely coupled to CBF in children (*flow-metabolism coupling*). In children, $CMRO_2$ is higher at 5.2 ml/100gm/min than 3.5 ml/100gm/

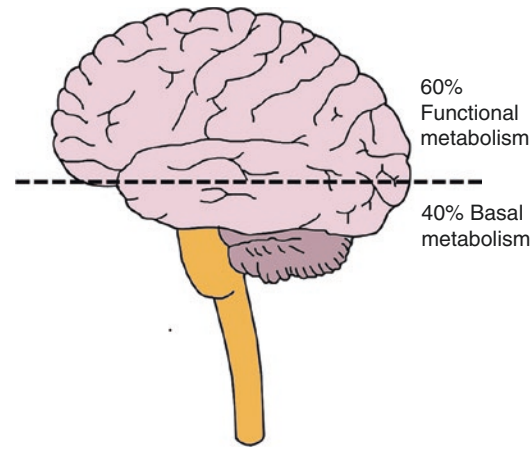


Fig. 2.11 Normal energy requirement of the brain

min in adults. Their higher CBF and increased glucose utilization are appropriate for this increased $CMRO_2$. Neonates have a lower $CMRO_2$ (2.3 ml/100gm/min) and a lower CBF and have relative tolerance to hypoxemia. CMRglu is around 60% of adult values at birth and rapidly increases to over 200% of adult values by the age of 5 years, and then it slowly decreases to adult levels at adolescence (13–16 years of age).

Studies have shown that, in healthy adults, the global $CMRO_2$ averages 3.2 ml (143 μmol)/100gm/min (gray matter 6 ml/100gm/min vs. white matter 2 ml/100gm/min) [36]. The information regarding $CMRO_2$ in children is limited. Kennedy and Sokoloff [25] using modified nitrous oxide method have reported higher $CMRO_2$ and lower CVR in healthy awake children aged 3–11 years than in young adults: $CMRO_2$ 5.2 ml (231 μmol)/100gm/min vs. 4.2 ml (187 μmol)/100gm/min and CVR 0.8 mmHg/100gm/min vs. 1.4 mmHg/100gm/min. Similarly, healthy anesthetized children also show an increase in $CMRO_2$ with increasing age after infancy: 104 μmol/100gm/min in infants [37] vs. 135 μmol/100gm/min in children from infancy up to 14 years old [38]. A positron emission tomography (PET) study on infants showed that regional $CMRO_2$ was lower in children than in adults [39].

CMRglu in children is lower at birth (13–25 μmol/100gm/min), increases slowly and peaks by 3–4 years (49–65 μmol/100gm/min) and remains high until 9 years of age. CMRglu then decreases and reaches adult values (19–33 μmol/100gm/min). The changes in $CMRO_2$, CMRglu, and CBF parallel each other and peak during early childhood, indicating maturational changes during this period. A thorough understanding of the age- and gender-related differences in these physiological variables is not possible as data regarding age-related changes in CMR in healthy children and children with traumatic brain injury is lacking.

2.5.3 Cerebral Autoregulation (CA)

CA is the intrinsic ability of cerebral blood vessels (small arteries and arterioles) to maintain a nearly constant CBF across a range of varying CPP. CBF becomes passive once the CPP crosses above the upper or below the lower limit. A sudden increase in CPP above the upper limit leads to cerebral edema or hemorrhage, while a sudden decrease in CPP below the lower limit leads to cerebral ischemia. CA is a composite feedback-based homeostatic process comprising at least two mechanisms that take effect at different time scales. A *rapid response*, otherwise called *dynamic autoregulation*, is a change in CBF in response to pressure pulsations observed in a time scale of seconds. This is followed by *a slow response or static autoregulation* in which there is a change in CBF in response to the change in MAP that is observed and averaged over several minutes to several hours. Various hypotheses involved in CA are discussed in detail as below (Fig. 2.12).

1. **Myogenic Hypothesis (Bayliss Effect):** The myogenic response is the intrinsic property of vascular smooth muscle to react to intravascular pressure changes. A rapid change in transmural pressure (ΔP) of about 10 to 25 mmHg/sec triggers this response with a latency period of less than 250 ms. Smooth muscle of small arteries and arterioles vasoconstricts with increased pressure and vasodilates with a decrease in pressure. Stretch induced activation of nonselective cation channels leading to an influx of calcium through the Ca^{2+} channels, which causes membrane depolarization and smooth muscle vasoconstriction. This process, in turn, activates the calcium-activated K^+ channel, which causes smooth muscle hyperpolarization leading to vasodilation; thereby, the balance between vasoconstriction and vasodilation is maintained.
2. **Metabolic Hypothesis:** Synaptic activity releases glutamate from the presynaptic nerve ending, which causes activation of glutaminergic receptors in the postsynaptic neuron, which stimulates the calcium entry. This results in the release of arachidonic acid (AA), prostaglandins (PGs), and nitric oxide (NO) and causes cerebrovascular dilation. Apart from this, the accumulation of metabolic by-products such as K^+, H^+, lactate, adenosine, and ATP all leads to cerebral vasodilation.

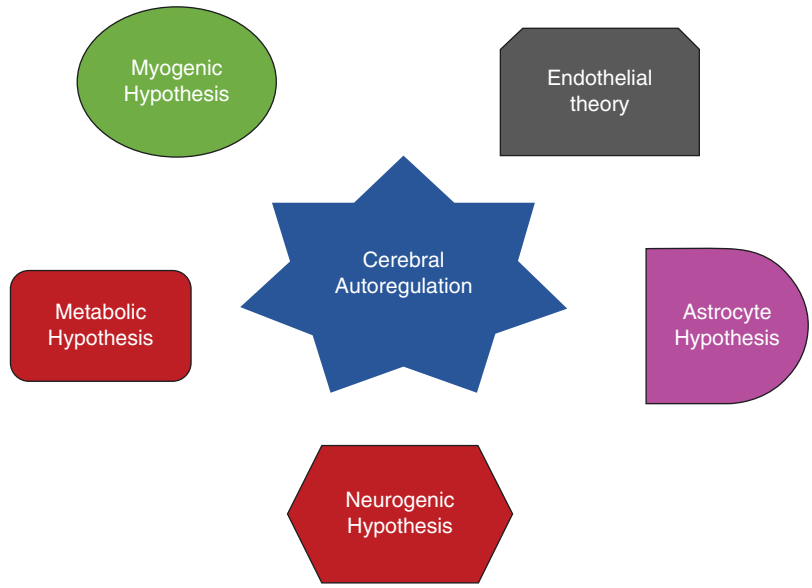


Fig. 2.12 Proposed hypotheses for cerebral autoregulation

Glutamate also activates metabotropic glutamate receptors (mGluR) in astrocytes, causing intracellular calcium entry, which activates the phospholipase A2 (PLA2) and releases AA, epoxyeicosatrienoic (EET) acid, and prostaglandin E2 (PGE2). The latter two AA metabolites contribute to cerebral dilation. In contrast, AA gets converted to 20-hydroxyeicosatetraenoic acid (20-HETE) in vascular smooth muscle and causes cerebral vasoconstriction. Figure 2.13 shows the flow of metabolism coupling.

3. **Neurogenic Hypothesis:** Two distinct mechanisms exist in the neural control of CBF; they are extrinsic and intrinsic neurogenic pathway. **The extrinsic neurogenic pathway** innervates the extra parenchymal cerebral blood vessels till it reaches the Virchow-Robin space, at which extra parenchymal vessels enter the brain parenchyma. The *extrinsic neurogenic pathway* consists of sympathetic and parasympathetic fibers, which cause cerebral vasoconstriction and vasodilation, respectively, through various mediators (Table 2.7). The *intrinsic neurogenic pathway* innervates the vessels from Virchow-Robin space to deep inside the cortex and the subcortical areas. Neurons arising from the subcortical areas such as nucleus basalis, locus coeruleus, and raphe nucleus send projections to interneurons and astrocytes and blood vessels (neurovascular unit) which are located in the cortical area which release various vasoactive mediators to act on the various receptor in the cerebral blood vessels and mediate either vasodilation or vasoconstriction. The components of intrinsic neurogenic fibers, the mediator, secreted, and its vasomotor response are given in Table 2.8.
4. **Astrocyte Hypothesis**: Astrocytes have a unique anatomical location to control the CBF. On one side, astrocytic processes extensively surround brain capillaries, and on the other side, it encircles the neuron, forming a link between the cerebral microvasculature and synapses. The cellular components of the neuron-astrocyte-arteriole conduit are often referred to as the "neurovascular unit."

   During neuronal stimulation, glutamate, an excitatory neurotransmitter, is released from the presynaptic nerve endings. It stimulates the astrocyte resulting in an increase in intracellular Ca^{++}, thereby causing vasodilation of arterioles contacted by astrocyte foot processes. Initially, astrocytes were considered to

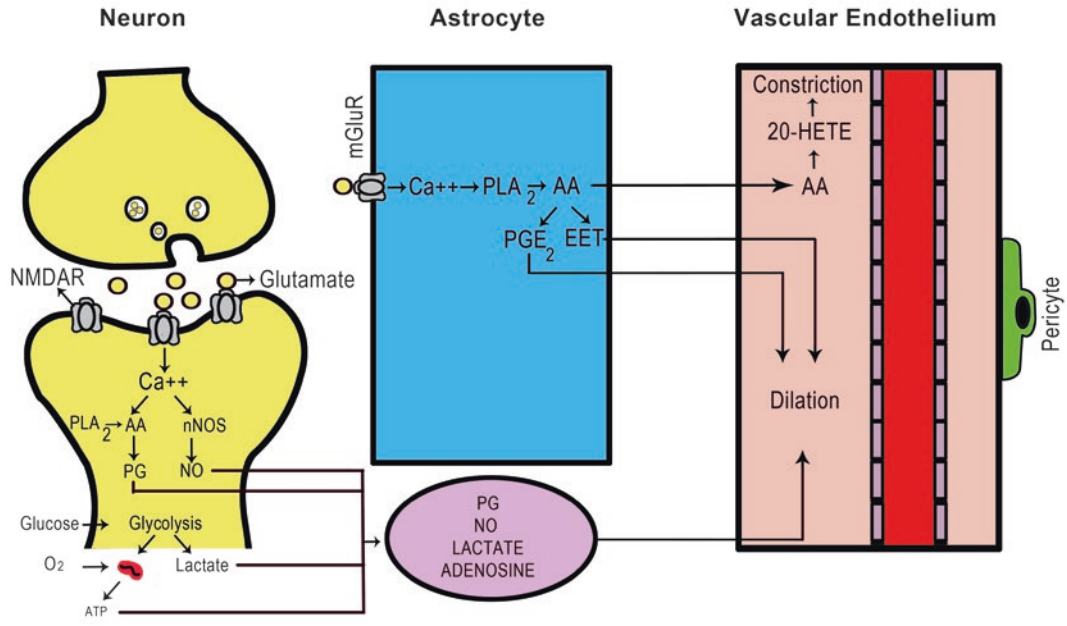


Fig. 2.13 Flow metabolism coupling

Table 2.7 The extrinsic neurogenic pathway involved in cerebral autoregulation

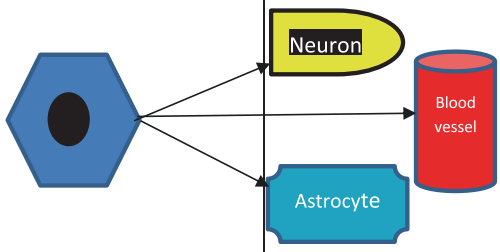
Types of fibers arise from	Vasoactive mediator	Vasomotor response
Sympathetic		
Postganglionic fiber from superior cervical ganglion	Norepinephrine, neuropeptide Y	Cerebral vasoconstriction
Parasympathetic		
Sphenopalatine and otic ganglion	Acetylcholine, vasoactive intestinal peptide (VIP)	Cerebral vasodilation
Sensory fibers		
Trigeminal ganglion	Substance P, calcitonin gene-related peptide	Cerebral vasodilation

be involved in the clearing of excess extracellular K^+. The absorbed K^+ is shunted to the foot process of astrocyte around the microcapillaries, leading to cerebral vasodilatation (K^+ induced). Recent in vitro studies show that astrocytes mediate cell-to-cell communication through gap junctions, modulating neuronal and vascular function.

5. **Endothelial Hypothesis:** The cerebrovascular endothelium is a dynamic organ playing an important role in the control of CBF by forming a physiologic connection between the blood vessel lumen and the surrounding smooth muscle. It consists of four main chemical substances, such as nitric oxide (NO), endothelium-derived hyperpolarization factor (EDHF), eicosanoids, and the endothelins, which are responsible for cerebral dilatation/vasoconstriction.
6. **Microvascular Communication Theory:** The cerebral blood vessels communicate within themselves at the microvascular level to regulate CBF. The connexin (Cx) protein, which is located in the endothelium (Cx 40, Cx 43, Cx 45), and the vascular smooth muscles are involved in this microvascular communication. This connexin protein has electrical and conductive properties. This is the proposed mechanism involved in spreading cortical depolarization, responsible for

Table 2.8 Intrinsic neurogenic pathway involved in cerebral autoregulation

Subcortical Area	Cerebral cortex	Vasoactive mediators released	Response to vasoactive mediators
Nucleus Basalis Locus Coeruleus Raphe Nucleus	Neuron Astrocyte Cerebral Blood vessels	NO, ACh, VIP	Vasodilation
		GABA	Vasodilation
		Neuropeptide Y	Vasoconstriction
		ACh	Vasodilation
		5HT	Vasoconstriction
		PGE_2	Vasodilation
		20-HETE	Vasoconstriction



NO nitric oxide, *Ach* acetylcholine, *VIP* vasoactive intestinal polypeptide, *HT* hydroxy tryptamine, *PGE_2* prostaglandin E_2, *HETE* hydroxyl-eicosatetraenoic acid

vasospasm and the delayed cerebral ischemia (DCI) after subarachnoid hemorrhage (SAH).

2.5.3.1 Cerebral Autoregulation (CA) in Neonates

Studies have shown that in the fetal and newborn lambs, the CA is preserved in a 40–80 mmHg MAP range during the neonatal period. Due to ethical reasons, it is not possible to study CA in human neonates by experimentally producing changes in MAP. Hence, our understanding of CBF and CA is largely based on impromptu observation of events occurring at the neonatal intensive care unit. Most studies are done in sick preterm or term babies who were mechanically ventilated. There are varied controversial results on the relationship between the CBF and CPP. In one study, it has been shown that the CPP is maintained constant with the mean BP range between 25 and 40 mmHg. Others have shown that the CA range is narrow in the mature neonates, ranging from 20 to 60 mmHg (Fig. 2.14) [40]. A study investigating CA in 57 mechanically ventilated preterm infants with normal brains showed that neonates who had shown pressure passive flow (altered CA) developed severe ICH [41]. TCD- and NIRS-based CA studies have shown the absence of dynamic CA in sick, low birth weight neonates [42]. Many studies have shown a positive association between the impaired autoregulation and a poor neurological outcome in the neonatal population [43–46]. The pressure autoregulation responds much faster in neonates (within 2 s) compared to adults (within 4–10 s) [3].

2.5.3.2 Cerebral Autoregulation (CA) in Small Children

No study is available on CA in healthy awake children. Low-dose sevoflurane anesthesia in healthy children showed no differences in autoregulatory capacity based on age [47]. The lower limit of CA in younger children aged between 6 months and 2 years was 60 ± 9 mmHg, which is contrary to the belief that the lower limit of CA is lower in small children [48]. Hence, lowering the blood pressure beyond the lower limit of CA to provide deliberate hypotension in certain therapeutic procedures in anesthetized young children may result in cerebral ischemia.

Clinicians have not demonstrated age- or gender-related differences in CA in healthy children. Based on extrapolation from adult studies, which show that women have higher CBF than men [49], the gender-related differences in pediatric CA is assumed [23, 31]; but this is yet to be studied in children. The latency of CA between children and adults may also be different. Adolescents have a somewhat delayed return of

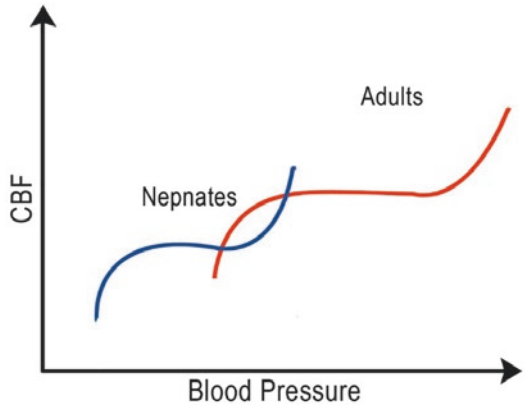


Fig. 2.14 Cerebral autoregulation in neonates and adults

CBF in response to transient hypotension compared with adults [31]. Our understanding of normal CA mechanisms in healthy children is still incomplete. A combination of myogenic, neurogenic, and metabolic processes that regulate CVR to maintain CBF during hypotension may be involved. Both anatomic and physiologic development play a role in the evolution of a fully mature autoregulatory response.

Since there is a gross variability (both intra- and inter-individual variation) in the CA range, it is better to determine the optimal CPP in the presence of pathological disease or brain injury. The middle of the autoregulatory curve, where the variation in arterial diameter in response to CPP changes is maximal, and the autoregulatory function is most robust, is the optimal CPP. Any deviation from this optimal CPP makes CBF pressure-passive in a graded manner to the extent of complete failure of pressure reactivity at the extremes.

The term *impaired autoregulation* is used to denote complete pressure passivity in CBF at all blood pressures or shifts in the blood pressure limits of autoregulation. Raised ICP shifts the lower limit of autoregulation (LLA) to higher blood pressure. Similarly, when the child's blood pressure falls below the LLA despite autoregulatory limits being within range, elevating the blood pressure above the lower limit may restore a stable CBF. It is important to determine an individual child's LLA and the blood pressure range over which autoregulation is optimum (neuroprotective hemodynamic goals), despite the shift in autoregulation curve after brain injury. All pediatric patients have been considered at risk of CBF dysregulation during anesthesia as the autoregulatory limits are unknown. Prematurity, brain trauma, hypoxic brain injuries, intracranial hemorrhage, vascular anomalies, congenital cardiac lesions, and cerebral inflammation are some of the conditions that can disrupt autoregulation.

Sympathetic stimulation shifts the autoregulation curve to the right, which is protective as cerebral vasoconstriction reduces CBF and limits injury to the BBB. However, during periods of hypotension, sympathetic activation-induced vasoconstriction may reduce CBF ischemic levels. The role of parasympathetic innervation is not distinctly delineated, and its denervation is shown to augment CBF when arterial pressure drops below the LLA.

2.5.4 Cerebral Spinal Fluid (CSF) Dynamics

CSF is a plasma ultrafiltrate; it is secreted by the choroid plexus of the lateral, third, and fourth ventricles. Blood flow to the choroidal plexus is almost ten times greater than that of the cerebral cortex. Unlike those found in most other areas of the brain, the capillaries of the choroid plexus have large fenestrations that offer little resistance to the passage of fluid, ions, and small macromolecules. The choroid plexus is supplied by the anterior and posterior choroidal arteries, which are the branches of internal carotid arteries and the posterior cerebral arteries, respectively. The posterior inferior cerebellar arteries supply the choroid plexus of the fourth ventricle. The choroid plexus produces 70 to 90 percent of the CSF; the rest of the CSF is produced from the movement of brain parenchymal ISF across the ependyma into the ventricles and across the pial

membrane into the subarachnoid space. CSF production is less in children compared to adults. In children, the rate and volume of CSF production depend upon the height and weight. The total amount of CSF production is about 25 mL/day in newborns compared to adults; it is about 500 mL/day. The total CSF volume is less in term neonates and infants (about 50 mL) than adults (about 150 ml), with only a small percentage contained within normal-sized ventricles. Its formation and reabsorption occur at the same rate with a turnover of three to four times per day [50], by energy-dependent perfusion-related processes in the choroid plexus and by the ependymal lining of the lateral ventricles. CSF flow results from the pressure gradient that exists between the ventricular system and the venous system. The CSF flows from the lateral ventricle to the third ventricle through the foramina of Monro and then into the fourth ventricle through the aqueduct of Sylvius and then into the central canal of the spinal cord and the subarachnoid spaces through the median foramen of Magendie and lateral foramina of Luschka (Fig. 2.15). The subarachnoid villi finally absorb CSF into the cerebral venous sinuses. When the rate of CSF formation is greater than absorption, it leads to hydrocephalus.

The CSF provides both a protective and supportive cushion for the brain and removes the redundant and deleterious substances from the brain. The specific gravity difference between the brain and CSF provides buoyancy to the brain and reduces its weight to approximately 4% of its mass. It also provides the brain parenchyma with a steady biochemical environment for optimal function. The BBB maintains the differences in composition between plasma and CSF. The solute concentration of CSF is similar between the children and the adults. Studies have shown that the white blood cell count (WBC) values are higher in neonates (less than a week old) compared to infants between 1 and 8 weeks old. Older infants and children have normal WBC values similar to those of adults [51]. The total protein content of CSF is very low compared to the plasma concentration because of the blood-CSF

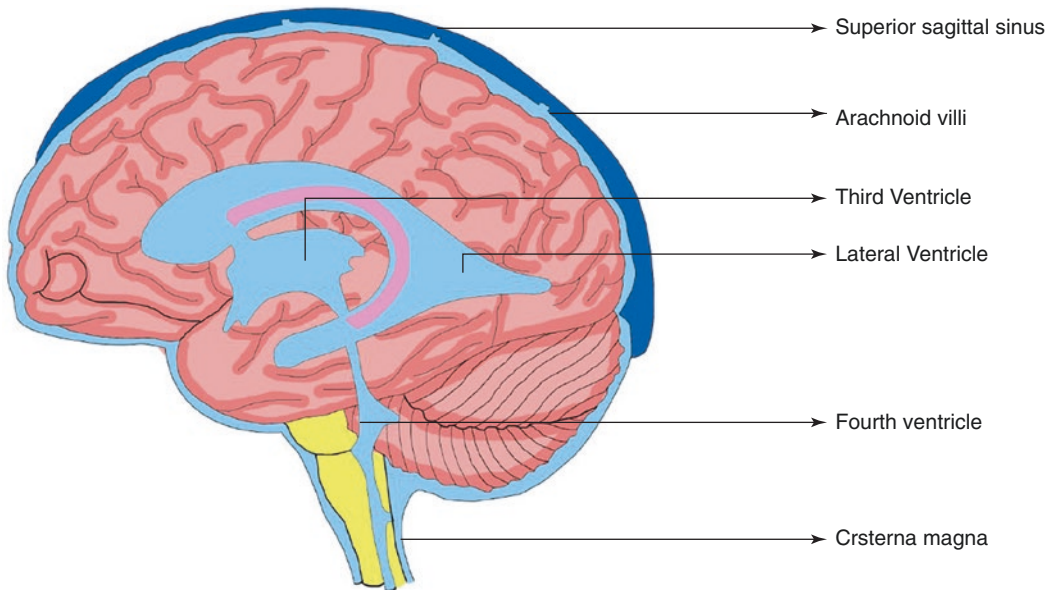


Fig. 2.15 The CSF pathway

barrier. The total protein concentrations are higher in neonates when compared to infants and older children. Protein levels also vary by the anatomic area from which the CSF is sampled. The CSF protein concentration is lower in the ventricle and the cisterna magna compared to the lumbar area; these regional differences could be due to the difference in the permeability of the blood-CSF barrier [52].

2.5.5 Blood-Brain Barrier (BBB)

The BBB is a physical barrier formed by the vascular endothelium with its basement membrane, the astrocyte foot processes, and pericytes (neurovascular unit). Cerebral capillary endothelium differs from other capillary beds by having a tight junction with a pore size of 7–9 Angstroms (A) compared to the capillary beds of other parts of the body, which has a pore size of 65A. BBB helps in maintaining a regulated intracerebral microenvironment for optimal neuronal function [53]. It limits the paracellular diffusion of various large molecular substances. It facilitates the receptor-mediated endocytosis of larger molecules and the transporter-mediated intake of smaller nutrients like glucose, insulin, and iron. It prevents the entry of harmful substances to the CNS [54]. The tight junctions are absent in certain brain areas, such as the choroid plexus, pituitary, and area postrema.

Earlier, the BBB was believed to be "incomplete" during fetal life. Recent researches are suggesting that the BBB is well developed at birth [55]. The formation of tight junctions occurs concurrently as angiogenesis phase, i.e., at the eighth week of postconceptional age. These blood vessels appear to be immature as they lack pericyte coverage or junctional organization. BBB disruption in children may occur in various conditions such as hypertension, stroke, trauma, status epilepticus, hypercarbia, hypoxia, and inflammation (chemical, infective, or autoimmune).

2.5.6 Intracranial Pressure (ICP)

ICP is the pressure inside the skull and, thus, in the brain tissue and the CSF. It is a direct determinant of the CPP and CBF. ICP is the sum pressure of parenchymal pressure, CSF pressure, and cerebral blood volume (CBV). At a steady state, it is calculated using the Davson equation; i.e., $ICP = P_{ss} + (I_f \times R_o)$ where P_{ss} is the sagittal sinus pressure, I_f is the rate of formation of CSF, and R_o is the resistance to CSF outflow. The normal value of sagittal sinus pressure (P_{ss}) is 5 to 8 mmHg; the normal rate of CSF formation (I_f) is 0.3 to 0.4 mL/min, and the normal resistance to CSF outflow (R_o) is 6 to 10 mmHg/mL/min.

In small children as well, the cranium is considered as a closed cavity occupied by the brain (70%), extracellular fluid (10%), CBV (10%), and CSF (10%). Under normal conditions, 0.35 ml/min of CSF is produced in children [56], and ICP is more dependent on CBF and CBV than CSF production. As the brain mass is relatively incompressible, CSF volume changes act as an initial buffer; and when it can no longer be absorbed, the ICP starts to increase. The pediatric patient can compensate for slow increases in ICP by suture and fontanelle expansion, but acute changes lead to an increase in ICP.

The anatomical contribution to the ICP by the supratentorial space accounts for 50%, the infratentorial space for 30%, and the spinal space for 20%. ICP is a dynamic pressure and fluctuates with arterial pulsation, position, respiration, coughing, and straining. Age, body position, and clinical situation affect the normal ICP values (Table 2.9). In a healthy adult, ICP varies from 7 to 15 mmHg in the horizontal position, and it is negative (average, −10 mmHg) in the standing position. Normal values for term neonate, infants, and younger children are 2–6 mmHg and 3–7 mmHg, respectively [57]. In adults, approximately 25 ml of fluid is required to raise baseline ICP by 10 mmHg, while only 10 ml is needed in infants [58]. Hence, children demonstrate rapid

deterioration in neurological function from being seemingly normal to almost coning in 30 min.

2.5.7 Cerebral Compliance (Intracranial Pressure-Volume Relationship)

The intracranial pressure and volume relationship in the brain are not linear (Fig. 2.16). Under physiological situations, due to various compensatory mechanisms, the brain volume varies without causing variations in ICP; but once its maximum capacity is reached, the ICP increases exponentially. When decompensation occurs, even small changes in CBV (e.g., 1 ml) can increase 7–8 mmHg in ICP. A slow-growing tumor remains asymptomatic due to the compensatory mechanisms which do not change the volume/pressure rate (V/P rate), while a rapidly expanding lesion can rapidly increase ICP. Compliance is expressed as changes of ICP to changes of intracranial volume: Compliance = $\Delta V/\Delta P$. Suppose the volume changes and pressure remain unchanged; the compliance increases. In infants with open cranial sutures and a non-ossified fontanelle, the system should be considered "open," and initial compensation occurs with bulging at the anterior fontanelle. In a slowly progressive change in volume, head growth will be affected by splaying the cranial sutures, as seen in hydrocephalus. On the other hand, the compliance decreases significantly if there are a minor increase in the volume and a major increase in the pressure. Adequate compliance indicates intact compensatory mechanisms.

Table 2.9 Factors affecting intracranial pressure (ICP) in children

Parenchymal brain swelling
Interstitial and vasogenic edema
Alterations in cerebral blood volume (CBV)
Obstruction of cerebrospinal fluid (CSF) outflow
Focal cerebral perfusion deficits
Variable levels of cerebral blood flow (CBF)
Cerebrovascular carbon dioxide (CO_2) reactivity
Cerebral vasculitis

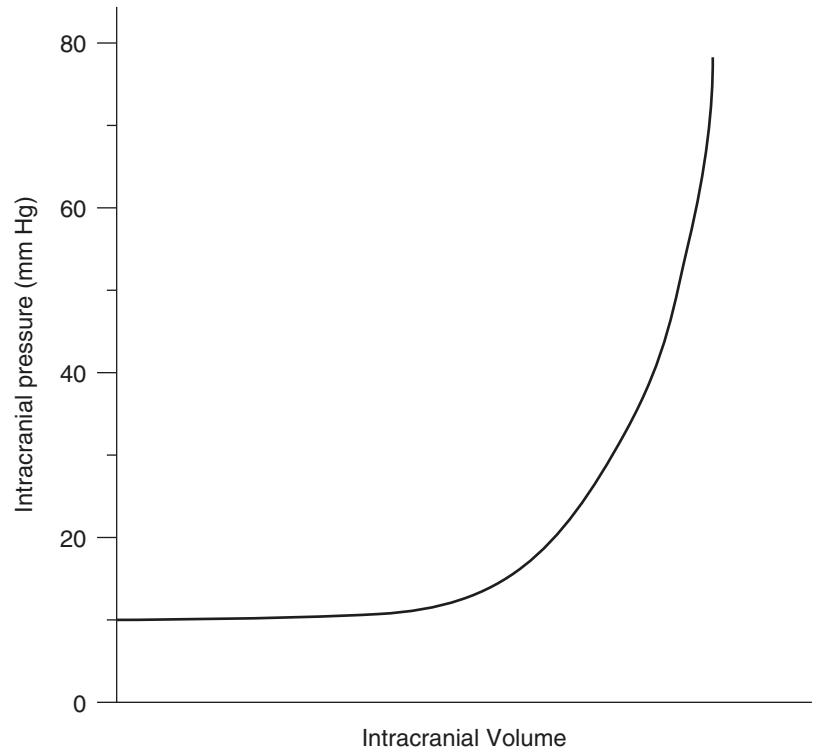


Fig. 2.16 Intracranial compliance curve

Compliance is evaluated along with ICP. The two methods to check cerebral compliance are both invasive and associated with complications (infections, herniation, bleeding): (a) intracranial pressure "reserve" test and (b) pressure-volume index (PVI). The *intracranial pressure "reserve" test* observes the variation in ICP while adding or removing 1 ml of fluid (saline solution or CSF). Normally, the increase of ICP is ≤2 mmHg when 1 ml is injected or when the ICP decreases with the draining of 1 ml of CSF. The *pressure-volume index (PVI)* depicts the volume of intraventricular fluid that has to be injected to produce an ICP increase of 10 mmHg. This volume is about 25 ml in adults and 10 ml in children. A value of less than 10 ml indicates greatly reduced compliance.

2.5.7.1 Intracranial Compliance

The Monro-Kellie doctrine states that the skull is a rigid container comprising the brain, blood, and CSF. An increase in the volume of one of these components is compensated by an equivalent reduction in the other components to prevent the increase in ICP [59]. Once the sutures and fontanelles have closed, the skull becomes a rigid structure that does not permit further expansion resulting in a constant intracranial volume irrespective of its content. Cerebral parenchyma (80%), CSF (10%), and blood (10%) are the three major compartments within the skull under normal conditions. An increase in the volume of any of these three compartments increases the pressure it exerts on the other two compartments. The total intracranial volume is constant as the three compartments of the intracranial vault are incompressible. When one of these compartments increases or another one is added (due to mass effect produced by lesions such as tumor or hematoma), one or more of the other compartments must contract in volume to prevent a rise in the ICP. A slow-growing cerebral lesion causes contortion or rearrangement of the parenchymal compartment to counterbalance the increased ICP. In cases of an abrupt increase in ICP, CBV and CSF act as buffers. CSF, which is the main compensatory system for increased intracranial volume, moves into the peri-medullary subarachnoid space until the displaced brain structures block the CSF flow. Next is the vascular compartment's compensation, which consists of the displacement of blood from the intracranial compartment to the extracranial compartment via jugular drainage. Children behave differently from adults in physiological and pathological states. Yet accurate data about normal neurophysiological variables in pediatric patients are limited, and these are commonly extrapolated from adult and animal data.

2.6 Spinal Cord Anatomy and Physiology

2.6.1 Spinal Cord Vascular Anatomy

The spinal cord receives its blood supply from a single anterior spinal artery and paired posterior spinal arteries, both originating from the VA (Fig. 2.17a, b). Radicular arteries originate from spinal branches of the ascending cervical, deep cervical, intercostal, lumbar, and sacral arteries supplement blood flow to the spinal cord at the segmental levels (Fig. 2.17c). The anterior spinal artery supplies the ventromedial aspect or motor area of the spinal cord. The two posterior spinal arteries supply the dorsolateral aspect or sensory area of the spinal cord. The arteria radicularis magna (great radicular artery of Adamkiewicz), a branch of the aorta, which usually originates from T9 and L5 on the left, reinforces the blood supply via the radicular arteries when the anterior spinal artery supply is deficient and collateral blood flow between the anterior and posterior circulations is absent. This makes the spinal cord vulnerable to ischemia at the upper thoracic and lumbar areas, especially during aortic or spinal surgery or following trauma. The venous drainage of the spinal cord is via two median longitudinal veins, two anterolateral longitudinal veins, and two posterolateral longitudinal veins that drain into the vertebral venous plexus and then into the segmental systemic veins and the portal system.

The principles of cerebral physiology apply to the spinal cord as well. Data in children regarding

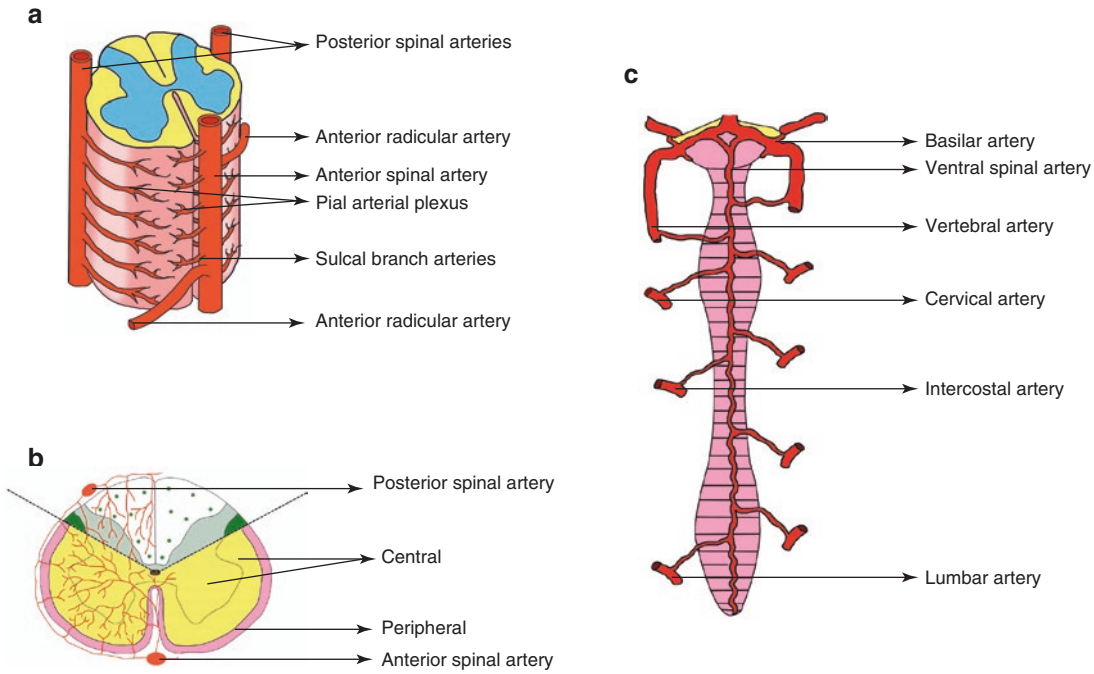


Fig. 2.17 Blood supply (**a**) of spinal cord; axial section (**b**); radicular branches (**c**) supplying the spinal cord

spinal cord physiology are limited. Blood flow to the spinal cord is approximately 40% of CBF, with the cervical and lumbosacral regions receiving twice that of the thoracic region [60]. Spinal cord blood flow (SCBF) autoregulates and responds to chemical factors similar to CBF [60, 61]. SCBF is constant between spinal cord perfusion pressures (SCPP) of 60 to 150 mmHg. Outside this range, flow is pressure dependent [62]. Ischemia occurs if SCPP falls below autoregulatory limits. SCBF responds to arterial oxygen and carbon dioxide tensions in the same manner as CBF. Hypocapnia decreases blood flow, while hypercapnia and hypoxia result in vasodilation and increased blood flow. Maintenance of SCPP during spinal surgery is essential.

The spinal cord is encased within the vertebral column, which is comparable to the bony cranium. As the canal cannot expand, the spinal cord may be compressed due to extrinsic factors (herniated intervertebral disc, tumors, etc.) or intrinsic factors (cord edema). The SCPP then becomes equal to the MAP minus the pressure exerted due to compression at that level. Therefore, with significant spinal cord compression, even mild hypotension may cause spinal cord ischemia/infarction at the compression level. Maintenance of blood pressure at or above baseline levels where the patient demonstrated to function in the awake state is important in spinal cord compression.

2.7 Neurotoxicity in the Immature Human Brain

The immature neurons are more vulnerable to toxic substances like alcohol, antiepileptic drugs, and anesthetic agents. These neurotoxic effects are marked during the intensive phase of brain development, and differentiation is called the "brain growth spurt," which in humans starts during the intrauterine life and lasts up to the second year of life. The immaturity of the BBB during the first few months of life also increases the susceptibility for toxic damage. There are theoretical models and mechanisms for anesthetic-induced neurotoxicity (Fig. 2.18).

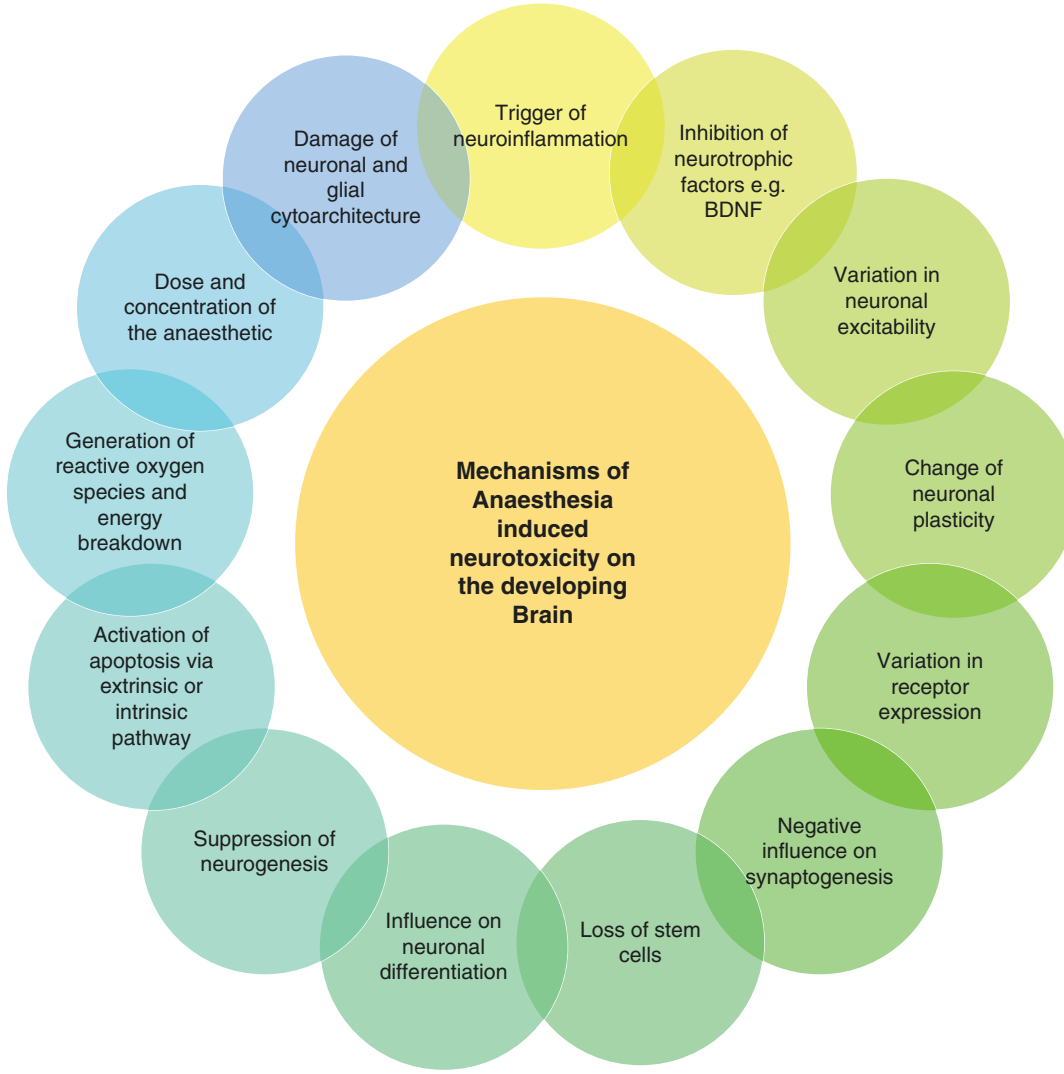


Fig. 2.18 Theoretical models and mechanisms of anesthetic-induced neurotoxicity

Data gathered from animal studies over the last decade prompted an investigation in children to study an association between anesthesia exposure in the first 3–4 years of life (the period corresponding with the brain growth spurt in humans) with learning and behavior abnormalities in adulthood. The multicenter *PANDA (Pediatric Anesthesia Neurodevelopment Assessment) study* [63], the *GAS (General Anesthesia and Spinal) study* [64], and the *MASK (Mayo Anesthesia Safety in Kids) collaborative cohort study* [65] were all randomized controlled prospective trials and did not show a significant risk of neurotoxicity in the exposed children. Further discussion on anesthetic neurotoxicity is beyond this chapter's scope and is discussed in detail in Chap. 35. The disturbance of physiological parameters such as hypotension, hypocapnia, hypoglycemia, or hypothermia should be avoided, as these changes also affect neurodevelopment.

2.8 Epileptogenesis in the Developing Brain

Epileptogenesis is the progressive development of epilepsy in the brain following an initial insult, evolving through acute, subacute, and chronic

phases. The propensity for epileptogenesis in infancy and early childhood is higher than in adulthood due to hyperexcitation and reduced inhibition in the developing brain.

Hypoxia, hypotension-induced ischemic insults, and CNS infection are some factors that make the developing brain more vulnerable to seizures. Structural brain abnormalities and genetic factors also contribute toward epileptogenesis in infancy. Several intrinsic factors like type, number, and distribution of ion channels, biochemical modification of receptors, activation of second messenger systems, etc. increase the susceptibility of the immature brain to produce seizures in contrast to the mature brain [66].

Children with epilepsy have more frequent cognitive impairment than the general population with IQ scores lower than children without epilepsy. Learning difficulties in certain specific areas with normal IQ can also be observed [67, 68] with a higher risk for academic underperformance. Numerous studies have demonstrated that recurrent seizures during the stage of brain development result in long-term changes [69]. Anticonvulsant medications currently available can only control seizures but fail to modify the epileptogenic process. Attacking the various phases of epileptogenesis with suitable treatment might help develop disease-modifying antiepileptogenic treatment regimens and prevent occurrence of cognitive deficits.

2.9 Neuroprotection

Neuroprotection refers to the actions taken to preserve the neuronal integrity and function against any insult to the brain or spinal cord. In pediatric patients, neuroprotection may be warranted in the following conditions in TBI, prolonged hypotension, meningitis, encephalitis, post-cardiac arrest, cardiac surgery, prolonged seizures, metabolic derangements, encephalopathies, and any event that leads to a sudden rise in ICP.

The causes for neuronal injury in pediatric patients include the immaturity of the CNS, abnormal development, chromosomal and genetic influences, and predominantly white matter injury. Several early surrogates/markers for an acute neurological injury help in the early application of neuroprotective strategies [70] and thereby produce a favorable neurodevelopmental outcome. These include monitoring modalities and biomarkers (Table 2.10).

Table 2.10 Markers/surrogates for neurological injury

Monitoring modalities	Near-infrared spectroscopy (NIRS)
	Electroencephalogram (EEG)
	Magnetic resonance imaging (MRI)
Biomarkers (older)	Creatine kinase-brain band (CK-BB)
	Neuron-specific enolase (NSE)
	S100B
Inflammatory markers	Interleukin (IL)-1B, 6, 8
	Tumor necrosis factor (TNF)
Newer CNS-specific biomarkers	Glial fibrillary acidic protein (GFAP)
	Ubiquitin C terminal hydrolase L1 (UCH-L1)
	Phosphorylated axonal neurofilament heavy chain (pNF-H)

Neuroprotective strategies and treatments (Table 2.11) can be classified as preventive, reactive, or reparative. Preventive strategies are therapies instituted before an anticipated neurological injury or insult. Reactive strategies are therapies started in response to a recent neurological insult or injury. Reparative strategies are treatments given after a known neurological injury. Neuroprotective strategies should be commenced in all children at risk of developing neurological insult/injury to avoid further secondary injury and reduce the risk of developing irreversible damage and thereby have a favorable neurological outcome. Some of the neuroprotective measures are discussed here, briefly.

2.9.1 General Measures

These aim to prevent secondary brain injury by preventing cerebral hypoxia and ischemia. They include maintaining the airway and adequate oxygenation to prevent hypoxia and adequate ventilation to maintain normocarbia. MAP

Table 2.11 Neuroprotection strategies and treatment

General measures
• Airway control and ventilation • Maintenance of cerebral perfusion pressure (CPP) • Control of intracranial pressure (ICP) • Seizure prevention • Glucose and electrolytes • Fluids • Nutrition
Anesthetic agents
Therapeutic hypothermia [71–74]
Hypoxic-ischemic preconditioning [75, 76]
Remote ischemic preconditioning [77]
Erythropoietin [78, 79]
Progesterone [80, 81]
Neurotrophic factors [82, 83]
Stem cell treatment [84, 85]

should be meticulously maintained to achieve adequate CPP. ICP should be controlled by careful positioning of head and neck, hyperosmolar therapy, sedation and analgesia, and surgical decompression when required. Normoglycemia should be maintained and dyselectrolytemia avoided. Seizures should be prevented and controlled with anticonvulsant medications. Judicious fluid therapy should be employed to protect the brain, and nutrition should be established as soon as possible to enable wound healing by tissue repair and optimal functioning of all organs. Other conditions like hyperthermia, anemia, and coagulopathy must be recognized and corrected.

2.9.2 Anesthetic Agents

A variety of anesthetic agents, including volatile anesthetics, intravenous anesthetics, and adjuvant drugs, have neuroprotective actions. The detailed discussion of this is beyond this chapter's scope and discussed in detail in Chap. 3.

2.9.3 Temperature Control: Therapeutic Hypothermia

Hyperthermia is detrimental to the injured brain and worsens secondary brain injury by increasing CMR, promoting inflammation, and lowering the seizure threshold. Hence, the temperature must be aggressively controlled to maintain normothermia. Hypothermia produces cerebral protection by many proposed mechanisms such as decreased global cerebral metabolism, maintenance of membrane ion channel integrity and preservation of ion homeostasis, decreased release of excitatory neurotransmitters and decreased calcium flux, prevention of inflammation and lipid peroxidation, and the maintenance of BBB. Therapeutic hypothermia holds promise for cerebral protection after neonatal hypoxic-ischemic encephalopathy [71] and post-cardiac arrest [72] but not in TBI in children [73, 74].

2.9.4 Hypoxic-Ischemic Preconditioning

A mild dose of ischemia and/or hypoxia of a short duration ahead of a major hypoxic-ischemic insult is neuroprotective by limiting the expanse of brain injury [75, 76]. This was clinically observed that stroke patients who experienced transient ischemic attacks before a major stroke had better long-term outcomes. Extremely complex transmembrane and intracellular signaling mechanisms result in neuroprotection from hypoxic-ischemic preconditioning that prevents excitotoxic and apoptotic cell death.

2.9.5 Remote Ischemic Preconditioning

The hypothesis that ischemia in a remote organ can bring about protective effects in other organs like the heart-brain is known as remote ischemic preconditioning [77]. The exact mechanisms of signal transduction or humoral changes involved are yet to be elucidated. Nevertheless, due to its simple and noninvasive nature, this therapy is easy to adopt clinically and has significant neuroprotective potential.

2.9.6 Erythropoietin (EPO)

Among the multiple biological effects of erythropoietin (EPO), its neuroprotective and cardioprotective effects are of immense value to us. EPO

exerts its neuroprotective effects by many cellular mechanisms, including anti-apoptotic, anti-inflammatory mechanisms, and reduced excitotoxicity. Clinical studies of EPO have demonstrated its therapeutic neuroprotective role in a variety of settings of CNS insults [78, 79].

2.9.7 Progesterone

Progesterone is a pleiotropic agent which favorably influences secondary injury cascades that are triggered following CNS injury. Several proposed mechanisms of its neuroprotective effects, such as its maintenance of BBB integrity, decrease inflammation, limit apoptosis, increase remyelination, decrease lipid peroxidation and free radical generation, potentiate GABA receptors, and decrease excitotoxicity.

In a single-center study performed in extremely preterm infants, the improved neurodevelopmental outcome was demonstrated using combined exogenous estrogen and progesterone administration [80, 81]. This opens up prospects to further investigate this agent to reduce long-term disability and produce a favorable outcome in head-injured children and other forms of pediatric acute brain injury.

2.9.8 Neurotrophic Factors

The essential growth factors for normal CNS development, and other factors associated with hypoxic-ischemic injury and other brain insults, have been studied for neuroprotection. ***Brain-derived neurotrophic factor (BDNF)*** is the most extensively distributed neurotrophic protein factor, and animal studies hypothesize it to be a promising neuroprotective agent in humans [82, 83].

2.9.9 Stem Cell Treatment

Stem cells are undifferentiated pluripotent cells with extensive proliferative capacity and self-renewal [84]. The therapeutic potential for stem cells in CNS injury makes this an important research area for the future. Human umbilical cord blood cells have stem cells and are being used for hematological malignancies and other neonatal diseases for many years [85]. Its use in several animal models of stroke and TBI has shown improvement in functional recovery and makes it a candidate for future trials.

The neuroprotection field for pediatric patients is still in its infancy and warrants carefully planned studies in the future to support them. Novel anti-inflammatory and anti-apoptotic therapies are promising. A combination of different therapies using multiple agents or modalities may be successful.

2.10 Cerebral Physiology in Pathological States

CA is impaired in pathological states such as TBI, SAH, and IVH, which vary from mild impairment to complete absence. The integrity of the BBB is also impaired in the pathological state. Many vasoactive neurotransmitters released during brain injury produces marked changes in CBF and ICP. Since there is an impairment in CA and BBB integrity, optimal CPP had to be maintained to avoid ischemia (hypotension) or cerebral edema and hemorrhage (hypertension). The optimal CPP in an injured brain shows regional and temporal variation. CBF is reduced during the first 24 h after TBI; hence, normocapnia should be maintained during this period. Hyperventilation-induced hypocapnia will further decrease CBF and lead to cerebral ischemia. Hyperoxia can worsen neurological injury by releasing oxygen free radicals. Maintenance of normoxia is associated with the best outcome following brain injury. Hence, the oxygen delivered should maintain arterial oxygen saturation > 96%, which is especially important in children who had a return of spontaneous circulation after cardiac arrest. The brain can recoup for short periods of high metabolic demands, but prolonged episodes (like seizures) of increased CMR result in irreversible neurological damage and warrant immediate attention.

2.11 Conclusion

Sound knowledge of the unique neurodevelopmental events and neurophysiological principles applicable to pediatric patients is paramount for the safe and effective perioperative care of infants and children at risk for neurological injury. Neuroanesthesia, as a specialty, continuously adds to the increasing volume of knowledge to reduce the maleficent effects of illness on the developing human brain. Further polishing of anesthetic practices intended to protect normal neurodevelopmental processes is expected. The combination of neurodevelopment principles, the intracranial compartment physics, and neurovascular physiology can improve our decision-making for enhanced patient outcomes.

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Effect of Sedatives and Anesthetics on Cerebral Physiology in Children

3

K. R. Shwethashri and M. Radhakrishnan

Key Points

- General anesthetics do not interfere with the cerebral autoregulation and cerebrovascular reactivity in clinically used concentrations.
- Requirement of anesthetic agents (MAC) is dependent on the age of the child.
- Both volatile and intravenous anesthetic agents are cerebral metabolic depressants except for ketamine and nitrous oxide.
- Volatile anesthetics tend to increase cerebral blood flow (CBF) due to vasodilation, while intravenous anesthetics decrease CBF, which is coupled to metabolism.
- Intravenous anesthetic agents are preferred in children with raised intracranial pressure and when intraoperative neurophysiologic monitoring is planned.
- Long-term neurocognitive effects of anesthetics are debatable.

3.1 Introduction

Children should not be considered as miniature adults as their anatomical and physiological parameters are unique. Thorough knowledge of the developmental physiology of the brain is required for better understanding of the effect of various anesthetic agents on the developing brain in normal and in different pathological conditions. This sound knowledge of anesthetic neuropharmacology will help in better management of pediatric neurosurgical patients. Most of the data are derived from adult human or animal studies, and data from the pediatric population is limited. This chapter aims to provide comprehensive details in understanding the cerebral physiological effects of various anesthetic agents on the child's brain.

Central nervous system (CNS) development is not complete at birth. CNS maturity is attained around the age of 2 years. Cerebral blood flow (CBF) is around 40 ml/100gm/min at birth [1]. It increases and reaches a peak around 2–4 ears of age (100–120 ml/100gm/min) and starts to decrease in adolescence phase to reach adult values (50 ml/100gm/min) [2]. At around 1–3 years, global CBF is approximately 40–50% of cardiac output and makes this age group vulnerable to cerebral ischemia following systemic hypotension. Children have a higher cerebral metabolic rate of oxygenation ($CMRO_2$) with 5.2 ml/100gm/min versus the adults 3.5 ml/100gm/min. Cerebral autoregulation is present in preterm and term neonates and operates in a narrow range in children less than 5 years [3–5]. Cerebrovascular reactivity to carbon dioxide (CO_2) is impaired in premature neonates but better preserved in infancy. In neonates, cerebrospinal fluid (CSF)

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volume is around 50 mL. The rate of production remains at around 0.35 ml/min across all ages.

Cranial sutures and fontanel remain open at birth and final closure occurs at around 10 years of age. Open fontanel and sutures compensate for slow expansion of any of the intracranial components (cerebral blood volume, CSF volume, and parenchyma) but not during an acute increase. This can result in intracranial pressure (ICP) increase like that seen in adults. Typical ICP values range from 1.5 to 6 mmHg in term infants, 3 to 7 mmHg in younger children, and 10 to 15 mmHg in older children.

3.2 Effect of Specific Anesthetic Agents

3.2.1 Inhaled Anesthetics

Inhalational agents are flow-metabolism uncouplers causing increased CBF with decreased $CMRO_2$. However, these changes are dose-related. Children have increased sensitivity to cerebral vasodilatory effect of inhaled anesthetic agents than adults [6]. Inhaled anesthetics are the most commonly used induction agents in children. They act as gamma-aminobutyric acid-A ($GABA_A$) agonists and N-methyl D-aspartate (NMDA) antagonists. In healthy child's brain, volatile anesthetic agents increase CBF, decrease $CMRO_2$, and retain CO_2 vasoreactivity till 1 minimum alveolar concentration (MAC) [6, 7]. The MAC changes with age. The MAC value is least in the newborn period, then gradually increases, and peaks at infancy, and it subsequently decreases with age and reaches adult values by 10–12 years. At equilibrium, the blood gas coefficients of the inhaled anesthetics are least in children in comparison to the adults. Also, infants have a greater alveolar ventilation and reduced functional residual capacity that result in rapid wash-in of the anesthetic vapors but requiring higher MAC values. The MAC values of volatile anesthetic agents with respect to age are mentioned in Table 3.1 [8–14]. The MAC values required to achieve EEG burst suppression with various agents as suggested by various literature [15, 16] have been tabulated (Table 3.2).

3.2.1.1 Nitrous Oxide

Nitrous oxide (N_2O) acts by antagonizing NMDA receptors. It increases the neuronal mitochondrial activity and increases $CMRO_2$, CBF, and ICP

Table 3.1 Minimum alveolar concentration (MAC) based on the age of the child [8–14]

Agent	Age group	Minimum alveolar concentration (%)
Halothane	Neonates	0.87 ± 0.03
	1–6 months	1.20 ± 0.06
	4–18 years	0.9 ± 0.02
	Adults	0.77
Sevoflurane	Neonates	3.3 ± 0.2
	1–6 months	3.2 ± 0.1
	6–12 months	2.5
	1–12 years	2.5
	Adults	1.77
Isoflurane	Neonates	1.6
	1–6 months	1.87
	6–12 months	1.8
	1–3 years	1.6
	3–5 years	1.6
	Adults	1.15
Desflurane	Neonates	9.16 ± 0.02
	1–6 months	9.42 ± 0.06
	6–12 months	9.92 ± 0.44
	1–3 years	8.72 ± 0.59
	3–5 years	8.62 ± 0.45
	5–12 years	7.98 ± 0.43
	Adults	6

Table 3.2 Minimum alveolar concentration (MAC; adults vs. children) to achieve EEG burst suppression with various agents [15, 16]

Agent	MAC value at EEG burst suppression (adults)	MAC value at EEG burst suppression (children)
Isoflurane	1.2 MAC	1.5 MAC
Sevoflurane	>1.4 MAC	1.5 MAC
Desflurane	1.3 MAC	>1.5 MAC

MAC minimum alveolar concentration, *EEG* electroencephalography

[17, 18]. CO_2 vasoreactivity is preserved when N_2O is combined with other inhalational agents up to 1 MAC. With hypocapnia, this reactivity is impaired in children [7]. Induced hyperventilation for intraoperative brain bulge might not be beneficial under N_2O-based anesthesia. CO_2 vasoreactivity and pressure autoregulation are better preserved when N_2O is combined with propofol infusion than with inhalational agents [17]. Incidence of postoperative nausea and vomiting is high with N_2O as it increases the acetylcholine (Ach) secretion in area postrema, a circumventricular organ in the medulla oblongata. It expands the volume of gas in closed spaces.

The role of N_2O in neurotoxicity is controversial. Most studies were conducted in animals and in cell line cultures. Being an NMDA receptor antagonist, it provides protection against excitotoxic cell damage [18]. NMDA antagonists and $GABA_A$ agonists are known to induce apoptotic neurodegeneration in the brain during synaptogenesis [19]. Prolonged exposure to N_2O causes neuronal death, and short-term exposure is shown to cause reversible neurotoxic vacuole reactions [20].

3.2.1.2 Halothane

Halothane is the most potent vasodilator among all inhalational agents. Halothane increases cerebral blood volume (CBV) by 20.5%, whereas sevoflurane increases it by 9.0% [21]. At equivalent MAC, halothane causes lesser $CMRO_2$ suppression than isoflurane and sevoflurane. Hence, a tremendous increase in CBF to achieve the desired $CMRO_2$ suppression is seen with halothane [22]. Transcranial Doppler studies with halothane have shown maximal cerebral vasodilation at a much lower concentration in children (0.5–1 MAC) when compared to adults (up to 1.5 MAC) [23]. On decreasing the MAC, cerebral blood flow velocity (CBFV) remains elevated for up to 35–40 min. The mechanism behind this cerebrovascular hysteresis is uncertain [24]. Though a suitable agent for induction, such wide fluctuation in the CBFV makes it unsuitable for clinical use in the children with raised ICP. But CO_2 vasoreactivity remains intact up to 1 MAC, similar to isoflurane [6].

3.2.1.3 Isoflurane

Isoflurane increases global CBF and decreases $CMRO_2$ in a dose-dependent manner. At MAC values of 0.5 to 1.0, isoflurane maintains constant cerebral blood flow velocities [25]. CO_2 vasoreactivity is maintained up to 1 MAC in healthy children [6]. Unlike sevoflurane, persistent frontal predominant EEG activity is not seen with isoflurane in children [26]. When compared to sevoflurane and desflurane, rapid emergence from isoflurane anesthesia for quick neurologic assessment is less likely due to its physicochemical properties [27]. By using balanced anesthesia technique with opioid infusions like remifentanil, the requirement of isoflurane can be reduced in children [28].

3.2.1.4 Sevoflurane

The physical properties (low blood-gas and tissue-blood partition coefficients) of sevoflurane make it the most frequently used inhalational agent in children, both for induction and maintenance of anesthesia [28]. Sevoflurane causes dose-dependent cerebral vasodilation resulting in increased regional and global CBF and also ICP [29]. The ICP changes can be controlled with simultaneous hyperventilation [30]. Addition of N_2O to sevoflurane further increases the ICP similar to that of isoflurane [31]. Studies measuring CBFV, a surrogate measure of CBF, in children have shown a significant reduction in CBF with a decrease in MAP in children less than 6 months of age as compared to older children [32]. In older children, CBFV remained constant despite a 40% reduction in baseline MAP. In healthy children, CO_2 reactivity is preserved up to 1 MAC

[33]. Dynamic autoregulation is well preserved up to 1.5 MAC in young children [34]. During revascularization procedures, inhalational agents like sevoflurane induce global cerebral hyperemia associated with intracerebral steal phenomenon. As a result, regional cerebral blood flow and regional oxygen saturation decrease with a potential for focal cerebral ischemia [35, 36].

Sevoflurane tends to produce epileptiform discharges (simple/complex/polyrhythmic spikes) on EEG in the vulnerable pediatric population, including children on antiepileptic drugs, and with raised intracranial pressure [37]. Frank seizure-like activity is seen at doses causing burst suppression [38]. Premedication with benzodiazepines or co-induction with intravenous anesthetics reduces EEG discharges [39]. Higher alveolar concentrations of sevoflurane have been shown to decrease ophthalmic artery blood flow and retrobulbar circulation predisposing them to retinal ischemia [40].

3.2.1.5 Desflurane

Desflurane has a rapid onset and offset of action because of its low blood gas solubility. This makes it an ideal agent for induction and maintenance of anesthesia. However, because of its pungent property, desflurane is not preferred for anesthetic induction. The incidence of arterial desaturation, breath-holding, laryngospasm, and airway hypersecretions is significantly higher with desflurane [41, 42]. It causes a dose-dependent increase in CBFV and CBF in children [43]. It reduces $CMRO_2$, increases ICP, and retains CO_2 vasoreactivity till 1 MAC in the healthy brain [44]. Addition of nitrous oxide does not further increase the CBFV as desflurane by itself is a potent vasodilator [45]. In children with raised ICP, at equivalent MAC doses (0.5–1 MAC), ICP and CPP changes were comparable between the three agents, namely, isoflurane, sevoflurane, and desflurane [27]. Desflurane does not produce epileptiform discharges on EEG.

3.2.1.6 Xenon

Xenon is a newer inhalational agent introduced into the anesthetic practice. Being an inert gas, it has analgesic property and results in faster emergence with minimal hemodynamic fluctuations, postemergence agitation and vomiting, and organ protection. However, not many studies are available on its use in children because of its cost and limited availability. Xenon has been administered to children for dental procedures and for cardiac catheterization procedures [46]. The latter study showed better preservation of regional cerebral oxygen saturation with xenon when compared to sevoflurane. To achieve anesthesia, a concentration of around 70% xenon is required, which limits the inspired oxygen concentration. Xenon is very expensive limiting its routine use in clinical practice. More studies are required to justify its use in the pediatric population, especially for neurosurgical procedures.

3.2.2 Intravenous Anesthetics

Intravenous agents are cerebral blood flow-cerebral metabolism couplers that reduce both CBF and $CMRO_2$. Intravenous anesthetics directly suppress neuronal metabolism and decrease CBF (except ketamine). They are preferred during procedural sedation and for neurosurgical procedures in children. The doses of commonly used intravenous anesthetic agents are enumerated in Table 3.3 [47, 48].

3.2.2.1 Propofol

It is the most commonly used nonbarbiturate intravenous induction agent. It has direct vasoconstrictive property on cerebral vasculature and reduces CBFV, $CMRO_2$, and ICP [49, 50]. Cerebrovascular reactivity to carbon dioxide is preserved in healthy children [51, 52]. Autoregulation is maintained with propofol and remifentanil anesthesia in children [53]. Time to recovery from propofol sedation is lesser than that of barbiturate sedation in children with traumatic brain injury (TBI) because of its shorter elimination half-life [54]. Propofol is used as a continuous infusion to maintain anesthesia in children requiring intraoperative neurophysiologic monitoring. Propofol has been shown to maintain better ICP and frontal cerebral blood flow during revascularization surgery for moyamoya disease [55].

Table 3.3 Doses of commonly used intravenous anesthetic agents [47, 48]

Agent(s)	Age group	Bolus dose	Infusion dose
Thiopentone (when opioids are used as adjuncts for induction)	Neonates (<10 days) up to 12 months Children	2.5–3 mg/kg 6–7 mg/kg 5 mg/kg	Not more than 4–5 mg/kg/h
Propofol	Neonates 1 month–3 years 3–8 years >8 years	2 mg/kg 2–3 mg/kg 3 mg/kg 2–3 mg/kg	EC50 3.7–3.81 μg/ml[a]
Etomidate	Neonates Children Children (PR)	0.2–0.3 mg/kg 0.3–0.5 mg/kg 6–8 mg/kg (PR)	—
Ketamine	Children (IV) Children (IM)	1–2 mg/kg (IV) 5–8 mg/kg (IM)	2–4 mg/kg/h

[a]*EC50* effect-site concentration of propofol at half-maximal effect, *PR* per rectum, *IV* intravenous, *IM* intramuscular

3.2.2.2 Thiopentone

Thiopentone causes a reduction in CBFV due to direct vasoconstriction of cerebral blood vessels [56]. It also decreases CBV, $CMRO_2$, and ICP in a dose-dependent manner. It maintains CO_2 vasoreactivity and autoregulation. Dose-dependent reduction in $CMRO_2$ occurs until an isoelectric EEG is achieved.

Effective dose (ED_{50}) required for satisfactory induction for anesthesia in neonates is 60% of that of infants due to decreased synaptogenesis at birth [57]. It is metabolized slowly and, hence, gets accumulated in the body. Thiopentone clearance from the body is 2–5 days in children who are on continuous infusion [58].

Thiopentone causes cardiovascular depression in children secondary to direct depression of vasomotor center and myocardium, making it unsuitable for its use in children with unstable cardiac conditions [59, 60].

3.2.2.3 Etomidate

Etomidate, a nonbarbiturate imidazole carboxylated derivative, induces anesthesia by its action on GABAergic system and chloride conductance across neuronal membrane. Etomidate decreases regional cerebral blood flow and $CMRO_2$ [61]. In children, it has stable cardiac effects and maintains blood pressure, ICP, and CPP better than thiopentone and propofol [62–64]. This property makes it suitable for use in children with altered hemodynamics secondary to head injury [65]. Head-injured children, especially less than 4 years, have impaired cerebral autoregulation irrespective of the severity of injury [66]. Minimal changes in the blood pressure can thus have significant effects on the cerebral hemodynamics. It induces EEG activation and increases the signal to noise ratio during neurophysiologic monitoring [67]. Following intravenous administration, it causes pain, involuntary movements, and adrenocortical suppression cautioning its use in the pediatric population.

3.2.2.4 Ketamine

Ketamine is a phencyclidine group of NMDA receptor antagonist. It is a direct cerebral vasodilator. It increases CBF, CBV, $CMRO_2$, and ICP and retains CO_2 vasoreactivity. Ketamine increases cerebral glucose utilization rate at higher doses. Positron emission tomography (PET) studies have shown that sub-anesthetic doses of ketamine increase global CBF without any changes in $CMRO_2$ [68]. Ketamine has anti-inflammatory properties. Changing the route of administration of ketamine or adding premedication does not reduce the ventricular fluid pressure in hydrocephalic children [69]. It also increases

lumbar CSF opening pressure and should be used with caution in children with raised ICP [70]. Though it increases ICP, a single bolus dose (1–1.5 mg/kg), by maintaining stable hemodynamics, prevents ICP increase during stressful interventions in children with refractory intracranial hypertension [71]. Hence, ketamine is a viable alternative agent for induction in hypotensive head-injured children. Ketofol (low dose of ketamine and propofol), the most comfortable regimen in procedural sedation, is shown to increase total cerebral blood volume in opposition to propofol infusions alone that decrease CBV [72]. Ketamine increases the alpha motor neuron excitability and improves the amplitude of evoked potentials. It can be used as an adjunct during intraoperative neurophysiologic monitoring [73]. A single bolus dose of ketamine on EEG produces high-frequency gamma bursts with high amplitude delta waves which are interspersed at regular intervals [74].

3.2.3 Other Agents

3.2.3.1 Opioids

Effect of opioids on cerebral hemodynamics is controversial. In general, opioids cause a mild reduction in CBF, $CMRO_2$, and ICP in the normocapnic range. Studies in sick newborn children (without cerebral pathology), receiving fentanyl sedation, have shown stable mean CBFV and pulsatility index (PI). Fentanyl boluses maintain regional cerebral oxygenation, cerebral tissue oxygen extraction, and cardiac output in preterm infants with stable hemodynamics [75]. On the other hand, when fentanyl bolus induces hypotension, it is associated with autoregulatory compensatory cerebral vasodilation to maintain CBF, thereby transiently increasing the ICP. Fentanyl blunts the stress response and CBFV changes to intubation by inhibiting the catecholamine release [76]. It was found to be more effective than remifentanil in reducing the CBFV changes to intubation [77]. An equipotent dose of infusions of fentanyl and remifentanil with nitrous oxide retains CO_2 reactivity in a healthy brain [78, 79]. Opioids cause neuroexcitation, manifested as nystagmus, rigidity, and tonic-clonic seizure-like activity in healthy neonates [80]. Such reactions are not observed in the regular therapeutic doses but can be seen in moderately higher doses of fentanyl (>10 μg/kg). Hence, opioid dosing is crucial in the susceptible pediatric population [81].

3.2.3.2 Benzodiazepines

Benzodiazepines (BZD) are GABA agonists that cause anxiolysis in children. Commonly used BZD include diazepam, midazolam, and clonazepam. In children, midazolam is the most commonly used benzodiazepine for premedication to achieve anxiolysis and amnesia. It causes dose-dependent reduction in CBF and $CMRO_2$ that follows flow-metabolism coupling [82].

3.2.3.3 Muscle Relaxants

Non-depolarizing muscle relaxants, like atracurium, maintain stable cerebral hemodynamics at conventional doses. But at higher doses, it can cause histamine release. This results in hypotension and a compensatory increase in CBF. Its metabolite, laudanosine, a CNS stimulant, crosses blood-brain barrier and precipitates seizures [83, 84]. Although described in animal studies, such incidences are not reported in children [85]. Cisatracurium is better than atracurium as it causes less histamine release and laudanosine generation. Vecuronium maintains stable cerebral and cardiac hemodynamics.

Children with raised ICP are at risk for aspiration, and hence, rapid sequence induction should be considered in them. Succinylcholine or rocuronium is the preferred agent. Succinylcholine causes EEG arousal, increase in muscle spindle activity, and fasciculations that can transiently increase ICP. Prior administration of a higher dose of propofol or precurarizing dose of rocuronium can reduce these fasciculations [86, 87]. Studies in preterm neonates using succinylcholine for nasotracheal intubation have not shown any increase in ICP [88]. Pretreatment with atropine might be required if the baseline heart rate is less.

3.2.3.4 Dexmedetomidine

Dexmedetomidine is a highly selective alpha-2 agonist. It causes anxiolysis, analgesia, and sedation without respiratory depression. It decreases CBFV and $CMRO_2$ like that seen in adults and has no direct effect on ICP and maintains CO_2 vasoreactivity. It induces sleep similar to that of Stage II non-rapid eye movement (NREM) sleep and does not hinder electroencephalography (EEG) interpretation, making it suitable for sedating children for EEG recording [89, 90]. Dexmedetomidine infusion interfere with electrocorticography, functional mapping, and evoked potential monitoring and, hence, is used as an adjunct for neurophysiologic monitoring and for awake craniotomy [91, 92]. Functional magnetic resonance imaging (fMRI) studies have shown better neuronal connectivity in higher-order networks [93]. This reduces agitation at emergence, and hence, dexmedetomidine is used most often for procedural and ICU sedation [94–96]. Prolonged infusion results in delayed recovery from sedation in contrast to propofol infusion.

3.3 Anesthetic Neuroprotection in Children

Both the inhaled and intravenous anesthetics are shown to provide neuroprotection in in vitro and in animal models. Shorter duration of exposure and single exposure are found to provide neuroprotection. On the other hand, prolonged and repetitive exposure is found to cause neuroapoptosis in the neonatal animal models. There is no data supporting a single drug as the best agent in causing neuroprotection. Anesthetics have been found to be neuroprotective in focal cerebral ischemia (e.g., moyamoya disease) but not in global ischemia (e.g., cardiac arrest). Every agent has its own advantages and disadvantages.

Isoflurane activates Akt pathway and adenosine triphosphate (ATP)-sensitive potassium channels, regulates intracellular calcium responses, and reduces endothelial matrix metalloproteinase (MMP)-2 and MMP-9 activation [97, 98]. These effects have been shown to have a preconditioning effect in the ischemic brain in in vitro and in animal experiments. However, the literature on documenting these effects in the pediatric population is scarce. Exposure to isoflurane in early childhood can disturb the mTOR (mammalian target of rapamycin) pathway in the hippocampal dentate gyrus. This pathway is involved in the cognitive development of the brain [99].

A single exposure to sevoflurane achieved neuroprotection in animal models by activating AKT/GSK3β signalling pathway. However, repeated and prolonged sevoflurane exposure induced neurotoxicity by inhibiting the same AKT/GSK3β signalling pathway [100]. This phenomenon has been described with all inhalational anesthetic agents antagonizing NMDA receptors in the hippocampus. NMDA antagonism at hippocampus interferes with the spatial learning and memory and, thus, induces deficits in learning and cognitive performances when exposed at a very young age [101, 102]. In addition, sevoflurane increases pro-apoptotic proteins Bax and caspase-3 and reduces anti-apoptotic protein Bcl-2 in in vitro models, together explaining its neurotoxic effects on the brain [103].

Desflurane provides neuroprotection in adults by inhibiting ischemic tissue acidosis and increasing the brain tissue oxygenations levels.

Thiopentone's neuroprotective properties during cerebral ischemia appear superior to propofol in in vitro studies [104]. It reduces glutamate release and prolongs the onset of anoxic depolarization in the ischemic brain and inhibits cortical intracellular calcium increase [105, 106].

The neuroprotective effects of etomidate remain controversial. In experimental models, it is shown to induce focal ischemia by inhibiting the endothelial nitric oxide synthase activity [107]. This increases cerebral vascular resistance (CVR), leading to CBF reduction far below than those that cause a decrease in $CMRO_2$ [108].

In animal studies, ketamine caused a longer duration of NMDA receptor blockade in immature neurons predisposing them to neurotoxicity [109]. When used in infants (<6 weeks) for cardiac surgeries, it was found to be safe without causing any neurodevelopmental delay at

the subsequent ages [110]. Clinical data on the neurotoxic effects of ketamine are limited in children as ketamine is never used as a sole anesthetic agent.

Experimental studies have shown that dexmedetomidine possesses some neuroprotective properties. In vivo and in vitro studies have shown increased expression of brain-derived neurotrophic factor (BDNF), and inhibition of procaspase 3 activation, both of which lead to neuro-apoptosis [111]. It also upregulates tyrosine kinase activity required for cellular plasticity [112].

3.4 Conclusion

In pediatric neurosurgical procedures, anesthetic agents should be chosen to achieve stable hemodynamics, which would have less effect on the cerebral blood volume. In children with poor intracranial compliance, intravenous anesthetics would be preferable, which has the additional benefit of facilitating neurophysiologic monitoring. Inhalational anesthetics facilitate rapid recovery. There is no robust clinical evidence to prove the neurotoxic potential of anesthetic agents.

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4 Preoperative Evaluation and Preparation of Children Undergoing Neurosurgery

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Key Points

- Infants and children undergoing neurosurgical procedures present unique challenges for the neuroanesthesiologist.
- Although the basic principle of neuroanesthesia remains the same even in children, physiologic and anatomical differences in young age should be carefully considered along with a detailed understanding of pediatric cerebral physiology, surgical condition, and clinical presentation.
- A detailed history should include both past and present illnesses, neurologic examination, complete systemic examination, risk stratification, and appropriate investigations.
- Adequate preoperative preparation of the children may help to prevent mishaps in the operating room.
- Specific conditions requiring meticulous attention are children with hydrocephalus with the features of increased intracranial pressure, meningomyelocele, craniosynostosis, brain tumors especially posterior fossa tumors, and vascular lesions.
- This chapter discusses the preoperative evaluation and preparation of children for neurosurgical procedures in detail, both in elective and emergency settings.

4.1 Introduction

Preoperative evaluation and planning are the keys to the successful anesthetic management of pediatric neurosurgery. Children should not be considered mini-adults as the pediatric population's anatomy and physiology is unique [1]. Intensive and plenary care of the pediatric neurosurgical patient requires a thorough understanding of the surgical condition and clinical presentation, a thorough knowledge of the cerebral physiology during childhood, and an awareness of the specific issues pertinent in providing overall anesthesia care for children [2]. Detailed history, general and systemic examination, risk stratification, investigations, proper planning, optimization, informed risk consent, premedication, and preoperative orders are the important requisites of preoperative evaluation and preparation for neurosurgery in children, which will be discussed in this chapter.

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4.2 History Taking in a Child Posted for Neurosurgery

The details of the history are obtained from the primary caretaker, mostly from the mother. A good rapport needs to be established with the child, parents, and other family members for gaining the confidence and trust for the further conduct of proper planning and execution of anesthesia and surgery [3]. The psychological status of the patient varies. It depends on the child's age, parents attitude and lifestyle, awareness regarding surgery and anesthesia requisites, complications, history of previous anesthesia exposure, and hospital stay. An audiovisual demonstration and net search of anesthesia management and surgery streamlines parents thought process and removes perioperative management disbeliefs per se. In emergency conditions like head injury, one needs to gather information from the witnesses and the attending resuscitation staff.

It starts from detailed data on demographics such as name, age, sex, and address. This provides the identification of the child, its diagnosis, type, and site of surgery. Age is an important parameter as the growing child changes its physiology over time [1].

Other aspects of history should include the following:

- Chief complaints: These include easy fatigability, lethargy, drowsiness, increasing head size, vomiting, bulging fontanelles, visual disturbances, difficulty in swallowing, abnormal back swelling, and other varied features depending upon the type of lesion.
- History of presenting illness: Presenting symptoms and its course of progression – static, increasing severity, or improving; acute, subacute, or chronic presentation; frequency; duration; the pattern of involvement; associated symptoms; relieving and aggravating factors; and treatment history.
- Features of increased ICP: Includes a range of mild symptoms like nausea, lethargy, and increasing head size to late severe symptoms like hypertension, bradycardia, and irregular respiration.
- Patients presenting with focal signs and symptoms: Guides us toward the tumor's location and its surrounding areas, e.g., lesions in the motor cortex area presenting with weakness of the arm, legs, or face, and brain stem lesions with lower cranial nerve palsies (e.g., difficulty in swallowing). The commonly encountered pediatric neuro-lesions and their presentation are described in Table 4.1.
- History of other comorbid illnesses: Congenital heart disease, prematurity, upper respiratory tract infection, urinary tract infection, diabetes, meningomyelocele, and hydrocephalus. History of seizures due to head injury, febrile convulsions, status epilepticus, and meningitis.
- History of previous hospital events: Previous exposure to anesthesia and surgery; any associated events or complications like difficult airway, cardiac arrest, or anaphylaxis; duration of hospital stay; history of tracheostomy/intensive care admission/ventilator days; history of blood transfusion or any bleeding disorders; accident history, repeated exposure to surgery and anesthesia, e.g., repeated shunt surgeries in children with hydrocephalus, spina bifida, and Arnold-Chiari malformations. Latex allergy is commonly seen in these patients [13]. Detailed anesthesia and postoperative record provides vital information about the condition of the child and airway problems.
- Birth history: Gestational age, maternal diabetes, exposure to illicit drugs or alcohol, intrauterine infections, complications during pregnancy (e.g., pregnancy-induced hypertension) and delivery (e.g., meconium aspiration, abruption placentae, premature rupture of membranes), history of spontaneous abortions in mother, APGAR scores, and history of fetal distress or any congenital disabilities. Other signs like respiratory distress, apneic episodes, seizures, bleeding, and duration of hospital stay may provide a clue to some neurological problems [14, 15].

Table 4.1 Commonly encountered neurosurgical pathologies and their presentations

Neurosurgical pathologies	Presentations
Hydrocephalus [4]	Increasing head size (in infants), irritability (infants)/headaches (young children), projectile vomiting, and diplopia, with increasing severity, may present with decreasing consciousness, loss of upward gaze, and palsies of third and sixth cranial nerves
Meningomyelocele [5]	Mass in the spine, paresis/paralysis of lower limbs, sometimes associated with Chiari malformations and hydrocephalus. With Chiari II malformation: Apnea, stridor, autonomic instability, and respiratory problems (features of brain stem compression)
Posterior fossa tumors [4]	Signs of obstructed hydrocephalus, lower cranial nerve involvement
Craniopharyngioma [6]	Endocrine disturbances (hypothalamo-pituitary dysfunction), thyroid and adrenal abnormalities
Head injury/intracranial hemorrhage [7]	History of accident; signs and symptoms of increased intracranial pressure: In infants, irritability, lethargy, failure to feed, decreasing consciousness, bulging Fontanelle, cranial nerve palsies, and loss of consciousness; in older children, early morning headaches, vomiting without nausea, double vision, and papilledema; in severe cases, Cushing's triad
Epilepsy [8]	Type and frequency of seizures, associated signs and symptoms, number of antiepileptic drugs (AEDs) for treatment
Craniovertebral junction abnormalities [9, 10]	Signs and symptoms depend on the site of neural compression: Paresis or paralysis of the lower and upper limbs, respiratory compromise
Craniosynostosis [11]	Usually, a cosmetic complaint; may be associated with Apert and Crouzon syndrome
Vascular anomalies [12]	MC is cerebral arteriovenous malformations (AVMs) followed by spinal AVMs, congenital venous malformations, and telangiectasia; the most common cause of spontaneous intracranial hemorrhage

- Developmental history: Assessed in four categories: motor, adaptive, language, and personal-social behavior [16]; Denver II test—most commonly used to identify the milestones [17]. Adaptive and language behavior has shown to be strong predictors of cognitive outcome. Any deterioration in school performance is a significant indicator of an acquired or progressive neurological problem.
- Drug history: List of medications the patient is taking, dosage, any side effects encountered, any other form of supplements the child is administered with (homeopathic, herbal, or Ayurvedic drugs), allergy to drugs and latex, and immunization history. Common drugs used in neurosurgical practice include mannitol, antiepileptics, and steroids.
- Family and social history: Family history of congenital health problems, epilepsy, muscle dystrophy, bleeding tendencies, neurodegenerative disorders, genetic diseases, or cancerous growths; consanguineous marriage; the anesthetic-related history of malignant hyperthermia and prolonged paralysis (pseudocholinesterase deficiency) should be asked for; social history gives us the information regarding its family environment and intellectual growth of the child.
- Dietary history: Whether the child is on breastfeed/artificial feeds/normal adult diet; vegetarian/nonvegetarian; any history of nausea and vomiting interfering with the feeds and its severity.
- Airway related: A list of questionnaires should be entreated to highlight the same. This includes complications during birth, trauma or surgery of airway, previous airway history, snoring, apneic attacks during sleep, difficulty in breathing or speaking, hoarseness, and noisy breathing.

At the end of history taking, the neuroanesthesiologist gets an idea about the child's medical condition, identifies risk factors and expected complications associated with the condition, and contemplates both anesthesia and surgical risks relevant to the patient.

4.3 Physical Examination

It is challenging to get full cooperation from the child during physical examination. Infants and young children are most comfortable in their mother's lap. The examination should be tailored as per each child's level of understanding and developmental level. We should observe the child closely during its interaction with the parents and during activities. This gives a lot of information regarding motor activity, mental status, coordination, and cranial nerve function [18].

4.3.1 General Examination

An overall general examination should include body habitus, general condition or look of the patient, gait, developmental milestones, and any signs of icterus, pallor, edema, lymphadenopathy, clubbing, tremor, or cyanosis.

Body habitus: Weight, height, and, notably, the body surface area provide an understanding of the growth physiology according to the child's age. The growth chart provides a clear indication of the nutritional status of the pediatric patient. Stunted growth is seen in conditions like malnutrition, emaciation due to chronic vomiting, poor financial condition, and repeated upper respiratory tract or urinary tract infection leading to loss of appetite; nutritional and electrolyte deficiencies are usually associated with underweight and emaciated children. On the other hand, the overweight child is a major concern in urban cities due to their junk food habits. A close correlation was observed between obesity and children with neurosurgical conditions like Chiari malformation, meningomyelocele, suprasellar tumors, and craniopharyngioma [19–21]. An obese child is prone to difficult intravenous cannulation, difficult airway management, increased snoring incidence, and positioning problems. Obstructive sleep apnea should be ruled out in obese patients. They require specific and unique perioperative care for a successful outcome [22]. Drug dosage calculation is based on the ideal body weight rather than the actual body weight.

The next important parameter is head circumference, especially in children less than 2 years of age. This is especially useful in the diagnosis and management of hydrocephalic babies [23, 24]. This is measured by placing a flexible tape around the broadest part of the forehead, just above the eyebrows and ears, and at the midpoint of the back of the head. ***Lasso-o™ tape*** is recommended for accurate measurement of head circumference [25]. The tape should be placed at the largest measurable circumference, especially in patients with an abnormal head like craniosynostosis and low hairline, e.g., Klippel-Feil syndrome [26, 27]. These measurements should be taken to the nearest millimeter and plotted in decimals on a centile chart. It should be recorded with the increasing age of the infant. The weight of the child is also recorded at the same time.

A normal growth chart is interpreted if the plotted line runs almost parallel to one of the printed lines. Abnormal growth is interpreted once the plotted line falls outside 99.6th or 0.4th centile on the chart or more than 2 centile lines above or below their length measurement.

General appearance: Some neurosurgical conditions present with a characteristic appearance. Hydrocephalic infants will have a large head, full fontanelle, widely separated cranial sutures, and sunset sign. Craniosynostosis occurs due to the premature fusion of one or more cranial sutures. Children may present with abnormal head shapes, e.g., Pfeiffer syndrome, Apert syndrome, and Crouzon syndrome. And when associated with other body deformities, this is called syndromic craniosynostosis [28].

Vital signs include pulse rate, rhythm, volume, blood pressure (noninvasive), and respiration pattern. The abdomino-thoracic type of respiration is seen in infants compared to thoracoabdominal in adult patients.

The examination of the skin and whole body has been [3] described in Table 4.2.

Intravenous (IV) Access: The skin and whole body are screened to identify an easy access for an IV-line placement. Intravenous cannula placement is a nightmare in a specific pediatric population, like children with multiple skin lesions and anatomical variations and severely malnour-

Table 4.2 Whole-body examination and abnormalities associated with neurologic lesions

Examination	Lesions	Conditions
Skin	Neurocutaneous lesions	Tuberous sclerosis (ash leaf spots) Neurofibromatosis (café au lait spots)
	Angiomas	Sturge-weber syndrome
	Axillary freckling	Neurofibromatosis 1 (optic gliomas, sphenoid wing dysplasia)
	Adenoma sebaceum, shagreen patches	Tuberous sclerosis
Hair	Hair whorl	Cerebral malformations
	Friable kinky hair	Menkes kinky hair—Mental retardation, optic atrophy
Palm	Palmar creases	Genetic syndrome
Thumbnails	Abnormality in size or convexity	Growth disturbance—Sign of hemiparesis
The midline of the back and neck	Sacral dimples or tufts of hair	Spinal dysraphism
Abdomen	Hepatosplenomegaly	Inborn errors of metabolism

Table 4.3 Skull abnormalities with its varied presentations and associated lesions

Skull abnormalities with presentations	Associated lesions
Microcephaly	Congenital, maternal exposure to rubella, chicken pox, and cytomegalovirus, substance abuse, malnutrition, Down's syndrome
Macrocephaly	Congenital, hydrocephalus, intracranial hemorrhage, neoplasms
Ridging of the cranial sutures	Premature closure of the fontanelles (craniosynostosis)
The prominence of scalp veins, Macewen or cracked pot sign, and bulging anterior Fontanelle	Increased intracranial pressure
Flattening of the occiput	Hypotonia
The prominence of the occiput	Dandy-Walker syndrome
Areas of tenderness (on percussion)	Osteomyelitis
Intracranial bruits (on auscultation, heard over—Globes, temporal fossa, and retroauricular areas)	Angiomas, anemia, thyrotoxicosis, meningitis

ished, extremely obese, and post-radiotherapy patients (small-caliber veins). Multiple pricks, difficult access, and accidental puncture of major arteries during central line placement may be further complicated by hypothermia, hemodynamic instability, and even hemorrhagic shock due to varied reasons [29]. Pediatric expertise in line placement and the use of currently available armamentarium like ultrasonography and transillumination methods for IV access may curtail the number of pricks, trauma, and a prolonged time for placement [30, 31].

Examination of the Skull: Before the neurologic examination, the skull examination [2, 32] gives a lot of information (Table 4.3).

4.4 Neurologic Examination

This is an important aspect of system examination in pediatric neurosurgical practice [18, 33, 34]. At the same time, it is tough to elicit in young pediatric patients. A friendly rapport needs to be established with the child to gain confidence. Neurological status is best described by the age-specific Glasgow Coma Scale (GCS) score (Table 4.4) [35]. The score varies from a minimum of 3 to a maximum of 15 points. GCS score correlates well with the clinical presentation. A reduced GCS score indicates increasing intracranial pressure (ICP); GCS <8 carries the risk of aspiration and needs airway protection.

Table 4.4 Age-specific Glasgow Coma Scale (GCS) score

Best motor response	>5 years	<5 years	
6	Obeys commands	Normal spontaneous movements	
5	Localizes supraorbital pain		
4	Withdraws from nail bed pain	–	
3	Flexor response to supraorbital pain	–	
2	Extensor response to supraorbital pain	–	
1	None	–	
Best verbal response	*>5 years*	*2–5 years*	*<2 years*
5	Oriented	Appropriate word use (to usual ability)	Smiles, follows objects, and interacts
4	Confused	Inappropriate words (less than usual ability)	Cries but consolable
3	Inappropriate words	Persistent cries and pains	Inconsistently inconsolable
2	Incomprehensible sounds	Grunts and moans to pain	Grunts, agitated and restless
1	No response to pain	–	–
T	Intubated	–	–
Eye opening			
4	Spontaneous		
3	To voices		
2	To pain		
1	None		
C	Closed (swelling, dressing)		

In infants with increased ICP or hydrocephalus, the signs of full fontanelle and widely separated cranial sutures may be elicited and in young children, papilledema with the fundoscopic examination. With increasing severity, they may present with Cushing's triad (bradycardia, irregular respiration, and hypertension), suggesting impending cerebral herniation. Other late signs include pupillary dilation, pupillary asymmetry, third and sixth cranial nerve palsies, Cheyne-Stokes respiration, and hypotension. Apart from examining the state of consciousness, the child's behavior should also be noted.

Cranial nerves are examined with various tests for infants, newborns, and young children (Table 4.5). The examination of the olfactory nerve is usually not recommended.

Motor Assessment: In neonates and infants, observe for the posture, spontaneous inherited movements and other movements when the patient is actively playing. The examiner assesses the tone of the muscle by passive manipulation of the limbs or spine. Normally, extended posture in preterm newborn changes to flexed posture in full-term newborn and finally attains normal tone by 6 months of age. Hypertonia is usually seen in patients with upper motor neuron disease. Hypotonia is seen in both central and peripheral nervous system pathology. ***The bulk*** of the muscle is usually evaluated by inspection and palpation. Due to the increased adipose tissue content in the limbs, it is difficult to assess the muscle bulk in newborns. Rather, it is assessed best in the tongue muscle. Atrophy indicates denervated muscle or decreased usage. Hypertrophy is seen in patients with increased usage of certain muscles to compensate for the weakness in other muscles, or apparent increase in size is seen when normal muscle tissue is replaced by abnormal tissue (e.g., amyloidosis) or due to some underlying inhderited muscle pathology (e.g., Duchenne's muscle dystrophy).

In infants and young children, withdrawal from noxious stimuli gives a rough estimate of motor strength. The child should be observed for daily activities like walking, standing, sitting, crawling, running, and cycling to gauge the motor power in young children. Motor examination in older children is carried out similarly to

Table 4.5 Cranial nerve examination in children

Cranial nerves	Infants and newborns	Young children
II	Optical blink reflex Pupillary	Snellen chart, picture chart, visual field: Let him focus on an object in front of his eyes and then wave a hand in the periphery
III, IV, VI	Oculocephalic doll's eye maneuver Gaze and track (hold infants up)	Ask the child to follow an object or doll with his eyes
V	Rooting reflex Sucking reflex Corneal reflex—Sensory	Chewing movement Corneal reflex, touching face with cotton
VII	Facial asymmetry and forehead wrinkle	Observe facial movement—Show teeth, puff cheeks
VIII	Acoustic blink reflex Doll's eye maneuver	Turn to sounds, whisper, hearing screen
IX, X	Swallowing and gag reflexes	Gag reflex
XI	Observe for the side movements of the neck; for head flexion on traction response (once the arms are pulled in the supine position, the newborn lifts both the head and trunk—Normal)	Ask the child to turn his head against resistance (sternocleidomastoid muscle)
XII	Coordinated suck and swallowing	XI, XII: Shrug shoulder, stick out tongue

Table 4.6 Grading of muscle power [26]

Grading	Muscle power
0	No contraction
1	Flicker or trace of contraction
2	Active movement with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

adults; grading of the muscle power is given in Table 4.6 [36].

Coordination examination is mainly done to assess cerebellum functions, sensory control, pyramidal and extrapyramidal tracts of motor control. Since sufficient voluntary control is not established until 4–5 months of age, it is difficult to conduct tests in infants. Coordination tests include finger-nose test in upper extremities and heel to shin test in lower extremities. This can be substituted in young children by asking them to reach an object or touch an interesting toy. The alternate method is utilized in young children by testing for high five in the upper extremity and kicking the examiner's hand in the lower extremity. For sensory abnormality, this is checked with eyes closed. ***Dysdiadochokinesis*** is defined as impaired rapid and alternating oscillating movements due to cerebellar abnormality. This is evaluated by rapid finger-to-thumb tapping, patting movements of the hand, and toe-tapping in older children. ***Romberg test*** is done for assessment of proprioception. In cerebellar disease, these are usually associated with hypotonia and decreased or absent deep tendon reflexes.

Gait is examined as the child enters the examination room. They should be watched for their steps when crawling, walking with and without support, running, playing, and climbing stairs. This has given an indirect clue to the lesion involved. Wide- and broad-based gait are commonly seen in the cerebellar vermis dysfunction, and narrow stance and stiff gait are seen in children with corticospinal tract lesions.

Sensory Examination: Sensory modalities include touch, pinprick (sharp), temperature, position sense, and vibration. Tingling instead of pinprick can be used in children because of the similar pathways for these two modalities. The part affected and the pattern of distribution (dermatomal/neural) determine the neurologic abnormality. Pain or tickling sensation can be elicited in a neonate, whereas more formal examination can be carried out in older children as in adults.

The sensory level should be searched for, especially in patients with spinal cord abnormality. Modalities like vibration and proprioception are difficult to elicit in young children, requiring good counseling and cooperation even from older children. Other higher sensory modalities like higher cortical sensory perception (like point localization) and discrimination are possible in older children and usually done as part of the mental status examination.

Reflex testing is easily carried out as it does not require a conscious and cooperative child. The type of reflexes includes deep tendon, superficial, and pathological reflexes. For deep tendon reflexes, the circuit includes:

Stimulus: A stretch of a tendon (by tapping with a percussion hammer) stretches the muscle's sensory organs, leading to the muscle's reflex contraction. Common reflexes used for testing include jaw jerk (V), biceps reflex (C5–C6), triceps reflex (C6–8), brachioradialis reflex (C5–C6), patellar reflex (L2–4), and ankle reflex (S1–2). Jaw jerk is difficult to elicit in the older child. Loss of reflexes suggest lesion of the sensory nerve or root, and exaggerated reflexes suggest a lesion of the upper motor neuron.

Superficial Reflexes: These are polysynaptic reflexes, and the responses are elicited by skin stimulus. These reflexes are lost in lesions of the upper motor neuron. They include corneal reflex (V and VII), palatal reflex (IX), abdominal reflex (T7–10), cremasteric reflex (L1–L2), and plantar response (Babinski response). *Babinski response* (L5/S1) is unique in newborn infants as they exhibit extensor plantar response instead of the normal flexor response, which is seen after 1 year of age.

Primitive reflexes are present at birth and disappear with time, almost by 5–6 months of age. These include the sucking reflex, Moro's response, rooting reflex, and grasp reflex. These reflexes are diminished or lost in neonates and young infants with a depressed, nervous system.

4.5 Airway Assessment

The relatively large head size and small neck compared to adults make it a difficult airway in infants and small children. In adjunct, they have large tongues and short mandible in young children. The additional presence of tonsils and adenoids in obligate nasal breathers also contributes to difficult mask ventilation and intubation. This is especially challenging in children with craniofacial abnormalities or occipital dysraphism [37]. Airway assessment initially starts with a proper history taking; a list of questionnaires should be entertained to highlight the same. Proper assessment paves the path for effective planning and successful execution of airway management.

4.6 Cardiovascular Examination

In addition to the routine screening of cardiovascular signs, a thorough CVS examination is advocated in pediatric patients coming for neurosurgical procedures in the sitting position, which carries the highest risk for venous air embolism (VAE). Atrial septal defect or patent foramen ovale increases the risk for paradoxical air embolism in these children. Routine echocardiography screening might help avoid the sitting position and plan the surgery in a different approach in this subset of patients [38]. Children with congenital cyanotic cardiac anomalies like tetralogy of Fallot are associated with a cerebral abscess and present with signs and symptoms of increased ICP [39].

4.7 Respiratory Examination

The respiratory system's routine examination should include stepwise assessment such as type and rate of breathing, bilateral air entry, presence of any wheeze or crepitations, and use of accessory muscles (nasal flaring). Reactive airway disease, asthma, or upper respiratory tract infection (URTI) may complicate the perioperative care. A child with cold or URTI is a common finding and needs to be optimized before surgery. The child may be assessed for URTI from history and physical examination; those with mild-to-moderate symptoms, such as a recent history of URTI, runny nose, dry cough, no wheeze, and fever for 1 or 2 days, may proceed for surgery. Children with severe URTI features such as productive

cough, mucopurulent secretions, fever >38 °C, wheeze, and lethargy should be deferred and re-evaluated after 2 weeks. Extra precautions are needed whenever surgery is planned in children aged less than 1 year (infants) and with history of passive smoking and asthma [40].

However, the risk-benefit should be weighed for deferring the neurosurgical procedure and perioperative adverse respiratory events, which can be minimized by administering salbutamol at least 10–30 min before the induction of anesthesia and also by avoiding any major respiratory stimulus that may lead to bronchoconstriction [41]. Premature babies and obese children with severe sleep apnea are at risk of pulmonary dysfunction such as pulmonary hypertension, apneic episodes, and infection. Hence, a thorough examination of the respiratory system should be done [3].

4.8 Other Systemic Examinations

The child needs to be screened for the presence of an endocrine abnormality [3]. The most common endocrine abnormalities found in pediatrics are thyroidal dysfunction, insulin-dependent diabetes mellitus, obesity, and precocious puberty. In the presence of a pituitary tumor, dysfunction of growth hormone leading to either cretinism or stunted growth is commonly seen, along with diabetes, hyperprolactinemia, thyroid dysfunction, and cortisol dysfunction. Thus, the child is examined for signs such as tachycardia, dysrhythmias, difficult intubation, and autonomic dysfunction. Examination of the abdomen for renal tenderness, hypospadias, hepatomegaly, splenomegaly, and borborygmi is done. Hematological abnormalities like sickle cell disease, thalassemia, and purpura are widespread in this group of patients. The presence of pallor, petechiae, rash, bruises, or other skin lesions, associated or not associated with hepatosplenomegaly, should be examined. The presence of ascites, icterus, and pedal edema should be thoroughly evaluated as they could indicate an underlying hepatic or renal pathology.

4.9 Preoperative Investigations

Pediatric neurosurgical patients are usually referred to the neuroanesthesiologist for evaluation with a confirmed diagnosis. A neuroanesthesiologist requests investigation on the diagnosis and perioperative requirements. The investigations are listed along with their implications in Table 4.6. A review of neuroradiologic investigations is also necessary for the overall intraoperative anesthetic planning and management (Table 4.7).

The American Society of Anesthesiologists (ASA) published an updated practice advisory for preanesthesia evaluation, which states that preoperative tests should not be ordered routinely and should only be ordered on a selective basis to improve perioperative patient management [42]. The National Institute for Health and Care Excellence (NICE) guidelines recommend that all children older than 16 years scheduled for neurosurgical procedures should undergo preoperative testing such as renal profiles, complete blood count, coagulation profile, and urine analysis, only when indicated [43]. However, NICE guideline 2016 update does not include recommendations on children and patients undergoing cardiothoracic and neurosurgery.

4.10 Risk Stratification

Risk stratification in neurosurgery is an essential tool not only for the accurate prediction of clinical and perioperative risk but also for comparative audit and outcome measurements. It guides the parents and older children to understand and sign the consent for surgery and clinical decision-making during the perioperative period. Though some risk stratification tools are described for adult neurosurgery, pediatric neurosurgery literature is sparse [44, 45]. The risk of morbidity and mortality is very high for infants and patients with severe comorbid conditions; emergency surgeries further increase the risk. Four major institutional audits [46] have suggested the following:

Table 4.7 Investigations for pediatric neurosurgical practice and their implications

Investigations	Neurosurgical indications	Implications
Hemoglobin, hematocrit (surgeries where significant intraoperative bleeding is anticipated)	• Craniotomies • Malignancy • Vascular malformations • Vascular tumors • Trauma • Poor nutritional status • Associated chronic cardiovascular, pulmonary, renal, or hepatic disease	Hb less than 10 gm/dl signifies anemia (varies according to age) Hb, more than 16 gm/dl, signifies polycythemia making more prone to thrombosis. Also, can suspect congenital cyanotic heart disease and needs further evaluation
Total leucocyte count	• To exclude any infection source • Patients on steroid therapy	Patients on steroids are more prone to infection
Blood grouping and crossmatching	All craniotomies and major spinal surgeries	Blood can be kept ready for transfusion whenever required
Coagulation profile: Platelet count, Bleeding time (BT), Clotting time (CT), Prothrombin time (PT), Activated partial thromboplastin time (aPTT)	• History of bleeding diathesis • Patients on anticoagulant therapy	Abnormality can be detected and optimized
Liver function test	Patients on anticonvulsant and antitubercular therapy	Need to titrate anticonvulsant and anesthetic drug dosages
Renal function tests (blood urea, serum creatinine, serum electrolytes)	Congenital anomalies Patients on diuretic therapy Pituitary and adrenal disorders Type I diabetes	Cautious fluid therapy and titration of drug dosage required in deranged renal function
Viral markers (HBsAg, HIV)	All the patients coming for surgery	Routinely carried out; universal precautions in positive cases
Electrocardiograph	Suspected heart disease, head injury, vascular malformations, intracranial hemorrhage, subarachnoid hemorrhage, type I diabetes, congenital malformations	It helps in differentiating cardiac disease from the changes caused by neurological insult
Echocardiography	Congenital heart disease, valvular heart disease, surgery in sitting position	Helps in the planning and execution of perioperative management To exclude patent foramen ovale
Chest roentgenogram	Cardiac disease, pulmonary disease, malignancy	To exclude major pathology To exclude tumor metastasis
Arterial blood gas (ABG) analysis	Significant pulmonary disease, scoliosis, cervical pathology	Assessment of respiratory reserve and optimization The decision for postoperative mechanical ventilation
Sleep apnea tests	History of sleep apnea Morbid obesity	The requirement for postoperative oxygenation Explain for the requirement for continuous positive airway pressure (CPAP) machine Titration of anesthetic drugs to prevent hypoxia

- Infants are at greater risk of complications.
- Infants have predominantly respiratory complications.
- Postoperative vomiting is common among older children.
- ASA grade III patients are at greater risk: ASA grading is controversial for its application in the neurosurgical patient population. ASA grade V neurosurgical patients have shown to have a better outcome when compared with other non-neurosurgical ASA V patients [47]. It has been less reliable in children and may still be difficult to apply further in pediatric subpopulations [48]. The search

for a more specific physical grading system to predict the perioperative outcome in pediatric age group is still on, considering the associated factors such as congenital conditions, syndromes, and other acute illnesses [48].

Massive hemorrhage and its consequences are the most common identifiable cause of anesthesia-related cardiac arrest and other major morbidity resulting in litigations. Craniotomy, craniofacial, and spinal surgeries have been identified as high-risk surgeries for major blood loss, particularly in infants. Proactive and appropriate planning like a timely replacement of blood and blood products along with IV fluids with continuous monitoring of fluid status, hematocrit, vitals, sugars, and potassium will help tide over the crisis. The most common equipment-related (iatrogenic) cause of severe morbidity is the insertion of central lines [46].

Pediatric spinal deformity correction is a challenge. The newly established model for risk stratification includes clinical and radiological factors that can guide the perioperative planning and meticulous surgical and anesthesia management for a better outcome. Osteotomy and resection procedures were independent predictors of postoperative neurologic complications [49].

As per Rotterdam CT score categories, children with TBI and less severe injuries will have better survival than the adults, but those with higher score categories will have worse survival

Table 4.8 Neuro-specific diagnostic imaging modalities and their implication

Modality	Neurosurgical condition(s)	Implications
Computed tomography (CT) and magnetic resonance imaging (MRI)	Head injury: Detects subdural, extradural, and subarachnoid hemorrhage, parenchymal bleeds, cerebral contusions, and skull fractures Spine injuries: Detects fracture, dislocation, and compression	CT scan is the most preferred modality in head injury patients; it also helps in rapid screening of cervical spine injuries Hemorrhages are seen as areas of white density (CT)
	Tumors: Site, the extent of the lesion and mass effect, associated hydrocephalus, vascularity, and edema	This helps planning for surgical position, CSF drainage options for deep lesions, blood conservation techniques, and arrangements of blood and blood products
	Cerebral edema: Hypodense (black) on CT On MRI: Seen as a decreased signal (black) on T1-weighted and increased signal (white) on T2-weighted studies	
	Detects herniation syndromes and hydrocephalus (both communicating and non-communicating)	
	Detects pneumocephalus	Pneumocephalus: After skull fractures, postoperative, after pneumocephalograms and lumbar punctures Nitrous oxide to be avoided
	Raised ICP: Seen as effaced cortical sulci, loss of gray and white matter distinction, basal cisterns, and interhemispheric fissures, compressed ventricles, and herniation syndromes	
Plain skull films	Detects fractures, penetrating injuries, foreign bodies, site and relationship of depressed skull fractures, pneumocephalus	
Positron emission tomography (PET)	In vivo evaluation of brain physiology and metabolic activity Identifies grades of glioma and can differentiate recurrent tumor from radiation-induced necrosis	
Angiography	Identifies vascular lesions, the site of origin, vessels at risk, vascularity of the lesion, presence of cross-filling, risk of bleeding (in AVMs), etc. Embolization of feeding vessels in highly vascular tumors and AVMs to decrease bleeding risk, plan surgical access, prepare for transfusion of blood and blood products, and maintain temperature	

than adults. Hence, this score can be used accurately in children with moderate or severe TBI for risk stratification [50]. This scoring system includes basilar cistern status, midline shift, subarachnoid hemorrhage (SAH), or intraventricular hemorrhage (IVH). This shows more favorable outcomes with epidural hematomas (Table 4.8).

4.11 Other Considerations

4.11.1 The Child with Physical or Mental Handicap

Children with physical or mental handicaps frequently come for surgery. They need care with expertise and compassion from a thoroughly coordinated team. Many children who survive traumatic brain damage, hypoxic encephalopathy, or post-infectious encephalopathy come for various surgical procedures, same with children having drug-refractory epilepsy and mental retardation for epilepsy surgery. These patients should be assessed in terms of neurological status, shunt patency if a shunt is in situ, respiratory compromise due to repeated aspirations, tracheal stenosis if there is a history of tracheostomy, and presence of gastrostomy tubes. Any old injuries, deformities, and scars should be noted to avoid future legal liability [51].

Cerebral palsy patients should be assessed for their intelligence in addition to the neurological status and deformities [52]. Children with mental retardation, especially Down's syndrome, need special assessment for congenital heart defects and other congenital anomalies. The latter include blunting of the second cervical vertebra's styloid process combined with ligament laxity, causing atlantoaxial subluxation leading to spinal cord injury [53].

4.11.2 Drug Abusing Child and Adolescent

With the increasing incidents of trauma in children, the anesthesiologist should be aware of drug abuse signs and symptoms that mimic neurological disability. Patients with cocaine abuse are particularly prone to myocardial ischemia and infarction in younger age groups. They are also associated with ventricular hypertrophy, dysrhythmia, cardiomyopathy, etc. There is also an increased incidence of hemorrhagic cerebrovascular accidents in these children. Ulcers in the nasal mucosa may pinpoint to drug abuse. Similarly, the neuroanesthesiologist should be aware of other commonly used drugs like amphetamine, marijuana abuse, and their consequences for guiding them during the perioperative period [54].

4.12 Preoperative Preparation

4.12.1 Preoperative Visit

The anesthesiologist's preoperative visit eases the emotional stress and builds the patient's and parents' confidence. Thorough knowledge of the pathological condition, expected surgical procedure and patient's medical history is of utmost importance. A preoperative visit wearing OR attire may help; the child may feel familiar when meeting the anesthesiologist inside OR.

4.12.2 Informed Consent

Generally, a consent form signed by parents is to be obtained for children age less than 12 years. Between 12 and 18 years, only a restricted consent, not involving risk of life, is valid. For most neurosurgical surgeries, the signature of both parents shall be preferably obtained. Consent in pediatric patients remains distinctive as parental responsibility and understanding. A child's capacity to consent and follow legal guidelines play an important role. All parents should understand the primary diagnosis, type of surgery, procedure-specific risks, and management options. Parents should be informed about the probable requirement for postoperative mechanical ventilation, tracheostomy, and ICU stay [55].

4.12.3 Fasting Guidelines

Preoperative fasting is of paramount importance as it allows sufficient time for gastric emptying and prevents aspiration of gastric contents. The benefits of fasting should be weighed against prolonged hours of fasting leading to dehydration, hypoglycemia, and discomfort to the patient, especially in patients with raised ICP associated with vomiting. During preanesthetic visit, clear written instructions and verbal communication to the parents about fasting is mandatory. It is important to instruct these patients due to unpredictable surgery, cancellations, and observance by both patients and parents. Many studies have shown no increase in the risk of aspiration for elective surgery if clear fluids are given up to and at 1 h preoperatively against 4 h for breast milk, 6 h fasting time for light meals and milk, and 8 h for fatty meals [56]. Current guidelines also favor early initiation of oral intake within hours of surgery [56].

It is important to ascertain that solids should not be allowed after admission for children coming for emergency neurosurgical procedures. Fluid status should be maintained with intravenous therapy.

4.12.4 Premedication and Review of Current Medications

Sedatives and opioid premedication are avoided in pediatric neurosurgical patients, especially with raised ICP. This may aggravate hypoxia, as well as hypercarbia which increases the ICP. However, a very anxious child may be premedicated with midazolam (oral 0.7 mg/kg; nasal 0.2 mg/kg) [57]. Oral midazolam in optimum dosage did not cause respiratory depression and increased $PaCO_2$. Children with vascular anomalies should be premedicated with midazolam under supervision, which helps control anxiety and, in turn, hypertension, which prevents the vessels' rupture. Antisialagogues are not recommended as per ASA guidelines to decrease the secretions and hence the risk of aspiration. These pre-medicants may be advocated in certain neurosurgical procedures requiring significant airway manipulations like the spine and cranial procedures in prone and sitting position and cervical spine procedures [58].

Drugs like fentanyl and digoxin may potentiate the side effects of dexmedetomidine like bradycardia; hence, caution has to be exercised [59]. On the other hand, perioperative β-blockers may be given to attenuate hypertension during the induction of anesthesia. Oral propranolol may be given in the dosage up to 1 mg/kg, in divided dosage, the night before, and in the morning of surgery. Ketamine should be avoided as it increases the cerebral blood flow and ICP. If the child is on medication with steroids and anticonvulsants, they need to be continued perioperatively. Application of a eutectic mixture of local anesthetics (EMLA cream) one hour before surgery helps secure an IV access.

Antiepileptics, steroids, beta-blockers, and others like antipsychotic medications should be continued on the day of surgery. Children undergoing epilepsy surgery come under a special category. The need to continue or stop antiepileptic agents depends on the severity and frequency of seizures and electrocorticography monitoring during the intraoperative period. Medications that need to be stopped on the day of surgery include insulin, diuretics, and other antihypertensives like angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blocking agents, etc.

4.13 Conclusion

The pediatric neuroanesthesiologist must understand the anatomical and physiological differences. They also need to deal with the emotional reaction of different age groups. Though, premedication can help in allaying fear and anxiety in some patients, there is no substitute for a thoughtful preoperative visit. In a nutshell, detailed preoperative evaluation and optimization, proper planning and execution of perioperative management, and communication and documentation improves the overall outcome.

Conflict of interest None.

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5 Airway Equipment and Difficult Airway Management During Pediatric Neurosurgery

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Key Points

- Pediatric patients with congenital hydrocephalus, craniofacial dysmorphic syndromes, and cranio-spinal dysraphism represent a subset of patients with anticipated difficult airways during neurosurgery and therefore pose unique airway challenges.
- Several unique neurosurgical scenarios may threaten the pediatric airway and make airway control difficult during the perioperative period.
- The difficult airway is a major contributor to anesthesia-related morbidity and mortality in children undergoing neurosurgical procedures.
- True difficult laryngoscopy may be rare, but associated problems include the fact that pediatric patients cannot be intubated awake. Many of them might undergo induction without an intravenous cannula.
- Airway anatomy and physiology, especially in neonates and infants, are at marked variance from adults, marking these patients as a category with increased risk for airway complications.
- Thus, it is essential that anesthesiologists need to have adequate training and resources in terms of airway equipment, staffing, and help, to deal safely with this vulnerable class of patients.

5.1 Introduction

Airway issues in the pediatric age group contribute to significant morbidity and mortality under anesthesia [1]. Neonates and infants are the most susceptible age group [2]. Oxygen utilization in this age group is substantially higher, and this imparts poor tolerance to apnea, implying that pediatric patients can develop significant hypoxemia very rapidly, with ensuing profound bradycardia [3, 4]. While true difficult laryngoscopy is rare (1.3%) [5], airway management in many pediatric patients presenting for neurosurgical procedures has certain unique considerations, including the fact that unlike adults, they cannot be intubated awake, and may often have to be induced without intravenous access.

5.2 Infant Versus Adult Airway

- The head size in the pediatric population is much larger relative to the body, making positioning difficult.

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- A child's nostrils, oropharynx, and nasopharynx are significantly narrower than that of an adult (Fig. 5.1). Hence, the development of airway edema following inflammation or injury in any of these anatomical areas can hamper airflow quite perilously.
- Similarly, the anatomy of the tongue, larynx, epiglottis, vocal cords, the narrowest part of the airway, the type of cartilages, and also the lower airway make the infant airway different from that of an adult (Table 5.1).
- Infants are obligate nasal breathers until about 5 months of age. Thus, placement of an esophageal temperature probe or a Ryle's tube through the nose might impede spontaneous respiratory efforts.

5.3 Predicting Difficult Airway in Children

This may be easier said than done, since even adequately trained anesthesiologists, who do not regularly manage children in their operating rooms, could face challenges, even with what would seem like a routine pediatric airway [6]. Table 5.2 lists certain issues to consider while assessing a difficult pediatric airway. Even in seemingly emergent situations, it is always worthwhile spending some time, if possible, to

Table 5.1 The infant and adult airway

	Infant	Adult
Head	Large occiput	Flat occiput
Tongue	Large in comparison to oral cavity	Smaller when compared with total space in oral cavity
Larynx	Placed much higher, at the level of C2/C3 vertebrae	At the level of C4/C6 vertebrae
Epiglottis	Ω-shaped, soft	Flat, flexible
Vocal cords	Short, concave	Horizontal
Smallest diameter	Cricoid ring below cords (has been challenged recently)	Vocal cords
Cartilage	Soft, less calcified	Firm, calcified
Lower airway	Smaller and less well-developed	Larger and has more cartilage

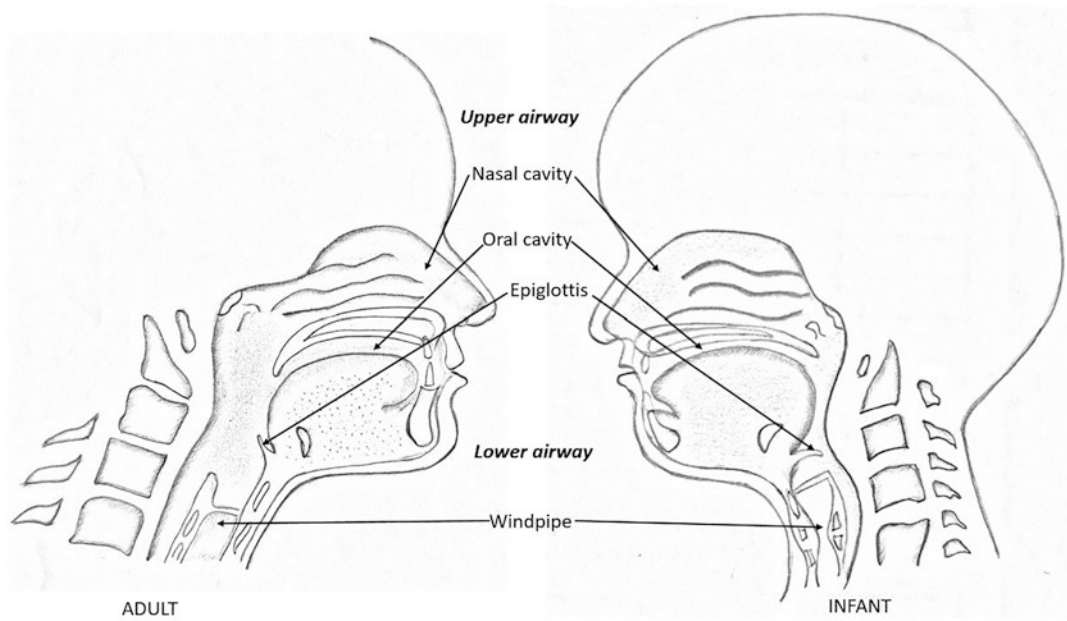

Fig. 5.1 Comparison in terms of sizes in between the adult and the infant airway

Table 5.2 Airway concerns during preoperative evaluation of pediatric neurosurgical patients

• Would it be possible to mask ventilate the patient?
• Would an adjuvant such as an oropharyngeal or nasopharyngeal airway be required to facilitate or improve mask ventilation?
• What will be the alternate plan if mask ventilation is not successful?
• Would it be possible to insert a supraglottic device?
• Would it be possible to perform a direct laryngoscopy?
• Would tracheal intubation be possible?
• Is infraglottic airway access an option?

Table 5.3 The modified Mallampati score

Class	Anatomy
Class I	Soft palate, uvula, fauces, pillars visible
Class II	Soft palate, uvula, fauces visible
Class III	Soft palate, base of uvula visible
Class IV	Only hard palate visible

assess the airway of a child before the initiation of anesthesia [1].

Assessment of the pediatric airway begins with reviewing the patient's history for previous airway manipulation and difficulties there. The subsequent physical examination directed at the airway should focus on any obvious anatomical abnormalities of the facies, any restriction of mouth opening, the mento-hyoid and thyromental distances, and any possibility of restricting neck movements. The thyromental distance might indicate micrognathia, which could make intubation difficult by restricting the space available for the displacement of the tongue when laryngoscopy is attempted. Thyromental distance is assessed using the child's own fingers, and three such fingerbreadths or more would be deemed reassuring. The modified Mallampati score [7], although commonly used in adults to predict probable difficult endotracheal intubation (Table 5.3), may also be employed in cooperative children. In contrast, the Cormack-Lehane grading [8] (Table 5.4) of the direct laryngoscopic view of the glottis should be done before the insertion of the tube to serve as a guide for practitioners handling the same child's airway at later dates.

Table 5.4 Cormack-Lehane classification

Grade	Anatomy
Grade 1	Almost entire glottis can be seen
Grade 2	Only posterior part of glottis or
Grade 3	arytenoid cartilages are seen
Grade 4	Only epiglottis but no part of glottis is seen
	Neither glottis nor epiglottis are visible

Most of the predictors for a difficult airway in an adult could predict difficulty in the pediatric population, as well. Further, some phenotypic features have been recognized as being associated with difficult airway management (Table 5.4). Another anatomical anomaly associated with difficult airway management is the abnormality of the pinna, especially microtia [9]. The difficult airway may also be anticipated in children with syndromes such as Goldenhar or Treacher Collins syndrome, as well as the Pierre Robin sequence [6]. Butler et al. have enumerated various syndromes and their impact on the management of the airway [10]. Diverse acquired situations can also impact the airway and may expedite progression to a difficult airway. These involve infection, trauma, burns, tumors, surgical changes, radiation to the airway, and anaphylaxis.

Patients who have features of obstructive sleep apnea (OSA) constitute another group at risk for a difficult airway. Most of our current understanding of OSA is derived from the adult population, in whom airway management and endotracheal intubation incur additional risk [11]. However, in children with craniovertebral junction (CVJ) anomaly, a central type of sleep apnea on polysomnography [12, 13] might exist and should indicate the need for foramen magnum decompression. This can cause upper airway obstruction and may predict a difficult airway. Neck circumference might also be a predictor of difficult intubation [14]. The ratio of the neck circumference to the thyromental distance (NC/TM) correlated well with difficult laryngoscopy incidence in 123 obese adult individuals [14]. However, given that none of the tests or physical characteristics tend to have 100% sensitivity or specificity for a difficult laryngoscopy or

intubation, it would seem prudent to combine more than one test to predict the possibility of a difficult airway, a strategy which might also hold for pediatric patients.

5.4 Planning and Investigations

It might be useful to record the saturation of a child with an expected difficult airway preoperatively based on feasibility. In patients with respiratory distress, an arterial blood gas might help assess the severity and progression of such distress. If possible, pulmonary function tests to obtain in a child cooperative enough might help distinguish respiratory obstruction due to extrathoracic causes from those due to intrathoracic etiology. Chest X-rays or CT or MRI scans help localize the cause and site of obstruction while identifying bony or soft tissue abnormalities. For children with OSA, sleep studies might indicate severity, although they are not practical for use in most clinical settings. Recording the incidence of desaturations overnight may be a more practical option.

The anesthetic plan should take into consideration any signs suggestive of congenital or acquired deformities of the airway. The child's clinical presentation, whether stable, having respiratory embarrassment, or presenting in an extremely moribund state, also needs due consideration.

Upper respiratory tract infections (URTIs) can upset even the most carefully laid plans and need meticulous evaluation for presence and severity. The determination of whether surgery needs to be rescheduled or not, especially in pediatric patients with URTI, should be individualized because of the risk factors and the anesthetist's experience with anesthetizing kids with URTI. It would be reasonable, under most circumstances, to progress with the anesthetic if the child looks healthy with no features other than clear rhinorrhea. However, rescheduling an elective neurosurgical case may be considered if the child has purulent nasal voiding, vigorous cough, or fever or there are clinical signs of lower respiratory tract complicity such as desaturation or wheeze. Under such conditions, it may be prudent to consider repealing the operation if the child has come in for major elective neurosurgery. The determination of appropriate time of elective neurosurgery in a child with URTI rests on the anesthetist after conferring with the surgeon and parents who should be informed about the risks either way.

The kind of airway device the particular surgical procedure requires, an endotracheal tube, or a supraglottic airway, also needs to be incorporated into planning for the difficult airway. It is a good idea to garner all the help one can get in pediatric patients with anticipated difficult airways. It might also be a good idea to involve the ENT surgeon early if infraglottic airway access is considered a distinct possibility.

5.5 Conducting the Anesthetic

It would always be a safe practice to maintain spontaneous ventilation for as long as possible while inducing anesthesia and proceeding in a stepwise fashion, reassessing the airway after each step, in cases with an anticipated difficult pediatric airway. If difficult mask ventilation is anticipated, the choice of the induction technique needs to be chalked out with due care; for example, with Apert syndrome, CVJ anomaly with the central type of sleep apnea, or adenotonsillar hypertrophy, spontaneous breathing from a face mask might lead to obstruction. Still, intubation does not pose a significant problem in these cases, justifying intravenous over inhalational induction. In contrast, children with certain mucopolysaccharidoses and those with achondroplasia [15] have difficult mask ventilation and difficult intubation. Hence, a careful inhalational induction might be most prudent.

5.6 Equipment for Airway Management in Children

5.6.1 Pediatric Masks

Anatomical masks and round clear PVC or silicon masks are commonly used in pediatric patients for ventilation. While the Rendell-Baker-

Soucek (RBS) mask has less dead space, disposable clear masks with inflatable cuffs are preferred for their uniform seal. Clear masks also allow visualization of secretions and vomitus during induction. Different sizes of pediatric masks available are 0, 1, 2, and 3 (Fig. 5.2).

5.6.2 Pediatric Laryngoscopes

Miller straight blade and Macintosh pediatric blades are most commonly used for conventional laryngoscopy. Straight blade is preferred in infants, but it limits movement and retraction of the tongue. The curved Macintosh blade may also be used, which can retract the tongue (Fig. 5.3).

5.6.3 Airway Adjuncts

Oropharyngeal airways and nasopharyngeal airways, bougies, stylets, and tracheal tube exchangers are commonly used airway adjuncts in pediatrics. Appropriate size selection ensures easy insertion. Hypertrophied adenoids and turbinates should be excluded while considering the insertion of the nasopharyngeal airway. Pediatric bougies are available in 8 and 11 Fr sizes (Fig. 5.4).

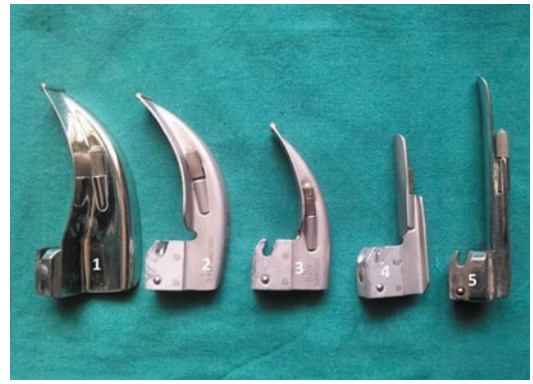

Fig. 5.3 Different sizes and types of conventional laryngoscope blades

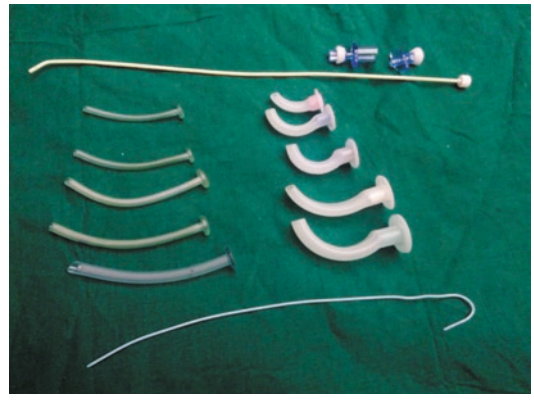

Fig. 5.4 Airway adjuncts: stylets, oral airways, nasal airways, and tracheal tube exchangers

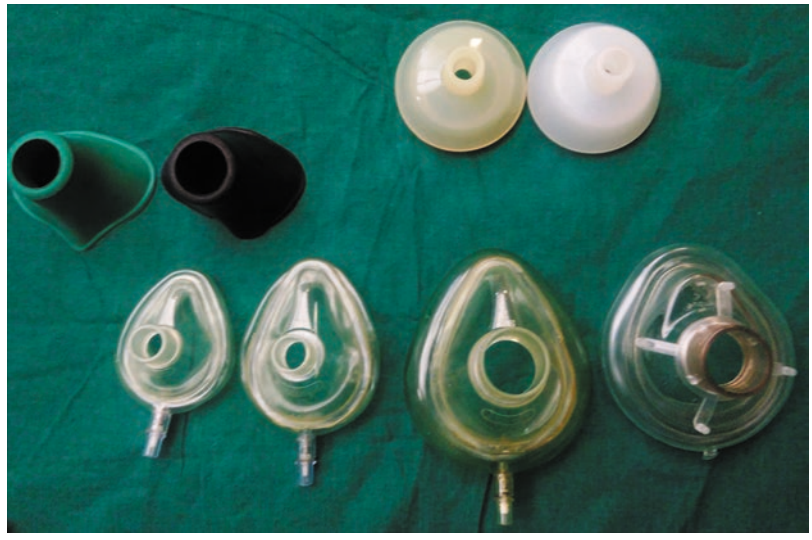

Fig. 5.2 Different sizes and types of pediatric face masks

5.6.4 Tracheal Tube Exchangers

Tracheal tube exchangers (TTEs) are available in different sizes [16], such as 8, 11, and 14 Fr, which can accommodate sizes 3, 4, and 5 ID size ET tubes for pediatric use. These help exchange endotracheal tubes in conditions where there is a significant leak around a previously placed endotracheal tube after intubating a difficult airway, to replace a laryngeal airway with an endotracheal tube in case of difficult intubation, and for extubation of a child who has had difficult intubation.

5.6.5 Cuffed Endotracheal Tubes in Pediatric Patients

It is compelling to note that our understanding of the danger of the use of cuffed ETTs in pediatrics has changed. Until the early 1990s, these were shunned due to their perceived disadvantage of causing potential injury to the laryngeal mucosa. Earlier thinking was mostly based upon the use of older high-pressure, low-volume cuffed ETTs. This fear was overcome to a large extent when companies began to assemble new high-volume class, low-pressure ETTs. These confer several benefits: low fresh gas flow, reduced gas impurities in the theatre, a smaller number of airway manipulations, substantially less aspiration risk, and better end-tidal gas monitoring. Further, the diminution of nitrous oxide, which might enter the cuff leading to an increase in cuff pressure, in most neurosurgical operating rooms, has also paralleled greater acceptance of high-volume, low-pressure ETTs.

5.6.6 Reinforced Endotracheal Tubes in Pediatric Patients

A metal or nylon spiral stiffened wire is engulfed within the PVC or silicone tube wall, coming up with more resilience to kinking or constriction. The greater resilience may make fitting it into the pediatric airway tougher. If bitten, the tube can be divided or indelibly damaged. Reinforced tubes come in small sizes and are singularly useful for many neurosurgical procedures as they are resistant to surface load from instrumentation or positioning. Excessive flexion of the neck may cause intraoral kinking of PVC ETT; hence, one might elect to go in for reinforced ETTs in cases where this is a possibility. While cuffed reinforced ETTs are available down to size 6.0 ID, many manufacturers also market cuffless reinforced Magill tip ETTs without Murphy eye down to a 2.5 mm ID size. However, the availability of smaller-size reinforced ETTs locally may be an issue.

5.6.7 Frova Intubating Introducer

This introducer catheter [17] (Fig. 5.4) comes with a hollow lumen and has a blunt curved tip. It comes in 8 Fr size, which allows placement of endotracheal tubes down to 3 mm ID size. It has a stiffening cannula with two Rapi-Fit adaptors to connect ventilator devices (anesthesia circuit—15 mm connector or to the jet ventilator). The introducer is also available in 14 Fr for a 6 mm ID endotracheal tube.

5.6.8 Laryngeal Mask Airways (LMAs) and Other Supraglottic Airway Devices (SADs)

Supraglottic airway devices (SADs) have been integral parts of airway management in children. A supraglottic airway can be inserted to sustain oxygenation and ventilation in a situation of not being able to intubate and ventilate. With SADs, surgery can continue, depending upon the nature and duration of the surgery. SADs can be used as conduits [17–19] for endotracheal intubation with the help of pediatric fiberoptic bronchoscopes or tube exchangers (Fig. 5.5a–d). Fiberoptic visualization techniques have a greater degree of success in intubations through the intubating LMA due to epiglottic down-folding potential in children [19]. SADs also help in maintaining patency of the airway during emergence from anesthesia and following accidental extubation. If inadvertent extubation occurs,

SADs can be inserted for maintaining ventilation and oxygenation, not only in supine position but also in the lateral or prone position. SADs used in children (Table 5.5; Fig. 5.5a–d) are LMA Classic, intubating LMA (ILMA), ProSeal LMA [20], i-gel [21, 22], LMA Supreme [20], Ambu laryngeal airway [23], Air-Q [21], laryngeal tube (LT and LTS) [24], etc. ProSeal LMA, i-gel, air-Q, and LMA Supreme are widely used for maintaining patency of the airway with effective sealing pressures during the perioperative period in children [20, 21, 23]. SADs have also been shown to produce less cardiovascular responses to anesthesia during neurosurgical procedures [25]; however they cannot guarantee the prevention of aspiration and displacement during the surgical intervention [26].

5.6.9 Video Laryngoscope

Pediatric video laryngoscopes have been recently introduced and are available in different sizes for intubation in both normal and difficult airway scenarios [27]. The devices currently available include [27, 28] Airtraq, GlideScope, Storz C-MAC, Truview PCD, McGRATH [29], Pentax-AWS [30], and Ambu King Vision [31] (for larger children) and the Bonfils fiberscope [32] (Fig. 5.6). These video

Table 5.5 Supraglottic airway in children

Supraglottic airway in children	Different sizes available	Conduit for fiberoptic intubation
LMA classic	1, 1.5, 2, 2.5.3	Good
ProSeal LMA	1, 0.5, 2, 2.5.3	–
LMA supreme	1, 1.5, 2, 2.5.3	–
ILMA	3 can be used in larger children	Good
i-gel	1, 1.5, 2, 2.5,3	Good
Ambu LMA, Ambu AuraGain	1, 1.5, 2, 2.5.3	–
Air-Q	1, 1.5, 2, 2.5	Good
Laryngeal tube suction (LTS, LTSD)	0,1,2,2.5,	–

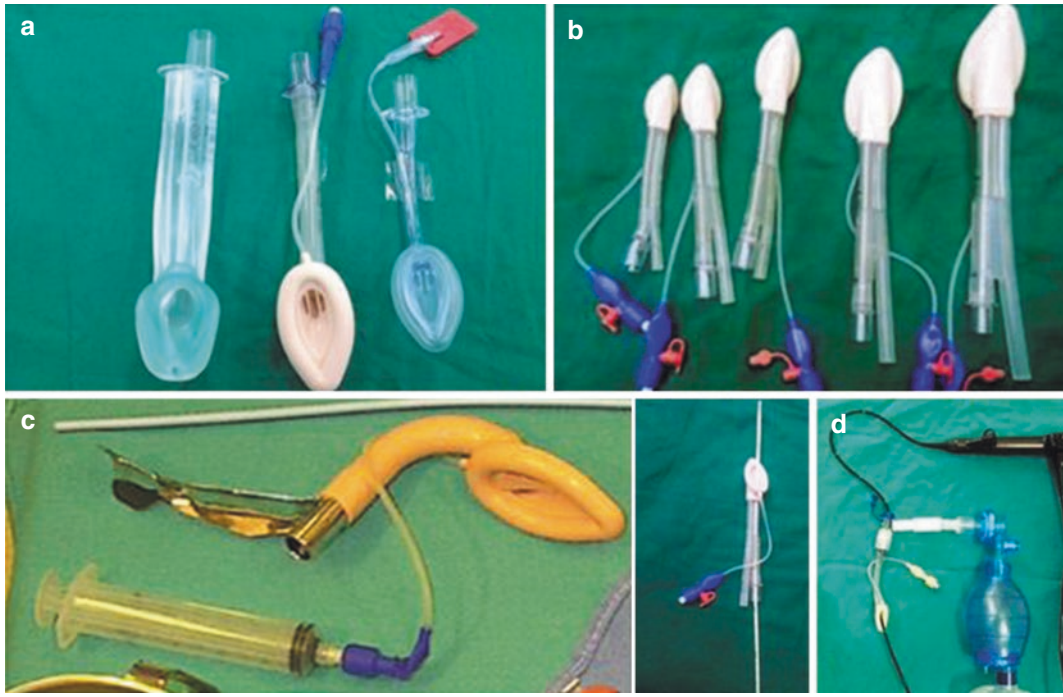

Fig. 5.5 (**a**, **b**, **c**) Different types and sizes of pediatric supraglottic airways. (**d**). LMA used as bridge to intubation with tracheal tube exchanger and/or fiberoptic bronchoscope

laryngoscopes are available with pocket monitors along with the scopes and/or can be connected to a standalone monitor/external monitor. Some of the video laryngoscopes have provisions for detachable blades (TruView, Pentax-AWS, King Vision, etc.). Airtraq and King Vision also have a channel to pass the tracheal tube. In a recent meta-analysis [33], video laryngoscope improved visualization of the glottis in pediatric patients but at the expense of prolonged times to intubation and increased failures. However, with experience and familiarity with the devices, video laryngoscopes can improve intubation success rates.

There are several advantages of video laryngoscope. They do not require hyperextension of the neck and permit intubation of patients in virtually any position, particularly in pediatric patients with cervical spine instability requiring manual in line stabilization. These cause minimal hemodynamic responses to intubation compared to conventional laryngoscopy and improved glottic exposure (Table 5.6).

5.6.10 Fiberoptic Bronchoscope

Fiberoptic bronchoscope (FOB) is considered to be the best method for intubating the (Fig. 5.7) uncompromised difficult airway [34, 35]. Fiberoptic intubation is not advisable in an emergent situation of compromised airway with desaturation. Children require induction with general anesthetic agents for fiberoptic intubation. Both inhalational and intravenous induction may be used in children with difficult airway, with the former being preferred because of better titration. If feasible, securing an IV access before induction with local anesthetics like EMLA cream is preferred. Under inhalational anesthetic, one has to perform fiberoptic intubation within a limited time frame while maintaining patency of the air-

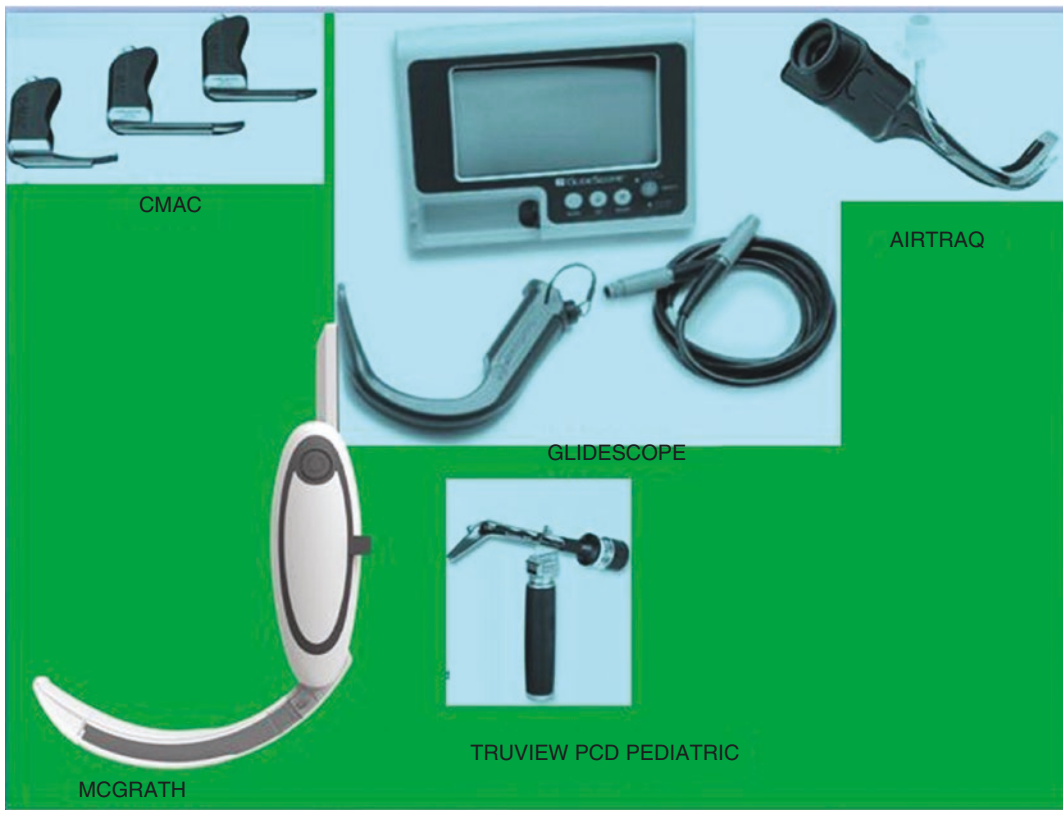

Fig. 5.6 Pediatric video laryngoscopes

Table 5.6 Pediatric video laryngoscope

Video laryngoscope	Pediatric sizes and specifications	Antifogging	Channeling
Airtraq	Infant, 2.5–3.5 ETT; pediatric, 4–5.5; small, 6.0–7.5); can be connected to smart phone	No	Yes
C-MAC (Storz)	Both pocket and standalone monitor, size, miller 0, 1; C-MAC, 2; D-blade pediatric	Yes	No
GlideScope AVL	Pocket monitor	Yes	No
Trueview PCD	Standalone, suction channel	No	No
Pentax-AWS	With a pocket monitor, also support external monitor. Size, 1. Infant, 2. Pediatric blade	Yes	Yes
McGRATH	Pocket monitor	No	No
Ambu king vision	Pocket monitor (size 3) can be used in larger child. Mouth opening of 1.5 cm can be intubated	Yes	Available in both blade
Bonfils rigid fiberscope	It is a rigid, straight fiberoptic device with a 40-degree curved tip and facilitates targeted intubation (retromolar approach). Requires an external monitor. Helpful in patient with limited mouth opening and cervical spine instability. It requires an initial training and is operator dependent	No	–

Fig. 5.7 Pediatric fiberoptic bronchoscope

way [36]. Various options are available to administer anesthesia during fiberoptic intubation procedures continuously. Usually a 3.7–3.8 mm FOB with a working channel is used for pediatric intubations in children above 1 year. Smaller sizes (2.2–2.5 mm ultrathin FOB with suction channels) are also available for intubation of neonates and infants. A nasopharyngeal airway with a 15 mm universal connector can be used to administer anesthesia and maintain the airway [37] during fiberoptic intubation. Oral intubation or nasotracheal intubation through the other nostril can be performed by this method. Video-assisted FOB [36] has also been described with an adult FOB. Methods involving the insertion of a guide wire through the working channel of an adult FOB can be performed for fiberoptic intubation in children [38, 39]. Specialized masks may also be used to continue administering anesthesia while conducting the fiberoptic intubation procedure in children [40, 41]. While performing mask ventilation with a nasopharyngeal airway, partially closing the pediatric breathing circuit's APL valve creates continuous positive airway pressure (CPAP). This helps to open the airway in syndromic children like those with Crouzon, Apert, Goldenhar, Klippel-Feil, Treacher Collins, Pierre Robin, and obstructive sleep apnea syndromes as well as CVJ anomalies. Spray as you go (SAYGO) technique is commonly used for airway anesthesia. In a situation of not being able to intubate and not ventilate (CICO/CICV), SADs can be used as a rescue device and as conduits [42] for endotracheal intubation with the help of pediatric fiberoptic bronchoscopes.

5.6.11 Pediatric Anesthetic Circuit During Neurosurgery

Jackson-Rees' modification of the Ayre's T-piece (JRMATP) system, by adding an open-ended bag, has been the most admired system for anesthetizing pediatric patients, with many advantages. The

bag serves as a respiratory monitor during spontaneous ventilation. It is easy to institute manual controlled ventilation and to apply PEEP.

In able hands the JRMATP is the best system for induction of anesthesia. The utilization of CPAP/PEEP props up the upper airway and boosts the ease of ventilation, though, in less adept hands, the T-piece may have its own problems. These include improper ventilation, inflation of the stomach, high peak inspiratory pressures, and barotrauma.

It is accepted practice to use adult circuits in pediatric patients more than 20 to 30 kg. To avoid carbon dioxide rebreathing under controlled ventilation, minimum required fresh gas flow can be calculated as 1000 + (200 × kg) (minimum 3 L/min), or 1.5 × minute ventilation. During spontaneous ventilation in pediatric patients, the end-expiratory pause is absent. The requirement of fresh gas flow is at least two times as that needed for controlled ventilation, which would work out to around thrice the minute ventilation.

The earlier versions of the circle breathing system were beset with problems like a high work of breathing owing to the resistance posed by the unidirectional valves. These problems are alleviated to a large extent in the modern circle systems. However, there are several other problems associated with the use of the circle system. A leak at the level of the endotracheal tube could make use of low flows difficult. The volume of the circuit is large, giving longer equilibration times than in adults. The compression volume of the tubing may alter aspects of ventilation. This can be avoided by using inflexible tubes and pediatric bellows. Circle breathing circuits meant for children do not preserve the temperature or humidity of inspired gases.

5.7 Pediatric Neurosurgical Patients with Difficult Airway

5.7.1 Rapid Sequence Induction

Emergency pediatric neurosurgical cases, like head trauma, raise the specter of a full stomach. This means that a rapid sequence induction (RSI) and intubation would be reasonable for this subset of patients. However, RSI can be very challenging in pediatric patients and can make the airway more difficult. This is especially true since many of these patients would need to be intubated along with manual in-line stabilization (MILS) of the cervical spine.

Older kids are habitually pre-oxygenated before the induction of anesthesia before RSI. Pre-oxygenation may not be easy to perform in very young kids, who may not accept a face mask deployment. High flow oxygen can be applied by a mask placed as close to the child's face as possible, to enrich the air drawn in with oxygen. The use of apneic oxygenation may be used for all pediatric patients considered at risk for difficult intubation.

If performed properly, direct laryngoscopy and intubation are safe in the pediatric patient with cervical spine injury. During intubation, the front portion of hard cervical collar can be taken out to facilitate the procedure.

5.7.2 Difficulty Securing the Airway

Halo fixation in pediatric patients (Fig. 5.8) suspected to have a cervical spine injury may aid in the workup and management of these patients. Pediatric trauma victims on halos pose a signifi-

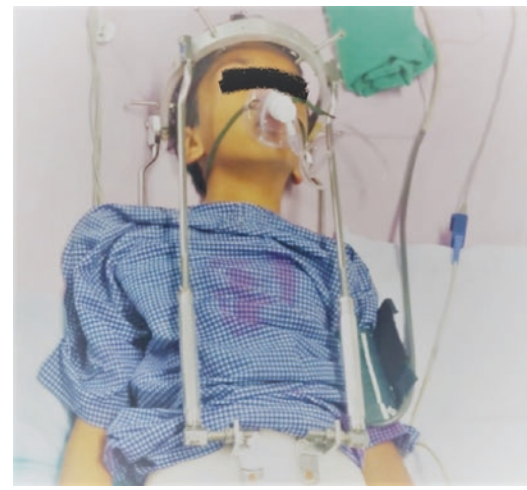

Fig. 5.8 Pediatric cervical halo fixation

cant airway dilemma for the anesthesiologist. The halo frame does not allow free access of the anesthesiologist to the pediatric airway, restricting craniovertebral junction (CVJ) movement. While supraglottic airway access may be feasible, its success would depend upon other anatomical factors of the individual child. In the backdrop of a non-emergent situation, fiberoptic bronchoscopy can be used for intubating these patients, notwithstanding the problems of conducting this in the pediatric age group. Still, during emergencies, these intubations can be extremely challenging. Sims and Berger [43] propose early tracheostomy in trauma victims with halos with other associated risk factors. A sudden airway emergency in the patient donning a halo frame is a grave catastrophe. In case of inability to intubate, use of bailout equipment such as the Bullard laryngoscope, LMA, ILMA, Combitube, GlideScope, and fiberoptic intubation could be options. Pediatric patients presenting for elective surgery with a halo in place need to have anesthesiologists skilled in various airway equipment attending on them. It is imperative that the neurosurgeon be available to quickly take out the halo if the airway is threatened. An alternate bailout plan for such "cannot oxygenate" scenarios must be in place for these children.

Stereotactic localization of lesions is also widely used in current neurosurgery. Utilization of stereotaxis is currently widespread for several indications. Having a calm and composed subject is vital to the success of these surgeries. Thus, children confer greater airway care considerations. The laryngeal mask airway may be used as the sole airway in children having these interventions supine. Just like with the halo frame, the anesthesiologist must be skilled in using a variety of airway devices and a must have a plan B ready, should problems arise.

5.7.3 Difficulty in Maintaining the Airway

Kinking of the endotracheal tube intraoperatively is a clear and present danger in many neurosurgical procedures. *Fish hook retractors* applied to skin flap during craniotomies for better exposure have been reported to result in kinking of polyvinyl chloride (PVC) endotracheal tubes [44]. *Positioning* during neurosurgery has often compromised the integrity of the PVC endotracheal tube. While this is common during positions other than supine, for example, prone positioning for posterior fossa or cervical spine surgeries, it can occur even with the patient supine, with change in head orientation, when the neck is flexed or due to excessive angulation of an endotracheal tube that is made soft by exposure to the patient's body temperature, typically, intraoperatively, after the surgery has commenced. Due to the very nature of their access, several specific surgical procedures can impinge on the endotracheal tube and kink it, and this can manifest at inopportune moments intraoperatively. These include *transnasal*, *transsphenoidal pituitary surgery*, *craniovertebral junction surgery*, and *trans-oral odontoidectomy* to name a few. While using a *reinforced endotracheal tube* may reduce the incidence of intraoperative kinking, whether they should be routinely used for all neurosurgical procedures, even when these are being conducted in supine position, is extremely debatable. Moreover, the availability of these tubes in the pediatric population is quite limited in the sizes that are typically required for the pediatric patient. This underlines the fact why careful attention to detail while positioning, to prevent excessive flexion of the atlanto-occipital joint, vigilance, and situational awareness during surgery are so important in pediatric neuroanesthesia practice.

Craniosynostosis consists of premature fusion of one or more cranial sutures. *Apert*, *Crouzon*, *and Pfeiffer* are the common syndromes associated with craniosynostosis [45]. *Apert syndrome* is an autosomal dominant disorder characterized by craniosynostosis, craniofacial anomalies, and the syndactyly of the hands and feet. Neurological involvement includes ventriculomegaly, hydrocephalus, and developmental delay. There is fusion of the cervical spine, mainly at C5–C6, a distinguishing feature from *Crouzon syndrome* (at the C2–C3 level) [46]. Upper airway obstruction can occur due to reduced nasopharyngeal

volume and choanal atresia. Obstructive sleep apnea and cor pulmonale may result because of this obstruction. They can have complete or partial cartilage sleeve abnormalities of the trachea and can cause lower airway compromise. Presence of midfacial abnormality and proptosis can make mask ventilation difficult. High resistance to mask ventilation can occur due to some degree of choanal atresia. A well-lubricated oropharyngeal or a smaller nasopharyngeal airway with CPAP is usually effective for bypassing the obstruction [45]. Inhalational induction with the maintenance of spontaneous ventilation is preferred in this group of patients. Though they have fused vertebrae, direct laryngoscopy is usually possible. FOB should be kept ready in case of failed laryngoscopy guided intubation. An ETT about one size smaller than predicted is preferred for intubation because of airway narrowing. Children who have undergone previous fronto-facial advancement surgeries can have difficulty during intubation because of reduced temporomandibular joint movement [47]. This group of patients would require fiberoptic intubation or tracheostomy. Postoperative tongue edema can occur due to prolonged neck flexion. Minimal changes in neck position during surgery, anti-edema measures, and extubation when fully awake over a tube exchanger will help prevent airway catastrophes during extubation. *Crouzon* and *Pfeiffer syndromes* also have similar facial appearances. Severe forms of *Pfeiffer syndrome* can lead to the closure of all the cranial sutures (cloverleaf skull deformity) [48].

Other congenital craniofacial abnormalities (a list of which is indicated in Table 5.7) that may alter normal anatomy are cleft lip and palate, whether or not associated with Pierre Robin syndrome (Fig. 5.9a), mandibulofacial dysostosis/Treacher Collins syndrome, arthrogryposis,

Table 5.7 Pediatric neurosurgical conditions that present with a difficult airway

Congenital anomalies predicting potential difficult airway		
Anatomical location	Syndrome	Anomaly
Head	Hydrocephalus	Macrocephaly
Mandible	Pierre Robin sequence Treacher Collins syndrome	Micrognathia Mandibular hypoplasia
Midface	Apert, Crouzon, Pfeiffer	Maxillary hypoplasia
Temporomandibular joint	Arthrogryposis Cocayane syndrome	Ankylosis
Mouth and tongue	Down's syndrome (trisomy 21) Mucopolysaccharidosis Freeman-Sheldon syndrome Neurofibromatosis Sturge-weber syndrome	Macroglossia Macroglossia Microstomia Masses obstructing airway Masses obstructing airway
Dental	Cocayane syndrome	Cocayane syndrome
Cervical spine	Klippel-Feil syndrome Down's syndrome Mucopolysaccharidoses	Limited mobility Instability Instability

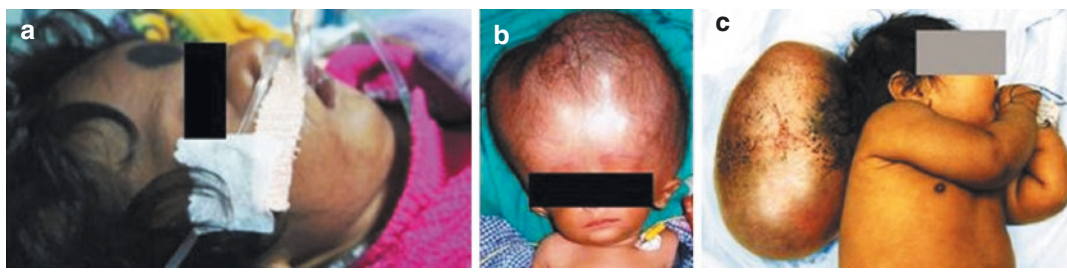

Fig. 5.9 (**a**) Pierre Robin syndrome; (**b**) hydrocephalus; (**c**) encephalocele

hemifacial microsomia, Cocayane syndrome, Klippel-Feil syndrome, mucopolysaccharidosis, Beckwith-Wiedemann syndrome, Freeman-Sheldon syndrome, and Down's syndrome.

Encephalocele is a neural tube defect causing protrusion of the brain and meninges through a defect in the cranium [48, 49]. When the size of the sac is larger than the head, it is called a giant encephalocele. Hydrocephalus is the most common complication of encephalocele (Fig. 5.9b, c). Occipital encephalocele is the more common presentation. The other sites are frontal, ethmoid, anterior, and cervical. Most commonly, intubation is done in lateral position in these cases [49]. Other maneuvers used are supporting the lesion within a doughnut, putting the head over the edge of the operating table while being held by other personnel, and ultrasound-guided needle aspiration to decrease the volume and content [50]. However, ultrasound-guided aspiration can cause brain herniation, hypoxia, and bradycardia during decompression of contents of the sac.

Meningomyelocele, cervical spine instabilities, CVJ anomalies, and endocrine disorders like acromegaly, Cushing's syndrome, etc. may also account for difficult airway scenarios in pediatric patients undergoing neurosurgical procedures.

5.7.4 Difficult Extubation

Awake extubation with the child fully active is preferred in children with difficult intubation and more so when a child undergoes neurosurgery. Following multiple attempts at endotracheal intubation, administration of dexamethasone 0.25 mg/kg IV to decrease the airway edema may be considered reasonable. Difficult extubation is expected in various clinical situations like intubation in a case of difficult airway; intraoperative airway deterioration like airway edema; tongue edema, which could be position-related, occurring commonly in the sitting and prone position; cervical spine implant fixation; and vocal cord edema and palsy during cervical spine surgery, intraoral surgery, prolonged procedures with fixed neck, procedures which have involved major fluid shifts, etc. In these situations, postoperative ventilation, initiation of anti-edema measures, and extubation performed over a tracheal tube exchanger [16] may be warranted. Before extubation, one needs to anticipate the possible causes which can compromise the airway. In case imminent reintubation is required, a fiberoptic-assisted reintubation (fiberoptic-guided visualization of vocal cord through one of the nostrils) with the passage of the tracheal tube over the tube exchanger may be performed, as blind intubation, even over the tube exchanger, can cause the ETT to hold up at the glottis. Accidental extubation in a pediatric neurosurgical patient with a difficult airway is a life-threatening situation. Laryngeal mask airway can be used as a rescue device in this situation.

5.8 The Pediatric Emergency Difficult Airway Cart

The purpose of having a pediatric emergency difficult airway cart (Table 5.8) for all units that operate on pediatric neurosurgical cases is to be able to mobilize airway equipment at a moment's notice, to deal with an unexpected difficult airway. Such ability may be invaluable in situations where one can mask ventilate, but not intubate while realizing that eventual airway control must be obtained at all costs. It could also be used in the cannot intubate, cannot oxygenate scenario.

5.9 Escape Route for Cannot Intubate, Cannot Oxygenate (CICO) Scenarios

In most children, a well-lubricated oropharyngeal airway or a soft seal nasopharyngeal airway bypasses the airway obstruction. In situations of not being able to intubate and ventilate, a laryngeal mask airway can be inserted if there is adequate mouth opening. In a predicted difficult airway, it might be worthwhile to mark the cricothyroid membrane and trachea before anesthesia induction. Ultrasound of the airway helps in identifying the cricothyroid membrane and tra-

Table 5.8 The pediatric emergency difficult airway cart

- Masks of different sizes (0, 1, 2, 3): Anatomical mask, PVC/silicon mask, Rendell-baker-Soucek (RBS) mask.
- Supraglottic airways (sizes: 1, 1.5, 2, 2.5, 3)
- Pediatric stylets
- Frova intubating catheter
- Pediatric tracheal tube exchangers (8, 11, 14 Fr size)
- Endotracheal tubes (sizes in ID: 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6)
- Laryngoscopes and video laryngoscopes
- Fiberoptic bronchoscope, guide wire, 1–2% lignocaine hydrochloride (2–5 ml)
- Pediatric suction and infant feeding tube
- Pediatric cricothyroidotomy and tracheostomy set
- Transtracheal jet ventilation with infant and pediatric modes (e.g., Manujet)

cheal rings. A large-bore IV cannula can be inserted through the cricothyroid membrane in children (below 6 years) or between the tracheal rings in case of infants [51]. This can be connected to a self-inflating bag or jet ventilator for sustaining ventilation and oxygenation. Oxygen delivery could be sustained up to the time a definite airway can be obtained. A decision to wake the patient up is taken or arrangements for a formal tracheostomy made. One needs to always allow ample time for expiration to occur during jet ventilation so that hyperinflation of the lungs is avoided during ventilation through the cannula inserted via the cricothyroid membrane. The Melker cricothyroidotomy-guided tracheostomy is associated with fewer complications than a scalpel-bougie technique in a cadaveric "infant airway" animal model [52]. ASA and Difficult Airway Society (DAS), UK, have formulated algorithms for difficult airway in a "cannot intubate, cannot oxygenate" (CICO) situation, which is more or less similar in both adult and pediatric patients [53].

5.10 Pediatric Tracheostomy

Pediatric tracheostomy in the neurosurgical setting may be warranted in an emergent setting of a CICO, as indicated above, if the child is less than 6 years of age, in which case, an emergency cricothyroidotomy may be contraindicated. It could also be undertaken in pediatric patients who are on long-term ventilation. However, unlike in the adult patient, there is no defined number of days for which a pediatric patient may remain intubated before deploying a tracheostomy tube. In the emergent setting, in children less than 6 years, emergency tracheostomy is typically preferred, as the cricothyroid membrane may be tiny and difficult to cannulate. In elder kids, needle cricothyroidotomy may be preferentially used rather than surgical cricothyroidotomy, mainly due to anesthesiologists' familiarity with this technique. Further, the percutaneous approach mitigates injury to the vocal cords and other important structures in the vicinity. The sizes and types of various tracheostomy tubes used in the pediatric population are given in Table 5.9.

5.11 Conclusion

Thus, pediatric airway management, whether routine or difficult, requires substantial foresight and training in children undergoing neurosurgical procedures. It is essential that such training be imparted upon every neuroanesthesiologist to ensure safe conduct of anesthesia for this vulnerable population. The difficult airway during neurosurgery not only is resultant of certain unique anatomical considerations that many of these pediatric patients have, including congenital conditions, but also depends on surgical considerations such as for the cervical spine, positioning issues, prolonged procedures, having the patient on specialized halos or stereotactic devices, the surgical access required for specific surgeries, etc. All this implies that the clinician handling

Table 5.9 Pediatric tracheostomy tube sizes

Brand and tube	Size	ID (mm)	OD (mm)	Length (mm)	MRI (yes/no)
Bivona					
• Neonatal cuffless and TTS cuffed	2.5	2.5	4.0	30	No
	3.0	3.0	4.7	32	No
	3.5	3.5	5.3	34	No
	4.0	4.0	6.0	36	No
• Neonatal Flextend TTS cuffed	3.0	3.0	4.7	32	No
	3.5	3.5	5.3	34	No
	4.0	4.0	6.0	36	No
• Pediatric cuffless and TTS cuffed	2.5	2.5	4.0	38	No
	3.0	3.0	4.7	39	No
	3.5	3.5	5.3	40	No
	4.0	4.0	6.0	41	No
	4.5	4.5	6.7	42	No
	5.0	5.0	7.3	44	No
	5.5	5.5	8.0	46	No
• Pediatric Flextend cuffless and TTS cuffed	3.0	3.0	4.7	39	Yes
	3.5	3.5	5.3	40	Yes
	4.0	4.0	6.0	41	Yes
Shiley					
• Neonatal cuffless	3.0	3.0	4.5	30	Yes
	3.5	3.5	5.2	32	Yes
	4.0	4.0	5.9	34	Yes
	4.5	4.5	6.5	36	Yes
• Pediatric cuffless	3.0	3.0	4.5	39	Yes
	3.5	3.5	5.2	40	Yes
	4.0	4.0	5.9	41	Yes
	4.5	4.5	6.5	42	Yes
	5.0	5.0	7.1	44	Yes
	5.5	5.5	7.7	46	Yes
• Pediatric cuffed	4.0	4.0	5.9	41	Yes
	4.5	4.5	6.5	42	Yes
	5.0	5.0	7.1	44	Yes

ID internal diameter, *OD* outer diameter, *MRI* magnetic resonance imaging compatibility, *TTS* tight-to-shaft, *LPC* cuffed with inner cannula, *CFS*, cuffless with inner cannula

the pediatric airway during the perioperative period should be adept with a wide range of airway equipment and be aware of the special challenges this vulnerable patient population poses.

Conflict of Interest Nil.

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6 Anesthetizing Pediatric Neurosurgical Patients: A Practical Approach

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Key Points

- There are many challenges unique to neurosurgical pathologies in the pediatric age group, thus necessitating a specialized approach in safe anesthesia delivery.
- A focused preoperative evaluation and assessment is an essential part of the composite anesthesia regimen, which has a significant bearing on overall outcomes.
- There have been gigantic strides in neuromonitoring techniques that have considerably increased the scope of pediatric neurosurgery.
- Tailoring the perioperative management to specific neurosurgical entities, being prepared for intraoperative catastrophes, and accounting for the interactions of the anesthetic agents with immature and developing organ system are important considerations for this patient population.
- Adequate care to ensure the process of smooth emergence from anesthesia as well as comprehensive postoperative management, including judicious use of pediatric neurocritical care modalities, goes a long way in improving patient care.

6.1 Introduction

The perioperative management of a child posted for a neurosurgical intervention is based on a robust understanding of the pediatric neurophysiology, the pathophysiologic effects of myriad neurosurgical entities, and the interplay between anesthetic drugs and cerebral pathophysiology in this subset of patients. From the preoperative period, until the child is discharged to the wards, the anesthesiologist's role is paramount in achieving the harmonious amalgamation of safe neuroanesthesia principles with high-end pediatric neurocritical care. There have been giant strides in modern-day neurosurgical practice, and it is imperative to develop high-level sub-specialty pediatric neuroanesthesia and neurocritical care to improve outcome measures. The ensuing treatise attempts to present practical aspects for the hands-on management of children presenting for neurosurgical procedures.

6.2 Preoperative Preparation

While evaluating children for neurosurgery, two significant evidentiary facts should be considered in the preoperative period, especially in emer-

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Table 6.1 Conditions with special anesthetic implications

Problem	Presentation	Anesthetic implication
Syndromes with associated airway anomalies	Usually well documented and anticipated	Difficult airway plans in place prior to induction
Respiratory illness	Usually have history of previous admissions or multiple hospital visits	History of steroids and bronchodilator drugs which may affect the anesthetic plan
Autistic child	Usually documented by the anesthetist during preop visit Parents can guide regarding the coping methods	Sedative anxiolysis Nonpharmacological methods like parental presence during induction of anesthesia (PPIA)/distraction Possibility of restraint may be discussed with the parents and due consent obtained Documented plan to abort anesthesia if needed
Cardiac comorbidities	Failure to thrive Cyanotic spells Frequent lower respiratory infections	Cardiology consult and ECHO Endocarditis prophylaxis Specialized centers if needed
Trisomy 21	History of noisy breathing or excessive drooling Behavioral issues and seizures	Evaluation for coexisting cardiac and noncardiac conditions Documentation of atlantoaxial stability/instability
Prematurity	History of chronic pulmonary disease Failure to thrive Frequent seizures and developmental delays Gastroesophageal reflux disease (GERD)	Anticipate perioperative apnea and bradycardia <60 weeks' gestational age needs mandatory postoperative observation with oximetry

gency conditions. First, neonates and infants have the highest risk of mortality and morbidity during the perioperative period [1]. Second, respiratory and cardiac events account for most of the anesthetic complications in children [2]. A pediatric neuroanesthesiologist should always be wary of the neurosurgical entity necessitating surgery in the neonatal and infantile age groups and keep a careful watch for common comorbidities in the pediatric age group known to have disastrous consequences. A tabular format of such common conditions in the children presenting for surgery has been given as a ready reckoner (Table 6.1). Preoperative checks and operating room preparation have special significance in ensuring patient safety in this highly susceptible patient population. These aspects and anxiolysis in children with varied and obtunded neurological symptomatology are covered in more detail next.

6.2.1 Preoperative Checks

6.2.1.1 Preoperative Assessment

While preoperative evaluation is covered in Chap. 4, the practical points while assessing children during the preoperative period are covered consequently. Children presenting for neurosurgery essentially fall under any of the following categories: (a) those who are systemically well and require minimal assessment, (b) children with debilitating inborn diseases and rare syndromes which mandate a discrete and individualized preoperative management, and (c) otherwise fit children presenting for emergency surgery who exhibit rapid clinical deterioration—adequate care and vigilance is necessary for such children to avert catastrophes and facilitate urgent preoperative optimization and stabilization of the overall clinical condition. Also, psychosomatic issues are common in children presenting for neurosur-

gery and have a predilection toward complicating the anesthetic course, especially during induction and in the postoperative period [3–5].

As most neurosurgical procedures are emergencies, a comprehensive preoperative assessment is not always possible. Considering systemic effects of general anesthesia (GA) and the inherent stress because of surgery, it is advisable to assess the individual organ system in tandem with the developmental stage. Because some children would not have fully acquired the faculty of speech and may not fully comprehend their medical illness, in more cases than not, it becomes vital to establish meaningful communication with either their parent or primary caregiver. A detailed patient history goes a long way to identifying patients who would benefit from a focused evaluation and optimization in the preoperative period. As in standard anesthesia practice, the investigative modalities employed in the preoperative phase should be based on the history, clinical signs, and the neurosurgery planned.

A child's neurologic condition varies greatly and should dictate the specifics of the preoperative assessment. A relevant example would be wariness of latex allergy symptoms in children undergoing multiple neurosurgical procedures, especially in children with meningomyelocele [6]. Dehydration, fluid and electrolyte anomalies, obtunded upper airway reflexes, and use of steroids and antiepileptics are the specific points of interest while examining a neurologically injured child during the preoperative period. Especially in children on antiepileptic drugs (AEDs), therapeutic levels of AEDs and hematologic and hepatic systems' affliction because of long-term use and interactions with anesthetic agents assume significance [7, 8].

The preoperative examination should include a meticulous central nervous system (CNS) examination, especially because postoperative neurologic function vis-à-vis the preoperative state plays a vital role in the neurosurgical decision-making during the postoperative period. A note should be made of signs and symptoms of the brain stem and CNS dysfunction, muscle power, bulk and weakness, physical signs of dehydration, and recording an accurate body weight to facilitate judicious use of anesthetic drugs, intravenous (IV) fluids, and blood products [9].

One should be more vigilant while dealing with emergency surgery because of the unplanned nature, and consequent probability of more blind ends and a tumultuous course during the management of these cases. A neurologically deteriorated, fearful, or a child in pain may be easily mistaken for a quiet or shy child. Any signs of underlying critical illnesses like tachypnea, recession, grunting, accessory muscle use, gasping, bradycardia, or a prolonged capillary refill time should be sought after. Such a child should be resuscitated and optimized either before or during the surgery to avoid hemodynamic and cardiorespiratory catastrophe. Adhering to the ABC framework keeps things simple and ensures adequate stabilization of a decompensated critically ill child before anesthetic induction. Especially in emergent situations, a risk-benefit decision should be taken in inadequate fasting, and rapid sequence induction should be planned. Bradycardia and reduced consciousness are usually terminal signs and should herald ominous warning bells for severe intracranial hypertension and consequent herniation.

6.2.1.2 Fasting and Consent

The importance of preoperative fasting and instructions regarding regular medication cannot be overstated. There are many reasons to encourage clear fluids up to 2 h before surgery [10, 11]. These include the fact that infants and small children cannot tolerate dehydration, nausea and vomiting are more frequent in prolonged starvation, and hypoglycemia can be avoided. There is a paradoxical increase in gastric secretion after prolonged fasting, and children become more irritable at induction.

The preoperative visit should be utilized to obtain consent for the procedure from the parents, nearest blood relatives, or the legal guardians. Adequate time and effort should be devoted to explaining the surgical procedure and anesthesia techniques clearly and the potential perioperative complications [3]. The perioperative sequence of events to the parent/custodian and, if

possible, to the child should be explained clearly. All concerns and questions that the parents and guardians have should be addressed adequately. In addition to the verbal information and use of written preoperative directives, it is mandatory to reduce confusion and increase compliance [3].

6.2.1.3 Radiology and Labs

A review of the neuroradiological scans in conjunction with the neurosurgical team is important to confirm the primary pathology, associated conditions such as hydrocephalus, compressed cisterns, and midline shifts as well as to plan the intraoperative positioning and other ergonomic issues [12]. Preoperative laboratory tests should include the hematocrit, coagulation parameters, and electrolytes as these patients may be receiving decongestant therapy or may be prone to dyselectrolytemia due to intracranial pathology. Adequate blood product estimation and preparation are important preoperative steps, as is an endocrinology evaluation in children with suprasellar pathologies [12]. In children on long-term anticonvulsants, preoperative liver function tests and a coagulation profile assume significance.

6.2.1.4 Checklist

The impact of iatrogenic diseases and human error on patient safety came to the forefront in medicine only at the turn of last century with the publication of a seminal treatise by the Institute of Medicine—"To Err is Human: Building a Safer Health System" [13]. A landmark event in improving patient safety was the publication of the WHO Surgical Safety Checklist in 2009 [14].

There has been an increase in the use of checklists throughout all specialties of medicine in the last decade, especially in the realm of surgery, anesthesia, and critical care [13, 15, 16]. However, evidence on the use of preoperative checks in pediatric neurosurgical patients is less common [17, 18]. Institutions should develop pediatric checklists, especially for the common neurosurgical procedures. The aim should be to adapt universal WHO surgical safety checklist principles while including points specific to the pediatric age group (e.g., checking for parental involvement) and the aspects specific to the pathology itself (e.g., check for prior chemotherapy, radiotherapy, or dural resection in tumor surgeries). An illustrative example is given in Fig. 6.1; the utility of such checks needs to be validated further.

6.2.1.5 Anxiolysis on Day of Surgery

Confirmation of fasting, reviewing the preassessment record, and a change in the child's clinical status should be a mandatory protocol in all pediatric neurosurgical units. A child-friendly environment and allowing the child to enter the theater zone in his own clothes, if possible, go a long way in establishing a rapport between him and the anesthesiologist. Premedication, including sedatives for anxiolysis, should be considered on an individual basis [5].

An uncooperative child is frequently encountered in anesthesia practice, sometimes requiring physical restraints during anesthesia induction [19, 20]. Anxiety because of an alien environment, painful procedures, hospital personnel in scrubs, or just the fear of parental separation is at the root of this behavior. It must be addressed with due sincerity to ensure compliance during the induction of anesthesia [21].

Postoperative behavior changes may be related to these stressful experiences, which, though transient in most cases, may sometimes persist, thus being a cause of concern for both the parent and the treating neuroanaesthesiologist [22]. Apart from age, other factors predicting heightened anxiety are the child's temperament, anxious parents, a preceding morbid hospital stay, and a previous vaccination-related unpleasant experience. A shy, inhibited, dependent, and/or withdrawn child is a definite red flag [5]; contrary to popular belief, gender does not play a role in predicting anxiety.

Psychological interventions like presurgical programs, play therapy, and parental presence during induction of anesthesia (PPIA) have been tried as potential strategies to allay anxiety prior to induction along with distraction (for IV) or engagement (for inhalation) at the time of induction [22, 23]. Although parental presence may be useful in reducing their own stress, the same may not hold true for the child being anesthetized.

Fig. 6.1 Illustrative preoperative checklist to be filled by the child with the help of the caregiver

Small infants [weight < 5 kgs], anticipated airway problems, critically ill children, and emergency procedures should ideally be excluded from this approach [24].

The use of sedatives given in the preinduction period significantly reassesses the transition from the holding area into the operating room. Midazolam remains the most commonly used pharmacological agent to allay anxiety, reliably providing sedation and anxiolysis at induction and a much calmer child postoperatively. An oral dose of 0.5 mg/kg usually initiates sedation within 5–10 min (peak 20–30 min) and lasting up to 45 min to an hour. The IV route of midazolam (0.1–0.2 mg/kg) may be preferred in children with features of raised ICP, especially when such access has been established, as the response is more predictable and quicker. However, it should be administered only under monitoring as CO_2 retention may cause catastrophic decompensation, and one should watch out for paradoxical agitation, which has sometimes been reported [25].

Supervision is mandatory even with the oral route of administration of midazolam with its superior safety threshold. Hence, the drug administration is usually withheld until the child arrives in the theater's safety. Reduced crying associated with this medication is particularly beneficial in children with vascular lesions where any agitation can be catastrophic but may be a delicate issue in a child with raised ICP (decreased consciousness, irritability, lethargy, failure to feed, bulging fontanelle, and cranial enlargement) as it may potentially unleash a vicious cycle of hypercapnia and intracranial hypertension by its negative impact on the medullary respiratory center. Analgesia-sparing effects are, however, speculative. Other routes are intranasal and rectal but do not usually find favors due to poor patient compliance [12, 25, 26]. Oral lorazepam and temazepam have also been tried (Table 6.2) in older children who require doses beyond midazolam safety ceiling, especially in longer surgeries [23].

Clonidine is another sedative with an excellent therapeutic index and minimal hemodynamic changes in healthy children. Administered orally (4 μg/kg) or intranasally (2 μg/kg), it provides preoperative anxiolysis, acts as an analgesic, decreases the requirement of volatile agents (hence a favorable impact on the CBF), and improves hemodynamic stability [26]. The IV preparation is tasteless and can be administered orally. Oral transmucosal fentanyl (given as lollipops) is an approved alternative and provides excellent conditions at induction. However, its use is constrained by the frequent occurrence of pruritus and vomiting, as well as the potential risk of respiratory depression [23, 27].

6.2.2 Operating Room Preparation

Apart from the standard operating room preparation before any neurosurgical procedure, specialized modifications are required for pediatric surgery, starting from the modalities to maintain body temperature to resuscitate the child. Before receiving the child in the operating room (OR), the temperature must be maintained in the range of 25–27 °C. Adequate warming apparatuses like warm blankets, air mattresses, or forced air devices, fluid warmers, etc. need to be available and set at appropriate temperature values. It is always advisable to prepare the IV fluid of choice in the correct amount according to the body weight, especially if a neonate is to be operated on. Adequate infusion sets and infusion pumps should be available, loaded with correctly labeled syringes. The anesthetic drugs should be calculated and prepared beforehand, considering the amount of fluid in each syringe. Some anesthesiologists prefer to have a leaflet of measurements and drug dose calculations for each patient ready in the OR beforehand to avoid miscalculations in stressed conditions. It is always advisable to use low-volume syringes (1 ml, 2 ml, and 5 ml) to prepare injectable medications to limit the volume of fluid infused through them, especially in babies prone to get volume overloaded easily. Pediatric-size equipment for positioning should be present beforehand according to the surgeon's discussion regarding the surgical procedure.

The monitor parameters and alarm limits, anesthesia workstation ventilator settings, and breathing circuit should be objectively tailored to

Table 6.2 Summary of anxiolytic premedicants

Agent	Dose and route	Onset	Duration	Contraindications	Special remarks
Midazolam	0.25–0.75 mg/kg (oral) 0.05–0.15 mg/kg (IV) 0.2–0.3 mg/kg (intranasal) 0.5–1.0 mg/kg (rectal) 0.2–0.3 mg/kg (sublingual)	Approx. 20 min on oral administration	45 mins	Emergency surgery Upper airway disease Hepatic/renal derangements Respiratory depression	Paradoxical reactions on IV administration Burning sensation after intranasal spray
Lorazepam	50–100 μg/kg (oral) in children 5–12 years; 1–4 mg (oral) in children 12–18 years	60 min	8–12 h (peak at 2 h)	Respiratory depression	Preferred in bigger children and longer procedures
Temazepam	10–20 mg crushed tablet or as elixir	60 min			
Fentanyl	15–20 μg/kg (transmucosal)	15–20 min			Vomiting Pruritus Respiratory depression
Clonidine	4 μg/kg (oral) 2 μg/kg (intranasal)	30–60 min	6–10 h (peak 2–4 h)	Bradyarrhythmia	Analgesia Anesthesia sparing

IV intravenous

the weight- and surgery-specific intraoperative requirements. The airway and intubation devices should be checked and laid out properly in a separate trolley for easy access. Care should be taken that adequate-size IV cannula is available in sufficient numbers and appropriately sized adhesive tapes are available to secure them. Proper oxygenation and transport equipment/devices should be ready for the child's swift shifting to the postanesthesia care unit (PACU) or pediatric intensive care unit (PICU).

On arrival in the OR, the patient surgical safety checklist should be filled confirming the identity, surgery, surgery site, etc., and standard monitoring should be attached to the child. Anesthesia should be induced with IV medications if the venous access is in place, or one should proceed with inhalational induction in the absence of an IV line.

6.3 Intraoperative Management

6.3.1 Vascular Access

All children presenting for neurosurgery require a properly functioning peripheral IV access appropriate for the neurosurgical entity and its expected perioperative course. In an emergency, intraosseous access should be considered early [28]. Considering the difficulty in obtaining IV access in children as well as the morbid and prolonged nature of hospital stay in children, the choice and site of central venous access should be a carefully weighted one. The decision to institute central venous access in the OR should be based on issues such as expected blood loss/fluid shifts/electrolyte imbalances, procedures at high risk for venous air embolism (VAE), diabetes insipidus (DI), and severe neurological impairment (traumatic brain injury, tumors) expected to require prolonged inotropic and ventilatory support.

A crucial consideration during the placement of IV access is to be mindful of and take effective steps to allay the child's anxiety. Parental presence, breastfeeding, distraction techniques, local anesthetic (LA) creams, and oral sucrose have been shown effective in reducing anxiety and procedural pain during IV access in children [29–32]. Tourniquet, tapping over the vein, local warming, transillumination, and near-infrared devices are established aids that should be considered routine in pediatric neuroanesthesia setups [33–35].

Sedation, GA, and strict asepsis are essential for any procedure establishing central venous access [36–38]. Among the various routes, the internal jugular vein (IJV) and subclavian vein (SCV) are the most preferred central venous catheter (CVC) placements in pediatric neuroanesthesia. However, the femoral route does provide ease of access, lack of interference with cerebral venous return, and avoidance of pneumothorax [39]. In all types of vascular accesses, peripheral, central, and arterial, the role of ultrasound (USG) is well established. USG-guided cannulation is highly useful in guiding catheter placement and determining the appropriate catheter size, confirming catheter-tip placement, and preventing catheter-related complications [40].

In difficult IV access cases in critical scenarios, intraosseous (IO) access is a rapid alternative with a high success rate [29]. In younger children, the proximal tibia, anteromedial aspect, is preferred, whereas, in older children, the distal tibia is a good site [29]. The technicalities of achieving arterial access in children are the same for adults, except that in newborn babies, the umbilical artery also presents itself as a viable option [41].

6.3.2 Induction of Anesthesia

The goal of anesthetic induction is to avoid intracranial hypertension because of associated hypoxia, hypercapnia, and inhalational agent-induced increases in cerebral blood flow (CBF) while avoiding a significant decrease in blood pressure (BP) [42]. The use of thiopentone, propofol, and neuromuscular blockade is commonly practiced in neurosurgery; however, etomidate may be preferred in unstable hemodynamic states [43–45]. Except for ketamine, all IV induction agents cause a reduction in ICP [46, 47]. Inhalational induction with sevoflurane should be preferred in children without IV access or with difficult IV access. The concomitant use of hyperventilation should blunt its effect on increasing ICP. Additionally, sevoflurane has shown beneficial effects on regional cerebral oxygenation and lesser myocardial depression than less-irritant agents such as halothane [48, 49]. In full stomach scenarios with a high risk for gastric aspiration, rapid sequence anesthetic induction with thiopentone or propofol followed by rapid-acting muscle relaxants such as succinylcholine/rocuronium should be practiced. Succinylcholine is contraindicated in spinal cord injury and denervation syndromes; rocuronium is an ideal alternative for rapid sequence induction (RSI) in these cases [50, 51]. The effect of the individual anesthetic agents on neurophysiology is covered in Chap. 3.

Once IV access is secured, boluses of thiopentone (1–2 mg/kg) or propofol can be used to decrease the laryngoscopy response [38]. As all volatile anesthetics increase the CBF, and consequently, the ICP, efforts should be instituted to control ventilation as early in the course of anesthesia as possible.

6.3.3 Intubation (Airway Management)

The principles of airway management in children presenting for neurosurgical procedures have been covered in great detail in Chap. 5. However, from a practical standpoint, this crucial aspect requires an amalgamation of the knowledge of airway peculiarities in the pediatric age group and a high skill level in the use of various airway equipment. It is also imperative to consider the potential interactions of such management with the neurophysiological variables [52–55]. These challenges are further magnified by disease-related distortions of airway anatomy in children presenting for specific neurosurgical procedures (hydrocephalus, craniosynostosis, craniovertebral junction anomalies, etc.). In these patients, especially in view of intracranial hypertension, airway management should be tempered by concomitant use of opioids and hypnotics to avoid any increase in ICP stringently.

The use of cuffed endotracheal tubes (ETTs) is increasingly frequent in pediatric neurosurgery, and there is evolving evidence to suggest an association of uncuffed tubes with subglottic mucosal trauma and laryngospasm especially in

the event of selecting inappropriately larger tube not taking into account the height and weight of child [53, 56]. In cases where cuffed ETT is used, processes should be developed to monitor and adjust cuff pressure [53] routinely.

While oral and nasal routes are used for intubation, the oral route is more extensively used, and the nasotracheal route is limited exclusively to specific indications in pediatric neurosurgery. The nasal route of intubation is especially preferred in complex craniofacial surgeries and some procedures performed in the prone position in small children requiring small-size endotracheal tube. In this group of children, it offers the advantage of increased stability, comfort, and the low propensity of intraoperative kinking in their tiny oropharyngeal cavities [57]. In conditions where nasotracheal intubation is planned, use of topical vasoconstrictors (0.25% phenylephrine or oxymetazoline on cotton-tipped applicators) and gentle dilatation of nares go a long way in decreasing the risk of a nosebleed [58]. However, nasal intubation is contraindicated in the transsphenoidal procedure, choanal stenosis, basilar skull fracture, and sinusitis. Some practical tips during the use of nasotracheal routes include keeping the tube's direction toward the chin and using sutures and wires to secure the tube in prolonged complex neurosurgical and craniofacial procedures.

Especially in neurosurgical positions requiring extreme neck flexion and twisting, the tube's proper length to be fixed should be decided in conjunction with the neurosurgical team to avoid inadvertent migration of the ETT during the procedure. Notwithstanding the intubation route, it is imperative to check for bilateral equal air entry after final positioning and secure the tracheal tube with care and caution to avoid intraoperative airway disasters in a compromised position with limited airway access. In cases of inadvertent extubation, direct laryngoscopy is the go-to rescue airway technique. However, in limited-access conditions, an adequately sized LMA is an important adjunct to maintain oxygenation and ventilation [59]. In "cannot intubate, cannot ventilate" situations during induction as well as in intraoperative airway disasters, the protocols are nearly the same as for an adult population except that a surgical approach is preferred in children <5–6 years of age as the compressible nature of structures precludes a needle cricothyrotomy [60].

The process of extubation in pediatric neurosurgery presents its own set of peculiar considerations. While there is a predilection toward extubation in a deeper plane, the evidence lacks that such a process results in significantly better effects on neurophysiological variables [61–63]. Besides neurosurgical pathologies hampering respiration (e.g., posterior fossa lesions, Chiari malformations), another phenomenon interfering with extubation includes airway edema, macroglossia, and pre-existing pulmonary dysfunction [64, 65]. Generally, an awake child adhering to extubation criteria is a good candidate for the same [66]. However, in problematic cases, prolonged ventilation, head up positioning, and diuresis may need to be employed to mitigate airway edema, while tracheostomy may be needed in severe unresponsive cases [67–69].

6.3.4 Maintenance of Anesthesia

There is ample evidence showing that low exhaled inhalational agent concentration with mild hyperventilation has favorable effects on ICP [39]. There is very little to choose between the use of total IV anesthesia (TIVA) and the administration of volatile agents at the minimum alveolar concentration (MAC) less than 1 (sevoflurane, isoflurane, desflurane). More often than not, a combination of these modalities is used and is acceptable. Opioids such as fentanyl or remifentanil, with or without nitrous oxide, and ventilation with neuromuscular paralysis are part of the standard anesthetic regimen [39, 70]. Halothane, on account of being a potent cerebral vasodilator and consequent intracranial hypertension, is currently out of favor in neuroanesthesia. Sevoflurane is the established agent of choice for inhalational induction. For maintenance of anesthesia, while TIVA is commonly practiced, among inhalational agents sevoflurane and desflurane are preferred to isoflurane because of

their superior recovery profile [70, 71]. Nitrous oxide has been shown to increase ICP and cerebral metabolism, increase the propensity of postsurgery pneumocephalus as well as postoperative nausea and vomiting (PONV) and interfere with intraoperative neuromonitoring. Hence, its routine use may be discouraged in pediatric neuroanesthesia.

While choosing a muscle relaxant, train of four (TOF) monitoring is useful to maintain optimal neuromuscular blockade. The choice of the agent should be based on individual patient characteristics. However, in surgeries requiring intraoperative neuromonitoring (IONM) and intraoperative wake-up (e.g., during spinal cord surgery), the muscle relaxant regimens need to be tapered or abolished completely for a transient period. Subsets of patients on antiepileptic medications usually require larger than normal doses of non-depolarizing muscle relaxants and opioids because of hepatic enzyme induction.

Whereas fentanyl is a commonly used opioid, an increasing half-life on repeat dosing precludes its use in preterm infants with immature hepatic metabolism owing to the possibility of prolonged sedative and respiratory depressive effects. Remifentanil infusions offer the benefit of rapid recovery; however, it is associated with delirium and suboptimal analgesia. There is an increased use of α2-agonist dexmedetomidine in pediatric neurophysiologic monitoring, certain specific procedures such as awake craniotomies, and facilitation in the rapid wake-up after surgery [72–75]. For a detailed effect of anesthetic effects on CNS physiology, the reader is referred to Chap. 3.

6.3.5 Monitoring

The details of monitoring both routine and IONM are interesting and covered in detail in Chap. 8; some salient practical points are highlighted in the next few paragraphs.

An electrocardiography, pulse oximeter, noninvasive BP, sphygmomanometer, capnograph, and a thermometer comprise minimal monitoring for pediatric neuroanesthesia. While instituting neuromuscular blockade monitoring, it is important to remember that nerve stimulator should be placed at a normal neurologic function site to avoid overdosing, which might go undetected if a neurologically depressed nerve is chosen. In surgeries at high risk for venous air embolism (VAE), precordial Doppler ultrasound is recommended. A precordial Doppler, used in conjunction with capnography and arterial catheter, helps detect even minute VAEs. The site just on the right sternal border at the fourth intercostal space on the anterior chest is the best location for the Doppler probe [76]. In surgeries planned for IONM, electroencephalogram (EEG) and other electrophysiological paraphernalia need prior installation in closed coordination between neurosurgeon, neuroanesthesiologist, and neurophysiologist. Urinary output should be measured during prolonged procedures, in cases with anticipated large blood loss, and when diuretics or osmotic agents are administered [76].

6.3.5.1 Hemodynamic Monitoring

Pediatric neurosurgery warrants intense hemodynamic monitoring because of the risk of hemorrhage, VAE, herniation, or brain stem manipulation. Arterial cannulation is the cornerstone of hemodynamic monitoring in such cases. In addition to providing a real-time account of blood pressure, it allows sampling for serial measurements of blood parameters, thereby influencing appropriate metabolic, fluid, and blood component management. The arterial transducer should be ideally zeroed at the level of the head (lateral corner of the eye or the external auditory meatus) to provide an accurate mirror of cerebral perfusion pressure (CPP) [57].

The use of central venous catheters as a vascular access device has already been discussed. The fact that neither do they reliably predict intravascular volume, nor do they seem to be effective in aspiration of air in the event of VAE, has discouraged routine use of a central venous catheter (CVC) in children [77]. However, as reiterated before, CVC (subclavian, IJV, or femoral) might be required in certain neurosurgical scenarios, especially in surgeries expected to have significant blood loss and hemodynamic perturbations [78–80].

6.3.5.2 Neurophysiologic Monitoring

Advanced neurophysiologic monitoring, monitors of cerebral oxygenation, and seizure detection modalities (electrocorticography (ECoG), EEG, electromyography (EMG), transcranial Doppler (TCD), somatosensory evoked potentials (SSEP), motor evoked potentials (MEPs), etc.) are an important cog in increasing the safety profile in cranium and spine surgeries. These are dealt with in more detail elsewhere (Chap. 8). The ergonomic considerations of instituting such monitoring and interaction of anesthetic regimens with such monitoring are important in the perioperative period.

6.3.6 Positioning

The small size of children and the intricacies of neurosurgical access make positioning in pediatric neurosurgery a challenging paradigm. The physiologic effects, indications, and salient points of different neurosurgery positions are similar to those in adults and are elucidated in detail in Chap. 7. Specific implications of positioning in children include generous use of padding, avoidance of head pinning systems in the neonate and small infants, proper positioning of instruments and grounding wires, pinpoint positioning of the tracheal tube in the airway, access to the airway and vascular ports under drapes, and avoidance of extreme head positions with a propensity for brain stem compression and cervical spinal cord ischemia [57, 81]. Positioning is an integral part of neuroanesthesia care and is covered in detail in Chap. 7.

6.3.7 Fluid and Blood Component Therapy

Blood component therapy in pediatric neurosurgery should elicit close cooperation between the anesthesiologist and the neurosurgeon. Important factors to consider would be the preoperative hematocrit, the child's weight, the location and type of surgical pathology, and comorbidities affecting tissue oxygenation. Especially in surgeries where life-threatening bleeding is expected, a clear management plan encompassing blood conservation strategy, an accurate estimation of ongoing blood loss, and keeping blood products ready and accessible are critical to the overall outcome of the surgery [82]. Assessing ongoing blood loss in neurosurgery, especially in children, is an onerous task because of drapes and use of Mayo trolley. Use of overhead cameras, monitoring of suctioned blood in calibrated containers, serial hematocrit estimations on arterial blood gas (ABG) analysis, and monitoring of coagulation parameters on thrombo-elastography (TEG) are recommended to guide blood component therapy [57]. There is no definite transfusion threshold. Factors enumerated before should be used to decide when to transfuse. However, blood product administration usually commences at a hematocrit of 21–25%, to which point of time losses should be managed by crystalloids and colloids [39].

The intricacies of fluid management will be covered in Chap. 10. However, it is important to understand that perioperative fluid management affects cerebral blood flow, potentially worsens brain edema, and affects electrolyte and glucose homeostasis. Generally speaking, normal saline is a common fluid in perioperative pediatric neurosurgery, barring premature infants in whom glucose-containing solutions assume significance [83]. However, certain caveats to the routine use of normal saline are beyond the scope of this chapter. Especially in lesions affecting the pituitary, such as craniopharyngioma, alternative IV fluids may need to be considered [84]. The routine use of cerebral decongestant therapy in mannitol and hypertonic saline also greatly affects perioperative fluid therapy. Simultaneously, loop diuretics have a place only in the scenario of fluid overload [57].

6.3.8 Glucose Homeostasis

Children are at significant risk of developing and suffering the disastrous effects of hypoglycemia. These are more pronounced in premature infants and sick neonates due to their limited gluconeo-

genesis and scarce glycogen reserves. The increased vulnerability of children to perioperative hypoglycemia necessitates stringent monitoring of glucose levels and may mandate continuous infusions of glucose at a rate of 5–6 mg/kg/min if blood glucose levels drop below 60 mg/dl [85]. At the other end of the spectrum, the relative insulin resistance caused by the stress response to surgery and critical illnesses has a high propensity to cause hyperglycemia with deleterious effects in the neurologically injured patients in the setting of cerebral ischemia [86, 87]. There is no doubt that hyperglycemia causes significant secondary damage to the already neurologically compromised brain, but a tight glycemic control with resultant hypoglycemia has shown no advantage either [88]. More recently, there has been a trend to steer clear of tight glycemic control practice because of significant evidence of the detrimental effects of resultant hypoglycemia [89]. In the present scenario, it is pertinent to diligently monitor and maintain the blood glucose levels at a conservative value of less than 180 mg/dl in an attempt to thwart the disastrous effects of hypoglycemia resulting from tight glycemic control, keeping in mind the vulnerabilities of the pediatric age group.

6.3.9 Temperature Regulation

Whereas thermoregulation is discussed in Chap. 9, preserving body heat in children during anesthesia is vital to decrease oxygen consumption and prevent hypoxemia. Maintenance of OR temperature of 25–27 °C, warm air convection blankets, heater humidifiers in the breathing circuit, overhead heaters, heating mattresses, and fluid warmers are effective strategies to regulate body temperature [90].

On the other end of the spectrum, despite favorable effects in traumatic brain-injured children, the incidence of complications such as coagulation abnormalities prevents the routine use of hypothermia in pediatric neurosurgical practice [91]. Hence, normothermia using active warming modalities is the intraoperative temperature goal [91].

6.3.10 Intraoperative Complications

Major adverse events in children undergoing neurosurgery are an important cause of morbidity and mortality associated with these procedures. The intraoperative complications might be surgical, anesthesia-related, pathology-related, or a result of the underlying critical illness. These complications are reported in up to 40–50% of cases. The most commonly encountered are hemorrhage, seizures, fluid and electrolyte disturbances, and coagulation disorders besides anesthesia-related complications specific to children [92]. Various factors like the urgent nature of these procedures, inherently associated comorbidities (such as prematurity), difficulty in establishing vascular access, and problems specific to the neurosurgical subgroup like impaired communication, sedation, and neurological deficits have been shown to increase morbidity and mortality in these patients [93].

Anesthesia-related complications might be mild, such as vomiting, laryngitis, and mild oral cavity lesions, or have serious ramifications. These include hypoxia, bradycardia, cardiac arrhythmia after anesthetic induction, dental fractures (intubation), bronchospasm, aspiration pneumonia, postoperative apnea, and anaphylaxis [94]. Besides the demographics like age, physiological, immunological, and laboratory conditions, a major contributor to these complications is the duration of anesthesia and surgery [95].

Every possible precaution should be taken to avoid an increase in ICP during the anesthetic and surgical maneuvers in these subsets of patients who are already at the edge of intracranial decompensation due to the underlying pathology. Steps should be tailored to prevent catastrophic consequences like mass effect and brain herniation as a result of even the smallest hemodynamic or ventilatory change. Pharmacological intervention should be preemptively undertaken at the time of ICP elevating procedures like laryngoscopy, rapid sequence orotracheal intubation, pin insertion, periosteum elevation, etc. [93, 96].

At all points of time in the intraoperative period, a meticulous awareness of the volume losses and prompt replacement with fluids and blood component therapy as necessary go a long way in preventing complications related to anemia and dehydration, especially in high-risk cases like craniosynostosis repairs, craniopharyngiomas, meningiomas, and vascular neurosurgeries. Intraoperative hypothermia and hyperthermia contribute to secondary brain injury and should be watched out for [93, 97].

A notorious intraoperative complication closely associated with intracranial surgeries is VAE. Augmented by the pressure discrepancy between the operative site and the heart (the heart is lower than the operative field) and a low central venous pressure (hypovolemia), it results in significant air entrainment in the central circulation. The inability of dural venous sinuses to collapse and the presence of spinal epidural and bridging veins predispose these children to the consequences of VAE. The management of VAE is largely based on actions to identify the problem, stop further air entrainment, and support the circulation, the details of which are explained in Chap. 7.

6.3.11 Emergence

Needless to say, the process of emergence and extubation is highly critical to the outcome of neurosurgery because of effects on ICP and postsurgical bleeding inside close cavities (cranium and spinal canal). PONV in neurosurgery is multifactorial, but in general, it is mostly because of the high emetic potential of blood in CSF compounded by headache and use of opioids. Multimodal techniques should be used to ameliorate the same and are discussed in great detail in Chap. 37. Among intravenous agents explored to control the extubation reflex in children undergoing neurosurgery, fentanyl, lignocaine, and dexmedetomidine have shown promise as effective agents. Autonomic blockers such as labetalol are effective in adolescents. However, while shown to be effective in the adult population, esmolol does not fulfill the safety criteria for use in children because of its predominant effect on the heart rate, a vital cog of the cardiac output in children. Adequate pharmacological reversal of neuromuscular blockade, confirmation of spontaneous ventilation and oxygenation, and an awake child are prerequisites for extubation in a child who has undergone neurosurgery. In cases of a stormy intraoperative course or children not meeting respiratory and neurological criteria for extubation, it is advisable to shift the child to a facility for postoperative ventilation while simultaneously employing methods to monitor intracranial hypertension (ICP monitoring and CT evaluation) [57].

6.4 Postoperative Care

6.4.1 PACU Considerations

Postanesthesia care should address concerns of the pediatric age group and oversee the recovery of the CNS. It should be viewed as a high specialty continuum of care from the intraoperative period [98, 99]. For clarity, practical recommendations for the organization of neurosurgical PACUs, care during the transition of these children from the operating room to these PACUs, and the specific entities requiring specialized care have been presented.

6.4.1.1 Organization of PACU

The pediatric neurosurgical PACU should be designed keeping in view the following factors [100]—(1) pediatric age group anthropometrics and relevant infrastructure in terms of monitoring, beds, drugs, airway, and other equipment and drug cards detailing pre-calculated drug dosage [101], (2) provisions to include the child's family in the postoperative care of these patients [100], and (3) a team having expertise in pediatric neurocritical care with evolving competencies in pediatric and neonatal advanced life support [102, 103].

6.4.1.2 Transport and Handover

Ideally, the PACU should be located as close to the operating room as possible. Before transport

to the PACU, a clear chain of communication with certain specific points should be established like patient specifics, the perioperative course, and specific concerns, if any. The postoperative plan, including clinical decision regarding extubation and need for mechanical ventilation, should also be clearly communicated to the PACU team [100, 104]. Important considerations should be ensured while shifting (Table 6.3).

6.4.2 Specific Entities in PACU

6.4.2.1 Emergence Delirium

A thrashing, disoriented, crying, screaming, and inconsolable child in the PACU is common, especially in the age group of 2–6 years [105, 106]. It has shown an association with the newer inhalation anesthetics, and it is usually a one-off self-limiting episode [107, 108]. In neurosurgical subsets, it has the potential to increase ICP. Several drugs such as dexmedetomidine, propofol, ketamine, magnesium, and midazolam and modalities such as regional anesthesia and acupuncture have shown efficacy in prophylaxis. IV agents may at times be required to treat intractable cases albeit with parental consent [100].

Table 6.3 Important considerations during ICU handover

• Detailed monitoring preferably under the direct supervision of the anesthesia team in the operating room
• Lines and catheters should be ensured to be in working condition; emergency drugs should be handy
• Keep the child warm during transit
• Keep transit times as a short as possible in children
• Adequate provisions for ventilatory, hemodynamic, and other emergency supports
• Effective pre-shifting communication to the patient receiving team
• In children who are awake and extubated—a high index of suspicion for hypoxic events, adherence to stringent monitoring protocols as well as safety in the form of guard rails, padding, and lateral decubitus position
• A detailed handover with the incorporation of checklist and protocols—efforts to decrease human error while shifting are warranted in pediatric PACUs [99]
• Advisable for the operating room team to remain with the child during the initial stabilization and handover in the PACU the receiving team has comfortably assumed responsibility of the child

6.4.2.2 Pain Management

Till not so long ago, pain perception in children was highly trivialized, to the point of being virtually nonexistent. However, in the past two decades, there has been a burgeoning amount of evidence that neonates and young children perceive and react to pain just the same as adults [109]. Another postulate that has been challenged recently is intracranial structures being pain insensitive. Post-craniotomy pain is a significant entity and requires optimum management in the postoperative period, especially in children [110]. In pediatric neurosurgery, the present pain management method is a multimodality approach targeting pain at various peripheral, spinal, and supraspinal sites. This approach results in better pain management than targeting only one site and is the underlying principle of treating pain in a multimodal fashion [110, 111]. It offers the advantage of utilizing various drugs described in the subsequent text to obtain maximum pain relief and minimize drug-related adverse effects on the CNS in children. The intricacies, routes, and dosages of postoperative pain management in children undergoing neurosurgeries will be covered in Chap. 38. Here, the general considerations of the two major pharmacological groups for postoperative pain, i.e., opioids and non-opioids, are elaborated.

Opioids

Opioids have been the mainstay of postoperative pain management. Still, their common side effects like nausea, vomiting, and sedation have deleterious effects on cerebral physiology in the form of increased $PaCO_2$ and cerebral vasodilation, consequently leading to cerebral edema and a disastrous increase in ICP. Despite these potential pitfalls, they continue to remain an integral part of perioperative pain management. The choice of opioid, dose, and administration route is based on practitioner preference, institutional protocol, and drug availability.

However, IV route should be preferred in the contiguous postoperative period. For IV therapy, drugs found efficacious are morphine, fentanyl, and hydromorphone. Among oral opioids, oxycodone is preferred over codeine. One should always be aware of the common side effects of opioid use like nausea, vomiting, pruritus, constipation, and urinary retention while being vigilant of the more ominous respiratory depression necessitating increased monitoring such as capnography and integrated acoustic sensors [111, 112].

Non-opioids

The non-opioid analgesics, even though exhibiting lesser efficacy than their opioid counterparts, have effectively reduced opioid requirements. They are a quite diverse and heterogeneous group of anesthetic adjuvants. The most common non-opioids used in postoperative pediatric neurosurgery are acetaminophen (paracetamol) and nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, ibuprofen, naproxen, and the selective cyclooxygenase (COX-2) inhibitors (celecoxib) [113]. They have myriad actions of analgesia, antiplatelet, and antipyretic effects. They also have anti-inflammatory action by blocking peripheral and central prostaglandin and thromboxane production by inhibiting cyclooxygenase types 1, 2, and 3 and can be administered through various routes. A significant limitation of this class of drugs is a ceiling effect, which has led to an offshoot of combination forms with opioids such as codeine, oxycodone, or hydrocodone. However, inadvertent liver toxicity, especially with acetaminophen formulation, is a real concern and must be avoided [114]. The major non-opioids in addition to those enumerated above are used as adjuncts and are corticosteroids, α2 adrenergic agonists (clonidine, dexmedetomidine, tizanidine), local anesthetics (lignocaine, bupivacaine, ropivacaine), nerve blocks (scalp block), and NMDA receptor antagonists (methadone). Details about mechanisms, routes, dosages, efficacy, side effects, and practical implications of these adjunct pharmacological agents in pediatric neurosurgical practice are covered in Chap. 38.

6.4.2.3 Adverse Respiratory Events and Mechanical Ventilation

Adverse respiratory events are common and represent an alarming two-thirds of critical events during the perioperative period in children [115]. The affliction of the CNS, which houses the vital respiratory centers, complicates matters manifold. A very close watch is mandated for respiratory insufficiency in neurosurgical children extubated, whether on the OR table or in the PACU.

A number of pediatric neurosurgical patients require ventilatory support, the period of ventilation is within 24–48 h to allow for effects of surgery to wear off, and assisted modes of ventilation are recommended to allow for ongoing neurological assessment. In children with poor lung mechanics, the effects of a conventional lung-protective strategy of low tidal volume, pressure-limited approach should be weighed against the effects of carbon dioxide retention and intracranial hypertension [39]. Effects on ICP are absent as long as the sutures and fontanelles are open [116]. A sizeable number of neonates and infants require controlled ventilation and sedation with muscle relaxants primarily because of severe neurological injury. The multiple systemic effects of the same, however routine use, are not advocated [117].

6.4.2.4 ICP Monitoring and Management

In children presenting with trauma and tumors, ICP monitoring is a routine of care at many centers and signifies ongoing intracranial hypertension even in CT changes [118]. Among the modalities available, intraventricular catheters offer therapeutic options and are the most widely used [39]. The methods used to manage intracranial hypertension include hypertonic saline (beware of hypernatremia), crystalloid therapy, use of steroids, and limited hyperventilation. Hyperventilation has been associated with reversible ischemia in children and should always be done in conjunction with monitoring blood gas and end-tidal carbon dioxide values [100].

6.4.2.5 Fluid and Electrolyte Disturbances

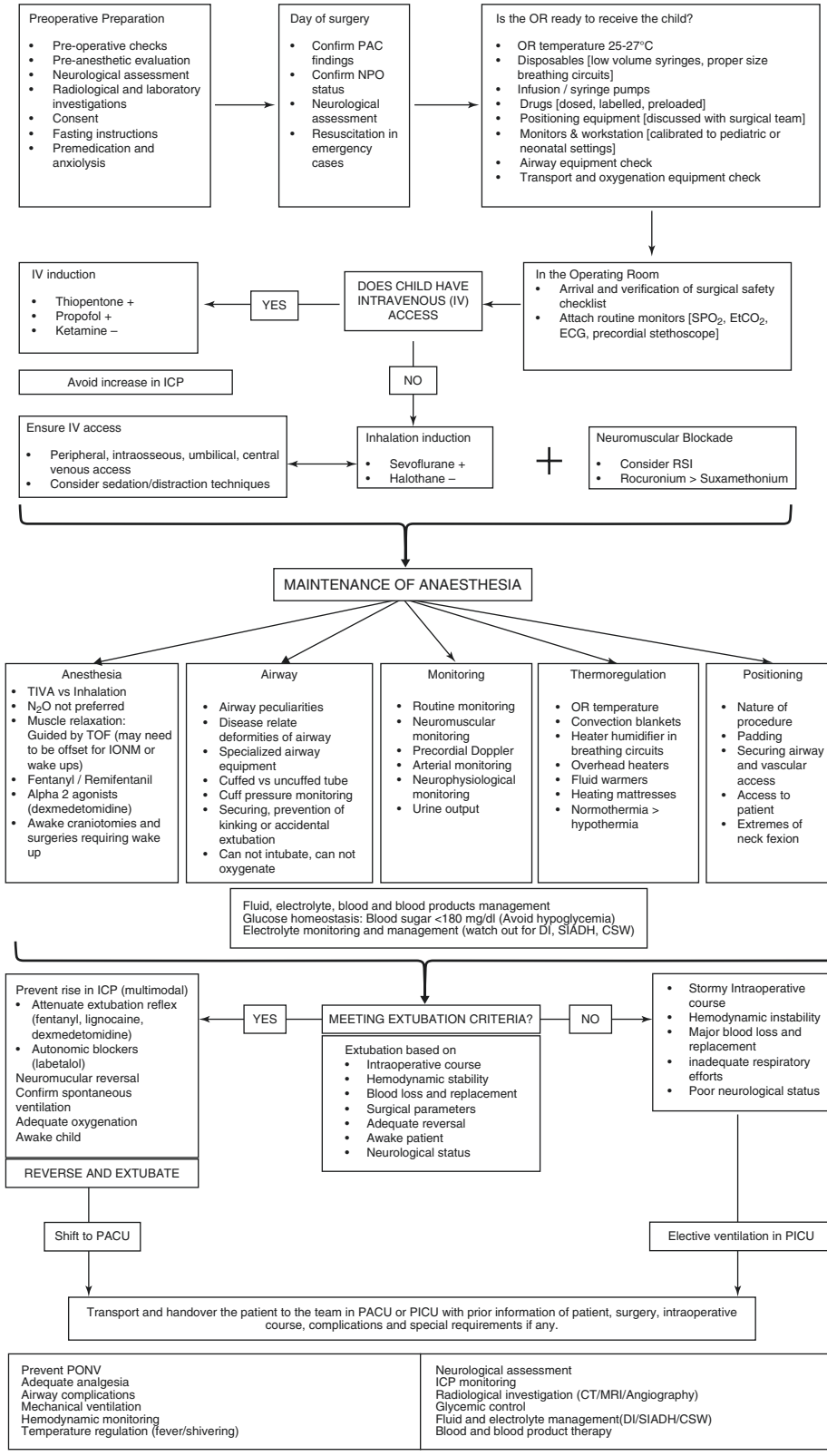
Inherent physiological considerations of pediatric neurosurgical patients like minuscule size, immature renal function, and impaired or varied intake of fluids, magnified by the effects of existing pathology and surgery on the brain, disrupt electrolyte fluid control mechanisms. This leads to severe disturbances in serum sodium and osmotic pressures in up to 10% of children undergoing neurosurgery and usually results in one of the three essential perioperative fluid and electrolyte disorders—viz., SIADH, diabetes insipidus, and CSW [119]. The details of these disorders are presented in Chap. 10. However, it is important to be very watchful for their timely diagnosis during the perioperative period as well as take timely and prompt corrective measures to mitigate evolving systemic and neuronal injury. Protocol-based diagnosis is especially important, especially because treatment modalities of these disturbances are radically different and should combine lab values of electrolytes and osmolarity in conjunction with urine output and subtle clinical signs such as hyponatremic seizures. The importance of having a strong suspicion for and dismissing and treating these disorders timely cannot be overstated, and they have a significant effect on the neurosurgical outcome.

6.5 Conclusion

Anesthetizing children for neurosurgery is challenging; nonetheless, applying sound pediatric neuroanesthesia principles in conjunction with effective postoperative neurocritical care should go a long way in delivering state-of-the-art, safe anesthesia care. An attempt to schematically represent children's care presenting for brain tumor surgery has been made as a case in point (Fig. 6.2). The aim should be to develop evidence-backed protocol-based processes involving multiple disciplines to improve outcomes and decrease morbidity in children undergoing neurosurgical procedures.

Conflict of Interest Nil.

Fig. 6.2 Schematic flow diagram of the entire perioperative management of a pediatric neurosurgical patient. Abbreviations: *PAC* pre-anesthetic checkup, *NPO* nil per oral, *OR* operating room, *IV* intravenous, SPO_2 pulse oximetry, $EtCO_2$ end-tidal carbon dioxide, *ECG* electrocardiogram, *ICP* intracranial pressure, *RSI* rapid sequence intubation, *TIVA* total intravenous anesthesia, N_2O nitrous oxide, *TOF* train of four, *IONM* intraoperative neurophysiologic monitoring, *DI* diabetes insipidus, *SIADH* syndrome of inappropriate antidiuretic hormone secretion, *CSW* cerebral salt wasting, *PICU* postanesthesia care unit, *PONV* postoperative nausea and vomiting, *CT* computed tomography, *MRI* magnetic resonance imaging


Preoperative Preparation
Pre-operative checks
Pre-anesthetic evaluation
Neurological assessment
Radiological and laboratory investigations
Consent
Fasting instructions
Premedication and anxiolysis
Day of surgery
Confirm PAC findings
Confirm NPO status
Neurological assessment
Resuscitation in emergency cases
Is the OR ready to receive the child?
OR temperature 25-27°C
Disposables [low volume syringes, proper size breathing circuits]
Infusion / syringe pumps
Drugs [dosed, labelled, preloaded]
Positioning equipment [discussed with surgical team]
Monitors & workstation [calibrated to pediatric or neonatal settings]
Airway equipment check
Transport and oxygenation equipment check
In the Operating Room
Arrival and verification of surgical safety checklist
Attach routine monitors [SPO2, EtCO2, ECG, precordial stethoscope]
DOES CHILD HAVE INTRAVENOUS (IV) ACCESS
YES
IV induction
Thiopentone +
Propofol +
Ketamine –
Avoid increase in ICP
NO
Ensure IV access
Peripheral, intraosseous, umbilical, central venous access
Consider sedation/distraction techniques
Inhalation induction
Sevoflurane +
Halothane –
Neuromuscular Blockade
Consider RSI
Rocuronium > Suxamethonium
MAINTENANCE OF ANAESTHESIA
Anesthesia
TIVA vs Inhalation
N2O not preferred
Muscle relaxation: Guided by TOF (may need to be offset for IONM or wake ups)
Fentanyl / Remifentanil
Alpha 2 agonists (dexmedetomidine)
Awake craniotomies and surgeries requiring wake up
Airway
Airway peculiarities
Disease relate deformities of airway
Specialized airway equipment
Cuffed vs uncuffed tube
Cuff pressure monitoring
Securing, prevention of kinking or accidental extubation
Can not intubate, can not oxygenate
Monitoring
Routine monitoring
Neuromuscular monitoring
Precordial Doppler
Arterial monitoring
Neurophysiological monitoring
Urine output
Thermoregulation
OR temperature
Convection blankets
Heater humidifier in breathing circuits
Overhead heaters
Fluid warmers
Heating mattresses
Normothermia > hypothermia
Positioning
Nature of procedure
Padding
Securing airway and vascular access
Access to patient
Extremes of neck fexion
Fluid, electrolyte, blood and blood products management
Glucose homeostasis: Blood sugar <180 mg/dl (Avoid hypoglycemia)
Electrolyte monitoring and management (watch out for DI, SIADH, CSW)
MEETING EXTUBATION CRITERIA?
YES
Prevent rise in ICP (multimodal)
Attenuate extubation reflex (fentanyl, lignocaine, dexmedetomidine)
Autonomic blockers (labetalol)
Neuromuscular reversal
Confirm spontaneous ventilation
Adequate oxygenation
Awake child
REVERSE AND EXTUBATE
Shift to PACU
NO
Extubation based on
Intraoperative course
Hemodynamic stability
Blood loss and replacement
Surgical parameters
Adequate reversal
Awake patient
Neurological status
Stormy Intraoperative course
Hemodynamic instability
Major blood loss and replacement
inadequate respiratory efforts
Poor neurological status
Elective ventilation in PICU
Transport and handover the patient to the team in PACU or PICU with prior information of patient, surgery, intraoperative course, complications and special requirements if any.
Prevent PONV
Adequate analgesia
Airway complications
Mechanical ventilation
Hemodynamic monitoring
Temperature regulation (fever/shivering)
Neurological assessment
ICP monitoring
Radiological investigation (CT/MRI/Angiography)
Glycemic control
Fluid and electrolyte management(DI/SIADH/CSW)
Blood and blood product therapy

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Positioning Children During Neurosurgery

7

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Key Points

- A wide range of surgical positions is required, in children, for optimal access during different neurosurgical procedures, with each position having its own physiological consequences.
- The unique concerns are related to physiological differences of children from adults and appropriate equipment required due to the variations in the physical dimension.
- Safe and comfortable positioning of the patient is teamwork involving close communication between the surgeons, anesthesiologists, and operating room staff.
- The ideal position is a balance between optimal surgical access and patient safety.
- Efforts to maintain appropriate temperature are mandatory when a prolonged positioning period is required.
- Commonly, the supine, lateral, prone, or sitting position and their modifications are used.
- It is important to maintain the patient's physiology as close to normal as possible and minimize the complications that can occur due to various positioning with anticipation and continuous vigilance.
- Prevention of inadvertent neurologic injury by adequate padding cannot be overemphasized.

7.1 Introduction

Positioning refers to the body position in which a patient is placed for a surgical procedure. The optimal patient position should facilitate maximum surgical access with minimum physiologic perturbations or physical injury without compromising patient safety. The fundamental considerations about the position for neurosurgery aim to (a) provide the most acceptable access to the anatomical target, ensuring the comfort of the surgeon and patient and access to the anesthesiologist and adequate access for monitoring, (b) avoid brain retraction, (c) minimize intraoperative bleeding, (d) reduce intracranial pressure (ICP), (e) ensure adequate cerebral perfusion, (f) prevent compression or traction injuries (skin dehiscence, ocular injuries, peripheral nerve injuries), and (g) increase the likelihood of a successful surgery with a good outcome. Table 7.1 enumerates the goals for patient positioning for surgery. The optimum positioning of children for neurosurgery poses unique challenges due to the anatomical and physiological differences and the age-wise variations in surgical lesions. Safe and comfort-

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Table 7.1 Goals of surgical positioning

• Patient comfort
• Patient dignity
• Maintain physiological homeostasis
• Protect anatomical structures of patient's body to prevent injuries and complications
• Access to surgical site without posing undue stress on the patient's body
• Access to anesthesiologist to intravenous (IV) sites to administer medications, fluids, blood and blood products, anesthetic agents
• Allow positioning of surgical equipment (e.g., C-arm, operating microscope) for easy use by surgical team

able positioning of the pediatric patient is of paramount importance. Knowledge, planning, and teamwork are the major components of attentive positioning, which fulfils the aim of the surgical procedure and prevents the ensuing complications, thereby reducing perioperative morbidity. This chapter describes the special considerations for positioning pediatric patients for the commonly performed neurosurgical procedures in commonly used positions (supine, lateral, prone, sitting) and their variations, how the position is established, associated complications, and measures to mitigate these complications.

7.2 Historical Aspects

Dutton, in 1933, gave an account of the effects of body position on anesthesia [1]. Slocum and Allen carefully documented the position related to cardiorespiratory and neurovascular complications [2, 3]. Then, there were subsequent reviews by several authors which clarified several aspects related to positioning [4–9].

The constantly evolving neurosurgical approaches have always demanded newer positions over time. Several challenges and hurdles encountered through trial and error have prompted numerous adjustments to make positioning of patient safety and formulate the standard of care for positioning for pediatric neurosurgical procedures.

The sitting position was first introduced in 1913 by Thierry de Martel for excision of the intracranial tumor under local anesthesia; however, Horsley performed many such procedures in the lateral oblique position as far back as 1906. In 1928, Frazier and Gardner used this position in the USA for surgery on the Gasserian ganglion. The 1960s and 1970s were the prime periods for the sitting position for neurosurgical procedures. Over time, neurosurgeons have transitioned to the prone position, limiting the sitting position and its variations to individualized and institutional practice.

7.3 General Principles Common to all Pediatric Positions

The ideal position of the child for pediatric neurosurgery is a balance between good surgical access and patient safety in terms of avoidance of associated complications. Patient positioning is a cooperative effort of the operating room (OR) team comprising of the neurosurgeon, neuroanesthesiologist, nursing staff, technical staff, and housekeeping staff. Proper positioning of the patient is one of the most crucial steps in neurosurgery. Multiple factors like child's age, weight, size, and medical diseases including cardiorespiratory disorders and evaluation of potential positioning risks help identify the patient's tolerance to the planned position and plan appropriate modifications to the position. Hence, considerations for patient positioning during surgery forms a vital component of the preanesthetic evaluation. Important issues in positioning are access to the child, head positioning, securing the airway, and adequate protection of the eyes, skin, and peripheral nerves. Table 7.2 shows a checklist for safe positioning of the patient for surgery.

Table 7.2 Checklist for safe positioning of the patient for surgery

Preoperative assessment	**Patient factors** (a) Age (b) Height (c) Weight (d) Skin integrity (e) Ranges of motion (f) Preexisting conditions—Allergies, cardiorespiratory, immune, neurological systems, nutritional condition (g) Poor vision or blindness (h) Impaired mobility (i) Development and mental competence (j) Prosthetic devices (k) Implanted devices—Shunt tubes, plates, and screws (l) External devices—Indwelling catheters **Procedure-related factors** (a) The surgical procedure to be performed (b) The estimated duration of the procedure (c) Surgeon's and anesthesiologist's preferred surgical position
Intraoperative considerations	**Before positioning** (a) Verify patient identity (b) Marking of surgical site (c) Procedure verified with patient or representative (d) Consent checked **During positioning** (a) Transfer by adequate personnel each knowing their predetermined role (b) Operating table and all positioning accessories clean and ready to use (c) Head immobilized in the preferred device (d) Eyes and face adequately protected (e) Pressure points well padded (f) Unlike adults, additional padding might be needed under edges of belt used for strapping/ wires/other monitoring aids (g) Cotton used for padding can get soaked in irrigating saline/sweat/ blood and can harden and lose cushioning effect and can worsen hypothermia. Hence caution must be exercised (h) Gentle application and removal of plasters and adhesives (delicate skin) (i) Diathermy cautery plate placed correctly and in contact with the body to prevent cautery burns (j) An in insulating layer of cotton or linen, may help prevent cautery burns due to the gel/ bolsters (k) Homeostasis maintained (l) All tubes, circuits, and monitors are free from compression and functional (m) All connections secured (n) Access to the patient is satisfactory (o) Measures to maintain temperature/normothermia (p) Patient strapped adequately **Post positioning** (a) Patient re-evaluated periodically (b) Pressure points checked from time to time in prolonged surgeries (c) Every time patient's/table position is altered intraoperatively, reassess patient
Postoperative assessment	**Check as the patient is undraped** (a) Assess the pressure points (b) Look for electrical burns, intactness of skin (c) Assess for signs of nerve compression **Documentation** (a) Outcome evaluation

7.3.1 Transport and Handling

The child must be handled gently during shifting from his/her hospital bed to the transport cart, transit through the corridors and elevators en route to the operating suite, and on transfer onto the operating table. Critically ill children should be monitored during transport and physiologic stability maintained [5]. Adequate team members should be available for the safe transfer of the child onto the operating table with the planned use of shifting aids like draw sheets, mechanical patient movers like body rollers, slide boards, etc. The person at the head end, usually the anesthesiologist, is overall in charge of shifting who ensures the stability of head and neck and airway patency. Vigilance regarding arms, vascular lines, and monitors can be designated to other team members. Careful planning with each member's predetermined role before shifting the patient results in safe patient handling in all circumstances. The movement of the child from the operating table to the recovery bed or cart should also be performed gently and by enough team members to allow smooth transition without provoking any complication.

7.3.2 Equipment

7.3.2.1 The Surgical Table

A standard operating table with the necessary attachments that aid the positioning required for a particular procedure is used for every neurosurgical operation. Specialized tables are available to meet the unique requirements of spine surgery, such as Allen's table and Jackson's table. Soft, segmented table pads are standard parts of all operation tables that adhere to metal surfaces. The advantage of this is that the leg part of the table can be detached in very small children to allow the anesthesiologist access to the child.

7.3.2.2 Accessories

Side rails are present on both sides and on the ends of the procedure table. Various sizes and designs of locking sockets and clamps that fit onto the side rails are also present. They allow the fitting of various accessories like leg holders; shoulder supports; skull clamps; arm boards; supplementary upper limb support systems, which are devised to support the upper arm, forearm, wrist, and/or hand; lateral positioning bars; and posts. Table 7.3 shows the desirable properties of positioning devices.

Table 7.3 Desirable properties of positioning devices

- Available in various sizes and shapes
- Durable (especially the reusable items)
- Conform to the patient's body and evenly distribute pressure
- Maintain a normal capillary interface pressure of 32 mmHg or less
- Resistant to moisture and microorganisms
- Radiolucent
- Fire resistant
- Nonallergenic
- Easy to use
- Easy to clean/disinfect (if not disposable)
- Easy to store, handle, and retrieve
- Cost-effective

7.3.2.3 Head Immobilization Devices

Head immobilization devices are used to immobilize the head, which can occur from surgical manipulation. They can be divided into rigid immobilization devices like cranial pin fixation or nonrigid immobilization frames like the horseshoe headrest. The utilization of skull clamps, though lower in children, is individualized on a case-to-case basis. Mayfield skull clamp is the most commonly used head immobilization device; others use the Sugita head clamp.

Guidelines for pediatric patients regarding the use of cranial pin fixation are unavailable. Its use is generally avoided in infants less than 1 year of age, and 5 years or more is often considered a safe age for the use of headpin by most neurosurgeons [10]. The practice regarding the size of pins and torque screw force pounds per square inch (lbs/psi) applied in children is extremely variable among the pediatric neurosurgical community [10]. The usual practice is that pediatric pins are used in smaller children and the pressure applied is 10 lbs./psi per year of age up to 30 lbs./psi. Children are more susceptible to complications associated with cranial pin fixation than adults due to their thinner bones [11], and

instances of depressed skull fractures, epidural hematomas, pneumocephalus, and venous air embolism (VAE) have been reported in literature [12–15]. Therefore, extreme caution should be exercised when using cranial pin fixation devices, and whenever possible, a padded horseshoe headrest may be used. There are some warning signs during pin application, and one must pause and reassess the patient's safety by using appropriate imaging. These signs include pin plunge (pins going too deep within the skull), crackling sound, higher than 30 lbs./psi torque, and inability to sustain the pressure.

Application of cranial pin fixation is associated with significant stimulatory effects resulting in tachycardia and hypertension, which may have several deleterious consequences. Hence, this response must be abolished by deepening the plane of anesthesia by administering additional boluses of anesthetic agents or by local anesthetic injection at the pin site.

7.3.3 Protective Padding

A direct contact between the patient and the operation table surface or accessories can be a potential cause of pressure-related injury. A range of protective padding and devices (arm pads, donuts, rolls, heel cups) is available, providing cushioning and distribution of pressure evenly over a wider area to decrease the pressure-related injury. The body parts particularly susceptible to positioning-related pressure injury in a certain position should be identified and padded well. Table 7.4 shows the various pressure points to be aware of in different positions.

Table 7.4 Potential pressure points in different neurosurgical positions

Position(s)	Pressure point(s)
Supine	Occiput Scapulae Thoracic vertebrae (spinous process) Olecranon Sacrum and coccyx Calves Calcaneum (heels)
Lateral	Dependent ear Acromion process Olecranon Dependent side ribs Iliac crest Greater trochanter Medial and lateral condyles Medial and lateral malleoli
Prone	Eyes Ears Malar prominences (cheeks) Acromion process Breasts Iliac crest Male genitalia Patellae Toes
Sitting	Occiput Scapulae Thoracic vertebrae (spinous process) Olecranon Sacrum and coccyx Buttocks Ischial tuberosity Thighs (posterior aspect) Popliteal fossa Calcaneum (heels)

7.3.4 Physiology of Patient Positioning

7.3.4.1 Respiratory Physiology

It is essential to keep the ventilatory parameters within normal limits during neurosurgery to prevent a rise in arterial blood carbon dioxide partial pressure ($PaCO_2$) and subsequent increase in ICP. Respiratory function can be compromised in certain positions like lateral or prone due to mechanical restriction of the chest wall, compression of the trachea [16], and reduced excursions of the abdomen, all of which can impair ventilation. Malposition of the endotracheal tube (ETT) is more common in children than in adults due to the shorter trachea. Extreme flexion of the neck may also cause kinking of the ETT [17] or endobronchial migration of the ETT in children and cause ventilation problems. Hence, it is better to decide the type of ETT (flexometallic vs. standard portex ETT) based on the intended surgical position. Once the desired position is finalized, the lung fields should be auscultated to assure proper placement of the tube confirmed by bilateral equal air entry; the mark on the tube at

the level of lips is rechecked, and the fixation of the ETT is well-secured. The breathing circuit is supported properly without any compression or pull or tug on the circuit, to ensure unhindered ventilation and oxygenation throughout the surgical procedure.

7.3.4.2 Circulation

Stable hemodynamics is vital to any neurosurgical procedure to maintain adequate cerebral perfusion. The circulatory changes to specific positions can sometimes be very rapid and have major consequences, especially in pediatric patients as they depend on heart rate to maintain cardiac output than stroke volume due to limited contractility of the myocardium in this age group and the myocardial depressant activity of most of the anesthetic agents used in children.

Neck positions like flexion, extension, or rotation may cause obstruction to arterial blood flow as well as impair venous return from the head and neck. The former can increase ICP due to impaired cerebral perfusion pressure (CPP), decreased oxygenation, and triggering of the cerebral vasodilatory cascade. On the other hand, the latter increases ICP due to increased blood volume due to impaired venous return. This also increases the chances of intraoperative venous bleeding from the surgical site and brain swelling resulting in difficult and prolonged surgery and higher chances of a patient being ventilated postoperatively, resulting in increased morbidity. This can also lead to airway edema and edema of the face and tongue, all causing postoperative respiratory compromise, especially after prolonged surgery in the prone position. This can be avoided by paying careful attention to the positioning of the head and neck during surgery.

Decreased systemic venous return can occur due to restrictions due to positioning aids in lateral or prone position due to the rolls and bolsters, which can increase intrathoracic and intra-abdominal pressures [18]. This, in turn, can cause a decrease in cardiac output and CPP. The increased pressures can be transmitted intracranially and cause a rise in ICP and increased bleeding in spinal surgery due to venous engorgement [19]. The fall in cardiac output can also cause decreased systemic perfusion resulting in ischemia of several organs like the liver, kidneys, and bowel [20–22]. This can be mitigated by careful positioning, avoiding abdominal compression.

7.3.4.3 Temperature Regulation

Maintenance of body temperature can be challenging when positioning a small child, especially due to the extended time required to establish the desired position before the final draping and start of surgery. Hypothermia is associated with complications like impaired coagulation resulting in increased intraoperative bleeding, surgical site infection, and delayed recovery [23]. Hence, efforts should be taken to maintain temperature during positioning. The operating room can be kept warm by adjusting the air-conditioning and room temperature when the child is brought in and till the final desired position is achieved and surgical draping is done. A heating mattress, overhead heating lamp, and blankets to cover the child may be used during the time of positioning. Forced air warmers (e.g., Bair Hugger) may be used after positioning as the position, and surgical procedure allows to maintain optimum temperature.

7.3.5 Head Position

The ideal head position should provide an optimal approach to the surgical target. The two principles that govern head position are as follows: (i) the imaginary trajectory joining the highest point of skull and the surgical target should be the shortest distance between those two points, and (ii) the perimetry of the craniotomy performed should be parallel to the floor [24].

Manipulation and positioning of the head for the neurosurgical procedure, if gone wrong, can have disastrous consequences. The safe margin allowed for head rotation is up to 45° away from the body, beyond which a pillow or roll must be placed beneath the opposite shoulder. The turning of the head must be done very slowly and smoothly, always supporting the neck and in alignment with the rest of the body as a single unit. Extremes of head position like hyperflexion,

hyperextension, rotation, and lateral flexion should be avoided. Always two fingerbreadths distance between the patient's chin and the nearest bony point should be ensured. The goal is to keep an adequate distance between these two points so that there is no or minimal increase in the airway pressure.

7.3.6 Repositioning During Anesthesia

The presence of disease, trauma, and anesthesia can depress or abolish the compensatory reflex responses during postural changes to maintain the systemic blood pressure and tissue perfusion. These changes can be accentuated during positioning, posing a serious threat to homeostasis if meticulous care is not taken. Adequate depth of anesthesia, adequate intravascular volume (replenish fluid deficits), and gradual and gentle change in the posture of the patient to attain the final position are mandatory steps for repositioning the patient for surgery after induction of anesthesia. A light plane of anesthesia may lead to tachycardia and hypertension due to stimulation during positioning, thereby causing increased ICP. Similarly, bucking or coughing on the ETT may cause raised ICP. However, an excessive depth of anesthesia also should be avoided, which might cause hypotension; it leads to inadequate cerebral and systemic perfusion, vasodilatory cascade, and, thence, increased CBV and ICP. The postural changes made at the termination of the surgery to bring the patient back to the supine position must also be gradual and be performed diligently. Hemodynamic instability at this time may occur due to iatrogenic and unrecognized intravascular volume deficits, hypothermia, electrolyte imbalance, and residual anesthetic effects. These factors must be kept in mind and corrected before normalizing the position to have a favorable outcome.

Frequent measurements of blood pressure, if not continuously monitored, should be performed throughout the change in patient position. Care must be taken to prevent dislodgement of ETT, indwelling catheters, indwelling cannula, and monitoring lines. The duration of loss of monitoring ("blackout" state) and disconnection from ventilation should be as minimum as possible during positioning. When the case permits, at least the pulse oximetry monitoring must be continued uninterrupted.

Once the final position is established, reevaluation of the respiratory and circulatory systems (airway patency, adequate ventilation, and oxygenation, peak airway pressure, adequate blood pressure to maintain cerebral and systemic perfusion), eyes (ointment and taped shut), all pressure points (adequate padding), intactness of vascular and monitoring devices, and access to the child should be made.

7.4 Basic Positions in Neurosurgery

Most of the neurosurgical procedures are performed with the patient in one of the variations of the four basic positions: supine, lateral, prone, and sitting. The exact position of the patient for a particular procedure is influenced by the type of surgery being performed, preferences of the surgical team, institutional practices, and choice of anesthesiology team. Neurosurgical procedures are carried out in different positions (Table 7.5), and the physiological changes associated with each of the positions may be different (Table 7.6). These positions are established stepwise in each position (Table 7.7). However, in smaller children, these steps can vary and modifications improvised on a case-to-case basis for the safe positioning of the child. These positions may have advantages as well as disadvantages. The common complications encountered in each of the positions and their subsequent management have been described in Table 7.8. The position-related complications among the different positions are also compared in Table 7.9.

7.4.1 Supine Position

This is the basic position for surgeries on the supratentorial part of the brain, the pituitary fossa, and sellar and suprasellar compartments. The lesions in the lateral part of the posterior

Table 7.5 Common pediatric neurosurgical positions and their indication(s)

Position	Indication
Supine	1. Craniotomies for supratentorial brain surgeries (a) Standard pterional craniotomy (b) Fronto temporoparietal (FTP) craniotomy (c) Bifrontal craniotomy (d) Anterior interhemispheric/transcallosal craniotomy (e) Temporal craniotomy 2. Craniotomies for lateral posterior fossa lesions in young children 3. Transsphenoidal pituitary surgery (in older children) 4. Craniosynostosis surgery (a) Strip craniectomy (b) Cranial vault remodeling (CVR) (c) Fronto-orbital advancement 5. Ventriculoperitoneal (VP) shunt 6. Endoscopic third ventriculostomy (ETV) 7. Repair of brachial plexus injuries 8. Vagal nerve stimulator placement 9. Transoral odontoidectomy 10. Anterior cervical spine surgery (traumatic) 11. Interventional neuroradiology procedures 12. Diagnostic computerized tomography (CT) scan, magnetic resonance imaging (MRI)
Lateral	1. Craniotomies, retro-sigmoid approach for cerebellopontine (CP) angle tumors 2. Theco-peritoneal shunt 3. Lumbar drain placement 4. Anterolateral approach to the thoracolumbar spine
Three-quarter prone/park bench	Midline posterior fossa lesions
Prone	1. Craniotomies (a) Midline posterior fossa lesions (b) Occipital (c) Posterior interhemispheric 2. Encephalocele 3. Foramen magnum decompression/cranio-cervical decompression 4. Atlantooccipital fixation 5. Spinal surgery (a) Posterior approach (b) Meningomyelocele (c) Detethering
Concorde (modified prone)	1. Craniotomies Occipital transtentorial Supra-cerebellar infratentorial Posterior fossa 2. Cervical spine surgery
Sphinx (modified prone)	Craniosynostosis (a) Cranial vault remodeling (b) Endoscopic-assisted sagittal strip craniectomy
Sitting	1. Craniotomies (a) Supra-cerebellar infratentorial approach to pineal region (b) Posterior transcallosal approach to pineal region (c) Posterior fossa 2. Upper cervical spine surgery

Table 7.6 Physiological changes associated with different neurosurgical positions

Position	Respiratory system	Cardiovascular system	Nervous system	Others
Supine	**Ventilation:** Breathing mainly due to abdominal movement Improved ventilation-perfusion matching More uniform ventilation per unit volume of lung **Perfusion**: The majority of pulmonary circulation in zone 3 (arterial pressure > venous pressure > alveolar pressure; blood flow determined by the difference between arterial and venous pressure; less gravity-dependent) **Lung volumes:** FRC ↓ TLC ↓ CV**:** CV exceeds FRC in the supine position in children <7 years; increased alveolar-arterial oxygen tension is seen CC ↔, ↑ (slight)	VR/CVP ↑ CO ↑ SV ↑ MAP ↓ (SP ↔, DP ↓, PP ↑, MAP ↓) HR ↓ SVR↓	JVF ↑, ↔ JVR ↓, ↔ CPP ↔, ↓ CSF drainage impaired ICP- ↑	Urine flow ↓ Esophageal sphincter tone ↑ Gastric emptying time ↑
Lateral	**Ventilation:** Dependent lung – ↓ → atelectasis Nondependent lung – ↑ **Perfusion:** Dependent lung – ↑ Nondependent lung – ↓ Ventilation-perfusion mismatch – ↑↑ **Lung volumes:** FRC ↓ TLC ↓	VR ↓ CO ↓ SV ↓ HR ↑, ↔ MAP ↓ SVR ↑ PVR ↑	JVF ↑, ↔ JVR ↓, ↔ ICP ↑	Decreased perfusion of dependent arm
Prone	Ventilation: ↑ Perfusion: ↑ Ventilation-perfusion ratio improved Lung volumes: FRC – ↑	VR ↓ SV ↓ CO ↓, ↔ HR ↑, ↔ MAP ↓, ↔	Head below the level of the heart JVF – ↑ JVR – ↓ ICP – ↑ Head neutral JVF ↑, ↔ JVR ↓, ↔	Decreased venous return from face and obstruction to lymphatics – Facial edema
Sitting	**Ventilation:** ↑ (diaphragm and abdominal contents pushed caudally due to the effect of gravity) **Perfusion:** ↑ Ventilation-perfusion ratio improved **Lung volumes:** FRC ↑ TLC ↑	VR/CVP ↓ CO ↓ SV ↓ PVR ↑ SVR ↑ HR ↔, ↑ MAP ↓	CPP ↓ (15%) (arterial pressure decreases by approximately 1 mm hg for every 1.25 cm distance above the level of the heart) Dural venous sinus pressure – ↓	

Abbreviations: *VR* venous return, *CVP* central venous pressure (mmHg), *CO* cardiac output (L/min), *SV* stroke volume (ml), *MAP* mean arterial pressure (mmHg), *SP* systolic pressure (mmHg), *DP* diastolic pressure (mmHg), *PP* pulse pressure (mmHg), *HR* heart rate (beats/min), *SVR* systemic vascular resistance (dynes/cm^2/s), *PVR* pulmonary vascular resistance, *JVF* jugular venous flow, *JVR* jugular venous resistance, *CPP* cerebral perfusion pressure (mmHg), *FRC* functional residual capacity (ml), *TLC* total lung capacity (ml), *CV* closing volume (ml), *CC* closing capacity (ml)
↑ increases, ↓ decreases, ↔ unchanged

Table 7.7 Steps for establishing the neurosurgical position(s)

Position	Steps to establish the position
Supine	• Operation table is well padded • Arms tucked comfortably along the side of the trunk • Place pillow under the knees to slightly flex the hips and avoid stress on back—Lawn chair modification or contoured supine position
Lateral	• The side of the surgery must be marked, specified on the consent form, and reconfirmed before positioning • After anesthesia is induced, IV accesses and catheters are secured with patient in supine position • Anesthesiologist takes control of the head and neck and coordinates with other team members in turning from supine to lateral • The alignment of the body must be maintained at all times to avoid stress on the spine • The downside arm must be abducted first to prevent it from being trapped under the laterally turned body • One assistant places one hand on the dependent shoulder and holds the nondependent shoulder with the other hand; the other assistant places one hand under the patient's dependent hips and grasps the pelvis and with the other hand holds the iliac crest of the nondependent side • Once the assistants are ready, the position is turned lateral at the call of the anesthesiologist on the count of three, who turns the head toward the direction of the turn keeping the head in the sagittal plane and moves it in alignment with the body • A padding is placed under the dependent chest to prevent compression of the axillary artery on that side and ischemia of the limb • The pelvis can be stabilized by flexing the lower leg at the hip and knee while keeping the upper leg straight. A pillow is placed between the legs • Padded rests are placed in front and back of the sternum and pelvis for further stability; the patient is strapped • The downside arm is abducted and flexed to not more than 90° and hung on a pillow and tied to the rail of the table at the head end. A crepe bandage may be placed in the dependent arm. The upper arm is on an armrest or pillow placed in front of the patient • **Park bench position** is a modification of the lateral position in which the upper arm is placed by the side of the patient along the trunk, and the shoulder is taped to the table • All pressure points must be well padded • All lines and monitors and peak airway pressure are noted and recorded for future management
Prone	• Once the patient is ready for turning prone, the bed or trolley is moved close and parallel to the operation table, and its height is adjusted to be level with the operation table • Bolsters or rolls or frames on which the patient is to be placed must be kept ready on the table • The anesthesiologist manages the head, neck, and airway and coordinates the turn, while two assistants (turner and receiver) are there on either side of the patient and one at the foot end. Smaller children can be made prone on the operating table itself • At the anesthesiologist signal, the breathing circuit is momentarily disconnected; the turner rotates the patient from supine to lateral to prone, in a slow and smooth manner. Simultaneously, the receiver receives the patient on the outstretched arms, and the anesthesiologist maintains the head in the sagittal plane always in alignment with the body and, then, rotates the head gently till it is face down and in the final desired position. Finally, the breathing circuit is quickly reconnected • In patients with less apneic reserve, especially in neonates, 100% oxygen should be administered before disconnections of the circuit • The trolley is then taken away, and all other monitors and lines are reattached, and their intactness checked • The arms are usually placed alongside the trunk of the patient. They may be placed above the patient's head for lower spine surgery. In that case, the shoulder is abducted and elbow flexed maximum up to 90°; hyperabduction of the shoulder and acute flexion of the elbow should be avoided • The abdomen must be free from compression. The supports should be at the upper chest and pelvis level and should not slip and compress vital structures in the neck or the abdomen, or lower limbs • The peak airway pressure is checked and should be within acceptable limits • All the pressure points must be well padded and all lines and tubes free from compression • The face should be padded and eyes protected from direct compression

Table 7.7 (continued)

Position	Steps to establish the position
Sitting	• The operating table should have a removable head section and separate controls for back and leg sections and flexion and head-down tilt • The table should be well padded • Compression stockings or Esmarch bandage applied to both lower limbs up to midthigh • A large and soft pillow should be placed at the thigh section on which the patient's buttocks will rest to prevent compression of the sciatic nerve by the ischial tuberosity. The pillow also elevated the patient's body above the back section of the table • The three-pinhead holder is placed in a supine position with the pins and holder placed away from the surgical field. Antibiotic ointment applied at the pin site helps prevent air embolism and provides antibacterial properties • Initially, the table is given a reverse Trendelenburg tilt to aid venous return from the lower limbs; then, the table is flexed fully at the back-thigh hinge. The foot is lowered 30–45° so that the knees are flexed and brought to the heart level, and thighs are flexed up to 90° over the abdomen. The combination of the back section of table elevation and foot end is coordinated and adjusted to maintain the horizontal position of the lower legs at the level of the heart. • All these maneuvers must be done very slowly and the blood pressure continuously monitored to detect any hypotension • The head holder is attached to a support frame inverted U-shaped, the limbs of which are attached along the back section of the table. This allows the sitting patient to be lowered rapidly to the horizontal position in case of severe hemodynamic collapse by simply lowering the back section • Correct positioning of head: Avoid extreme neck flexion, maintain two fingerbreadths (2–3cms) space between chin and anterior chest wall or the nearest bony prominence • All bony prominences should be well padded • Arms should be well padded and flexed across the chest or abdomen to remain within the inverted U-shaped frame and hands crossed over the lap • After the final position is achieved, the arterial transducer should be placed at the level of the operative site to reflect the perfusion pressure at the operative site. The right atrial catheter should be transduced at the level of the heart

Table 7.8 Risks and benefits of surgical position and complication management

Position	Benefits	Adverse effects	Management
Supine	The easiest position to achieve No special equipments required	Backache	Lawn chair or contoured supine position reduces stress on the back
		Pressure point retractions	Awareness of all the pressure points and generous padding
		Pressure alopecia	Use of soft head supports when possible; avoid hypotension and hypothermia
Lateral	Optimal position for unilateral posterior fossa approach and anterolateral approach to spine	Brachial plexus injury	Avoid stretch on the shoulder and thereby brachial plexus
		Entrapment neuropathy of suprascapular nerve	Avoid circumduction of arm across the chest and extreme lateral tilt of head toward the contralateral side
		Peroneal nerve neuropathy	Adequate padding of dependent lower limb
		Decreased perfusion of dependent arm	Avoid axillary artery compression—Chest roll, park bench modification
		Atelectasis of dependent lung	Recruitment maneuvers end operatively and continued in the postoperative period
		Ocular compression	Protect the downside eye
		Compression of the ear (downside ear)	Avoid compression of dependent ear

(continued)

Table 7.8 (continued)

Position	Benefits	Adverse effects	Management
Prone	Optimal position for posterior fossa surgery, posterior approach for spine Less chances of venous air embolism (VAE) compared to sitting position	Dropping the patient; loss of airway, vascular access lines, catheters, and monitors	Coordinated turning by a skilled team
		Injury to arms (shoulder dislocation, humerus fracture, soft tissue injury)	Awareness regarding the possibility of undergoing arm to fall into the gap between trolley and operation table and careful attention during turning
		Injury to eyes Corneal abrasions Ocular edema Postoperative visual loss (POVL)—Retinal ischemia, lens displacement, blindness	Ocular lubricants and tape eyelid shut, head elevation above heart, correct-size horseshoe headrest to prevent slipping of head and compression of eyes, adequate padding, avoiding hypotension and anemia
		Compression of ear (downside ear)—Cartilaginous damage, disfiguration	Avoid compression of dependent ear
		Injuries to facial and mandibular nerves	Avoid compression over the angle of mandible
		Neck torsion, flexion, and extension	Avoid extremes of neck position
		Intravascular volume pooling in lower limbs	Use compression stockings or Esmarch bandage from feet up to thighs
		Compartment syndrome	Avoid sharp angulation of knees or hips, tight wraps around lower extremities
		VAE	Monitoring, early detection, surgical steps to prevent air entrainment, air aspiration, and supportive management
		Nerve injuries, brachial plexus, ulnar neuropathy	Avoid stretch Padding of olecranon
		Thoracic outlet syndrome	A preoperative careful history, neck in the sagittal plane, arms tucked by the side without caudal stretch on shoulders or compression on the clavicle
		Breast injuries (adolescent female children)	Breasts to be placed in neutral or medial configuration, nipples not stretched,and supporting surface fixed and smooth
		Genital injuries (male children)	Check that external genitalia are free from compression after final position

Table 7.8 (continued)

Position	Benefits	Adverse effects	Management
Sitting	Optimal surgical exposure for posterior fossa surgery—Less tissue retraction and risks of cranial nerve damage, improved cerebral venous and cerebrospinal fluid drainage due to gravity, and less bleeding Patient's airway is easily accessible to the anesthesiologist	Hypotension	Fluid preloading Modify the anesthetic technique Fluid resuscitation and vasopressors Lower limb compression stocking to augment venous return Continuous monitoring and minimizing severity and duration of hypotension
		Endotracheal tube compression due to excessive neck flexion	Check peak airway pressures and compare to patient's baseline, two fingerbreadths between mandible and neck to avoid acute neck flexion
		VAE	Monitoring, early detection, surgical steps to prevent air entrainment, air aspiration, and supportive management
		Paradoxical air embolism	Rule out intracardiac defects
		Cardiac dysrhythmias	Monitoring, timely recognition, identifying and eliminating cause when possible, prompt use of medications to restore normal sinus rhythm
		Nerve injuries	Adequate padding
		Pneumocephalus	Occurs 100% in sitting, 72% in a park bench, and 57% in prone to keep in mind in case of delayed arousal, ventilate with 100% FiO_2, or give high-flow oxygen—Resolving spontaneously Tension pneumocephalus is an emergency and may present as worsening consciousness or seizures; treatment is twisted drill evacuation of air at the bedside
		Injuries to cervical vertebrae and spinal cord (mid-cervical flexion myelopathy)—Stretching of spinal cord due to excessive neck flexion resulting in spinal cord ischemia exacerbated by loss of autoregulation, intraoperative hypotension, and surgical retraction	Avoid extreme neck flexion, head positioning should be done slowly with careful torsion and flexion and never forced Avoid intraoperative hypotension and treat aggressively when occurs
		Edema of face, tongue, and neck—Venous and lymphatic obstruction of tongue, macroglossia	Avoid extreme neck flexion Use soft intraoral bite block to have more pace in oral cavity and therefore less compression of tongue
		Ischemia of lower extremities—Compartment syndrome	Avoid hyperflexion of thighs over the abdomen, maximum 90° flexion of thighs to prevent kinking of femoral vessels

Table 7.9 Comparison of complications in different neurosurgical positions

Complication(s)	Supine	Lateral/three-quarter prone	Park bench	Prone	Sitting
Nervous system					
Cerebral ischemia	0	0	+	+	++
Cervical spine ischemia	0	0	+	+	++
Nerve palsies					
Cranial nerve	?	++	?	++	+
Brachial plexus	?	++	++	?	+
Sciatic nerve	+	0	0	0	+
Peroneal nerve	?	?	?	0	+
Airway					
Edema of face, tongue	0	+	0	++	++
Endotracheal tube	+	+	+	++	++
migration	?	+	?	++	++
Postoperative respiratory obstruction					
Pulmonary system					
Ventilation-perfusion	0	+	+	+	+
abnormalities	0	0/ +	0	++	0
Increased airway pressures					
Cardiovascular system					
Hypotension	0	0/ +	+	++	++
Dysrhythmias	0	0/ +	++	++	++
Need for blood transfusion	+/ 0	+/ 0	+	++	+
Miscellaneous					
Eye compression	0	++	+	+++	0
Postoperative visual loss	0	+	+	+++	0
Compartment syndrome	0	0	0	0	+
Venous air embolism	+	+	++	++	+++
Paradoxical air embolism	?	?	?	+	++
Tension pneumocephalus	0	0	?	0	++

0, +, ++, +++, showing relative chance of occurrence 0 being no risk to +++ being very high risk;?, risk not known

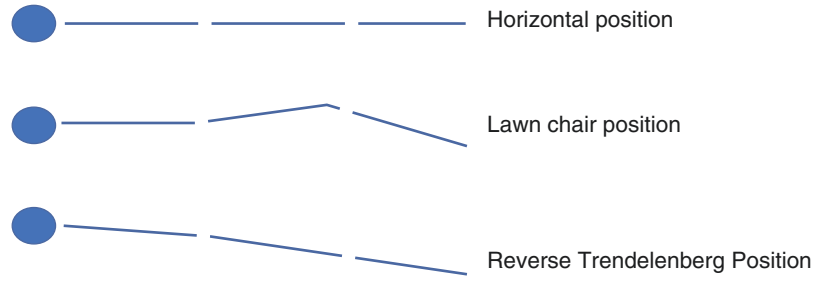

Fig. 7.1 Schematic diagram of variations of supine position

fossa may be approached with the patient lying supine with the head maximally turned to the contralateral side. The supine position avoids several of the complications accompanying other positions used in posterior fossa surgery. This position is easily achievable and does not require any special aids.

The three common variations of supine position (Fig. 7.1) used in neurosurgery are (i) ***horizontal position*** where the patient is placed with his/her back completely flat against the operating table, (ii) ***head-elevated supine position or the reverse Trendelenburg position*** where the whole body is tilted 10–15° above

horizontal axis from the head end, and (iii) ***lawn chair (contoured supine) position*** which results from 15° flexion at hips and knees and prevents stress on the back.

Pediatric patients are susceptible to airway obstruction in supine position due to neck flexion resulting from larger heads compared to torso. This can be prevented by placing a roll under the shoulders. If the head is turned to a side, there can be excessive tension due to stretch on the neck muscles and nerves, which must be avoided. All pressure points that are at risk in the supine position must be well padded.

7.4.2 Lateral Position

The lateral position is commonly used for access to the temporal lobe, skull base, and lateral posterior fossa lesions and also anterolateral approach to the thoracolumbar spine. It promotes gravity-aided retraction of the dependent cerebellum and allows CSF and venous drainage from the uppermost posterior fossa, thus making it suitable for unilateral surgical procedures. The incidence of VAE and postural hypotension is low compared with sitting positions. The patient is easily accessible. The major disadvantage is the possibility of peripheral nerve damage.

The positioning of patients must be performed scrupulously. The upper limb is usually stretched and taped to prevent the shoulder from coming into the surgeon's view. Excessive traction should be avoided to prevent brachial plexus injury. Evoked potential (EP) monitoring may help in the detection of neural ischemia. Head-up tilt of the operating table causes the shoulder to fall away from the surgeon and allows better drainage of CSF and blood from the surgical site. A roll is placed under the chest just below the dependent axilla. Migration of the axillary roll (a misnomer; correct is chest roll placed beneath the dependent chest to keep axilla free from compression) may cause compression injuries to the brachial plexus [25] and must be checked after the final position (Fig. 7.2). The dependent arm is positioned along the patient's side. The dependent leg should be positioned flexed with a pillow between the knees to avoid lateral popliteal nerve damage.

The upper leg is placed straight with adequate padding. The patient's head is usually immobilized with three-pin skull fixation. If a headrest is used, the dependent ear and eye should be protected from compression injury [25–27].

7.4.3 Park Bench Position

This is an adaptation of the lateral position resembling a drunk reclining on a park bench. The dependent shoulder and arm, supported by a sling, are positioned outside the operating table.

The patient is semi-prone and the head rotated and flexed with the brow facing the floor. This

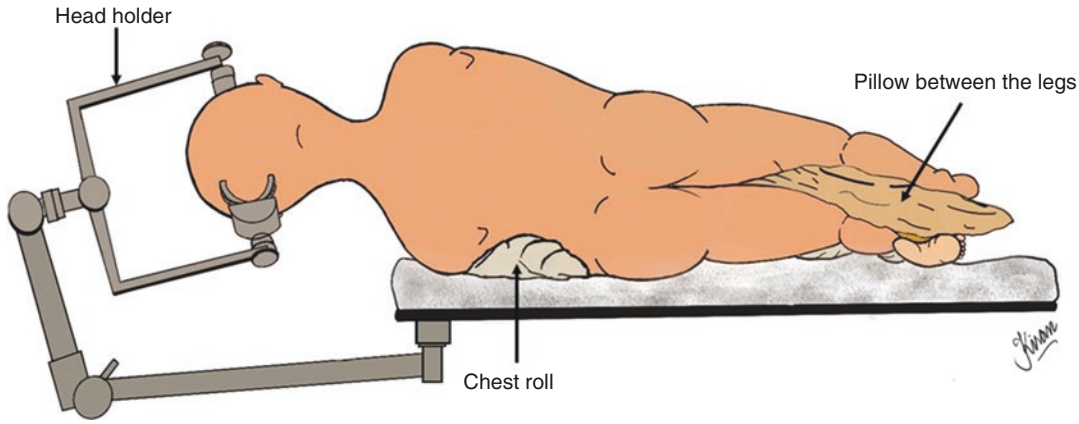

Fig. 7.2 Diagrammatic representation of lateral position

enables better access to midline structures than with the straight lateral position. The peripheral nerves have to be protected with good padding as well as with the lateral position. The incidence of venous engorgement and macroglossia is similar as with supine position with lateral head rotation [26, 28, 29].

7.4.4 Prone Position

The prone position is used to approach the midline posterior fossa structures, the cranio-cervical junction, and upper spinal cord and in major thoracic and lumbosacral spine surgery and detethering procedures of the spinal cord. The patients have to be carefully selected.

A "U-shaped" bolster is placed under the child to allow free movement of the abdomen and diaphragm and avoid ventilatory compromise in this position. Small rolls or bolsters can be placed under the upper chest and the pelvis in small children (Fig. 7.3). Displacement of the roll under the patient's abdomen would increase intra-abdominal pressure and compress the inferior vena cava and epidural veins, resulting in increased bleeding during spinal surgery.

The venous pooling in the lower limbs reduces the venous return, which may be poorly tolerated. The head is usually elevated to assist drainage of fluid from the surgical site, which predisposes to VAE, but its risk is less than the sitting position. VAE can occur in spinal surgeries, too, in the prone position [30]. If the horseshoe headrest is used, the eyes have to be protected and the face is adequately padded to avoid compressive complications [31]. Restricted access to the airway and monitoring apparatus is a major disadvantage of the prone position. Should cardiopulmonary resuscitation be required, it can be severely compromised due to inadequate access to the chest wall and delays due to repositioning the patient.

7.4.5 Head-Elevated Prone or Concorde Position

Head-elevated prone position is a modification of the prone position where the patient's head is flexed and is elevated above the level of the heart. Kobayashi described the Concorde position [32] to approach the pineal and cerebellar lesions via a suboccipital craniotomy. Here, the suboccipital craniotomy is done with the head neutral in the Sugita head clamp, and then, the head is tilted to the right with the face turned to the right to approach the surgical lesion [33, 34].

The modified prone positions allow safer access to the posterior fossa and cervical spine than the sitting position. Venous congestion at the surgical site is avoided due to gravitational drainage of blood. The head-elevated prone position based on the degree of head elevation above the level of the heart can cause cerebral hypoperfusion and VAE. Further, if resuscitation is needed, accessing the anterior chest for cardiac compres-

Fig. 7.3 Prone position in a 6-year-old child for midline suboccipital craniotomy and excision of posterior fossa tumor, placed on two bolsters at chest and pelvis (yellow arrows) wrapped with disposable warming blanket (blue arrow) of a convective temperature management system

sion may be difficult as it may be time-consuming and disrupt the surgical field. However, recent reports have described the successful resuscitation of pediatric patients undergoing neurosurgery by placing hands over scapulae and defibrillator pads in posterior lateral position while the patient still remaining prone [35, 36].

7.4.6 Sea Lion Prone or Sphinx Position

This is a modification of the head-elevated prone position [32] where the head is maintained in the midline. The neck is extended to allow maximum access to the top of the skull, and the back is arched or hyper lordotic. This position is used for craniosynostosis surgery.

7.4.7 Sitting Position

The sitting position bestows the surgeon with superior exposure of midline structures and the cerebellopontine angle. It minimizes the need for surgical retraction by promoting drainage of blood and CSF, and allowing the cerebellar hemispheres to fall away [37–39]. There are less bleeding, lower incidence of cranial nerve damage, and complete resection of the lesion. The anesthesiologist has unhindered access to the patient's airway, extremities, and monitoring apparatus. The chest wall is also accessible if there is a need for resuscitation. Ventilation is better than with other positions due to unrestricted diaphragmatic excursion, which is noted as improved vital capacity and functional residual capacity.

However, when alternative positions can be used more safely, the sitting position is infrequently used in most centers because of its possibility for serious and life-threatening complications [40] like significant hypotension, VAE, paradoxical air embolism (PAE), quadriplegia, pneumocephalus, and pneumoventricle [41]. Macroglossia and peripheral nerve injuries are much more likely to occur with the sitting position [42–45]. The incidence of VAE is found to be similar in adults and children [46]. A rare complication is bilateral posterior compartment syndrome. Tension pneumocephalus may occur if watertight dural closure is not done; the patient may present with altered sensorium and seizure postoperatively, which can only be relieved by immediate burr-hole drainage of air. However, with modern monitoring, early signs of VAE and brainstem compromise can be detected, and serious complications can be avoided. The relative contraindications for surgery in sitting position include open ventriculoatrial shunt, platypnea, orthodeoxia, diagnosed presence of patent foramen ovale (PFO), and extremes of age. Reports suggest this positioning is utilized safely for neurosurgery among children between 3 and 18 years of age [40], and even below the age of 3 years [43].

The patient is thus placed in the sitting position. The cranial fixation device, usually the three-pinhead holder, is applied following anesthesia induction. Thigh-high compression stockings are applied to the legs, ensuring that they do not act as a tourniquet and intermittent pneumatic compression throughout the surgery to prevent deep vein thrombosis (DVT). The cardiovascular parameters are closely monitored while the operating table is slowly flexed with the arterial pressure transducer at the level of the skull base. Before positioning, the patient is preloaded with intravenous fluids.

The final position is in-between semi-recumbent and full sitting, with the knees flexed and the feet at the heart level. Over flexion of the hip should be avoided as it can cause kinking of the femoral vessels, and traction on the sciatic nerve. The common peroneal nerve may be compressed at the fibular head, and adequate padding can avoid this complication. Over flexion of the neck must be avoided [28, 29, 42, 44]. There should be at least two fingerbreadths between the chin and the nearest bony prominence (Fig. 7.4). The tongue should not protrude between the teeth. The arms are folded with the hands resting on the lap with overlapping open palms ("Buddha" posture). All the pressure points at the elbows and lateral and medial aspects of the knees and heels should be sufficiently padded.

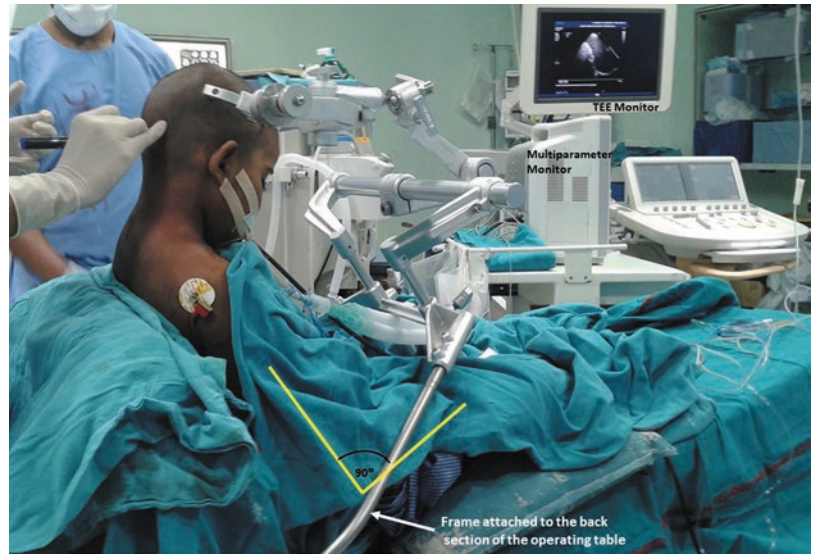

Fig. 7.4 Sitting position in a 9-year-old child for surgical excision of a fourth ventricular tumor

7.5 Conclusion

Good patient positioning is the first step to a successful surgery. Attention to small details during positioning can prevent major catastrophes. Understanding the physiology related to each position enables us to consider the favorable and adverse consequences before the child is positioned. As neurosurgery is continually evolving with new procedures necessitating different positioning, prior assessment complications and new problems can be done to avoid future mistakes. Close communication between the surgical team, anesthesia team, and operating room personnel is key to optimal pediatric patient positioning. Maintaining homeostasis during the perioperative period is vital for good patient outcomes.

Conflict of Interest Nil.

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8 Monitoring Children Undergoing Neurosurgery

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Key Points

- Minimizing secondary brain injury is the fundamental premise of perioperative management of neurologically injured children.
- Standard monitoring involves electrocardiogram (ECG), pulse oximetry (SpO_2), noninvasive blood pressure (NIBP), end-tidal carbon dioxide ($EtCO_2$), the fraction of inspired concentration of inhalational agents (FiAA), precordial stethoscope, temperature probe, peripheral nerve stimulator to monitor neuromuscular blockade, and a urinary catheter to monitor output.
- Multimodality neuromonitoring such as intracranial pressure (ICP) monitor, near-infrared spectroscopy (NIRS), transcranial Doppler (TCD), etc. can be used to determine adequate perfusion to the brain.
- Other modalities such as evoked potentials may be used to ensure the integrity of neurological tracts during surgery and prevent iatrogenic injury.
- Children have significantly different neurophysiology as compared to adults, which should be borne in mind when choosing parameters to monitor.

8.1 Introduction

Irrespective of the age of the patient, both anesthesia and surgery induce physiological changes, and therefore, there is a need for monitoring during the perioperative period. This need for monitoring continues into time spent in intensive care units (ICUs), with patients remaining in altered pathophysiological states. Advancements in surgical and anesthetic techniques have led to an increased number of complex neurosurgical procedures being performed in children and at an increasingly younger age. Perioperative monitoring in these children includes standard monitors suggested by the American Society of Anesthesiologists (ASA) as well as other special monitors such as neuromonitoring, depending on the requirement of the patient and procedure. This chapter aims to detail the role of perioperative neuromonitoring in pediatric patients.

Neurological assessment may be difficult among pediatric patients, and these children are at risk for neurological injury during surgery. Multimodal monitoring techniques can help provide data regarding the structural as well as functional integrity of neuronal structures and may help prevent damage via early identification of neural structures and detection of neurological

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dysfunction at a potentially reversible stage. The use of perioperative neuromonitoring during neurosurgery in children has progressed substantially over the last decade. The same techniques used in adults can also be applied to the pediatric population, despite the added considerations of the immature nature of the pediatric nervous system (incomplete myelination, reduced conduction velocities, etc.), which may increase the difficulty in obtaining the data and also contribute to the increased sensitivity of neural tissue to anesthetic agents. The equipment also requires certain modifications in terms of size to enable neuromonitoring in the pediatric population. In the interest of *do no harm*, neuromonitoring techniques should be utilized whenever a potential mechanism of injury exists.

8.2 Basic Monitoring

The choice of monitoring modality depends on the child's age, condition, and the nature of the surgery being performed. Standard monitoring for all pediatric neurosurgical patients (Fig. 8.1) involves electrocardiogram (ECG), pulse oximetry (SpO_2), noninvasive blood pressure (NIBP), end-tidal carbon dioxide ($EtCO_2$), a fraction of inspired concentration of anesthetic agents (FiAA), precordial stethoscope, temperature probe, peripheral nerve stimulator to monitor neuromuscular blockade, and also a urinary catheter to monitor the output. Intravenous (IV) catheters, arterial catheters, and nerve stimulators are placed on a limb other than that being used by the neurosurgeon to assess motor function. An arterial cannula is frequently cited in craniotomies since there is a risk for sudden and significant hemodynamic flux. Increased paradoxical pressure tracing in children on positive pressure ventilation is often used as surrogate marker for intravascular volume depletion.

Capnography or $EtCO_2$ monitoring is useful to detect events such as airway obstruction or reduced respiratory efforts, especially in remote access locations such as magnetic resonance imaging (MRI) suites, and may also be useful for early identification of venous air embolism (VAE) during neurosurgical procedures. Normocapnia is usually maintained during neurosurgeries. Continuous temperature monitoring constitutes part of basic intraoperative monitoring; however, it takes on added significance in the pediatric operative setting. In infants or children undergoing prolonged surgeries, heat loss exceeds heat generation since they have a higher surface area/mass ratio than the adults. Surgeries commonly performed in this population, such as

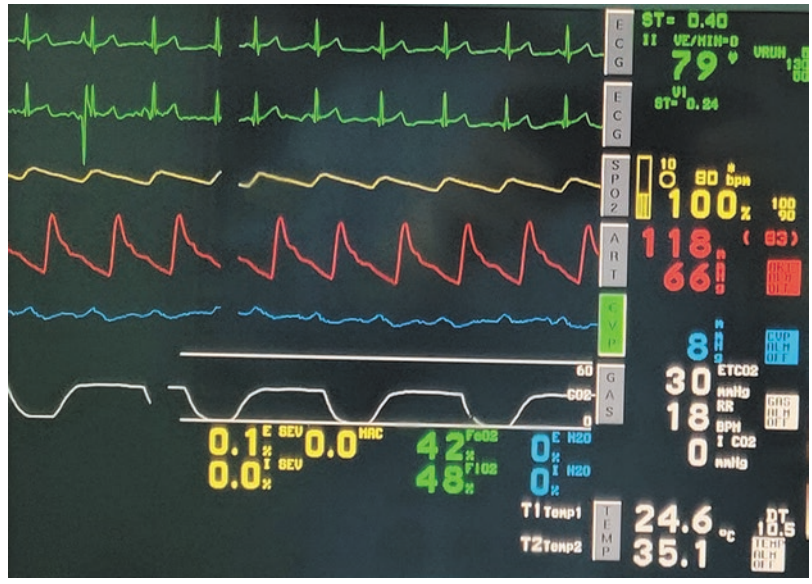

Fig. 8.1 Standard multiparameter monitoring in a 6-year-old child undergoing excision of a posterior fossa tumor

ventriculoperitoneal shunt surgery, endoscopic third ventriculostomy (ETV), etc., cause significant temperature swings, and physicians should be aware that hypothermia can lead to impairment of cardio-respiratory function and delayed recovery from anesthesia.

8.3 Special Monitoring

This chapter deals primarily with neuromonitoring modalities in the pediatric population. However, modalities of intraoperative monitoring with special applications in the pediatric setting are also discussed. Central venous catheters are usually inserted for surgeries where large fluid shifts are expected and may be positioned in the right atrium when VAE is an intraoperative possibility. The central venous pressure essentially reflects the right atrial pressure and, in the setting of a normal tricuspid valve, approximates right ventricular end-diastolic pressure, which is a marker of preload. Precordial Doppler ultrasound may also be used in children undergoing craniotomies to monitor for VAE events since the large size of the head in children relative to the body predisposes them to air entrainment, especially in the head-up position. Another useful modality to screen for intraoperative emboli is the use of transesophageal echocardiography (TEE). TEE is a more sensitive tool for the detection of VAE events than precordial Doppler and is, in fact, so sensitive that it can detect even microbubbles that may be hemodynamically insignificant. TEE requires special expertise to operate as well as interpret findings, making it a resource-intensive monitoring modality.

Devices to monitor cardiac output and fluid responsiveness are useful in the operating room (OR) as well as the intensive care units (ICUs). They may be classified as invasive such as arterial catheters, pulmonary catheters, or esophageal probes, or noninvasive such as thoracic bioimpedance, ultrasound-based CO monitoring, etc. Bioimpedance cardiac output monitoring has the advantage of being completely noninvasive and cost-effective; however, its accuracy is still being evaluated. The basic principle behind cardiac output measurement based on bioimpedance measurement is that the heart chambers are electrically insulated. Hence, changes in chest impedance and reactance are linked to variations of volume passing through the aorta.

Point of care (POC) testings for various parameters have improved to high standards and are now reliable tools with the added advantage of portability. Devices to monitor hemoglobin levels, viscoelastic tests of coagulation, arterial blood gases, etc. have been studied and validated in the pediatric setting [1]. In neurosurgical cases, where large fluid shifts and blood loss is anticipated, such as during vascular or large intracranial tumor surgeries, use of viscoelastic tests of coagulation such as thromboelastography (TEG), rotational thromboelastometry (ROTEM), or Sonoclot analysis as well as POC tests of hemoglobin may provide real-time feedback to treating physicians and guide hemostatic management. These tools may be especially beneficial in the pediatric population, which has limited hemodynamic reserve.

8.4 Monitoring the Nervous System

The fundamental premise of perioperative management of neurosurgical patients is the limitation of secondary injury to neural structures. In this regard, several new technologies (Fig. 8.2) have been developed in recent years, which help assess specific neural pathways at risk during certain surgeries. Children have an immature nervous system as compared to adults, with certain features such as incomplete myelination posing significant challenges to the monitoring of neural tracts.

8.4.1 Monitoring Intracranial Pressure and Cerebral Blood Flow

8.4.1.1 Intracranial Pressure (ICP)

Defining normal ICP values in children is difficult, as ICP may change as the child grows. The highest normal accepted value for ICP by con-

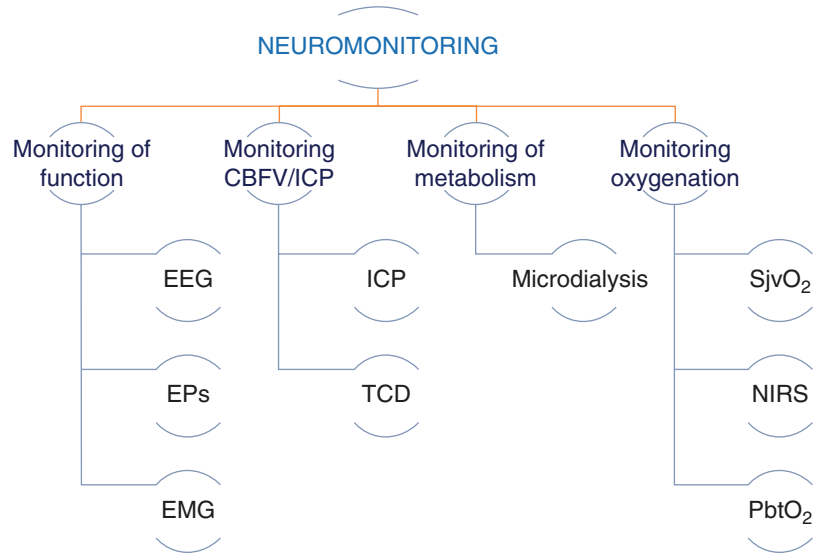

Fig. 8.2 Shows different modalities for neuromonitoring. Footnotes: *CBFV* cerebral blood flow velocity, *ICP* intracranial pressure, *EEG* electroencephalogram, *EPs* evoked potentials, *EMG* electromyography, *TCD* transcranial Doppler, $SjVO_2$ jugular venous oxygen saturation, *NIRS* near-infrared spectroscopy, $PbtO_2$ brain tissue oxygen saturation

sensus between the ages of 4 and 16 is 12.9 mmHg. In mechanically ventilated children below the age of 1 year, a value of 5 mmHg is regarded as the upper limit of normal for ICP. Older children in this scenario have a maximal allowable ICP of 10 mmHg [2]. There has never been a randomized controlled trial of ICP monitoring in this age group. However, Mehta and colleagues suggested ICP monitoring to target a CPP of 45 mmHg after TBI to avoid brain ischemia [3]. According to guidelines for brain injury management in pediatric patients, elevated ICP should be treated when greater than 20 mmHg (level III recommendation) [4]. Other than the neurological examination, one of the most basic rough assessment methods of raised ICP in the pediatric age group is palpation of an open, tense anterior fontanelle, increased head circumference, and splayed cranial sutures [5]. Few important radiological features are as in Table 8.1.

ICP monitoring can be carried out by direct and indirect methods.

Direct Methods

- **Ventricular Cannulation**: An external ventricular drain (EVD) is considered the gold standard of ICP monitoring, as they can be used for monitoring as well as therapeutic purposes. The EVD is placed via a burr hole at Kocher's point into the frontal horn of the lateral ventricle, and ICP can be measured via a pressure transducer [6]. The major advantage of using such a system to measure ICP is that drainage of cerebrospinal fluid (CSF) can be used to control spikes in ICP. There is a risk of CSF infection when monitoring is done for greater than 72 h. Cannulation may also be a challenge when ventricles are compressed or displaced due to pressure effects. Ngo et al. studied rates of EVD-associated complications, and found a complication rate of 26% (overall) in children, with the most frequent complication being catheter infection (9.4%) [7].
- **Epidural and Subdural ICP Devices**: Subdural bolts need to be fixed to the cranial vault following insertion, and hence are not used in very young children. Although this monitoring modality carries the advantage of lesser infection rate than EVDs, CSF drainage cannot be performed [8]. Extradural devices tend to be bulky, and insertion may lead to the formation of an extradural hematoma at the site of insertion. Extradural monitors also tend to underread ICP, particularly at higher pressures.
- **Intraparenchymal Devices:** These devices are easy to place and have fewer infectious sequelae as compared to EVD's [9]. Insertion

Table 8.1 Radiological features of raised intracranial pressure in certain conditions

Traumatic brain injury	Acute hydrocephalus	Chronic hydrocephalus
• Basal cisternal compression • Midline shift • Presence of epidural hematomas • Subarachnoid/intraparenchymal blood	• Enlarged temporal horns of lateral ventricles • Transependymal edema, or periventricular lucency • Outward bowing of the third ventricle • A distended fourth ventricle may suggest that the obstruction is at the level of the foramina of Luschka or Magendie	• Marked dilatation of the lateral and third ventricles • Thinned and elevated corpus callosum • Fenestration of the septum pellucidum • Obliteration of the suprasellar cistern • Forniceal depression

involves sitting a thin single-use catheter via a burr hole into the cranial vault, attempting to put it 1–2 cm into the brain parenchyma. Shifting of ICP trends was often encountered in earlier devices but is seen less frequently in current models [10]. The Camino ICP monitor is a fiber-optic device, which transmits light toward a movable mirror. Changes in ICP lead to changes in the position of the mirror, and changes in the reflected light are used to approximate an ICP value. The Codman sensor is a piezoelectric strain gauge device: changes in ICP cause bending of the transducer and change in its resistance; thus, ICP can be calculated (Fig. 8.3). One of the largest studies on ICP monitoring in pediatric trauma patients by Alkhoury et al. suggested a small survival advantage associated with ICP monitor insertion in patients with the most severe variants of brain injury, with a GCS of 3 [11]. However, children with ICP monitors had a prolonged ICU length of stay and more ventilator dependent days than children without ICP monitoring. Hence, more data is needed to define the proper use of ICP monitoring in this population. The *ADAPT* (Approaches and Decisions in Acute Pediatric Traumatic Brain Injury), *trial*, an observational study to evaluate the effectiveness of therapies that control intracranial hypertension, prevent secondary insults, and normalize metabolism, has recently completed recruitment of 1000 pediatric TBI patients over 2.5 years and 8 countries. This trial might answer some of the queries related to monitoring and acute medical management of children with traumatic brain injury soon.

Indirect Methods

These are noninvasive and include optic nerve sheath diameter and tympanic membrane displacement.

- **Optic Nerve Sheath Diameter (ONSD)**: An acute increase in ICP is reflected in the perioptic nerve sheath, which then manifests as increased optic nerve sheath diameter [12]. Transorbital sonography is a safe and noninvasive method to measure the optic nerve sheath diameter (ONSD) for the diagnosis of raised ICP in children; it may facilitate the initiation of early treatment (Fig. 8.4). ONSD is measured by insonating the orbit in the transverse plane, 3 mm posterior to the papilla bilaterally. Upper normal limits for ONSD are considered to be 4 mm in infants and 4.5 mm in older children [13]. Studies have also suggested that when pediatric patients present with an ONSD >6.1 mm following TBI, invasive ICP monitoring should be considered [14].
- **Tympanic Membrane Displacement (TMD):** This technique that was described nearly 20 years ago by Marchbanks is a safe, painless, and noninvasive means of estimating ICP. The reflex contraction of the stapedius and tensor tympani muscles upon sound is affected by changes in ICP, which forms the premise for this monitoring modality [15]. As CSF and cochlear perilymph are connected via the cochlear aqueduct, an increase in ICP is transmitted to the stapes, changing the direction and magnitude of eardrum movement in response to sound. Inward movement of the tympanic membrane suggests high ICP,

Fig. 8.3 Intracranial pressure (ICP) monitoring with Codman intraparenchymal catheter in a 2-year-old male child with severe traumatic brain injury

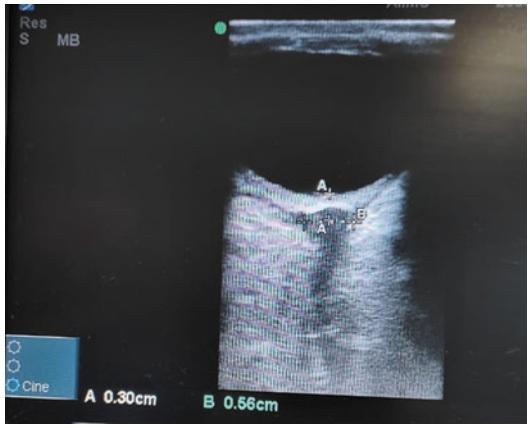

Fig. 8.4 Optic nerve sheath diameter (ONSD) measurement in a 2-year-old child with severe traumatic brain injury. ONSD measured 3 mm behind the papilla (*A*); a diameter of more than 4.5 mm (*B*) was considered as significant

and outward movement indicates normal or low ICP.

- **Quantitative Pupillometry:** This is a relatively new technology that can be used as a noninvasive tool to monitor the neurological status of patients. It provides an objective measure of velocities of changes in pupillary diameter and pupil size. Increased ICP has been associated with an increased latency in a change in pupillary diameter, which can be detected using this tool. Changes in pupil diameter can also provide an index of nociception through opioid-mediated constriction or dilation mediated by autonomic innervation of the muscles surrounding the iris, and pupillometry has previously been studied as an objective method to quantify pain intensity in children.

8.4.2 Monitoring Metabolism and Oxygenation

8.4.2.1 Near-Infrared Spectroscopy

Near-infrared spectroscopy (NIRS) is a noninvasive means of monitoring regional brain tissue oxygenation, using infrared light, in a similar manner to pulse oximetry to measure the absorption of infrared light, by tissue chromophores [16]. The basic principle underlying NIRS is a change in the absorption patterns for specific wavelengths of infrared light when hemoglobin binds to oxygen. The NIRS sensor consists of a diode that emits light and two sensors that pick up light, all placed at a fixed distance from each other (Fig. 8.5). The diode emits the infrared

light, which enters the superficial tissue, some of it is absorbed, and some is reflected back. The sensors are arranged in such a way that light reflected from superficial tissues reaches the closer sensor and light reflected from deeper tissues is picked up by a farther sensor. The reflected light is analyzed according to the Beer-lambert law. NIRS readings are interpreted as a single percentage value (rSO_2) between 15 and 95%, which is calculated as the ratio of oxyhemoglobin to total hemoglobin within the irradiated tissue. Dix et al. concluded that there was a good correlation between pediatric and neonatal NIRS sensors. However, a comparison between adult, pediatric, and neonatal sensors showed a difference in readings between 10 and 14%, with higher values in the pediatric and neonatal sensors [17].

Continuous monitoring of rSO_2 may help detect periods of decreased cerebral perfusion and help guide intervention at an early stage that may decrease the risk of neurological sequelae. Evidence suggests a potential benefit for its use in children during surgery for congenital heart defects in children [18]. Kurth et al. noted lower baseline rSO_2 in patients with cyanotic heart disease and found that rSO_2 values correlated with PaO_2 values. They suggested that NIRS use may be useful to identify the duration of cooling and cardiopulmonary bypass (CPB) before deep hypothermic circulatory arrest (DHCA) [19]. Current literature suggests that an absolute decrease of 20% from baseline NIRS values could serve as a trigger for intervention to prevent potential cerebral hypoxemia. NIRS may also find use as a prognostic indicator following TBI. Adelson et al. suggested that NIRS reliably detected changes in intracranial hemodynamics and may help understand the etiology of diffuse cerebral edema following pediatric TBI [20].

Within the OR or ICU settings, NIRS may also be used as a marker of cardiac output and tissue perfusion. NIRS may serve as a proxy for mixed venous oxygen saturation, and probes may be placed at various sites other than the head, such as in the abdomen, to measure mesenteric rSo_2 and renal area to predict ischemic renal injury.

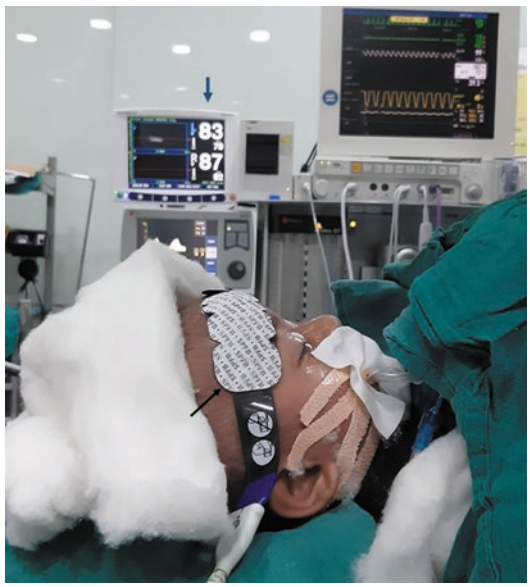

Fig. 8.5 Bilateral forehead NIRS (near-infrared spectroscopy) sensors (*black arrow*) and NIRS monitor (*blue arrow*) for regional cerebral oxygenation (rSO_2) monitoring (INVOS™ 5100C Cerebral/Somatic Oximeter) in a 3-year-old female child with retinoblastoma undergoing intra-arterial chemotherapy in the interventional neuroradiologic suite

8.4.2.2 Brain Tissue Oxygen ($PbtO_2$) Monitoring

Direct measurement of cerebral tissue oxygen tension serves as a reflection of cerebral perfusion and local oxygen extraction. The Licox monitor is basically a miniaturized Clark electrode, which continuously measures $PbtO_2$. The probe is typically inserted into the penumbra of injured tissue, through a burr hole into the right frontal white matter in the absence of localized lesions or else in the hemisphere having focal lesions. Oxygen from the tissue diffuses through a permeable membrane and creates a current proportional to the oxygen concentration within the tissue being sampled, typically an area of 18 mm^2. The Licox monitor converts the electrical current to a numerical value for $PbtO_2$. Normal $PbtO_2$ value is approximately 40 mmHg, and a value of 22 mmHg is considered to be the critical ischemic threshold of cerebral perfusion (18 ml/100 g/min) [21]. It has been suggested that the reduced values of $PbtO_2$ in children with TBI are associ-

ated with a poorer prognosis [22]. Due to the lack of evidence for $PbtO_2$ monitoring, recent pediatric TBI guidelines suggest a level III recommendation to target a $PbtO_2 \geq 10$ mmHg [16]. These devices may be used to measure brain temperature as well. Measurement of core body temperature often leads to underestimating brain temperature, and dissociation between the two could be an indicator of poor prognosis. Measurement of brain temperature and timely institution of therapeutic hypothermia could improve outcomes by reducing secondary brain injury in conditions such as status epilepticus, meningitis, TBI, etc.

8.4.2.3 Jugular Venous Oximetry

Jugular venous oximetry ($SjvO_2$) measures the balance between oxygen supply and demand. A catheter similar to standard catheters used for monitoring central venous pressure is inserted into the jugular bulb of the internal jugular vein (IJV) ipsilateral to the lesion, in a retrograde manner for continuous monitoring or sample aspiration [23]. On a lateral radiograph, the tip of the catheter is positioned at the level of the mastoid process and also above the lower border of the C1 vertebra. The jugular blood contains blood being drained from both hemispheres of the brain, 70% from the ipsilateral and 30% from the contralateral hemisphere. Oxyhemoglobin has a specific light absorption pattern, and this is used in the monitoring of $SjvO_2$. These catheters typically contain two optical fibers, one to direct light into the blood and another to direct reflected light into a sensor that measures the absorption of light.

Oxygen demand in the brain is primarily influenced by the cerebral metabolic rate of oxygenation ($CMRO_2$). Increases in $SjvO_2$ may suggest increased CBF, increased oxygen delivery, or reduced $CMRO_2$ [24]. Similarly, decreased $SjvO_2$ may be due to reduced brain perfusion, hypoxemia, or increased $CMRO_2$. The normal range for $SjvO_2$ in adults is 50–75%, but normal ranges for children have not been established. Perez et al. observed a significant association between two and more events of $SjvO_2 < 50\%$ with poor outcomes in pediatric TBI patients; however, values >70% were not associated with worsened outcomes [25].

8.4.2.4 Cerebral Microdialysis

Monitoring the milieu of the brain tissue may help identify secondary brain injury at an early stage and allow the application of neuroprotective therapies. Cerebral microdialysis is a monitoring device used increasingly in the intensive care setting to understand cerebral energy metabolism [26]. Essentially, the catheter consists of a double-lumen probe with a semipermeable dialysis membrane at a gold tip. The probe is placed into the brain parenchyma and perfused with fluid isotonic with brain tissue interstitium. The perfusate traverses the membrane and reaches the brain parenchyma, where the exchange of the substances along the concentration gradient occurs. The fluid exits into a collecting chamber from where it is taken for chemical analysis. Since the perfusate flows at a constant rate (0.3μl/min), the concentration gradient is maintained. Typically, metabolic markers (lactate, pyruvate, glucose), excitatory neurotransmitters (glutamate), and markers of tissue damage (glycerol) are measured. Tolias et al. used microdialysis in pediatric TBI and concluded that values for excitatory neurotransmitters in the pediatric population differed from previously defined values in adults [27]. Normal values have been established in the adult population but are still not defined in children [28].

8.4.3 Transcranial Doppler (TCD) Ultrasonography

Transcranial Doppler (TCD) has become a vital tool in adult neurocritical care, allowing continuous monitoring of changes in cerebrovascular blood flow [29]. It involves the use of a 2 Mhz probe to insonate basal cerebral arteries through certain windows within the cranial vault. The *Doppler effect* states that when sound strikes a moving object, the reflected wave undergoes a change in frequency directly proportional to the velocity of the reflector. This is the basis for calculating cerebral blood flow (CBF) velocity with

TCD, assuming that the insonation angle and the vessel diameter are relatively constant. The insonated artery is identified through characteristics such as acoustic window, flow direction, and velocity in addition to waveform changes following maneuvers such as carotid artery compression. Increased flow velocities may indicate stenosis, vasospasm, or hyperdynamic circulation, whereas decreased values may indicate hypoperfusion, reduced ICP, or brainstem death. Various other factors, such as increased cardiac output, reduced hemoglobin levels, increased $PaCO_2$, cerebral vasodilatory agents, and hyperthermia, may also increase recorded TCD velocities. Flow velocities are typically higher in children than adults, increasing from birth and reaching their zenith at 6–8 years of age and then declining to the adult range by approximately 18 years of age.

Gosling's pulsatility index (PI) [(Peak systolic velocity (PSV)-End diastoilc velocity (EDV))/ Mean flow velocity (MFV)] provides information about vascular resistance; the normal range is 0.5–1.19 [30]. In adults, PI has been shown to correlate positively with increases in ICP; a PI change of 2.4% correlates to a 1 mmHg change in ICP [31]. In the pediatric population, TCD can be used to indirectly monitor ICP and cerebral perfusion pressure (CPP), with studies finding an 80% sensitivity value [32]. In contrast, Figaji et al. stated that the pulsatility index of TCD might not consistently represent ICP in children, showing that further studies are needed to establish associations between PI and cerebral perfusion pressure (CPP) [33]. TCD may also be used to evaluate cerebrovascular autoregulation. Disordered autoregulation has been observed in up to 40% of pediatric patients with significant TBI and has been associated with worsening outcomes [34]. TCD has also found an application in evaluating the risk of stroke in children with sickle cell disease. It has been seen that chronic blood transfusions, when implemented in children with middle cerebral artery (MCA) flow velocity of >200 cm/s, may decrease the risk of stroke by as much as 92% [35]. TCD may also provide information on cerebral hemodynamics with TBI, intracranial hypertension, CNS infections, and diagnosis of brain death in pediatric patients.

8.4.4 Monitoring of Function

8.4.4.1 Somatosensory Evoked Potentials (SSEPs)

Somatosensory evoked potentials (SSEPs) comprise a volley of signals generated when peripheral nerves are electrically stimulated. These signals travel from the nerve stimulated and ascend via the ipsilateral dorsal columns into the medulla, where the response travels to the contralateral side at the level of the arcuate fibers. The impulse is then relayed to the ventral posterolateral thalamus via the medial lemniscus and into the cortex via the posterior portion of the internal capsule. Thus, monitoring SSEPs provides information regarding the integrity of neural tracts from the periphery to the primary sensory cortex. The cortical SSEP is depicted as a graph of amplitude (μV) against time (ms). The latency of each recording has a typical appearance, which is due to the velocity of conduction of the neural impulse, length of tract, and the number of intervening synapses. Hence, factors such as age, developmental status, height, temperature, and anesthetic regimen affect latency.

The most frequently used nerves are mixed peripheral nerves such as the ulnar, median, and posterior tibial nerves. Baseline amplitude and latency readings are obtained before the start of surgery to determine any preexisting anomalies. Intraoperative SSEPs are obtained at frequent intervals and evaluated against the baseline readings to identify intraoperative changes. Alternating unilateral stimulation is preferred to detect unilateral spinal cord injury. A change is considered significant if there is a more than 50% decrease in amplitude or a 10% increase in latency. Direct spinal cord trauma tends to cause immediate changes, whereas cord ischemia results in delayed changes. The disappearance rate reflects the severity of the ischemic event; acute loss of SSEPs necessitates immediate intervention by the surgical team [36].

Anesthetic agents may alter both the amplitude and latency of SSEPs in a dose-dependent manner. Subcortical SSEPs are relatively resistant to anesthetic drugs but are influenced by changes in body temperature and cord perfusion. Neuromuscular blockers do not directly affect SSEPs but may improve waveform quality by the elimination of EMG artifacts [37]. SSEP signals may be more difficult to obtain in young children (<2 years) since their waveform is influenced by the immaturity of the pediatric nervous system. Partially myelinated tracts result in blunted peaks with delayed latencies [38].

8.4.4.2 Motor Evoked Potentials (MEPs)

Motor deficits may occur intraoperatively without sensory defect when only SSEPs are monitored, necessitating the monitoring of motor tract integrity as well. MEP and SEP pathways are situated in different anatomical and vascular areas of the nervous system, and motor tracts are more susceptible to ischemia. Penfield's technique, the low-frequency (50–60 Hz) stimulation with biphasic stimuli (0.5 ms) delivered via a bipolar probe, was first described 70 years ago and was considered the gold standard in children. It is still used for language mapping but has been abandoned elsewhere due to the risk of triggering intraoperative seizures and the relatively low success rate in mapping the motor cortex in very young patients.

Transcranial MEPs are obtained by applying a stimulus directly over the scalp above the primary motor cortex. This electrical stimulus leads to depolarization of axons on pyramidal motor neurons (D wave) and interneurons (I wave) and then travels along corticospinal tracts, activating the spinal motor neurons [39]. The MEP recorded from electrodes placed in muscles of interest represents the compound muscle action potential (CMAP). D waves correlate with the number of functional fibers of corticospinal tracts and can be observed even at >1 MAC of anesthetic agents [40]. I waves are extremely sensitive to anesthetics and cortical hypoperfusion, showing a sudden fall in MEP amplitude of 50–75% [41]. In general, volatile agents have a negative effect on MEPs even at low doses, except for desflurane, which has been used at 0.5 MAC [42]. Total intravenous anesthesia (TIVA) is the preferred anesthetic technique when MEPs are required, along with avoidance of muscle relaxants.

Increases in the strength of stimulus required to obtain the MEP of >50 V, increase in the number of stimuli, or significant decreases in amplitude (usually >80%) are generally considered significant. Infants may require a greater charge delivered to elicit reliable MEP responses, and this monitoring modality has lower reliability as such in children aged less than 6 years. In very young children, two other factors may complicate the acquisition of MEPs. The immaturity of the motor tracts leads to an increase in threshold; this may be balanced by the reduced thickness of the skull, which leads to lower impedance. Also, even though children have slower conduction velocities due to the immature motor tracts, they have shorter limbs, and this may balance out each other. Monitoring of motor as well as sensory pathways is now considered standard of care during corrective surgeries for spinal deformities such as scoliosis repair surgery, which is usually performed in the adolescent age group.

8.4.4.3 Electromyography (EMG)

Electromyography (EMG) refers to the recording of electrical activity that is produced by muscles. Intraoperative neuromonitoring (IONM) using either triggered or spontaneous EMG has become widely used for preserving neurological function during surgery. Small electrodes are placed in muscles that are innervated by the nerve roots at risk of injury. Stimulation of nerve roots or peripheral neurons produces a characteristic burst (short duration of irritation) or train (sustained irritation) of motor potentials called "neurotonic discharges," which show the presence and location of a nerve, as well as the potential for damage. The major point is that a sharp nerve transection may not lead to any change in EMG, and stimulation of the nerve distal to the injury will result in a normal EMG response.

EMG is recorded from muscles innervated by cranial nerves during intracranial surgeries and somatic muscles for other neurosurgical procedures. The facial nerve is the most frequently

injured cranial nerve during cerebellopontine angle surgeries, and EMG patterns of the facial nerve have prognostic value for postoperative facial nerve function. Neuromuscular blocking drugs are avoided whenever cranial nerve EMGs are recorded, as muscles of the face are usually more sensitive to the effects of neuromuscular blockers (NMBs). In children, this technique is frequently used for monitoring lower limb, bladder, and anal sphincter integrity during excision and repair of meningomyelocele and lipoma as well as untethering of the tethered cords (Fig. 8.6).

8.4.4.4 Visual Evoked Potentials (VEPs)

VEP monitoring is performed to assess the visual pathway to prevent postoperative visual dysfunction. A light source is placed over closed eyelids, and each eye is stimulated separately by 40–100 flashes to obtain an averaged waveform. Recording montage includes electrodes placed over the occiput, in addition to an electroretinogram (ERG) reading to verify the arrival of light stimulus at the retina. Stable readings are difficult to obtain, and VEP data may not reach sufficient reliability to predict impending or established damage to visual tracts. Anesthetic agents significantly affect VEPs, especially volatile agents. This technique may be of use during surgeries that are adjacent to the optic tracts, as well as tumors involving or displacing the optic radiations [43]. Another potential application of VEP monitoring could be the assessment of development of children since the visual function triggers motor development and integrative functions. It has been observed that children with delayed VEP latencies showed more developmental delays than children with normal VEP latencies [44].

8.4.4.5 Brainstem Auditory Evoked Responses (BAERs)

BAERs are obtained by generating a series of repetitive sounds to stimulate the eighth cranial nerve while providing white noise to the other ear. The BAER is measured at the vertex, using an electrode placed over the mastoid as reference. Normal latencies are short; the total time for recording is usually about 10 ms, dividing BAERs into short-, medium-, and long-latency responses. Clinically relevant responses are short-latency values, which are resistant to the effects of anesthesia and are known as waves I–V. These represent the distal cochlea (I), proximal cochlea (II), cochlear nucleus (III), lateral lemniscus (IV), and inferior colliculus (V) [45].

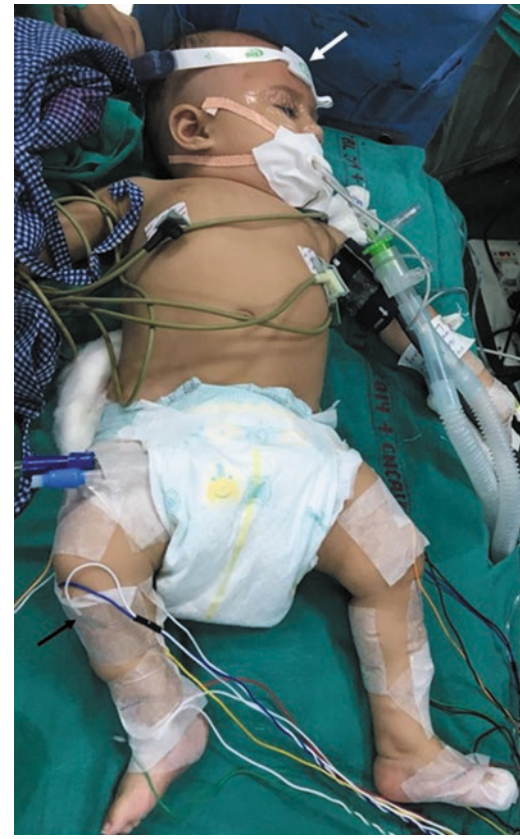

Fig. 8.6 Needle electrode placement (*black arrow*) in the lower extremities for triggered electromyography (EMG) monitoring during spinal surgery in a 2.5-year-old child with myelomeningocele; a pediatric bispectral index (BIS) sensor (*white arrow*) is attached for the depth of anesthesia monitoring

BAERs can identify injury to the vestibulocochlear nerve (CN VIII) during surgery or hypoperfusion within the brainstem during posterior fossa surgeries, acoustic neuroma resections, or resection of pontomedullary tumors [46]. Children with conditions such as Friedreich ataxia and Rett syndrome may have baseline aberrations in recorded BAERs. An amplitude reduction of >50% or an increase in absolute latency of any wave of >1 ms is considered to be

a significant change in BAER. Injury to the vestibulocochlear nerve at its point of exit near the brainstem may cause partial sparing of wave I but can affect other waves. Loss of wave I signifies a complete hearing loss in the affected ear. This modality may be useful during surgeries involving the posterior fossa, brainstem, or skull base.

8.4.4.6 Electroencephalography

Electroencephalogram (EEG) represents the summated excitatory postsynaptic potentials and inhibitory potentials of cortical neurons, with frequencies being limited by insulation generated by the skull, galea, and scalp [47]. The EEG is dependent on age as well as the anesthetic regimen used. Sharp waves and spikes are suggestive of seizure disorders. Abnormally slow EEG is representative of systemic metabolic abnormalities. Anesthetic depth of the patient can be evaluated on EEG by mapping frequency and amplitude of background electrical activity – α-activity of 8–15 Hz, β-activity of 15–25 Hz, γ-activity of 4–7 Hz, and δ-activity of 1–3 Hz. Infants usually display higher-frequency values for similar depths of sedation than older children. Commercially available EEG monitors such as bispectral index (BIS) can be used to evaluate the depth of anesthesia (Fig. 8.6) reliably. However, these monitors are subject to interference from multiple sources such as electrocautery, motion, EMG activity, etc., which may limit their use.

Intraoperative EEG may be used to interrogate cerebral perfusion and help in early identification of cerebral hypoperfusion, test for seizure activity after cortical stimulation, and also evaluate anesthetic depth. As CBF nears 15 ml/100gm/min, EEG demonstrates decreasing amplitude. When confounding factors are ruled out, an isoelectric EEG represents brain death or cessation of cortical blood flow, although children may show ongoing low-amplitude EEG activity even in the absence of cortical flow. Burst suppression induced by anesthetic agents is used as a technique for cerebral protection via a reduction in $CMRO_2$ [48]. Burst suppression is defined as periods of isoelectric EEG interspersed with burst activity. Factors that can affect intraoperative EEG recordings are hypothermia, hypoxia, metabolites, and surgical manipulation. Electrocorticography (ECoG) is another procedure in which the EEG electrode grid is placed directly over the exposed cortical surface following craniotomy and is used to identify areas amenable to resection in children undergoing epilepsy surgery. This technique may help in accurate resection of seizure foci while preserving the integrity of motor, sensory, and language tracts.

8.5 Conclusion

Monitoring during pediatric neurosurgical procedures may help reduce or avoid incidences of perioperative neurological dysfunction. Constant communication between the operating personnel and the anesthesiologist is vital to provide quality patient care during surgeries requiring neuromonitoring. A sound knowledge of the different IONM modalities and their response to various anesthetic protocols may help tailor the anesthetic plan.

Conflict of Interest None declared for each author.

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9 Perioperative Thermoregulation in Children and Temperature Monitoring

Barkha Bindu and Ashish Bindra

Key Points

- Intraoperative hypothermia occurs in up to 50% of children.
- Children and infants are more prone to perioperative fluctuations in body temperature than adults. This is owing to morphological and physiological differences.
- Perioperative hyperthermia can result in hypoventilation, apnea, sympathetic stimulation, increased oxygen demand, and increased rates of surgical site infections (SSI) in infants and children.
- The risk of intraoperative hypothermia is present under general and regional anesthesia, and appropriate strategies should be formulated for prevention.
- Higher ambient temperature is advised for children under anesthesia.
- Preoperative warming increases total body heat content and reduces the temperature gradient between the core and the peripheral compartment, decreasing intraoperative hypothermia.

9.1 Introduction

Human beings are homeothermic and tend to regulate their body temperature tightly within a narrow range of 36.5–37.3 °C. While thermoregulatory mechanisms are well developed in adults, they are relatively immature in children and infants, making them prone to fluctuations in body temperature. Exposure to anesthesia and surgery in pediatric patients further increases the incidence of temperature fluctuations. Understanding the thermoregulatory mechanisms in infants and children will help in the better perioperative care of these patients. This chapter discusses the physiology of thermoregulation in children, temperature monitoring, effects of anesthesia on body temperature, and methods to prevent perioperative temperature fluctuations.

9.2 Physiology of Thermoregulation

Thermal information is processed in three phases: afferent input, central regulation, and efferent responses. Hypothalamus is the principal site of thermoregulation in humans and integrates thermal information obtained from different body parts.

Afferent input: Thermosensitive receptors (both cold and warm) are located all over the body. Cold-sensitive receptors (maximum

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discharge rate of impulses at 25–30 °C) transmit to preoptic area of thalamus via Aδ fibers. In contrast, warm receptors (maximum discharge rate of impulses at 45–50 °C) transmit via unmyelinated C fibers and spinothalamic tracts. Brain, spinal cord, skin, deep abdominal, and thoracic tissues contribute 20% to thermal input.

Central regulation: Hypothalamus integrates all afferent thermal information and regulates various efferent mechanisms to keep body temperature normal.

Efferent responses: Deviations in temperature from the normal range activate various effector mechanisms that alter heat production or heat loss to bring the temperature back to normal. *Behavioral regulation* is the most important and most efficient of all mechanisms and involves voluntary movement, dressing, altering ambient temperature, etc. Autonomic responses include cutaneous vasoconstriction, non-shivering thermogenesis, shivering, vasodilation, and sweating. The first and quickest response to hypothermia is *cutaneous vasoconstriction*. It reduces blood flow through arteriovenous shunts in the skin and can reduce heat loss by up to 25%. *Non-shivering thermogenesis* is the mechanism of heat production without associated muscle activity. It is the mainstay of heat production up to 1 year of age but has an insignificant role in adults. It takes place in brown fat and, to a lesser extent, in the skeletal muscle, liver, brain, and white fat. Activation of brown fat causes direct warming of blood because 25% of cardiac output flows through it. The mitochondria of brown fat cells produce heat by uncoupling oxidative phosphorylation and almost double metabolic heat production. It is attenuated by inhalational anesthetics, fentanyl, and propofol and is nonfunctional under general anesthesia [1]. *Shivering* manifests as involuntary, irregular muscle activity. Shivering has a minor role in the thermoregulation of newborn and infant due to poor muscle mass. In older children, it can increase metabolic heat production up to sixfold and increase oxygen consumption and CO_2 production of up to 400–600%, along with an increase in cardiac output. Shivering also increases intraocular and intracranial pressure. *Vasodilation* is mediated by nitric oxide and inhibition of sympathetic activity by nerve blockade. *Sweating* helps in dissipating heat to the environment and is remarkably effective in reducing body temperature. Term neonates have the ability to sweat, but preterm infants of less than 30 weeks' gestational age have poorly developed sweat glands and weak sweat response. Common terminologies about thermoregulation have been described in Table 9.1.

Table 9.1 Definitions of common terminologies relevant to thermoregulation

Term	Definition
Threshold temperature	Temperature at which a response is triggered. Threshold for vasoconstriction is 36.5 °C and 36.0 °C for shivering
Inter-threshold range	The range of temperature over which autonomic responses are not activated. Bounded at its upper end by sweating threshold and lower end by vasoconstriction threshold. Normally, it is only a few tenths of a degree centigrade (thermoregulatory zone), but, under general anesthesia, the range can increase to up to 3–4 °C
Gain	The extent to which the intensity of thermoregulatory response increases with further deviation from the triggering threshold
Maximum intensity	When the intensity of the response no longer increases with further deviation in core temperature
Mean body temperature	Physiologically weighted average temperature from various tissues
Neutral temperature	Ambient temperature at which oxygen demand is minimal and thermoregulation is achieved through non-evaporative processes alone. Adults, 28 °C; neonates, 32 °C; preterm infants, 34 °C

9.2.1 Thermoregulation in Newborn

Newborns and infants are predisposed to hypothermia. In fact, the importance of thermoregulation in infants was recognized by Budin in the 1900s. He observed different mortality rates in infants with different body temperatures [2]. Large skin surface area to body mass ratio (neonates, 1.0; adults, 0.4), large head size (20% of body surface area), thin skull bones,

sparse scalp hair, the proximity of highly perfused brain to the skin surface, minimal subcutaneous fat, reduced keratin content of the skin, reduced ability to produce heat, and immature thermoregulatory responses contribute to the high incidence of hypothermia in infants and newborns. Low ambient temperature in the operating room, cold intravenous fluids, cold and dry anesthetic gases, type of surgery [3], and large surgical incisions further add to these predisposing factors.

9.3 Effects of Anesthesia on Thermoregulation

Both general and regional anesthesia cause a drop in core temperature of 1–3 °C. Contributing factors include anesthesia-induced 30% reduction in metabolic rate, exposure to cold operating room environment, anesthesia-induced inhibition of thermoregulation, and internal redistribution of heat. Behavioral regulation is irrelevant under anesthesia, so autonomic effector responses become more important, and these, too, are markedly impaired by anesthesia.

General anesthetics decrease the threshold for cold responses by ~2.5 °C and increase the threshold for warm responses by about 1.3 °C. There is a widening of the inter-threshold range to 2–4 °C [4]. Inhalational anesthetic agents produce nonlinear inhibition of thermoregulatory responses. They also inhibit non-shivering thermogenesis. Desflurane, in particular, reduces gain response in addition to reducing the vasoconstriction threshold. Nitrous oxide reduces vasoconstriction threshold lesser than volatile anesthetic agents. Among intravenous anesthetic agents, opioids cause a linear decrease in vasoconstriction and shivering thresholds. Propofol [5] and dexmedetomidine [6] increase the sweating threshold and cause a marked linear decrease in the cold response threshold. Propofol also inhibits non-shivering thermogenesis. Clonidine for premedication does not worsen hypothermia during general anesthesia [7]. Atropine inhibits sweating, increases sweating threshold, and may cause hyperthermia in children.

Regional anesthesia was earlier thought to protect against hypothermia due to the preservation of central thermoregulation mechanisms. But the incidence and magnitude of hypothermia after regional anesthesia may be almost similar to or even more than general anesthesia [2]. Neuraxial blockade inhibits both afferent and efferent pathways, preventing vasoconstriction and shivering in the blocked areas. The degree of inhibition of thermoregulation is directly proportional to the number of dermatomes blocked [8]. Supplementation of regional anesthesia with analgesics or sedatives or combination with general anesthesia can further severely impair thermoregulation.

9.4 Perioperative Hypothermia

Hypothermia is defined as a core body temperature of less than 36 °C. Intraoperative hypothermia is reported in up to 50% of children [9]. Balance between heat loss and heat-generating mechanisms determines the intraoperative body temperature. Heat loss from the human body can occur by four mechanisms: radiation, convection, conduction, and evaporation. Mechanisms of heat loss under anesthesia have been described in Table 9.2. Heat loss by *radiation* is the most important heat loss mechanism under anesthesia because of the larger surface area to volume ratio in infants and newborns. The amount of heat lost depends on the temperature gradient between the two surfaces and can be reduced by increasing ambient room temperature. Operating room temperatures of 27° and 29 °C are generally used for full-term and premature newborns, respectively [2]. *Convection* is the second most important heat loss under anesthesia and is proportional to the square root of air speed. Convective losses can be substantial in operating rooms equipped with laminar flow. *Evaporation* is an energy-dependent process, and losses occur through skin, respiratory tract, and surgical wounds. The velocity of airflow, relative humidity of inspired air, and

Table 9.2 Heat loss mechanisms under anesthesia

Mechanism	Definition	Contribution to heat loss under anesthesia
Radiation	Transfer of energy between two objects that are not in contact but differ in temperature	39%
Convection	Transfer of heat from an object to moving molecules like air or liquid	34%
Evaporation	Transfer of heat from body or mucosal surface using latent heat of evaporation	24%
Conduction	Transfer of heat between two surfaces in direct contact	3%

minute ventilation play an important role. Even the use of skin disinfectant solutions and wet drapes can cause evaporative losses. Heat loss via the respiratory tract contributes only 5–10% of total heat loss in adults. Still, it accounts for up to one-third of total heat loss in infants due to higher minute ventilation per kg body weight. This can be reduced by using warm moisturized gases. *Conduction* causes little heat loss under anesthesia since patients are well insulated from surrounding objects.

Various *heat-generating mechanisms* include voluntary muscle activity, non-shivering thermogenesis, shivering, and dietary thermogenesis. Non-shivering thermogenesis and shivering have been described above. *Voluntary muscle activity* does not contribute to heat production in the perioperative period, and *dietary thermogenesis* plays an insignificant perioperative role. Certain nutrients like proteins, amino acids, etc. are known to cause thermogenesis. Higher core temperature under anesthesia has been achieved using preoperative and intraoperative amino acid infusion [10]. Fructose administration also seems to have a similar effect.

For an easier understanding of the effect of anesthesia on body temperature, the human body can be thought to be divided into three compartments; central, peripheral, and skin (Fig. 9.1). (a) *Central (core) compartment* includes the vessel-rich group of organs such as the brain, heart, lungs, liver, kidneys, and endocrine glands. The temperature of this compartment represents the core temperature and is around 37 °C. It accounts for up to 22% of body weight in neonates and receives 75% of cardiac output. The size of this compartment increases under anesthesia due to the redistribution of heat. (b) The *peripheral compartment* includes the musculoskeletal system and acts as a buffer for any changes in core temperature by causing vasoconstriction or vasodilation. This compartment is typically 2–4 °C cooler than the core with a temperature of around 31–34 °C. (c) *Skin (shell) compartment* acts as a barrier between the other two compartments and the environment.

Hypothermia under *general anesthesia* develops in three phases [11]: initial rapid decrease, slow linear reduction, and plateau phase (Fig. 9.2). During the *initial rapid decrease phase, anesthesia*-induced peripheral vasodilation causes the redistribution of heat from the core to periphery, increasing the core compartment's size and resulting in a drop in core temperature by 0.5–1.5 °C while increasing peripheral temperature to around 35 °C. This redistribution of heat accounts for an 81% decrease in core temperature in the first hour of anesthesia. Rest 19% occurs due to decreased metabolic rate and increased heat loss. The *slow linear reduction phase* lasts up to 2–4 hours, and the core temperature falls at a rate of 0.5–1.0 °C. As body temperature falls, the gradient between skin and the surroundings reduces, resulting in reduced heat loss. *Plateau (rewarming) phase* occurred after 3–4 hours of anesthesia when heat lost equals heat produced. Body temperature stabilizes and remains unchanged thereafter. It is called a rewarming phase in children since thermoregulatory vasoconstriction in response to core hypothermia causes restriction of metabolic heat to the core. Studies have shown that preoperative warming helps prevent intraoperative hypothermia by increasing total body heat content and reducing the core to periphery temperature gradient [12, 13].

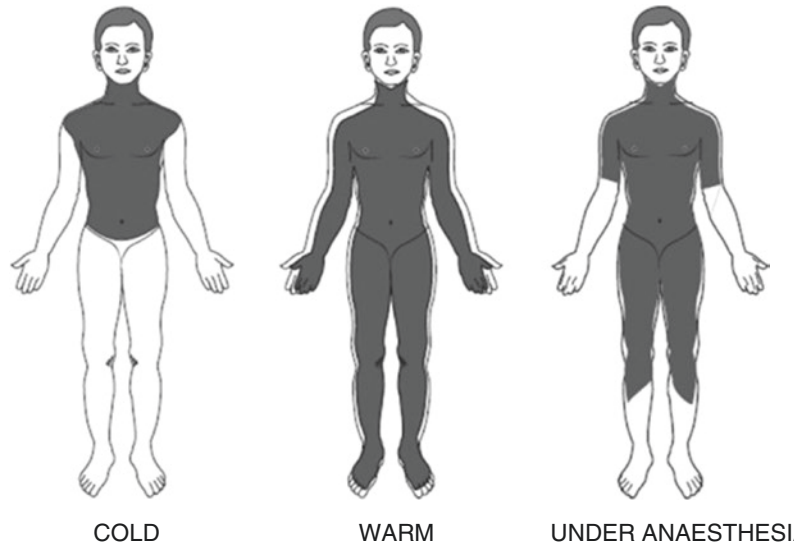

Fig. 9.1 Distribution of heat in three compartments of human body

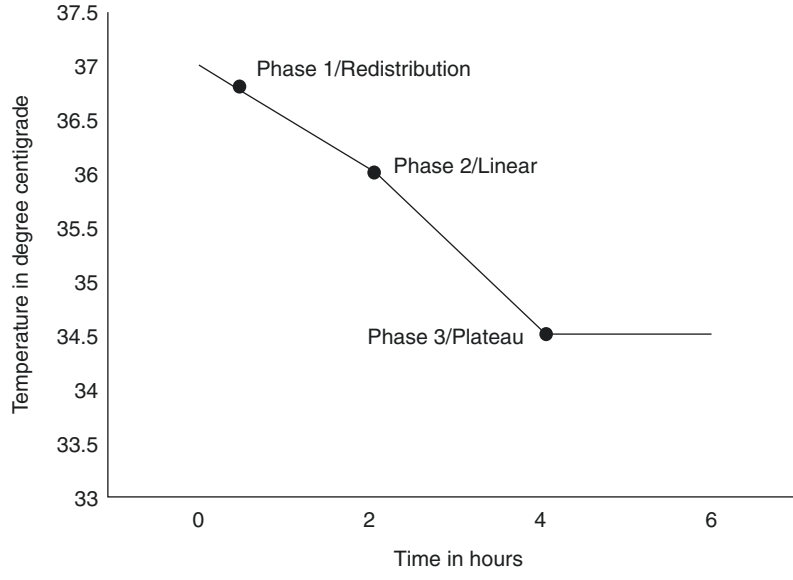

Fig. 9.2 The phases of hypothermia under anesthesia

Hypothermia during *neuraxial anesthesia* is as severe as during general anesthesia. Core temperature decreases by around 0.5 °C–1.0 °C. But these patients may not reach an equilibrium state since for plateau phase to occur, peripheral vasoconstriction must occur, which is inhibited by nerve block under regional anesthesia. Therefore, heat loss may continue until sympathetic function and vasoconstriction are restored, and hypothermia may be more severe than under general anesthesia. However, caudal block in children has been shown not to affect the vasoconstriction threshold, significantly [14].

9.4.1 Adverse Effects of Hypothermia

Hypothermia, defined as a temperature of less than 36 °C, is the most common thermal perturbation occurring perioperatively [15]. The risk is

higher with prolonged surgery and anesthesia time, extremes of age, patients with extensive burns, low preoperative temperature, severe trauma, and major fluid shifts.

The adverse effects of hypothermia include hypoventilation or apnea, precipitation of a preoperative cardiopulmonary deficiency due to increased oxygen demand, hypoxia and right to left shunt, anesthetic overdose, delayed recovery, sympathetic stimulation causing vasoconstriction leading to acidosis, impaired neutrophil function, wound infection, delayed wound healing, impaired platelet function causing impaired coagulation and hemostasis, increased blood loss, etc. [16, 17]

Another practically important consequence of hypothermia, postanesthetic shivering, has been reported in 6.6–66% of patients. It is an unpleasant sensation for the child and increases oxygen consumption by 200–500% [18] though the exact incidence of postoperative shivering in children is unknown, and the risk is higher in children. The use of intravenous induction agents, age older than 6 years, and prolonged surgery duration have been identified as risk factors [19]. Agents such as meperidine (0.35 mg/kg), clonidine, and dexmedetomidine (0.5 μg/kg slowly) are used to treat shivering [18, 20].

9.5 Perioperative Thermal Manipulations

Various options available to prevent and treat perioperative hypothermia include preoperative warming, use of warm humidified gases, warm intravenous fluids, warm operating rooms, intraoperative use of various passive and active cutaneous warming devices, etc.

National Institute for Health and Care Excellence (NICE) 2008 guidelines (last updated December 2016) recommend preoperative warming of patients using forced air warmers, if the temperature is less than 36 °C, in adults coming for surgery. These guidelines also recommend preoperative risk assessment of patients for inadvertent perioperative hypothermia based on the presence of risk factors [21]. In the absence of specific guidelines for pediatric patients, the American Society of Anesthesiologists (ASA) standards which state that "every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated or suspected" and for office-based sedation, regional anesthesia, or general anesthesia, "the body temperature of the pediatric patient shall be measured continuously" must be followed.

Preoperative warming increases the total body heat content and reduces the core to periphery temperature gradient, thereby reducing redistribution hypothermia. Skin surface warming for as little as 30 minutes before anesthesia induction has been shown to prevent redistribution hypothermia [22]. Subjecting patients to an ambient temperature of 26 °C in the induction room and operation theatre for 30–40 minutes before anesthesia induction has also been found to reduce intraoperative hypothermia [12].

Airway heating and humidification does not increase body temperature but does help in preserving body heat [23]. Heat and moisture exchangers and ultrasonic heated humidifiers can be used. Heat and moisture exchangers are safer to use since they do not because airway burns and can also filter infective particles. The risk of over humidification and overhydration is low with them [24]. A relative humidity of 50% maintains normal ciliary function.

Intravenous fluids and blood must be warmed before administration, especially when rapid fluid administration is required. But excessive heating may cause hemolysis of red blood cells, whereas slow administration of fluids may result in loss of heat in the tubing itself before reaching the body [25]. Irrigation fluids must also be warmed to body temperature before use. Various devices are available for warming intravenous fluids. Warm water baths through which intravenous tubing is passed (counter-current warming systems; Fig. 9.3), aluminum plates near the patient end of tubing (dry heat technology), fluid warming cabinets, and blood warmers (at 43 °C) are various options available.

Skin warming can be done by passive insulation or active warming. *Passive insulation* is

Fig. 9.3 (**a**) Fluid warming cabinet. (**b**) Forced air warming blanket

done applying *cotton blankets, surgical drapes, plastic sheets, reflective composites ("space blankets"), or sleeping bags*. It is the most commonly used mechanism. Insulation is provided by the layer of still air trapped beneath the blanket; the amount of insulation provided by different devices is almost similar. A single layer of most of these devices reduces heat loss by approximately 30%, and the addition of extra layers of insulation reduces the heat loss only slightly [26]. Therefore, only passive insulation is insufficient to prevent hypothermia. The use of reflective blankets is advised to cover uninvolved skin areas. Head, which accounts for up

to 20% of the total surface area, can be covered. *Active warming* devices include circulating water mattresses and garments, forced air warmers, resistive heating devices, negative pressure water warming systems, etc. (Fig. 9.3). *Circulating water devices* reduce conductive losses. They are available as both mattresses and garments, but their practical use is limited due to bulky nature. *Forced air warmers* are the most commonly used devices for active warming. They produce convective warming by circulating warm air around the patient. They have a fast warm-up time, have high warming capacity, do not produce burns, and are convenient to use. *Resistive heating devices* transfer heat by conduction through a mattress or blanket. Low-voltage electric current is passed through semi-conductive polymer or carbon fiber systems to generate heat. They are reusable, energy-efficient, easy to clean, and cost-effective and provide a practical alternative to forced air warmers [27] but can cause significant burns. *Negative pressure water warming systems* apply a subatmospheric pressure with a thermal load that opens arteriovenous shunts, promoting periphery to core heat transfer [28]. Their role in the intraoperative setting is doubtful. *Infrared radiant heaters* can be used before induction and in the postoperative period. But their prolonged use can increase insensible water losses, and skin burns can occur if placed too close to the patient.

Special care must be taken while transferring pediatric patients from the operating room to intensive care unit (ICU) or postanesthesia care unit (PACU). Neonates and infants must be transferred in an incubator, and older children should be covered with a warm blanket.

9.6 Temperature Monitoring

Intraoperative monitoring of temperature from at least one reliable site is essential to detect temperature fluctuations. Various devices to measure temperature are available. Earlier, *mercury-in-glass thermometers* were used; but they were slow and cumbersome. *Infrared thermometers* are used for tympanic membrane and skin measurements; they are unsuitable for continuous monitoring. They are usually used for intermittent temperature monitoring in PACU and wards and have a quick response time. *Electronic thermometers* use thermistors and thermocouples. They are the most commonly used devices for intraoperative temperature monitoring. They are sufficiently accurate and inexpensive. Other devices like *temperature-sensitive liquid crystals* are easy and convenient to use but not accurate enough and are used to measure skin temperature. *Handheld infrared scanners* measure core temperature by measuring skin temperature. They detect the highest temperature in the temporal or forehead region.

Both core and peripheral temperatures can be measured clinically. Core temperature represents the temperature of the hypothalamus and remains reliable during extreme temperature fluctuations. Skin temperature tends to be considerably lower than the core temperature. Various temperature monitoring sites, their advantages, and disadvantages have been described in Table 9.3 [29]. Core body temperature can be measured from the tympanic membrane, nasopharynx, oropharynx, distal esophagus, pulmonary artery, etc. or in the peripheral sites which include the axilla, rectum, skin, bladder, etc. (Fig. 9.4). Skin temperature over carotid artery has been shown to accurately estimate the nasopharyngeal temperature in infants and young children during general anesthesia [30]. The recommended sites for temperature monitoring by NICE include pulmonary artery catheter, distal esophagus, urinary bladder, sublingual, axilla, and rectum [21]. The site of temperature monitoring depends on the site of surgery and accessibility of various sites. Generally, the least invasive site that gives the most reliable estimate of core temperature is preferred [31]. Commonly used sites under anesthesia are nasopharynx and axilla. However, nasal bleeding due to adenoids, influence of hot and humidified inhaled gases, and leak of anesthetic gases when using uncuffed endotracheal tubes in children is a cause of concern.

Table 9.3 Temperature monitoring sites

Site	Remarks
Tympanic membrane	Ideal site. Probe need not directly touch tympanic membrane. Tympanic membrane perforation reported
Nasopharynx	Placed in posterior nasopharynx close to soft palate. Can cause nasal bleeding, especially in children with adenoids. Incorrect readings when used with uncuffed endotracheal tubes
Oropharynx	More inaccurate compared to nasopharynx
Distal esophagus	Placed with the help of esophageal stethoscope. Good option in pediatric patients. Inaccurate with high gas flows
Pulmonary artery	Invasive. Use limited to special situations like cardiac surgeries
Axilla	Widely used. Must be placed over axillary artery with arm closely adducted. Does not reflect fluctuations of body temperature
Rectum	Easily accessible. Probe should not be embedded in feces. Avoided in inflammatory bowel disease, neutropenia, thrombocytopenia, bowel/bladder irrigation. Widely used
Skin	Least invasive. Very unreliable
Bladder	Accurate reflection of core temperature if urine volume is high

Fig. 9.4 Pediatric invasive temperature monitoring probe

9.7 Perioperative Hyperthermia

Anesthesia increases the threshold for warm responses by only 1–1.4 °C compared to a decrease of 2.5–3.5 °C in the threshold for cold responses, i.e., under anesthesia, the body responds more strongly to hyperthermia than hypothermia. Vasodilation, which manifests as flushing, effectively dissipates heat. Term infants have the ability to sweat and dissipate heat when the ambient temperature rises. Premature infants of less than 30 weeks' gestational age have no sweating response due to poorly developed sweat glands [2]. Various causes of perioperative hyperthermia in children include primary central nervous system pathology, toxins, envenomation, sepsis, transfusion reaction, heat stroke, endocrinopathies, neuroleptic malignant syndrome, and malignant hyperthermia [32].

Intraoperative hyperthermia is associated with increased rates of surgical site infection (SSI) in infants aged 6 months or less [33], unlike in adults where hypothermia is known to be associated with higher SSI rates.

9.8 Malignant Hyperthermia in Children

The reported incidence of malignant hypothermia in children is around 17%. [34] Older inhalation anesthetic agents and succinylcholine are known to trigger MH. Desflurane and sevoflurane are weak triggers, while xenon and nitrous oxide do not trigger MH [35].

The most common initial signs are tachycardia and hypercarbia. Differences in clinical features among different age groups of children have been observed [36]. Since MH is primarily a disease of muscles, older children tend to have more severe symptoms (higher temperature, higher creatine kinase and potassium levels) due to greater muscle mass. Younger children have greater metabolic acidosis and lactic acid levels due to lower muscle reserve available to buffer the anaerobic metabolism during an acute MH episode. Active cooling, hydration, dextrose with insulin, and dantrolene (2.4 mg/kg initial dose, 5.9 mg/kg total dose) are the mainstays of treatment.

Though the relationship between muscular dystrophy and development of intraoperative hyperthermia has been commonly described, literature shows intraoperative heart failure,

inhaled anesthetic-related rhabdomyolysis (absence of succinylcholine), and succinylcholine-induced rhabdomyolysis and hyperkalemia as *common intraoperative* anesthetic complications in these patients. There was no increased risk of malignant hyperthermia as compared with the general population [37].

9.9 Targeted Temperature Management in Pediatric Neurointensive Care

Targeted temperature management (TTM) includes a range of interventions from inducing hypothermia to fever prevention. Hypothermia confers neuroprotection by reducing programmed cell death and secondary inflammatory cascade. Present indications for therapeutic hypothermia (TH) in children include acute neonatal hypoxic-ischemic encephalopathy and postcardiac arrest coma. The benefits of TTM in pediatric traumatic brain injury are still uncertain [38]. TH is being considered for the management of refractory status epilepticus [39]. However, continuous temperature monitoring and active fever prevention in critically ill pediatric neurological patients are of paramount importance.

9.10 Conclusion

Intraoperative fluctuations in temperature are common and can affect the outcome in children. Therefore, careful monitoring, prevention, and treatment of fluctuations in intraoperative temperature must be considered while formulating the anesthetic plan for pediatric patients. The site and device for temperature monitoring can be decided depending upon the surgical site and patient access.

Conflict of Interest None.

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10 Fluid and Electrolytes Management in Children Undergoing Neurosurgery

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Key Points

- The fluid management plan for children undergoing neurosurgical procedures should consider preoperative assessment, correction of existing deficit, calculation of intraoperative requirements and management thereof, postoperative management of the imbalances, and fluid therapy monitoring.
- Among children, a fall in blood pressure is usually a late sign of hypovolemia, and it should be rapidly corrected to maintain cardiac output and cerebral perfusion. Slower correction of dehydration, without the signs of hypovolemia, is acceptable.
- Avoid, if possible, colloids and glucose infusion. In the case of hypernatremia as a consequence of pituitary surgery (such as diabetes insipidus), infusion of 5% glucose solution may be considered.
- Electrolytes dysregulation, such as hyponatremia or hypernatremia, and K^+ alterations are associated with worsening of the outcome.
- Attention should be paid to postoperative complications, particularly after surgery for sellar lesions (diabetes insipidus, syndrome of inappropriate antidiuretic hormone secretion, cerebral salt wasting syndrome).

10.1 Introduction

Advances in neurosurgical techniques have changed the face of pediatric neurosurgical management, leading to generally improved outcomes. However, with the increasing demand, complexity, and improvement of care for children undergoing neurosurgical procedures, there is an increased need to develop guidelines to improve the level of care and assure uniform patient management. In particular, fluid and electrolytes management in the pediatric neurosurgical population requires careful attention to the intravenous (IV) fluid administration and close monitoring of fluid balance and assessment of the clinical status of the patient to prevent and correct perioperative complications. Neurosurgical patients are usually complex and often need a large number of fluids and hemo-components as well as postoperative monitoring in an intensive care setting. Moreover, several pathophysiological processes occur in this group of patients that make them vulnerable to peculiar electrolyte and fluid disturbances, including syndrome of inappropriate antidiuretic hormone (SIADH) secretion, cerebral salt wasting syndrome (CSWS), and cranial diabetes insipidus (DI). This chapter

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will review the main principles for fluid and electrolytes management in the pediatric population undergoing neurosurgical procedures.

10.2 General Considerations

Management of infants and children posted for neurosurgical procedures requires careful considerations of the unique challenges they present with. There are several important differences between the procedures performed in pediatric neurosurgical patients and those performed in the adult population, which are usually due to the anatomo-physiologic peculiarities of children. The types and characteristics of the central nervous system (CNS) tumors seen in the pediatric population are different from those in adults. Also, the management of some conditions (such as hydrocephalus) is much more challenging from both clinical and surgical perspectives, particularly when its onset is in infancy or childhood [1].

Because of the particular anatomical characteristics of the pediatric population, including a more compliant (viscoelastic) and not fully ossified skull, injuries to the brain mass (including tumors, hemorrhages, etc.) tend to progress indolently when compared with adult lesions. Additionally, considerations like the development of the spinal cord and associations with congenital disorders in pediatric patients also impact the decision-making process perioperatively compared to the adults.

Several anatomical, physiological, and anesthetic implications have to be taken into account (Table 10.1). A higher percentage of total body water in the pediatric population than adults makes them vulnerable to develop serious morbidity caused by fluid and electrolytic imbalance. They need a large volume of distribution for water-soluble medications, and low fat and muscle content provides a small reservoir for drugs that depend on redistribution into these tissues for their metabolism and the execution of their effect. Therefore, water-soluble drugs require larger doses for clinical effect (such as antibiotics and muscle relaxants), while drugs like thiopental (redistribution into fat) and fentanyl (redistribution into the muscle) have a longer clinical effect.

Table 10.1 Peculiar characteristics of neonatal physiology regarding fluid and electrolytes

Neonatal physiologic variables	Characteristics regarding fluid and electrolytes
Body water percentage and distribution	• Term neonates: 75% (40% ECF, 35% ICF) • Preterm neonates (23 weeks): 90% water (60% ECF, 30% ICF) • Adults: 60% water (20% ECF, 40% ICF)
Fluid losses	• Skin (70%) and respiratory tract (30%) are the major sources of insensible water losses (IWL) in neonates • Preterm infants have a generally higher IWL
Cardiovascular physiology	• Reduced cardiac contractility (low contractile mass/gram of cardiac tissue) • Reduced ability to ↑ stroke volume • Dependence on heart rate (↑ HR) to ↑ cardiac output (Treppe effect) • High sensitivity to hypovolemia and anesthetic agents
Renal function	• 25% functionality at birth with maturation by 2 years of age • $T_{0.5}$ of drugs excreted by glomerular filtration is prolonged • Normal urine osmolality: 50–600 mEq/L in preterm and (50–?) 800 mEq/L in term infants

ECF extracellular fluid, *ICF* intracellular fluid

Moreover, renal and cardiovascular physiology and fluid losses present some differences in the pediatric population compared with adults (Table 10.1), making them more vulnerable to fluid dysregulation. In children, the fall in blood pressure is usually a late sign of hypovolemia, and hence, it is to be corrected rapidly to maintain effective cardiac output and cerebral perfusion.

In addition to all of the above considerations, in-depth knowledge of anticipated major possible adverse events is also essential in managing some

of the unique surgical challenges. Fluid and electrolyte imbalance can also increase morbidity and mortality, and its prevention and prompt treatment should be a priority concern in pediatric neurosurgery.

10.3 Choice of Fluid During Pediatric Neurosurgery

Planning for fluid management in neurosurgical cases is extremely important, and communication between the surgeon and the anesthesiologist in this regard must be clear. In general, the target is to ensure euvolemia, avoiding both hypovolemia and hypervolemia and consequently hypoperfusion of the brain and other organs, and attenuate edema. Crystalloids should be the first choice, and in particular, 0.9% normal saline is commonly used because of its slight hyperosmolality (308 mOsm/L), which can help in attenuating the occurrence of brain edema (Table 10.2) [2]. Although there is no absolute contraindication, caution must be exercised with the use of colloids (hydroxyethyl starch). A recently published meta-analysis concluded that the established adverse effect profile of colloids such as renal injury and coagulopathy were not observed with their perioperative administration in noncardiac surgeries [3].

In patients with intracranial hypertension, osmotherapy using mannitol or hypertonic saline (3% or higher concentration) should be considered in order to reduce intracranial pressure (ICP). However, if possible, it is important to avoid using hypertonic solutions if a central line is not available so to avoid the risk of phlebitis. Attention should also be paid to the administration of diuretics (such as furosemide), which can be used to induce systemic diuresis, improve overall cerebral water transport, and decrease cerebrospinal fluid (CSF), but they can also determine hypovolemia and dehydration and reduced cerebral perfusion pressure (CPP).

Hypotonic saline solutions (including 0.45% NaCl, 0.45% NaCl +5% dextrose, 0.18% NaCl +10% dextrose, 0.18% NaCl +4% dextrose, and 10% dextrose solutions) should be used with extreme caution in neurosurgical patients, as they can worsen cerebral edema, and should only be used to treat acute hypernatremia (Na >150 mEq/L) [4]. In particular, small children and neonates are more susceptible to hypoglycemia than adults, which may occur after preoperative fasting. Thus, when initiating fluid management in neonates, the use of 0.9% NaCl and dextrose should be considered. Complications of hyperglycemia in neonates and preterm infants include dehydration due to diuresis and electrolyte disturbances and an increased risk of hypoxic-ischemic central nervous system (CNS) damage and have to be strictly avoided [5]. The current anesthetic practice involves dextrose solutions at a lower concentration (1–2%) instead of the traditional use of 5% solutions [6]. In children older than 5 years, in those who have a low risk of fasting-induced hypoglycemia, or in patients with documented hyperglycemia, 0.9% NaCl without dextrose is usually the standard of care [7]. Although a hyperglycemic response during surgery and anesthesia is anticipated (increased sympathetic system activity and gluconeogenesis), such a response may not occur in all patients and makes children especially prone to hypoglycemia. The incidence of intraoperative hypoglycemia has been estimated at 0–2.5% and

Table 10.2 Commonly used intravenous fluids

Types	Na^+	K^+	Cl^-	Ca^{2+}	Mg^{2+}	Acetate lactate	Glucose	Phosphate	Osmolality
NS	154		154						308
RL	1	4	109	3		9			274
Isolyte P	26	21	21		3	24	5	3	
Plasmalyte	140	5	98		3	27			295
Albumin 5%	150	<2.5	100						330
Hetastarch	154		154						310

NS normal saline, *RL* Ringer's lactate

is generally seen with longer fasting periods (8–19 h). Hence, it becomes essential to monitor blood glucose levels intermittently when fasting is prolonged and glucose is not being supplemented intraoperatively [8].

Fluid management for neurosurgical procedures can be divided into several phases [9]:

- Fluid considerations before surgery.
- Preoperative assessment for fluid deficits and methods for correction.
- Estimating the requirements for maintenance fluids.
- Management of other losses (blood and third space loss) during surgery.
- Postoperative fluid management and modalities to monitor fluid therapy.

10.3.1 Fluid Considerations Before Surgery

In the preoperative phase, fluids are best administered through the oral/enteral route. The literature is not clear about which is the safest preoperative fasting practice in infants. Some authors consider it safe to anesthetize a child 3 h after the last breastfeeding; some suggest this concept is valid only in infants under 6 months of age, and others would allow surgery 4 h after the last breastfeeding [10]. It is generally accepted that children aged 6 months or older should safely be allowed to have clear fluids 2 h before surgery and that withholding of solid food should be done 8 h before surgery. This is essential to prevent dehydration in the child and, at the same time, reduce the risk of hypoglycemia and aspiration. Under 6 months of age, breast milk is allowed up to 4 h before surgery [11].

10.3.2 Assessment and Correction of Fluid Deficit

The preoperative assessment of the pediatric population undergoing neurosurgical procedures should take into account several factors. An accurate collection of information about the patient's past medical history is necessary, focusing on congenital or acquired diseases that can increase the risk for dehydration or electrolyte imbalance (heart or kidney diseases, burns, etc.). Physical examination should include the weighting of the child (one of the most important criteria to assess the fluid balance in children) and the characteristics of the skin and mucosa (including dry mucosa, edema, and altered skin turgor). Clinical signs due to dehydration are tardive, in particular the hypotension. Therefore, trying to calculate the water deficit precisely using clinical signs may result in inaccuracies. In mild dehydration, the only clinical signs/symptoms may generally be just an increased thirst with dry mucosal membranes; in moderate dehydration, tachypnea, cool and pale peripheries with prolongation of capillary refill times, sunken eyes, reduced skin turgor, and low urine output can be useful additional clinical signs/symptoms. Finally, in severe dehydration, in addition to the signs of moderate dehydration, the child may be irritable and/or lethargic and have severe hypotension with deep acidotic breathing, which is late premorbid signs (Table 10.3) [12–14].

Laboratory tests should be obtained alongside the accurate clinical assessment, including serum electrolytes and plasma osmolality, blood urea, serum creatinine, urine electrolytes, and specific gravity, and, if necessary, arterial blood gases (ABGs).

Patients undergoing minor and elective surgery usually have only a minor fluid deficit, which is usually not necessary to correct. For major surgery, an initial bolus of 10 ml/kg of isotonic crystalloid (0.9% normal saline) or Ringer lactate or Hartmann's solution should be given in the first hour to correct the fluid deficit. The fluid normally used to replace this deficit should be isotonic, in particular, 0.9% sodium chloride. Should hypovolemia be present, a bolus of 10–20 ml/kg of an isotonic fluid must be administered and repeated as per Advanced Pediatric Life Support (APLS) guidelines [15].

Table 10.3 Signs and symptoms of dehydration

Grade of dehydration	Mild (<3% water loss)	Moderate (3–10% water loss)	Severe (>10% water loss)
General	Alert	Thirsty, lethargic	Cold, sweaty, limp
Pulse	Normal rate and volume	Rapid and weak	Rapid, feeble
Systolic pressure	Normal	Normal	Low
Respiratory rate	Normal	Increased, deep	Deep
Dry mouth	No	Yes	Yes
Eyes	Normal	Sunken	Sunken
Anterior Fontanelle	Normal	Sunken	Very sunken
Skin turgor	Normal (recoils instantly)	Reduced (1–2 s)	Severely reduced (>2 s)
Capillary refill	Not prolonged	Slightly prolonged	Prolonged
Neurological deterioration	No	Drowsiness	Severe
Urine output	Normal	Reduced	Reduced
Deficit	30–50 ml/kg	60–100 ml/kg	>100 ml/kg

Table 10.4 Holliday and Segar recommendations for fluid management (4-2-1 rule)

Body weight (kg)	Daily fluid requirement
0–10	4 ml/kg/h
10–20	40 ml/h + **2** ml/kg/h above 10 kg
>20	60 ml/h + **1** ml/kg/h above 20 kg

Table 10.5 Fluid requirements for neonates

Newborn term	Daily fluid requirement (ml/kg)
Day 1	50–60
Day 2	80
>Day 7	100–150

10.3.3 Maintenance Fluid Requirements

Fluid requirements due to fasting should be replaced according to the recommendations of Holliday and Segar for children and infants over 4 weeks of age, using the child's body weight (Table 10.4) [16]. According to Furman et al., the total amount of hourly maintenance requirements multiplied by hours of fluid restriction should be administered by giving 50% in the first hour and 25% during each of the next 2 h [17]. This management strategy was further modified by Berry et al., as they suggested the administration of a salty solution bolus during the first hour of the surgery (25 ml/kg for children 3 years old and younger, 15 ml/kg for older than 4 years) [18].

However, this formula should be just considered as a starting point only. Every individual child should always be monitored for response to fluid therapy, and adjustments should be made accordingly; in particular, clinical parameters to be assessed include heart rate, blood pressure, and capillary refill time.

In term neonates (>36-week gestational age), maintenance fluid requirements are reduced in the first few days after birth (Table 10.5). The normal infant will lose up to 10–15% of its body weight in water during this time. For the older children, the 4–2-1 rule (Holliday and Segar method) is followed. Certain conditions like burns, radiant heaters or phototherapy pyrexia, or excessive sweating result in hypermetabolic states resulting in increased requirements in maintenance fluids [19, 20].

During neurosurgical procedures, most children may be given fluids without dextrose. The maintenance fluid most commonly used during neurosurgery is an isotonic crystalloid, 0.9% sodium chloride. However, blood glucose and electrolytes should always be monitored, especially in long procedures, major surgery, or pituitary surgery. Perioperative dextrose (1–2.5% dextrose in Ringer's lactate solution) was shown to increase blood glucose in pediatric patients during surgery, which returned to normal levels about 1 h after surgery. The use of 2.5% solution was shown to yield a much greater increase in blood glucose, compared with 1% solution [21].

10.3.4 Management of Other Losses During Surgery

Generally, replacement of all losses during surgery should be done with 0.9% sodium chloride, or eventually Ringer lactate/Hartmann's solution, while colloids should be used only when deemed necessary. Intraoperative losses include third space loss and blood loss. During surgery, third space loss occurs due to extravasation of fluids from the intravascular compartments out to the tissues around the surgery site, and they should be replaced. It is generally accepted that superficial surgeries, including ophthalmic and neurosurgeries, result in the least amount of third space loss estimated at 1–2 ml/kg/h [22].

Even in this phase, it is important to assess clinical signs like heart rate, blood pressure, and capillary refill time to ensure adequate replacement. In case of bleeding, blood products transfusion should be considered. The determinants for blood transfusion are based on clinical signs, estimated blood volume (Table 10.6), preoperative hemoglobin and hematocrit values, and coexisting illnesses.

According to a study, a hemoglobin threshold of 7 gm/dL for red blood cell transfusion can decrease transfusion requirements without increasing adverse outcomes in critically ill children [23]. A fall in hematocrit of up to 25% from baseline values may be acceptable in children aged more than 3 months; however, in children with cyanotic congenital heart disease or severe respiratory diseases, a higher hematocrit target should be used to maintain appropriate tissue oxygenation. In infants younger than 3 months of age, it is not clear which is the hemoglobin and hematocrit threshold to consider for transfusion, but blood administration should be individually considered, according to the clinical conditions and the gestational age. However, mildly low hemoglobin and hematocrit values could be acceptable in small, older preterm infants [24, 25].

Table 10.6 The estimated blood volume in neonates and infants

Age	Estimated blood volume (ml/kg)
Premature neonates	95–100
Full-term neonates	85–90
Infants	80

10.3.5 Postoperative Fluid Management and Monitoring of Fluid Therapy

Regarding postoperative fluid management (Table 10.7), it should be considered that surgery, pain, nausea, and vomiting are all potential causes of dehydration and ADH release, as well as other peculiar complications related to neurosurgical procedures, including DI or other electrolyte disturbances. The literature is not clear about which is the correct maintenance fluid rate during the postoperative period. Holliday and Segar's formula may be followed; isotonic fluids may be used to replace ongoing losses from drains or nasogastric tubes, with or without added electrolytes. Serum electrolytes, as well as hemoglobin and hematocrit, should be measured pre- and postoperatively. Moreover, children should be weighed prior and after the prescription and administration of fluids [21]. During the postoperative period, serum electrolytes should be monitored every 24 h in all children on IV fluids (or more frequently if abnormal). Particular attention is paid to patients who underwent pituitary surgery and who are vulnerable to electrolytic complications. Fluid monitoring should include a fluid input/output chart, urine output monitored hourly and replaced every 2–4 h. Apart from routine clinical parameters, advanced parameters

Table 10.7 Goals of postoperative fluid therapy

Parameter	Target
Urine output	1–3 ml/kg/h
Allowable weight loss	1–2% per day in first week
Urine specific gravity	1005–1015
Euglycemia	75–100 mg/dl
Normonatremia	135–145 mEq/L
Normokalemia	4–5 mEq/L
Prevention of failure	Absence of edema/ dehydration/hepatomegaly

like dynamic indices of fluid responsiveness like stroke volume variation (SVV), pulse pressure variation (PPV), and plethysmograph variability index (PVI) may be employed whenever available. Although they have been validated in adults, the data available for the pediatric population is limited due to the anatomical and physiological variations in cardiorespiratory parameters that make their efficacy limited [26, 27].

10.4 General Principles for Electrolytes Management

Neurosurgical patients receiving IV fluids should have their electrolytes checked daily by capillary sampling or venous blood gas analysis. Hyponatremia is the most common electrolytic disorder in this group of patients, and if SIADH or CSWS occurs, sodium may fall very rapidly, and the treatment becomes a clinical emergency. In general, any neurosurgical patient with a drop in sodium of more than 4 mEq/L since the last measurement or a Na^+ <131 mEq/L should have an urgent clinical assessment. Repeat electrolytes and ABG analysis are to be done to confirm hyponatremia, and appropriate treatment is to be instituted. Any patient with Na^+ <135 mEq/L on routine blood tests should be reviewed urgently, including the assessment of fluid balance, IV or enteral fluids, and replacement of Na^+ losses [28]. Finally, patients with extraventricular drainage (EVD) in situ should have their electrolytes monitored twice a week.

10.5 Sodium Disturbances

10.5.1 Hyponatremia

Hyponatremia may occur in up to 20% of patients in the postoperative period and reach up to 50% of neurosurgical patients. The early signs of hyponatremia are nonspecific, and often the first presenting symptoms are neurological deterioration, seizures, or respiratory arrest. Headache is considered an early and common sign of hyponatremia, but this sign might not be obvious in young children. Initial symptoms may also include nausea or vomiting; and progress to confusion, seizures, stupor, and coma as hyponatremia worsens. Finally, severe hyponatremia may result in brain swelling (cerebral edema) and symptoms related to increased ICP. The magnitude of the symptoms is related to both the severity and the rate at which serum sodium levels drop [29]. Hyponatremia can increase mortality, which is significantly higher and directly related to the severity of electrolyte disturbance. Therefore, aggressive treatment as a medical emergency and pediatric intensive care admission is mandatory precaution [30].

There are several conditions which can lead to hyponatremia in the pediatric population (Table 10.8); however, in neurosurgical patients, the main causes of hyponatremia are the SIADH, resulting from excessive water retention after ADH secretion dysfunction, or the salt-losing brain syndrome, characterized by hyponatremia, polyuria, and severe dehydration [31]. Pituitary tumors are at higher risk for developing both these conditions, whereas in tumors not involving the hypothalamo-pituitary axis, SIADH occurs commonly. As the management of both these conditions is vastly different, accurate diagnosis and clinical and laboratory criteria are most essential (Table 10.9). Physiologically, ADH is secreted in cases of high plasma osmolality and decreased effective blood volume, which is detected by the osmoreceptors and baroreceptors in the aortic arch, carotid sinus, left atrium, and hypothalamus. ADH acts on the distal convoluted tubule and collecting ducts in the kidney in order to reabsorb water without reabsorbing solute.

Inappropriate ADH secretion occurs when this process happens in response to non-osmotic stimuli (Table 10.10). The main risk factors are stress, cerebral injury, mechanical ventilation, pain, and several drugs, including anesthetic agents and antiepileptic drugs. Patients affected by SIADH present with euvolemia or hypovolemia with hyponatremia, and therefore the clinical management should be based on Na^+ replacement and fluid restriction.

In the salt wasting syndrome, there is an excessive release of the natriuretic peptide, which

Table 10.8 Causes of hyponatremia in the pediatric population

Reduced total body sodium	Clinical presentations
Extrarenal	Vomiting, diarrhea Fluid sequestration (sepsis, peritonitis, pancreatitis) Cutaneous losses (burns) Ventriculostomy drainage
Renal	Cerebral salt wasting syndrome Diuretics (osmotic/non-osmotic) Tubulointerstitial diseases Adrenal insufficiency Congenital adrenal hyperplasia, Addison's disease Renal diseases (obstructive uropathy, nephritis, pyelonephritis, renal tubular acidosis)
Increased total body sodium	Congestive heart failure Cirrhosis Nephrotic syndrome Renal failure
Normal total body sodium	SIADH Glucocorticoid deficiency Hypothyroidism Infantile water intoxication Abusive water intoxication

Table 10.9 Differential diagnosis between SIADH and CSWS

Parameters	SIADH	CSWS
Extracellular fluid volume	Normal to high	Low
Fluid balance	Positive or neutral	Negative
Urine volume	Decreased or normal	Increased or normal
Central venous pressure	Normal to high	Low
Urine Na^+	High (20–40 mEq/L)	High (>40 mEq/L)

SIADH syndrome of inappropriate antidiuretic hormone, *CSWS* cerebral salt wasting syndrome

Table 10.10 The causes of syndrome of inappropriate antidiuretic hormone (SIADH) secretion

Central nervous system	Meningitis, encephalitis Multiple sclerosis, neuropathy Brain trauma, tumor, and abscess Hypoxia Hydrocephalus Drugs (vincristine, salicylates) Cerebral thrombosis of hemorrhage Subarachnoid hemorrhage or subdural hemorrhage
Pulmonary system	Pneumoniae Asthma Pneumothorax Positive pressure
Drugs	ADH analogs Barbiturates Haloperidol, tricyclic, indomethacin, interferon, ecstasy
Miscellaneous	Tumors Postoperative and postprocedural patients

leads to primary natriuresis and volume depletion, and therefore patients present with hypovolemia and hyponatremia. Thus, given the severe dehydration risk, an aggressive volume replacement with an isotonic solution and increased sodium supply is necessary.

In general, asymptomatic hyponatremia should be treated with enteral fluids as tolerated or with intravenous 0.9% sodium chloride solution and, eventually, fluid intake restriction if the child presents normal or increased volume. Patients with hyponatremic encephalopathy (seizure, coma) should be aggressively treated with an infusion of hypertonic 3% sodium chloride solution. 1 ml/kg of 3% sodium chloride will normally raise the serum sodium by 1 mEq/L, and attention should be paid to the rate of Na^+ increase, which should not be higher than 1–2 mEq/L/h to avoid complications such as pontine myelinolysis. Hypertonic saline should be administered via a central vein, but it is important

not to delay sodium administration for the insertion of the central venous line.

The amount of Na^+ required can be calculated as:

$$\text{mmol of } Na^+ \text{ required} = \left(130 - \text{present serum } Na^+\right) \times 0.6 \times \text{Weight}\left(\text{kg}\right)$$

Sodium should be raised aggressively until serum Na^+ reaches 125–130 mEq/L, or after clinical improvement. A slower Na^+ correction should take place at this stage, and a 0.9% sodium chloride solution should be used. The addition of dextrose to this solution is still controversial, as generating hyperglycemia might worsen brain injury, and thus, should be considered on a case to case basis. During Na^+ replacement, patients should be monitored for signs of increased ICP, and electrolytes should be rechecked every 4 h until Na^+ is >130 mEq/L and, then, at least twice a day for the following 48 h. Finally, particular attention should be paid to patients with EVDs in situ, who might be more prone to hyponatremia due to sodium loss in CSF. The Na^+ levels in CSF are similar to those of plasma, and when the EVD drainage rate is >10 ml/h, Na^+ loss should be monitored and accurately replaced [32–34].

10.5.2 Hypernatremia

In hospitalized children, hypernatremia (serum Na^+ >150 mEq/L) commonly occurs due to excessive water loss, restricted intake, or an inability to respond to thirst. It is, therefore, generally related to a systemic dehydrated status (Table 10.11). The magnitude of the hypernatremia signs is more severe when it develops rapidly or when serum Na^+ >160 mEq/L, while chronic hypernatremia is often well tolerated. The severity of dehydration might be underestimated if clinical signs alone are used, compared to weight loss.

Improvement of hydration and establishing euvolemia should be targeted with 0.9% sodium chloride, given in boluses of 20 ml/kg. Once the initial fluid replacement is done, complete correction of hypernatremia should be done very slowly over at least 48 h to prevent cerebral edema, seizures, and brain injury. The correction rate should be no more than 12 mmol/kg/day and done with 0.45% or 0.9% sodium chloride with dextrose [35].

10.5.3 Diabetes Insipidus (DI)

Neurosurgical patients, especially with suprasellar tumors, are at high risk for many postoperative complications, including DI (Table 10.12). The deficiency of ADH secretion

Table 10.11 Causes of hypernatremia in the pediatric population

Causes of hypernatremia	Clinical presentation
Low total body sodium	
Extrarenal losses Renal losses Inadequate intake	Vomit, diarrhea, profuse sweating Osmotic diuresis (mannitol, glucose, urea) Insufficient lactation
Increased total body sodium	
Increased Na intake	Excessive administration of Na^+, near-drowning (seawater)
Normal total body sodium	
Extrarenal losses Renal	Respiratory insensible losses, dermal insensible losses (fever, burns, radiant warmers, phototherapy) Diabetes insipidus

Table 10.12 Causes of diabetes insipidus

Central	Clinical presentations
Congenital Acquired	Inherited, idiopathic Cerebral trauma, sellar/suprasellar tumors Infections (meningitis, encephalitis) Post-neurosurgical procedures Vascular, aneurysms, thrombosis, etc.
Nephrogenic	
Congenital Acquired	Inherited, mutation Renal failure, tubular disease Hypercalcemia, K^+ depletion Drugs (alcohol, lithium, diuretics, amphotericin B, etc.) Dietary abnormalities (primary polydipsia, decreased sodium intake)

results in intravascular solvent loss, polyuria, and, dehydration, with consequent hypernatremia, which can occur within the first postoperative hours. In patients who underwent pituitary surgery, DI should always be suspected, and if serum Na^+ level increases over 150 mEq/L, with urinary sodium levels below 20 mEq/L, polyuria, and dehydration. The therapy for DI is desmopressin, a synthetic ADH analog, which should be administered early to prevent metabolic complications described above. This medication can be administered intravenously, orally, or intranasally. Hypotonic saline solutions (e.g., 0.45% NaCl, 0.45% NaCl +5% dextrose, 0.18% NaCl +10% dextrose, 0.18% NaCl +4% dextrose, and 10% dextrose solutions) should only be used to treat active hypernatremia (Na >150 mEq/L) [36].

10.5.4 Hyperkalemia

Hyperkalemia (serum K^+ >5.5 mEq/L in infants and >6 mEq/L in neonates) can cause general skeletal muscle weakness and substantial ECG changes, especially when serum K^+ >7 mEq/L. Hyperkalemia is most commonly an artifact due to either hemolysis or release of K^+ during clot formation in the specimen tube. Other causes of hypopotassemia are drugs, including β-blockers and digitalis, myonecrosis, and acidosis, as well as renal disorders or failure [37]. First-line treatment of hyperkalemia should include the administration of 100 μg/kg of 10% calcium gluconate. The second line of treatment consists of administration of sodium bicarbonate (1–2 mmol/kg), an infusion of 0.3–0.5 mg/kg/h of glucose with 1 unit of insulin for every 5 gm of glucose added, or an infusion of 2.5–5 mg of nebulized salbutamol (5 μg/kg in neonates, IV) to increase intracellular shift of potassium. Finally, the removal of potassium from the body is achieved by administering 125–250 mg/kg calcium resonium rectally or orally, by using either furosemide (1 mg/kg), dialysis, or hemofiltration.

10.5.5 Hypokalemia

Hypokalemia (serum K^+ <3.5 mEq/L) is usually caused by diuretic therapy. In intensive care and perioperative settings, additional causes include nasogastric suctioning, magnesium deficiency, and alkalosis or loss of K^+ as a consequence of vomiting/diarrhea. Children are usually asymptomatic until K^+ reaches 2.5 mEq/L, and then they might present with muscular symptoms such as cramps, cardiological complications (including arrhythmias, reduced cardiac contractility, ECG alterations like U waves, loss of T waves, and QT prolongation), and neurological deterioration. Hypokalemia is associated with poor outcomes in patients with aneurysmal subarachnoid hemorrhage and therefore should be aggressively treated [38]. This is also true for symptomatic hypokalemic children [39]. Management should focus on reversing the transcellular shifts (alkalosis) and on potassium replacement. Potassium can be administered orally (3–5 mmol/kg/day) or intravenously (recommended in severe hypokalemia, i.e., serum K^+ <3 mEq/L). Potassium correction should not be faster than 0.25 mmol/kg/h while using a maximal peripheral concentration of 40 mEq/L of KCl. When a rapid correction is being done, it is essential to carry out the administration via a central line while monitoring the patient in the intensive care unit [38].

10.5.6 Hypocalcemia

Hypocalcemia (defined as corrected total Ca^{2+} <2 mEq/L, or <1.5 mEq/L in neonates) may produce various symptoms, including perioral, finger, and toe paresthesia, spasm, cardiac alterations including prolonged QT interval, and reduced cardiac contractility. Immediate treatment includes 10% calcium gluconate (0.5 ml/kg, up

to a maximum of 20 ml over 10 min) or a solution of 10% calcium chloride (0.2 ml/kg, up to a maximum of 10 ml over 10 min), possibly through a central venous route. Newborns are prone to hypocalcemia due to physiologically lower albumin concentration, a normal fall occurring after birth, which later rises after the second day, and maternal diabetes mellitus. Other causes include encephalopathy, renal failure, DiGeorge syndrome, and disordered maternal metabolism [38].

10.5.7 Hypercalcemia

Hypercalcemia presents with a low incidence (<1% of hospitalized patients), and most of the cases are caused by hyperparathyroidism or malignant tumors. More rare causes include thyrotoxicosis and drugs. Presentation is nonspecific, including cardiovascular (hypotension/hypovolemia and shortened QT interval on ECG), renal (polyuria, nephrocalcinosis), and neurological alterations. Patients require treatment if symptomatic, or if ionized Ca^{2+} >3.5 mEq/L (14 mg/dL). Hypercalcemia can also produce hypercalciuria, which results in osmotic diuresis and hypovolemia. These patients are volume depleted and, therefore, require saline infusions; furosemide can be used to enhance excretion, but it can exacerbate hypovolemia and hypotension.

10.5.8 Hypophosphatemia

Hypophosphatemia is seen when serum phosphate levels fall below 0.8 mEq/L (or <2.7 mg/dL) and occurs in 17–28% of postoperative patients. When glucose moves into cells, phosphate usually follows it, and thus, glucose overloading is the most common cause of hypophosphatemia in hospitalized patients [35]. Hypophosphatemia is often clinically asymptomatic, and even at levels of <1.0 mg/dL, it may not produce any obvious effects. However, common symptoms include muscle weakness and respiratory depression, and therefore, phosphate levels are to be monitored with attention in the postoperative period. Hypophosphatemia can lower cardiac output (CO), and patients with low CO and heart failure may respond to supplementation [38]. Phosphate replacement can be started intravenously if levels are very low, but when phosphate levels are higher than 2.0 mg/dL, a replacement can be given orally.

10.5.9 Hyperphosphatemia

It usually occurs after renal insufficiency (decreased secretion), widespread cell death related to tumor lysis, or rhabdomyolysis. Sucralfate calcium acetate tablets or antacids can be used to reduce serum levels.

10.5.10 Hypomagnesemia

Hypomagnesemia is found in 15% of ward patients and 60% of ICU patients. Main causes include other electrolyte abnormalities (hypokalemia, hypophosphatemia, hyponatremia, hypocalcemia), drugs (diuretics, furosemide, aminoglycosides, digitalis, amphotericin, cyclosporine), diarrhea, alcohol, and diabetes. The clinical findings include cardiac manifestations, ischemia, arrhythmia, and neurological deterioration. Hypomagnesemia has been shown to be studied in relation to vasospasm in patients with SAH, in both animal and human models. In a study including 283 SAH patients, 4 days of magnesium treatment compared with normal saline showed a favorable trend in the development of delayed cerebral ischemia (reduced by 34%) and resulted in a better outcome at 3 months [40]. Still, its role in a SAH is considered controversial.

10.5.11 Hypermagnesemia

Hypermagnesemia is found in up to 5% of hospitalized patients. The risk factors include massive hemolysis, renal adrenal insufficiency, hyperparathyroidism, and lithium toxicity. Magnesium is a calcium channel blocker, and thus, the promi-

nent effects of hypermagnesemia are cardiac (ECG alteration, including prolonged AV conduction, heart block, and cardiac arrest). To treat hypermagnesemia, IV calcium gluconate (1 mg over 2–3 min) should be given, and eventually, if not effective, dialysis should be started. With preserved renal function, aggressive fluid resuscitation and furosemide are appropriate as well.

10.6 Conclusions

Recognizing the diverse nature of pediatric neurosurgery complications is imperative for appropriate patient management during the perioperative periods. Disturbances in salts and water balances are relatively common in children, and present diagnostic and therapeutic challenges, especially after brain surgeries for suprasellar and pituitary tumors. Sodium disturbances, and in particular hyponatremia, are the most common and critical disturbances, even if DI is commonly encountered as well. A proper fluid balance assessment and a prompt diagnosis are mandatory to improve the outcome of the pediatric neurosurgical population.

Conflict of Interest None.

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11 Blood Loss and Transfusion in Children Undergoing Neurosurgery

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Key Points

- Pediatric patients undergoing neurosurgical interventions are vulnerable to intraoperative bleeding.
- Pediatric physiology is diverse from that of adults, which precludes them from enduring even a small quantity of blood loss over a short duration.
- Various pediatric neurosurgical procedures are prone to massive blood loss, management of which requires a thorough understanding of body physiology, usage of blood products, and appropriate monitoring methods.
- Contemporary blood conservation techniques with special attention to the pharmacologic aspects of reducing transfusion requirements should be employed whenever deemed necessary.
- One should also know the adverse effects of blood transfusion, especially during a massive blood transfusion.

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11.1 Introduction

Pediatric blood transfusion practices during neurosurgical procedures differ from those of adults with regard to physiologic and hematologic considerations. Such differences dictate different guidelines for blood transfusion practices. In addition, pediatric patients are more susceptible to certain transfusion-related complications as compared to their adult counterparts [1]. A hemovigilance database that included both adults and children receiving transfusion revealed the incidence of reactions to be higher in children than the adults (6.2 vs. 2.4 per 1000 transfusions) [1]. The pediatric patients present with more incidence of allergic, febrile non-hemolytic, and hypotensive transfusion reactions [1]. Oxygen consumption in children is higher as compared to adults [2]. As the myocardium of a newborn operates to the full potential to meet the higher oxygen demand, it may not be able to compensate for diminished oxygen capacity by further increasing cardiac output and, thus, have a higher likelihood of cardiac decompensation and ischemia under stressful circumstances [2]. Optimal hemoglobin concentrations are, thus, higher in newborns as compared to the adults. The term neonate has mean hemoglobin values of 16.5 gm/dL [3], and the hemoglobin concentrations vary in children

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Table 11.1 Age-based hemoglobin levels in children and adolescents

Age		Mean hemoglobin level (gm/dL)	−2 standard deviations (gm/dL)
At birth (term infant)		16.5	13.5
1 month		13.9	10.7
2 months		11.2	9.4
3–6 months		11.5	9.5
6 months to 2 years		12.0	10.5
2–6 years		12.5	11.5
6–12 years		13.5	11.5
12–18 years	Males	14.5	13.0
	Females	14.0	12.0

and adolescents in an age-related manner (Table 11.1) [3]. Fetal hemoglobin (HbF) in the full-term newborn is highest at birth, decreasing at 5% per week until 6 months [4]. The basic differences between HbF and adult hemoglobin (HbA) are that HbF is of short life-span (90 vs. 120 days), poorly interact with 2–3-diphosphoglycerate (2–3-DPG), and have a decreased partial pressure of oxygen at which hemoglobin is 50% saturated (P_{50}; 19 vs. 27 mmHg) [5]. HbF shows a leftward shift of oxygen-hemoglobin (O_2-Hb) dissociation curve as a result of the high affinity of HbF for oxygen. Hence, younger infants have a lesser oxygen-carrying capacity, and thus, the target hemoglobin concentration for transfusion red blood cells (RBC) to begin in a neonate should be higher than a much older child or a healthy adult [2]. Compared to a full-term infant, premature infants have larger fractions of HbF and decreased erythropoietin production as an appropriate response to anemia [2]. Besides that, during early life (8–10 weeks of age), a gradual progressive decline in hemoglobin concentrations is observed in infants without any clinical evidence of anemia. This decline in hemoglobin is physiological and often referred to as "early anemia of infancy." [6] After reaching this nadir, hemoglobin concentrations begin to rise, ultimately attaining adult levels by 2 years of life [6].

11.2 Blood Volume Calculation

To manage blood loss and initiate blood transfusion, one must understand the maximum allowable blood loss (MABL) and estimated blood volume (EBV) [7]. The EBV is in the range of 90–100, 80–90, 70–80, and 70 ml/kg among preterm, neonates, infants, and children, respectively. The preoperative estimation of MABL may help to manage intraoperative blood loss and subsequent transfusions.

$$\text{MABL} = \frac{\text{Starting Hematocrit} - \text{Target Hematocrit}}{\text{Starting Hematocrit}} \times \text{EBV}$$

Blood transfusion is initiated once the estimated blood loss (EBL) reaches the calculated MABL [7]. However, preterm infants, children with comorbidities such as respiratory failure and congenital cyanotic heart disease, and those with mismatched ventilation and perfusion and a higher hematocrit (Hct) should be targeted for starting RBC transfusion [7]. The lost blood is usually replaced with either crystalloid in a ratio of 3 mL crystalloid for 1 mL of blood or in a ratio of 1:1 if colloids are preferred as a replacement [7]. However, in adults, studies have shown that the optimal ratio of crystalloids to blood loss is 1.5:1, which is more restrictive than the traditional 3:1 ratio [8].

11.3 Conditions Prone to Intraoperative Bleeding

Of particular note in pediatric neurosurgery, scenarios such as craniofacial surgeries, resection of vascular malformations (arteriovenous malformations), and highly vascular tumors (meningi-

Table 11.2 Pediatric neurosurgical conditions prone to intraoperative bleeding

Surgical procedure(s)	Neurosurgical condition(s)
Craniofacial surgeries • Cranial vault reconstruction • Fronto-orbital advancements	Craniosynostosis: • Syndromic: Apert's syndrome, Crouzon's syndrome, Pfeiffer syndrome • Non-syndromic: Multi-suture involvement
Resection of vascular malformations	• Intracranial aneurysm • Arteriovenous malformations • Vein of Galen malformation
Resection of intracranial vascular tumors	• Choroid plexus papilloma • Meningioma • Medulloblastoma (posterior fossa surgery) • Tumors involving large vessels and sinuses • Glomus tumor • Nasopharyngeal angiofibroma
Excision of CNS sarcoma (both cranial and spinal)	• Primary CNS sarcoma • Secondary metastatic CNS sarcoma.
Resective epilepsy surgery (hemispherotomy and hemispherectomy)	Medically intractable epilepsy due to unilateral hemispheric lesions: • Congenital (hemimegalencephaly, extensive porencephaly, and Sturge-Weber syndrome) • Perinatal disorders (Rasmussen encephalitis and Lennox-Gastaut syndrome)
Decompressive surgery for traumatic brain injury	• Acute extradural hematoma • Acute subdural hematoma and contusion
Spinal surgeries	
• Scoliosis correction surgery. • Transoral odontoidectomy and occipital-cervical fusion (posterior fixation). • Spinal instrumentations and multi-level fusion	• Scoliosis • Craniovertebral junction anomaly

CNS central nervous system

oma), sarcoma, neurotrauma, epilepsy surgery (hemispherectomy), and scoliosis correction surgery are prone to significant blood loss and massive fluid shifts (Table 11.2). In children undergoing excision of brain tumors, the predictors of intraoperative blood transfusion are age < 4 years, a preoperative hemoglobin <12.2 gm/dL, and the duration of surgery >270 min [9]. In pediatric patients with age less than 10 years, undergoing hemivertebra resection, preoperatively determined total Cobb's angle and the number of fused levels were independently associated with the total blood loss [10]. In children undergoing craniosynostosis surgery, younger age, lower weight, and longer duration of surgery predisposed the children to transfusion of more than 50% circulating blood volume (CBV) [11].

11.4 Blood Transfusion Goals [12]

The hemorrhage management goals in pediatric patients should target the following principles:

- Hemodynamic stability should be maintained.
- End-organ perfusion and oxygen delivery should be preserved.
- Avoidance of excessive transfusion by using the point-of-care (POC) modalities and apt use of blood products.
- Reduction and early recognition of adverse effects associated with transfusion.
- Prevention of the dangerous triad of acidosis, coagulopathy, and hypothermia.

The maintenance of hemodynamic stability is of utmost priority; hence, temporizing measures such as vasopressor support are often required to maintain the blood pressure [13]. The use of lactate, base-deficit measurements [14], urine output, and near-infrared spectrometry (NIRS)-based cerebral oxygenation monitoring can help monitor end-organ perfusion. POC modalities such as rotational thromboelastometry (ROTEM) guide blood and component transfusion, especially during massive transfusion (MT), effectively decrease transfusion requirements and associated complication rates, and ultimately reduce healthcare costs [15].

11.5 Perioperative Monitoring of Blood Loss

11.5.1 Perfusion of Vital Organs Monitoring

As discussed previously, the goal of blood transfusion is to maintain hemodynamic stability and ensure adequate end-organ perfusion and oxygen delivery [12]. The intensity of monitoring depends on the extent of surgery and, hence, depends on the expected blood loss. The American Society of Anesthesiologists (ASA) recommends heart rate, blood pressure, oxygen saturation, capnography, and urine output monitoring in addition to clinical evaluation as a part of management. Hemoglobin and hematocrit (Hct) monitoring and arterial blood gas (ABG) analysis are based on clinical signs and EBL. Monitoring with invasive arterial blood pressure and central venous pressure is decided as per individual cases. Mixed venous oxygen saturation (SvO_2) and regional cerebral oxygen saturation using NIRS technology can be considered additional monitoring modalities. However, the central venous oxygen saturation ($ScvO_2$) can be used as an alternate to SvO_2, the latter being more invasive [16].

11.5.2 Noninvasive Hemoglobin Monitoring

Technological advancements allow us to measure the real-time concentration of hemoglobin inside the operative room (OR), allowing us to decide on blood transfusion requirements. Numerous such devices exist, which measures the concentration of hemoglobin noninvasively [17]. One such device is the Radical-7 Pulse CO-Oximeter (Masimo Corporation, Irvine, CA), which can continuously estimate hemoglobin concentration (SpHb) in a noninvasive manner. A coefficient of correlation of 0.53 ($P < 0.001$) between SpHb and arterial sample hemoglobin (tHb) was observed in children undergoing neurosurgery [18]. However, the average difference (bias) between tHb and SpHb was 0.90 gm/dL (95% confidence interval [CI], 0.48–1.32 gm/dL), and 1 standard deviation of the difference was 1.35 gm/dL [18]. Hence, it was suggested that the SpHb values should be used cautiously while making transfusion decisions [18].

11.5.3 Intraoperative Blood Loss Estimation

Ongoing blood loss estimation is always a daunting task for anesthesiologists. Continuous visual assessment of the surgical field provides significant input, but inaccuracies always plague it. To improve the accuracy of visual estimation, one group of authors conducted an experiment where they mimicked surgical blood loss, using aspirated blood and different sizes of surgical gauze and photographed to create an analog of real surgical loss, which can be used to estimate the blood loss [19]. Quantitative measurement includes checking suction canisters, surgical sponges, and surgical drains. However, in pediatric patients, these methods might not be accurate. Therefore, it is of utmost importance to remain vigilant and observe the surgical field as well as use other adjuncts whenever available for making transfusion decisions.

11.5.4 Coagulation Monitoring [20]

Intraoperative coagulation monitoring can be theranostics, i.e., to diagnose and treat the underlying pathophysiological derangements during perioperative bleeding [15]. Periodic assessment of blood loss and communication with the surgical team are fundamental practices to detect impending or established coagulopathy. The utility of conventional coagulation tests, namely, prothrombin time (PT), partial thromboplastin time (PTT), and fibrinogen concentrations, during the intraoperative period is limited. Activated clotting time (ACT) monitoring is advised when a large intravenous (IV) dose of heparin is used intraoperatively or during interventional neuroradiological procedures.

11.5.5 Point-of-Care (POC) Coagulation Tests

Point-of-care (POC) tests [21] are employed to interpret the pathology rapidly and comprehensively, which allow the anesthesiologists to initiate the corrective measures early. POC coagulation tests such as thromboelastography (TEG), ROTEM, and sonoclot measurements are essential for patient blood management (PBM) [15]. The frequently used POC tests are TEG and ROTEM, which analyze the viscoelastic properties of blood, thus determining which component in the coagulation cascade is at fault. Age-specific reference ranges are described for all pediatric age group, which may be employed for monitoring coagulation in children [22].

11.6 Blood and Component Transfusion [23–25]

11.6.1 Red Blood Cell (RBC) Transfusion [24, 25]

The recommendations from Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) [24] provide essential guidance and applicable tools to reduce superfluous RBC transfusion in critically ill pediatric patients (Table 11.3). However, as per the consensus panel recommendation, it is advised to transfuse RBC if hemoglobin concentration is between 7 and 10 gm/dL in pediatric patients with acute brain injury (e.g., trauma, stroke) [25]. The use of brain oxygen monitoring to guide RBC transfusion is not advised due to the lack of supporting literature to date [25]. In a randomized control trial (RCT) in pediatric critically ill patients, the use of restrictive blood transfusion strategy (hemoglobin trigger of ≤7 gm/dL) was considered better regarding the hemodynamic and laboratory values during the early period as compared to liberal transfusion strategy [26]. The implementation of PBM with restrictive transfusion trigger (<7 gm/dL) along with the use of prophylactic tranexamic acid, intraoperative cell recovery, and goal-directed therapy as per TEG

Table 11.3 Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) recommendations [24]

Recommendations	Level of evidence/ recommendation
• RBC transfusion is recommended in critically ill children or those at risk for critical illness if the hemoglobin concentration is <5 gm/dL	Strong recommendation Low-quality pediatric evidence
• The TAXI cannot recommend a specific RBC transfusion decision-making strategy based upon physiologic metrics and biomarkers	Consensus panel expertise
• For critically ill children with stable hemodynamics and a hemoglobin concentration ≥ 7 gm/dL, RBC transfusion are not recommended	Strong recommendation Moderate-quality pediatric evidence
• There is insufficient evidence to recommend transfusion thresholds in critically ill children who have a hemoglobin concentration between 5 and 7 gm/dL	Consensus panel expertise
• After the transfusion, a reasonable hemoglobin goal should be in a range between 7.0 gm/dL and 9.5 gm/dL	Weak recommendation, low-quality pediatric evidence

resulted in a substantial reduction of transfusion in the adolescents undergoing correction of idiopathic scoliosis [27].

In most cases, a volume of packed RBC (PRBC) in the range of 10–20 mL/kg is often used for initial transfusion [14]. However, to avoid the risk of over-transfusion, a formula-based (as below) estimation of PRBC transfusion volume may be used in pediatric patients [28].

$$\textbf{PRBC volume}\,(\textbf{mL}) = \textbf{weight}\,(\textbf{kg}) \times \textbf{hemoglobin increment}\,(\textbf{gm/dL}) \times \textbf{transfusion factor}$$

[Transfusion factor = 3/Hematocrit of transfused PRBC]

Therefore, a 10 mL/kg of transfused PRBC (60% Hct) provides a 2 gm/dL increment of hemoglobin.

11.6.2 Platelet Transfusion [23, 29]

Platelets are indicated in the following situations.

(a) *Age of the infant less than 4 months*
- Platelet count <20–30,000/μL in infants lacking platelet production.
- Invasive procedures (other than neurological surgeries) or minor surgery: platelet count <50,000/μL.
- Neurologic invasive procedures: platelet count <100,000/μL.

(b) *Age of infant ≥4 months*
- Prophylactic platelet transfusion is indicated with a platelet count <10,000/μL, as these patients are prone to spontaneous bleeding.
- Transfusion of platelets is needed if the count <50,000/μL, preceding an urgent or emergent invasive procedure.
- A count of more than 100,000/μL of platelets is recommended in patients scheduled for neurosurgical procedures.

If the expected blood loss is more than 40% of CBV, the platelets and clotting factors may be transfused to maintain hemostasis. The platelet dose recommended for transfusion is 1–2 units/10 kg or 10–15 ml/kg [30].

11.6.3 Fresh Frozen Plasma [23, 29, 30]

Fresh frozen plasma (FFP) contains all the factors of coagulation. Transfusion of FFP is indicated in specific factor deficiency only when factors are not readily available. FFP can be transfused as a supportive treatment in hepatic dysfunction, disseminated intravascular coagulation (DIC), or vitamin K insufficiency. FFP can be considered for replacement therapy in protein C or S deficiency and congenital antithrombin deficiency. FFP transfusion is a part of a massive transfusion protocol (MTP) to replenish the clotting factors. The volume of FFP needed for transfusion is 1 unit/10 kg or 10–15 ml/kg [23, 30], which increases the concentration of coagulation factor by 15–25% [29].

11.6.4 Cryoprecipitate

One unit of cryoprecipitate (10–15 mL) contains fibrinogen (150–250 mg), factor VIII (80–

100 units), factor XIII, von Willebrand factor (VWF), and fibronectin. The recommended dose is 1–2 units/10 kg [23] or 5 ml/kg [29]. Cryoprecipitate is indicated [23] when there is bleeding in the presence of hypofibrinogenemia (fibrinogen <100–150 mg/dL), von Willebrand disease, hemophilia A, and factor XIII deficiency.

11.7 Massive Transfusion (MT) and Massive Transfusion Protocol (MTP)

Definitions of massive transfusion (MT) in adult patients do not apply to pediatric patients, and there are very few established definitions available. Blood transfusion in children is considered massive when the PRBC transfusion amounts to more than 50% of the total blood volume (TBV) in 3 h and >100% of TBV in 24 h or the PRBC transfusion supports to replace ongoing blood loss of >10% TBV per minute [31, 32]. MT involves selecting the appropriate type and amounts of blood components to be administered. The multipronged role of MTP is to help in guiding the ongoing resuscitation, providing logistic support, and preventing coagulopathy before it takes place. In adults, the application of MTP consequently achieved faster delivery of blood components, reduced rates of multi-organ dysfunction, and resulted in better 30-day survival [33]. Although MTP in pediatric trauma patients did not show any mortality benefit, the time to transfusion was reduced [34]. In MT, the blood component replacement is done to restore the hemostasis. Many adult MTP suggest a ratio of 1:1:1 of PRBC-FFP-platelets to represent whole blood loss best [32]. However, in pediatrics, most MT guidelines suggest a higher PRBC component advocating replacement in a PRBC-FFP-platelet ratio of 2:1:1 [32]. Nevertheless, a study in severely injured children receiving MT at a PRBC-FFP ratio of 1:1 showed the highest survival rate; the higher ratios, such as 2:1 or ≥3:1, were linked to increased mortality [35]. The use of POC coagulation tests significantly reduces the time for test results, thus guiding in transfusion.

Adjuvant therapeutic interventions, such as antifibrinolytics and local hemostatics, are frequently used to reduce perioperative blood loss. Clotting factor concentrates such as fibrinogen [36], prothrombin complex concentrate (PCC) [37], recombinant factors VIIa (rFVIIa), and factor XIII are used; their role in pediatric patients has not been studied adequately. As guided by the ROTEM analysis in children undergoing craniosynostosis repair surgery and requiring MT, administration of fibrinogen concentrate resulted in good hemostasis without adverse effects [36].

11.8 Consequences of Blood Transfusion

Blood transfusion carries various risks and consequences, starting from incompatibility, infectious risks, to various metabolic derangements. In a bleeding pediatric patient, the blood gas and electrolyte disturbances can magnify the risks to multiple levels.

11.8.1 Allergic and Febrile Non-hemolytic Reactions

Like adults, the children manifest allergic transfusion reactions and febrile non-hemolytic transfusion reactions (FNHTRs); however, these reactions occur variably. As compared to the adult population, the incidence of FNHTRs in

children is more (0.47 vs. 1.9 per 1000 transfusions; $p < 0.001$) [1]. The allergic transfusion reaction and FNHTRs have been observed in 0.9% and 0.2% of the total number of transfused products [38].

11.8.2 Hemolytic Transfusion Reactions and Other Immunologic Considerations

The risk of hemolytic transfusion reactions is approximately 1:70,000 per unit [39]. Human error is the most common cause of a transfusion mismatch resulting in ABO incompatibility and hemolytic transfusion reactions, which can be mitigated by careful vigilance. Acute transfusion reactions occur during or within 24 h after blood transfusion, whereas the delayed complications occur later than 24 h after the blood product's transfusion [39].

Transfusion-associated graft vs. host disease is a possibility when lymphocytes are present in a transfused blood component and react with the host tissue. This is more of a concern for patients undergoing chemotherapy, radiotherapy, or other immunosuppressive therapies or for premature infants with a birth weight of less than 1200 gm [23]. Thus, irradiation of cellular blood components with an of 25Gy is recommended to hinder the lymphocyte proliferation effectively, thus reducing the possibility of graft vs. host disease [23].

11.8.3 Risk of Infectious Disease Transmission

In recent years, the risks of infection via transfusion have decreased owing to vigilant screening methods. The WHO recommends screening of donated blood for human immunodeficiency virus (HIV), hepatitis-B virus (HBV), hepatitis-C virus (HCV), and syphilis [40]. In India, all donated blood units undergo testing for the HIV antibodies (HIV1, 2), hepatitis-B surface antigen (HBsAg), hepatitis-C antibody, and malaria parasites [41].

11.8.4 Metabolic Repercussions

11.8.4.1 Hypocalcemia

Citrate, a calcium chelating agent present in the blood units, can cause hypocalcemia by chelating divalent calcium ions. Hypocalcemia is most often noticed in neonates and patients with impaired hepatic function leading to impaired metabolism of citrate. It is also observed during whole blood and FFP transfusion, as these products contain more concentration of citrate per unit volume [2]. Cardiac dysfunction can be prevented by maintaining the rate of transfusion lesser than 1 ml/kg/min, particularly the citrate containing products [2]. Dose of calcium gluconate is 15–30 mg/kg to treat hypocalcemia resulting from rapid transfusion [2]. Calcium chloride yields three times more ionized calcium than calcium gluconate; hence, the dose of calcium chloride is proposed to be 5–10 mg/kg in such scenarios [2].

11.8.4.2 Hyperkalemia

Transfusion-associated hyperkalemia is a risk involved in large volume transfusions in neonates and infants, leading to lethal cardiac arrhythmias. There is a linear relationship between the stored blood and hyperkalemia [42]. The incidence of hyperkalemia was found to be 4% (defined as serum $K^+ \geq 5.5$ mEq/L) among a total of 160 units of PRBC transfused to 125 children; it further suggested that the hyperkalemia was more pronounced in patients who receive >12 days old stored blood [42]. Treatment of life-threatening arrhythmia caused by hyperkalemia warrants the use of calcium chloride (15–20 mg/kg). Alternately, calcium gluconate may be administered at a dose of 45–60 mg/kg. The other measures include administration of glucose and insulin, as well as administration of albuterol to shift potassium into the intracellular compartment [2].

11.8.4.3 Hypomagnesemia

Hypomagnesemia may also result in citrate chelating the divalent magnesium ions. In severe hypomagnesemia (<1.25 mg/dL), life-threatening arrhythmias can occur. The arrhythmias arising

after transfusion of blood products may not respond to calcium administration. In such cases, magnesium sulfate may also be given at a bolus dose of 25–50 mg/kg, followed by an infusion of 30–60 mg/kg/24 h [2].

11.8.4.4 Acid-Base Changes

Transfusion of blood initially leads to an increased load of accumulated carbon dioxide and lactic acid, which results in a momentary mixed respiratory and metabolic acidosis. Carbon dioxide is ventilated out, and the lactic acid is buffered, leading to a null effect on acid-base status. Metabolic acidosis that occurs as a result of MT may signify underlying hypovolemia, insufficiency in tissue perfusion, hypoxemia, or the presence of systemic infections. Metabolic alkalosis seen with MT may occur secondary to citrate metabolism. Therefore, it is logical to limit the administration of sodium bicarbonate to treat the acid-base abnormalities [2].

11.8.4.5 Hypothermia

With the relatively large head size and body surface area, pediatric patients can quickly lose body heat and become hypothermic. Hypothermia adversely affects coagulation, oxygen delivery to tissues, and drug metabolism. Therefore, it is imperative to avoid hypothermia, especially during rapid administration of cold blood and blood products. Various warming methods are employed to maintain normothermia. At high transfusion rates (>100 ml/min), devices using magnetic induction (FMS 2000; Belmont Instrument Corp., Billerica, MA, USA) and countercurrent exchange system (Level 1 fast flow H-1200; Smiths Medical, London, UK) can prevent transfusion-associated hypothermia. Direct warming of the blood transfusion tubing or using an in-line warmer (Buddy, Belmont Instrument Corp.) can also be effective in maintaining the desired temperature at lower flow rates [32].

11.8.4.6 Transfusion-Associated Circulatory Overload (TACO)

Transfusion-associated circulatory overload (TACO) may result from transfusion of blood and blood components, with an overall incidence of 1–5.8% [43, 44]. However, in pediatric patients, the incidence varies from 1.5% to 76%, depending on the definitions used [44]. The possibility of TACO should be considered in patients developing breathing difficulty or hypertension during or within 6–12 h of transfusion [45].

11.8.4.7 Transfusion-Related Acute Lung Injury (TRALI)

Transfusion-related acute lung injury (TRALI) is an acute transfusion reaction characterized by respiratory distress, hypoxia, and diffuse bilateral pulmonary infiltrates seen on chest radiography during or within 6 h of transfusion [46, 47]. The incidence ranges from 0.02 to 1.12% per transfused blood product; a higher incidence of TRALI exceeding 5 to 8% has also been described in critically ill patients [47]. Unlike TACO, the risk of TRALI is not associated with the volume of the transfusion.

11.8.4.8 Transfusion-Related Immunomodulation (TRIM)

Immunosuppression, as a result of ABT, is termed as transfusion-related immunomodulation (TRIM) [48]. The TRIM concept attributed to either transfusion of pure RBC or the intermediate products from a stored RBC [49]. One should differentiate TRIM from other transfusion reactions such as alloimmunization, graft vs. host disease, and anaphylactic reactions related to ABT. TRIM is described in adults and older children; however, in premature infants, the occurrence of TRIM is negligible owing to their immature immune system [49]. Increased concentrations of interleukin-8 (IL-8) and soluble intercellular adhesion molecule-1 (sICAM) are often considered markers of TRIM. In premature infants, both these TRIM markers were monitored in a study; however, the immunomodulatory effects of RBC transfusion were not observed [50].

11.8.4.9 Blood Transfusion and Postoperative Morbidity in Children

There are pieces of evidence in the literature which link transfusion of blood to several postop-

erative morbidities in adult patients, such as the increased likelihood of infective complications, organ dysfunctions, longer hospital stay, early and late mortality, and total cost [51]. The large volume of PRBC is associated with longer mechanical ventilation and longer intensive care unit (ICU) stay [52]. Among the pediatric patients (median age of 27.5 months), blood transfusion was found to be an independent risk factor for postoperative complications [53]. It was observed that postoperative cardiocirculatory and respiratory failure were common in the transfusion group. The most common postoperative infective complications were pulmonary and abdominal sepsis [53].

11.8.4.10 Clinical Effect of Aging of Stored RBC

Collection and storage of RBC for transfusion at a later time is associated with various morphological and biochemical changes. It includes membrane alterations leading to reduced deformability and potassium leakage from the RBC and decreased 2–3 DPG activities. However, the clinical implications of these changes are uncertain. There has been an ongoing debate on the transfusion of freshly collected RBC (<7 days old) versus prolonged storage of RBC (>7–14 days old), on the clinical implications. Lacorix et al. reported that stored RBCs more than 7–14 days old might impact the physiology of RBC and, thus, can have a negative impact on the susceptible population when transfused [54]. Subsequently, the same groups of authors have concluded that freshly collected RBC (<7 days) does not offer any clinical and economic benefit when transfused compared to standard aged RBC in critically ill adults [55]. A similar RCT on patients aged ≥12 years compared the fresher RBC (≤10 days old) with older RBC (≥21 days old). They maintained that the duration of storage was not associated with the occurrence of multi-organ dysfunction [56]. Also, it was observed that there was no difference in the rate of hospital-acquired infections, morbidity, and mortality in neonates based on the transfusion of stored RBC [57].

11.9 Perioperative Blood Conservation Strategies

Preoperative assessment of anemia and correction should begin at least 4–8 weeks before surgery [58]. Although hemoglobinopathies pose a unique challenge, adequate preoperative evaluation, and preparation, with an appropriate anesthetic plan, scrupulous surgery, and proper postoperative care, can result in good surgical outcomes in such patients [59]. Of particular importance are patients with sickle cell disease, where maximum care should be provided to avert a perioperative sickling crisis. The goal is to reduce the episodes of crisis by preventing precipitating factors such as hypoxia, acidosis, and dehydration [60].

Various pharmacologic and non-pharmacologic methods (Table 11.4) during preoperative and intraoperative periods are often utilized to reduce ABT. Preoperative optimization of erythropoiesis, autologous blood transfusion, and antifibrinolytics are often employed among at-risk bleeding patients to reduce the use of ABT. In pediatric patients undergoing reconstruction of the cranial vault, the antifibrinolytics were most often utilized for blood conservation [61]. The use of cell saver was the next frequent method to conserve blood resources [61]. Apart

Table 11.4 Perioperative blood conservation strategies

Preoperative erythropoiesis
• Erythropoietin
Local anesthetic infiltration
• With vasoconstrictor (epinephrine)
Autologous blood transfusion
• Preoperative autologous donation (PAD)
• Acute normovolemic hemodilution (ANH)
• Acute hypervolemic hemodilution (AHH)
• Intraoperative cell salvage
Antifibrinolytics
• Tranexamic acid
• Epsilon aminocaproic acid
Surgical techniques
• Electric cautery
• Vascular clips
Surgical local hemostatic agents
• Surgicel
• Gelfoam
• Flowseal
• Fibrin glue

from these physio-pharmacological manipulations under anesthesia, several surgical techniques are utilized to reduce blood loss during the intraoperative period, such as the use of electric cautery and vascular clips. A local anesthetic agent and epinephrine for vasoconstriction help reduce bleeding from the skin incision site. Surgical local hemostatic agents with nonspecific effects on clotting cascade are popularly used during neurosurgery [62]. Commonly used agents are Surgicel (oxidized cellulose), Gelfoam (gelatin), Spongostan (gelatin), Flowseal (gelatin-thrombin complex matrix), and Fibrin glue (thrombin-fibrinogen) and are utilized to achieve local hemostasis despite the limited literature that suggests their efficacy. Thrombin-gelatin matrix sealant has been opined to be a safe agent for strengthening hemostasis during posterior fossa surgery in pediatric low-grade tumors [63].

Preoperative erythropoietin (EPO) use increases hemoglobin levels, and consequently, perioperative transfusion is minimized [64, 65]. EPO in a subcutaneous dose of 100 U/kg thrice weekly for 3 weeks before the surgery and IV on the day of surgery increased the autologous blood donation and reduced the ABT in pediatric patients undergoing open-heart surgery [65]. For craniosynostosis surgery, preoperative EPO administration reduces the proportion of patients requiring ABT [64].

Autologous blood transfusion is employed in practice to avoid the risks associated with ABT and blood resource conservation. Autologous blood procurement can be done in three different ways, such as preoperative autologous donation (PAD), acute normovolemic hemodilution (ANH), and intraoperative blood salvage [66].

Preoperative autologous donation (PAD) should be considered in patients with a baseline hemoglobin level of more than 11 gm/dL. Although there is a dearth of literature on the pediatric population, no age and weight limits exist as far as the donors are concerned. The patients can donate up to 10.5 ml/kg and repeatedly donate (once per week); however, the previous donation should be at least 72 h before the scheduled surgery [66]. The volume of blood donated may be calculated using the formula [67].

$$\textbf{PAD Volume} = \textbf{EBV} \times \textbf{Hct1} - \textbf{Hct2} / \textbf{Hct1}$$

[EBV, estimated blood volume; Hct1, actual hematocrit; and Hct2, the target hematocrit]

Often the target hematocrit should not be less than 27% [67]. It has been observed in adult patients requiring neurosurgical intervention that the concomitant use of erythropoietin and PAD did not reduce the ABT. Moreover, the PAD resulted in anemia and increased transfusion requirements [68]. The findings are reasonable and may be extrapolated to pediatric patients as similar studies comprising of children are lacking. Moreover, the associated wastage of autologously donated blood was significant in this study [68].

Acute normovolemic hemodilution (ANH) removes whole blood from a patient shortly before the scheduled surgery and replaces the volume with acellular fluids [66]. Typically, 3 mL of crystalloids or 1 mL of colloid (albumin, dextran, starches) replaces for 1 mL of blood withdrawn. Like in PAD, a similar equation may be utilized for the removal of blood in ANH, as well [67]. The use of erythropoietin and ANH reduced the need for ABT in infants undergoing craniosynostosis surgery [69]. On the contrary, no difference in the incidence or amount of ABT was observed with ANH than the control group in an RCT of children undergoing craniosynostosis repair [70]. Because of the equivocal benefits it offers, the use of ANH as a strategy to reduce the ABT is not often employed as a part of a protocol.

Acute hypervolemic hemodilution (AHH) is another cost-effective method of RBC conservation, aiming to reduce ABT during surgery. Hemodilution is achieved by fast transfusion of crystalloids or colloids up to 20–30% of blood volume after anesthesia, to a target Hct value of not less than 25%. Both ANH and AHH were found to reduce the loss of red cells comparably, with AHH considered a simple technique as it does not involve withdrawal of blood [71]. AHH has been used safely in children undergoing spinal fusion [72]. Nevertheless, AHH may not replace ANH to reduce ABTs, but for expected blood losses less than 40% of blood volume, the

application of AHH could be superior [73]. Nonetheless, AHH as a part of a multimodal blood conservation protocol has recently been observed to reduce the rate of blood transfusion significantly in children undergoing craniosynostosis repairs [74].

Intraoperative cell salvage is the process of utilizing a patient's own blood retrieved from the surgical field to produce autologously transfused blood by filtering and washing it. Cell salvage, therefore, returns RBCs and reduces the requirement for ABT. The intraoperative cell salvage may be considered in patients with a weight of more than 10 kg and is indicated when the expected blood loss is more than 40% [13]. A systematic review involving patients of age group 10–19 years undergoing scoliosis correction concluded that the cell saver reduces intraoperative ABT [75]. Spinal instrumentation and fusion surgeries are associated with significant blood loss, and thus, the use of cell saver devices should be beneficial. A retrospective review of children undergoing posterior spinal instrumentation and fusion observed use of cell salvage reduced intraoperative ABT; however, no significant differences were observed in the use of ABT during the perioperative period [76]. Some fluid agents cause lysis of RBCs such as sterile water, hydrogen peroxide, alcohol, and hypotonic solutions and thus absolutely contraindicated to be mixed with the salvaged blood products. Other relative contraindications to cell salvage include clotting agents (Gelfoam, Surgicel, Fibrin sealants), irrigation solutions (betadine/chlorhexidine, topical antibiotics), contaminants (urine, fat, bone, bone cement, infection), and papaverine [77].

Antifibrinolytics such as tranexamic acid, epsilon-aminocaproic acid (EACA), and aprotinin play an important role in decreasing blood loss and, thus, allogenic transfusions. The effectiveness of **tranexamic acid** is demonstrated in various neurological surgeries such as craniosynostosis [78–80], scoliosis correction [81, 82], pediatric intracranial tumor resections [83], and major pediatric surgery [84]. In adult isolated traumatic brain injury, the clinical randomization of an antifibrinolytic in significant head injury (CRASH-3) trial demonstrated a reduction in mortality when tranexamic acid is given within 3 h from injury [85]. Similarly, in pediatric patients, the use of tranexamic acid within the first 3 h of trauma is suggested as beneficial [86]. The dose of tranexamic acid varies in different literature. A loading dose of 10 mg/kg over 15 min, followed by a 5 mg/kg/h maintenance infusion, may be used, which will maintain a required plasma therapeutic concentration of 16 μg/ml [87]. Two different dose regimens of tranexamic acid in pediatric patients undergoing correction of scoliosis were compared: a tranexamic acid loading dose of 10 mg/kg followed by a maintenance dose of 1 mg/kg/h (low-dose regimen) vs. 50 mg/kg loading dose followed by a maintenance dose of 5 mg/kg/h (high-dose regimen). The high-dose regimen was associated with reducing intraoperative blood loss and consequent transfusion requirements [88].

EACA, in a loading dose of 100 mg/kg, followed by a continuous infusion of 40 mg/kg/h, has been shown to maintain therapeutic plasma concentrations [13, 87, 89]. In children undergoing cranial vault reconstruction surgery, a loading dose of 50 mg/kg followed by an infusion of 25 mg/kg has significantly reduced intraoperative blood loss [90]. Aprotinin usage in this context is limited since there is no evidence to suggest that it is more effective as compared to tranexamic acid or EACA in reducing blood loss during major pediatric surgeries [84].

11.10 Conclusion

Institutional protocols must be devised to manage perioperative bleeding in pediatric patients undergoing neurosurgery. It should be borne in mind that pediatric patients are different hematologically and physiologically from adults. Therefore, strict application and adherence to a protocol for transfusion of blood and blood products are essential for a successful outcome in neurosurgery. The application of vigilant perioperative monitoring, restrictive transfusion strate-

gies, and apt blood conservation methods shift the pivot of care in bleeding pediatric patients from liberal protocols to minimal transfusion strategies.

Conflict of Interest None to declare.

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Part II

Anesthetic Management of Specific Problems

12 Hydrocephalus and CSF Diversion Procedures for Pediatric Neurosurgical Patients

Bhavna Hooda and Shalendra Singh

Key Points

- Hydrocephalus is the commonest neurosurgical condition in infants and children.
- The excess cerebrospinal fluid (CSF) accumulation in hydrocephalus presents as macrocephaly in infants (volume hydrocephalus) and as intracranial hypertension in older children (pressure hydrocephalus).
- CSF diversion procedures remain the gold standard to bypass the functional or physical blockage of CSF flow.
- Grossly hydrocephalic children in the emergency present challenges due to associated congenital anomalies, macrocephaly, difficult airway, and a full stomach.
- Maintaining the pediatric cerebral physiology, normothermia, and judicious fluid therapy while addressing these issues underpins the anesthetic management.
- Rapid sequence intubation (RSI) should always be considered in emergency shunting.
- This chapter provides a comprehensive review on the pathophysiology of disturbed CSF hydrodynamics in the hydrocephalus, CSF shunting procedure, anesthetic concerns, and recognition and management of shunt-related complications.

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12.1 Introduction

The writings about large hydrocephalic infant skulls in Egyptian medical literature can be found as early as 500 AD. A more scientific description is, however, credited to Hippocrates who coined the term "hydrocephalus" derived from the Greek word "hydro" meaning water and "kefale" meaning skull and described it as liquefaction of the brain with fluid accumulation surrounding the brain. The definition of hydrocephalus has since undergone several modifications. Simplistically, it was defined as the presence of dilated ventricles with an increased volume of intracranial cerebrospinal fluid (CSF) [1]. A more comprehensive definition as proposed by Rekate and adopted by the International Hydrocephalus Working Group defines hydrocephalus as active distension of the ventricular system that results from the inadequate passage of cerebrospinal fluid from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation [2].

Hydrocephalus presents with an overall prevalence of 1–1.5% with a childhood prevalence of 1–32 per 10,000 births depending on the population and the definition of hydrocephalus [3].

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There is a typical bimodal distribution with pediatric hydrocephalus at one peak and the normal pressure hydrocephalus of the elderly at the other. In children, it is the commonest neurosurgical condition, with congenital hydrocephalus occurring in 0.2–0.8/1000 live births and neonatal acquired hydrocephalus occurring in 3–5/1000 live births [4]. Although reliable data for developing countries is unavailable, nevertheless the incidence is likely to be much more due to the higher incidence of neural tube defects, low birth weight, perinatal infections, and lack of antenatal diagnosis. Both males and females are equally affected by this condition. An exception to this is the X-linked hydrocephalus that is exclusively seen in males [5].

12.2 CSF Dynamics and Pathophysiology of Hydrocephalus

CSF hydrodynamics are vital for brain homeostasis. Approximately 80% CSF is produced by the choroid plexus of the ventricular system, primarily the lateral ventricles, and the remainder by the ependymal lining of the ventricles and cerebral vessels at a rate of 0.35 ml/min to a total volume of about 150 ml in adults, 60–100 ml in children and 50 ml in infants. CSF is produced at a rate of approximately 20 ml/h in adults, and complete turnover occurs three or four times in 24 h [6]. Intuitively, CSF production in children should be proportional to the size of the brain for homeostasis. True estimates of CSF production in neonates and young children are difficult and are extrapolated from the hourly output from external ventricular drains. Studies suggest CSF production increases logarithmically with age and weight in children, reaching two-third adult levels by 2 years of age [7]. From the point of production, CSF circulates through the lateral ventricles into the slit-like third ventricle via the foramen of Monro. The third ventricle drains via the Sylvian aqueduct into the fourth ventricle which in turn circulates the CSF via a midline foramen of Magendie into the cerebello-medullary or basal cistern and laterally via the foramina of Luschka into the subarachnoid space of the spinal canal and the cerebral convexities. It is finally reabsorbed at the arachnoid granulations protruding into the dural sinuses, largely the superior sagittal sinus and the lumbar theca [6–8]. A hindrance anywhere from the point of production to the point of absorption results in hydrocephalus (Fig. 12.1).

The pathophysiology of hydrocephalus based on the traditional "bulk flow model" denotes a state of disturbed CSF hydrodynamics characterized by its excessive intracranial accumulation as a result of excessive production, impaired circulation, or absorption of CSF. There is ventriculo-

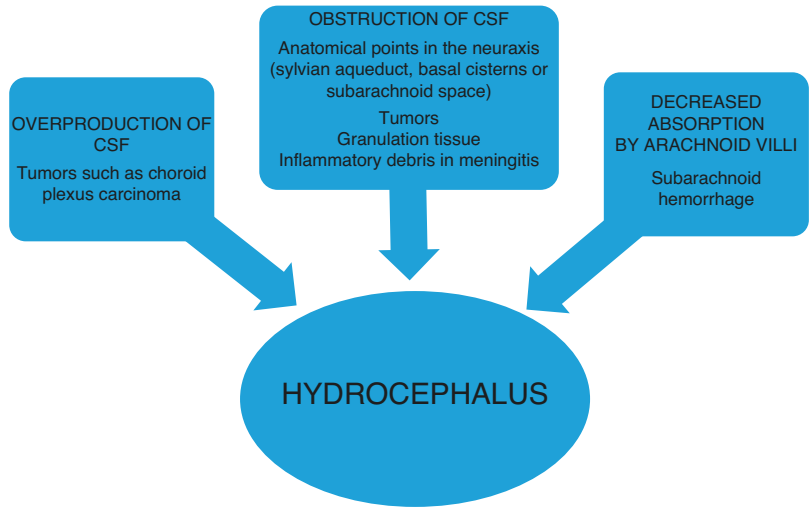

Fig. 12.1 Etiopathogenesis of hydrocephalus

megaly beginning with enlargement of the frontal and occipital horns of the lateral ventricles. As the pressure rises, the ependymal lining gives way allowing CSF egress into the periventricular parenchyma, with sub-ependymal edema and progressive white matter involvement. Progressive white matter atrophy occurs as the hydrocephalus progresses and there is the loss of sulci and gyri with the cerebral mantle compressed against the cranium [9, 10]. As new insights into the CSF hydrodynamics point toward a role of intracranial arterial pulsations, a "hydrodynamic model" of impaired dissipation of these pulsations by the subarachnoid spaces, venous capacitance vessels and choroid plexus pulsation, is being postulated as a cause of hydrocephalus [11, 12].

The manifestations are governed by the underlying condition, the speed at which it progresses, and compensatory mechanisms. Infantile hydrocephalus typically presents with marked macrocephaly with preserved brain parenchyma. Before the cranial sutures fuse, the skull enlarges mitigating the effects of raised intracranial pressure (ICP) [10, 13]. Additionally, the force of ICP is splayed over a large ventricular area, thus minimizing brain parenchyma damage, and a "volume hydrocephalus" develops. Hydrocephalus presenting in older children, after the fusion of the sutures, presents as a "pressure hydrocephalus." The rigid skull fails to expand, and as the compensatory mechanisms are exhausted, there is a rapid rise in ICP with brain parenchymal damage [13].

12.3 Classification

Historically, Galen classified the fluid collections surrounding the brain into four anatomic presentations: between the brain and meninges, meninges and pericranium, pericranium and skin, and bone and the skin. It was not until the twentieth century that Professor Walter Dandy researched on experimental animal models and classified hydrocephalus into communicating and non-communicating, terms which are still accepted worldwide. Based on the pathogenesis, onset, and genetic associations, hydrocephalus is classified as the following.

12.3.1 Communicating Vs. Non-communicating Hydrocephalus

In communicating or nonobstructive hydrocephalus (Table 12.1), the defect remains at the level of arachnoid granulations resulting in subnormal reabsorption of CSF. Typically imaging shows a pan-ventriculomegaly. In non-communicating or obstructive hydrocephalus, the site of obstruction is upstream of the arachnoid granulations. Imaging the brain would show an enlargement of the ventricles upstream of the site of obstruction, e.g., triventricular hydrocephalus in aqueductal stenosis (Fig. 12.2).

12.3.2 Syndromic Vs. Non-syndromic Hydrocephalus

Congenital hydrocephalus is described as non-syndromic when it occurs in isolation with no additional system involvement, viz., L1CAM-associated hydrocephalus, AP1S2-associated hydrocephalus (Fried syndrome), Walker-Warburg/muscle-eye-brain disease, autosomal recessive form, holoprosencephaly, agenesis of the corpus callosum, etc. Syndromic forms are numerous, to name a few, RASopathies, FGFR-associated skeletal dysplasias, VACTERL-H, mucopolysaccharidoses, etc.

12.3.3 Congenital Vs. Acquired Hydrocephalus (Table 12.2)

12.3.3.1 Congenital Hydrocephalus

(a) **Neural tube defects**: Neural tube defects (NTDs) are the commonest congenital malformations affecting 1:1000 live births [14]. Particularly, myelomeningoceles (MMC) show a strong association with congenital hydrocephalus and are considered its major cause. Overall, there is an estimated inci-

Table 12.1 Etiology of pediatric hydrocephalus

Communicating hydrocephalus	Non-communicating/Obstructive hydrocephalus
Leptomeningeal inflammatory debris: • Post-infectious (following TORCH infections) • Post-hemorrhagic (SAH/IVH of prematurity)	Obstruction at the foramen of Monro • Congenital atresia of the foramen of Monro
Congenital absence of arachnoid granulations	Obstruction at the aqueduct of Sylvius • Congenital aqueductal stenosis • Tectal gliomas • Posterior third ventricular mass lesions
Raised cerebral venous pressure • Sagittal sinus thrombosis • Craniostenosis	Obstruction at the fourth ventricle • Neural tube defects – Myelomeningocele and Chiari II malformation – Dandy Walker complex – Occipital encephalocoele • Posterior fossa tumors – Medulloblastomas, cerebellar astrocytomas, ependymomas • Developmental cysts • Tonsillar prolapse • Basilar impingement • Post-infectious or post-hemorrhagic ependymal scarring
Excessive CSF production and/or raised intraventricular CSF pulse pressure • Choroid plexus papilloma or hyperplasia • Choroid plexus carcinoma	
Raised CSF protein content • Spinal neurofibromas	
Carcinomatosis (meningeal infiltration)	

SAH subarachnoid hemorrhage, *IVH* intraventricular hemorrhage, *CSF* cerebrospinal fluid

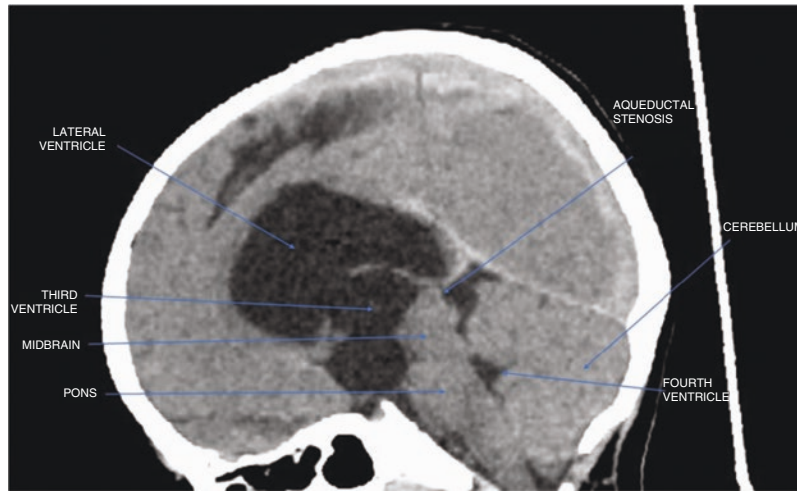

Fig. 12.2 Computed tomography brain image showing hydrocephalus due to aqueductal stenosis

Table 12.2 Congenital versus acquired classification of hydrocephalus

Congenital	Acquired
Neural tube defects	Post-hemorrhagic hydrocephalus
Primary aqueductal stenosis	Infections • Bacterial/viral meningitis, neurocysticercosis.
Secondary aqueductal gliosis • Germinal matrix hemorrhage • Infections	Posterior fossa tumors
X-linked hydrocephalus • Bickers-Adams syndrome	Low-pressure hydrocephalus
Chiari malformations	Constitutional ventriculomegaly
Dandy-Walker complex	Neurosarcoidosis
Vein of Galen malformation	Rarely associated with spinal tumors as neurofibromatosis due to ↑ protein, ↑ venous backpressure in the arachnoid granulations
Inheritable • Trisomy-13, −18, −9 • Triploidy • Walker-Warburg syndrome • MASA • Autosomal recessive hydrocephalus • Holoprosencephaly	Post-traumatic (severe traumatic brain injury)
Intrauterine infections • CMV • Toxoplasmosis • Syphilis • Zika	Increased venous sinus pressure • Craniosynostosis • Achondroplasia • Venous thrombosis
Posterior fossa arachnoid cyst	Iatrogenic (Hypervitaminosis A)
Choroid plexus papilloma or carcinoma	

dence of symptomatic hydrocephalus in 80% of children with MMC [15]. This is primarily obstructive hydrocephalus with a communicating component due to acquired Chiari II malformation causing a distorted skull base anatomy and fourth ventricular outflow tract obstruction. Another NTD commonly associated with developmental hydrocephalus is occipital encephalocoele, with as many as 50% infants developing hydrocephalus.

(b) **Aqueductal stenosis** is primarily obstructive hydrocephalus whereby the blockade in CSF flow can be primary or secondary to ependymal scarring following intrauterine infection or germinal matrix hemorrhage.

(c) **X-linked hydrocephalus** is the most common genetic form of non-syndromic congenital hydrocephalus affecting 1 in 30,000 male births [15, 16]. Typically, there is aqueductal stenosis with hydrocephaly, spasticity with corticospinal tract hypoplasia, corpus callosum agenesis, small brain stem, pachygyria, and pathognomonic clasped thumbs (cortical thumb sign).

(d) **Chiari malformations**: The most common and least severe Chiari malformation is type I that occurs in 1:1000 births with the hallmark of caudal displacement of cerebellar tonsils. In Chiari II, along with the cerebellar tonsils, the lower brainstem and the fourth ventricle descend past the foramen magnum and are almost invariably associated with myelomeningocele and spina bifida. The descent causes the CSF outflow tract to be obstructed at the foramen magnum producing an obstructive hydrocephalus.

(e) **Dandy-Walker malformation** is a less common cause of infantile hydrocephalus accounting for 2–4% of cases [17, 18]. There is an enlarged fourth ventricle continuous with a posterior fossa cyst, atresia of the foramina of Luschka and Magendie (Fig. 12.3), abnormal cerebellar development, and elevation of the tentorium causing supratentorial hydrocephalus in up to 90% of cases.

(f) **Intrauterine infection**s due to enterovirus [19], lymphocytic choriomeningitis [20], cytomegalovirus (CMV), and toxoplasmosis (TORCH infections) have all been associated with hydrocephalus by inducing secondary

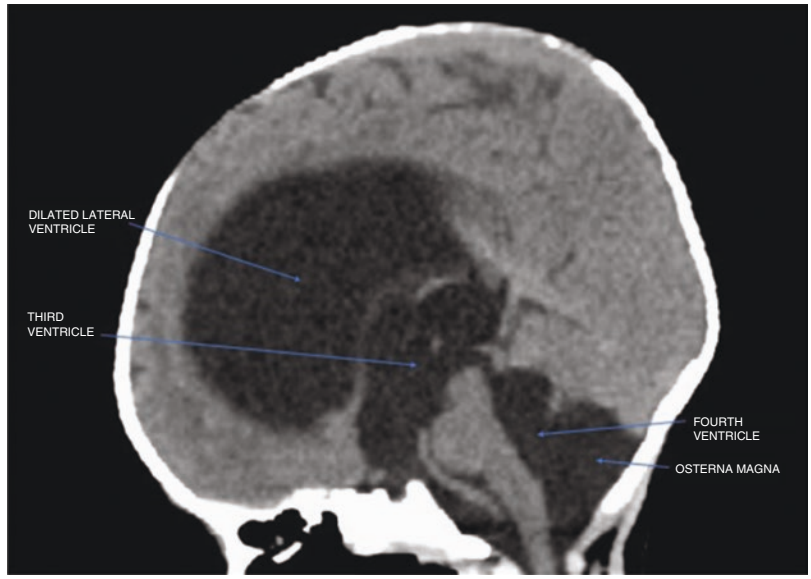

Fig. 12.3 Computed tomography brain image showing enlarged fourth ventricle continuous with a posterior fossa cyst, atresia of the foramina of Luschka and Magendie

aqueductal gliosis or impaired CSF absorption at the arachnoid granulations by inflammatory debris [21].

(g) **Arachnoid cysts** in the suprasellar region, quadrigeminal cistern, or the cerebellopontine angle may at times produce obstructive hydrocephalus in infants [22, 23].

12.3.3.2 Acquired Hydrocephalus

(a) **Post-infectious hydrocephalus**: Although in the developed countries majority of cases are attributed to post-hemorrhagic hydrocephalus following intraventricular hemorrhage of prematurity, globally, post-infectious hydrocephalus is the commonest acquired cause of pediatric hydrocephalus. There is also a wide disparity between the spectra of bacteria causing neonatal sepsis between the developed and the developing world, Gram-negative organisms and tuberculosis being the predominant infections in the developing world.

(b) **Post-hemorrhagic hydrocephalus** develops following intraventricular/subarachnoid hemorrhage as a result of prematurity (grade III or IV intraventricular hemorrhage), trauma, ruptured arteriovenous malformation, or systemic bleeding diathesis [24]. Although the initial presentation is obstructive type, they subsequently develop impaired absorption (communicating hydrocephalus). IVH is common in premature (≤32 weeks period of gestation) and very low birth weight babies (1500 g or less; 20% develop IVH) and extremely low birth weight preemies (1000 g or less; 45% develop IVH) with typical onset within 3 days postnatally [25]. An estimated 20–50% of infants develop permanent hydrocephalus.

(c) **Central nervous system (CNS) neoplasms** tend to predominantly involve midline posterior fossa, thus obstructing CSF flow at the fourth ventricle. In more than half the cases, hydrocephalus is present at the time of diagnosis or may be the initial presentation. Common etiologies are medulloblastomas, ependymomas, pilocytic astrocytomas, pineal region neoplasms, choroid plexus tumors, or rarely suprasellar extension of pituitary tumors [26]. Approximately 20% of patients develop permanent hydrocephalus postoperatively, which may be delayed for up to a year.

12.4 Clinical Presentations

The clinical presentation depends on the age at onset (with respect to the fusion of cranial sutures), underlying cause, rapidity of progression, duration, and presence of additional physical abnormalities. The common signs and symptoms are either a consequence of ventriculomegaly or raised ICP (Table 12.3).

- **During infancy**, the cranial sutures are open and allow the enlarging ventricles to be accommodated. A volume hydrocephalus develops whereby there is a large head with splayed sutures, ventriculomegaly, thin cerebral mantle, and low CSF pressure with minimal periventricular edema. Signs and symptoms are a consequence of the enlarged ventricles. The head enlargement is present if the occipitofrontal circumference (OFC) measurement is more than two standard deviations adjusted for a given age, gender, and gestational age (≥97th percentile) [27]. Macrocephaly is suspected if [28] any abnormal OFC measurement is recorded, serial measurements are suggestive of the crossing of major percentile lines (10th, 25th, 50th, 75th, 90th centile), or head enlarges at a rate

Table 12.3 Clinical presentation of hydrocephalus

	Infants	Older children
Symptoms	Irritability	Psychomotor slowing Delayed developmental milestones
	Poor feeding	Headache (particularly on waking up) associated with vomiting
	Failure to thrive	Neck pain
	Vomiting	Blurring of vision (papilledema)
	Lethargy	Diplopia • Due to third or sixth nerve palsy causing extra-ocular muscle paresis
	Reduced motor activity	Stunted growth, obesity, and defects in sexual maturation • Due to hypothalamic dysfunction due to the enlarged third ventricle
	Cushing triad • Widened pulse pressure (increasing systolic, decreasing diastolic) • Bradycardia • Irregular respirations	Spastic gait • Due to stretching of pyramidal tract in the periventricular region
		Somnolence
Signs	OFC at or above the 97th centile for age	Papilledema
	Frontal bossing	Upward gaze palsy
	Sutural splaying	Parinaud syndrome • Up gaze palsy • Convergence retraction nystagmus • Pupillary hyporeflexia
	Tense/bulging fontanelles	Collier sign (bilateral upper lid retraction)
	Dilated scalp veins	Convergence-retraction nystagmus
	Setting sun sign	Macewen sign (cracked pot sign)
	Increased limb tone	Unsteady gait due to spasticity
		Macrocephaly
		Unilateral or bilateral sixth nerve palsy

more than 1.25 cm/week, or increase in OFC of >2 cm/month (up to 6 months age).

Although increased OFC may be the earliest, most prominent sign in neonates and infants, other conditions such as subdural hematoma/hygroma, benign extra-axial fluid collections of infancy, inherited familial macrocephaly, fragile X syndrome, overgrowth syndromes such as cerebral gigantism (Sotos syndrome) and Weaver syndrome, lysosomal storage disorders (Tay-Sachs, mucopolysaccharidosis, and gangliosidosis), leukodystrophies, and megalencephaly (familial, Cowden syndrome, neurocutaneous disorders, achondroplasia, etc.) need to be ruled out. A good guide is to plot the head circumference on the age-adjusted growth charts, more specifically onto the Weaver charts (OFC charted as per parental OFC to rule out familial causes) and prematurity adjusted charts. Neonates may at times present with the Cushing triad of apnea and bradycardia with irregular respirations, though this is less apparent as the infant grows and macrocephaly becomes notable.

- **Older children and adults**: A pressure hydrocephalus develops as the sutures have fused and there is limited macrocrania, mild ventriculomegaly, thick cerebral mantle, high CSF pressure, and extensive periventricular ooze. As the child grows, the brain water content and, therefore, the brain compliance reduce and sutures fuse; the signs and symptoms of raised ICP manifest [29].

  Headaches (particularly on waking up) are common, associated with vomiting, worsened by recumbent position, coughing, crying, and micturition/defecation. In advanced hydrocephalus, focal neurologic deficits (bilateral sixth nerve palsy), Parinaud syndrome (dorsal midbrain syndrome characterized by up gaze palsy, downward gaze preference or setting sun sign, the large pupil with light-near dissociation, skew deviation of eyes, convergence-retraction nystagmus, bilateral ptosis, and abnormal upper eyelid retraction or Collier sign), and new-onset seizures may be the sinister presentation and mandate emergent intervention [29].

12.5 Diagnosis of Hydrocephalus

Different diagnostic modalities for hydrocephalus are available other than the clinical presentation in a child (Table 12.4); some of them are detailed as below:

(a) **Cranial ultrasound**: Antenatal ultrasonography may reveal hydrocephalus and other neurodevelopmental anomalies [30]. Screening cranial ultrasound is recommended for all preterms born at 30 weeks or earlier as a tool to identify ventricular dilation, periventricular leukomalacia (PVL), and IVH. Screening window is recommended on all infants of ≤30 weeks' gestation once between 7 and 14 days of age (preferably first 48 h) and repeated between 36 and 40 weeks' post-conceptual age [31]. The early examination rules out IVH and any developmental anomalies, while late one rules out ventriculomegaly and

Table 12.4 Diagnostic criteria of hydrocephalus

Diagnostic criteria	Corroborative criteria
Size of both temporal horns (TH) is ≥2 mm in width *Plus* Effaced Sylvian and interhemispheric fissures and the cerebral sulci	Ballooning of the frontal horns of lateral ventricles ("Mickey mouse" ventricles may indicate aqueductal stenosis) and/or rounding of the third ventricle
OR	
Both TH are ≥2 mm *Plus* Ratio of frontal horn width (FH) to internal diameter (ID: Measurement across the frontal horn between the inner table on each side) more than 0.5	Periventricular lucency on CT, or periventricular high intensity signal on T2WI on MRI fluid-attenuated inversion recovery [FLAIR] sequences
	FH to ID ratio > 0.5
	Evans ratio (ratio of FH to maximal biparietal diameter, BPD) more than 0.3
	Thinning/atrophy of corpus callosum (chronic hydrocephalus) or upward bowing of the corpus callosum (acute hydrocephalus)

progressive hydrocephalus. Though the cranial ultrasound hardly visualizes third and fourth ventricles, it serves as a useful guide as serial measurements of the lateral ventricle, is available bedside to follow up preemies with IVH, and helps decide upon need for surgical intervention. It also differentiates hydrocephalus from benign extra-axial fluid collections of infancy. The sonographic window is through the anterior fontanelle, and ventriculomegaly is present if ventricular atrium is more than 10 mm at term. If the posterior portion is larger than the anterior part of lateral ventricles (colpocephaly) and persists in the postnatal period, it is considered as abnormal. As the fontanelle closes by 12–18 months, the utility of this imaging is limited to infants. Progressive ventriculomegaly mandates additional imaging by CT/MRI.

(b) **Computed tomography**: Most of the time, it is the initial modality of imaging due to ready availability and faster acquisition time, especially in the setting of raised ICP. However, there are concerns about radiation exposure, particularly in the follow-up of patients with hydrocephalus. Additionally, it provides little information about the underlying cause, and further imaging with MRI is quintessential [32].

(c) **Magnetic resonance imaging** is the imaging modality of choice for suspected hydrocephalus as it delineates the ventricular system anatomically and pinpoints the pathologic processes causing altered CSF hydrodynamics [32]. The state of arachnoid membranes and trans-ependymal flow, tumor, or other pathologies is readily identifiable via MRI. T2-weighted images delineate the ventricular pathway and the basal cisterns [32]. Additionally, CSF flow studies are possible with turbo spin-echo (TSE), three-dimensional constructive interference in the steady state (3D-CISS), and cine phase-contrast sequences [33]. The need for sedation and longer acquisition time has precluded the use of MRI as routine imaging in infants and children. However, with the advent of ultra-fast MRI sequences (as half-Fourier acquisition single-shot turbo spin-echo (HASTE) or single-shot fast spin-echo T2-W sequences), it is possible to obtain images within 5 min without sedation [34]. Limited imaging using ultra-fast MRI is now seen as used as an alternative to ultrasonography in the evaluation of infantile hydrocephalus [35].

(d) **Skull radiographs**: The typical beaten copper or silver beaten appearance is pathognomonic of hydrocephalus. There may also be sellar erosion in chronic hydrocephalus. Except for historical significance, this imaging has no current role in the workup.

12.6 Management with CSF Diversion Procedures

Medical literature from the first millennium is replete with the research work of Arab physician Abu Al Qasim (Latinized as Abulcasis) on infantile hydrocephalus and ventricular drainage as a possible treatment. However, the renaissance era showed little research in this field, and it was only in the late nineteenth century when Kay and Retzius developed sterile ventricular puncture procedure and external CSF drainage. However, Mikulicz in 1893 is credited with the first ever ventricular-subarachnoid-subgaleal shunt [36]. Over the years, a myriad of ventriculoperitoneal, ventriculovenous, ventriculopleural, ventriculoureteral, and lumboperitoneal shunts came in use; but procedure-related mortality was exceptionally high. What revolutionized the management of hydrocephalus was the development of ball valve-type ventriculo-caval shunt in 1952 by Nulsen and Spitz and is the forerunner for modern-day shunt systems [37]. Hence, in the late 1950s, VA shunts were the mainstay of treating hydrocephalus. Almost 94% of CSF diversion procedures were VA shunts till the early 1970s. However, it was increasingly recognized that these shunts needed revision with the child's longitudinal growth, and these were associated with a high risk of potential complications of thromboembolism, pulmonary hypertension, shunt nephritis, and sepsis. By the late 1980s, with silicon-based shunt catheters, there was a

resurgence of the VP shunts, and soon these shunts evolved as a mainstay in over 90% of cases. Despite significant advancement in shunt technology over the last six decades, the management of pediatric hydrocephalus remains an enigma for neurosurgeons. It also continues to be a major health burden in terms of prolonged treatment, multiple hospital admissions, and poor neurodevelopmental outcome. The available modalities aim to achieve a CSF diversion across the point of the hindrance of CSF dynamics (Fig. 12.4, Table 12.5).

12.6.1 CSF Shunts Used for Diversion Procedures

An implanted shunt functions by diverting the CSF from the ventricles or the subarachnoid space surrounding the brain and spinal cord to another body cavity or systemic circulation. This provides an alternative route for removal of the excess CSF, thus restoring the balance between CSF production, flow, and absorption. Typically, the shunt has the following essential components:

(a) **Proximal ventricular catheter**: A catheter is placed into the frontal horn of the right or left lateral ventricle through a frontal or occipito-parietal burr hole (Fig. 12.5). The material for the catheters is silicone, and currently, antibiotic-impregnated and silver-impregnated polyurethane catheters are being increasingly used. It is speculated that these prevent a bacterial biofilm formation (silver) or form a zone of inhibition of bacterial colony growth (clindamycin and rifampicin impregnated), thus preventing shunt infection [35].

(b) **Unidirectional valves** are the interface between the proximal and distal catheters that function to control the rate of CSF drainage. Traditionally, these valves work on the principle of differential pressure (DP), i.e., the CSF pressure head across the valve that

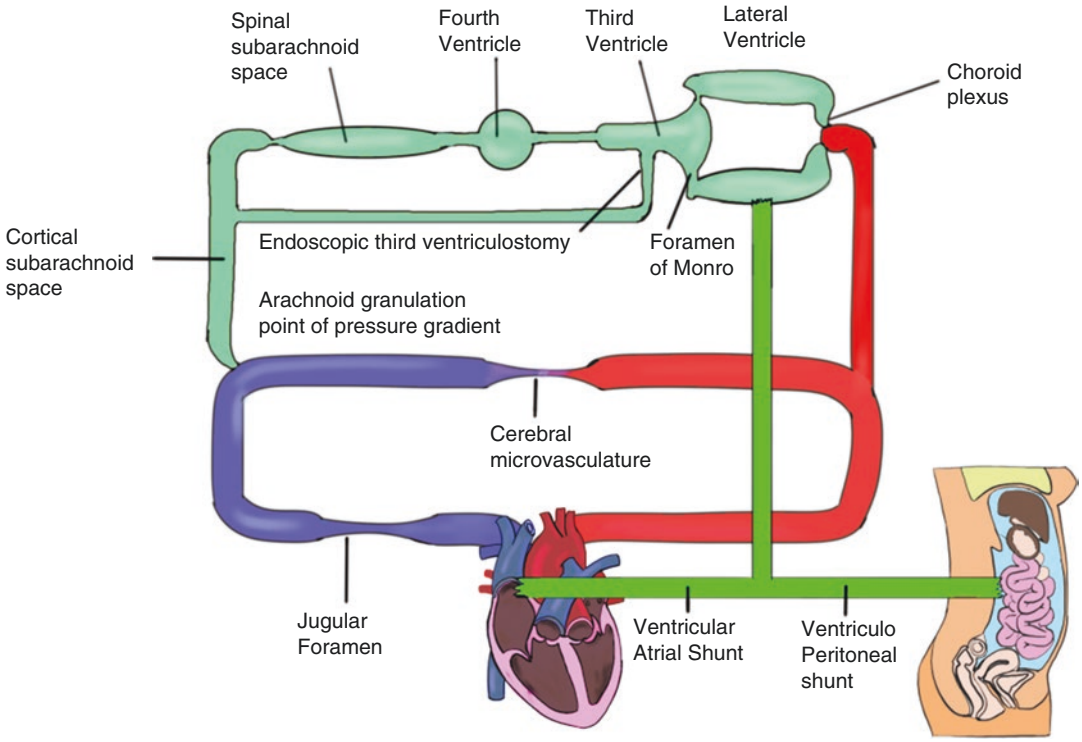

Fig. 12.4 Schematic diagram of CSF diversion procedures

Table 12.5 Available modalities for CSF diversion

Temporary	Permanent
External ventricular drainage	*CSF shunts* (a) Ventriculoperitoneal (VP) shunt • Lateral ventricle to peritoneal cavity (b) Ventriculo-atrial/caval shunt (VA) or vascular shunt • Lateral ventricle to the right atrium via the jugular vein and SVC • Typical candidates are those with morbid obesity, peritonitis, and extensive abdominal surgery or premature infants with necrotizing enterocolitis (c) Ventriculo-pleural shunt • Usually a second-line diversion technique • Recommended for patients above 7 years of age to avoid problems related to hydrothorax (d) Lumbo-peritoneal shunt • Communicating hydrocephalus, CSF fistula, and benign intracranial hypertension (e) Torkildsen shunt • Ventricle to cisternal space (f) Miscellaneous: • Arachnoid cyst or subdural hygroma to peritoneal cavity, ventriculo-ureteral, gall bladder, superior sagittal sinus, etc.
External lumbar drainage	Endoscopic third ventriculostomy (ETV)
Temporary intraventricular reservoirs with intermittent transcutaneous reservoir	

allows CSF outflow when the valve's opening pressure (OP) is exceeded. Newer generation valves are either DP-adjustable or flow-regulated valves [38]. The pressure-regulated valves work on the principle of differential pressure across the valve. The design may be slit valves, miter valves, diaphragm valves, or metallic spring-loaded ball-in-cone valves. Flow-regulated valves work by altering the resistance of the outflow tubing to maintain constant flow rate close to the rate of CSF secretion regardless of posture or straining, coughing, or Valsalva maneuver. These valves combine the features of a conventional DP valve with a variable flow restrictor to control the problems of siphoning.

Shunt technology is rapidly evolving with several new generation shunts in the market. It is therefore important to have a basic understanding of the valve mechanisms to allow clinicians to select wisely from the wide armamentarium of shunts for each patient.

Conventional differential pressure (DP) is further categorized as low (0–5 cmH_2O), medium (5–10 cmH_2O), or high (10–15 cmH_2O) pressure depending on the upper and lower pressure differential of the shunt. Though the indications determining the opening pressure gradient are relative, a common practical application is to place low-pressure shunts in infants with open fontanelles, medium-pressure shunt in older children, and high-pressure shunts in obstructive hydrocephalus in posterior fossa lesions.

Variable pressure valves may be (i) programmable valves or (ii) multistage flow-regulated valves. **Programmable valves** are essentially second-generation valves that can be adjusted noninvasively by changing the DP magnetically from outside the body. These are basically DP valves with a ball-cone mechanism controlled by a spring whose opening pressure can be altered using a magnetic field to alter the preload of the spring. These can be adjusted in the range of 10–150 cmH_2O and require a variable number of steps and, therefore, multiple office visits for the patient. The distinct advantage of programmability is the ability to fine-tune the valve performance for the patient without the need for revision surgery [38]. **Multistage flow-regulated valves** function by altering the caliber of the outflow tube in response to changes in the CSF pressure head, thus maintaining a constant flow.

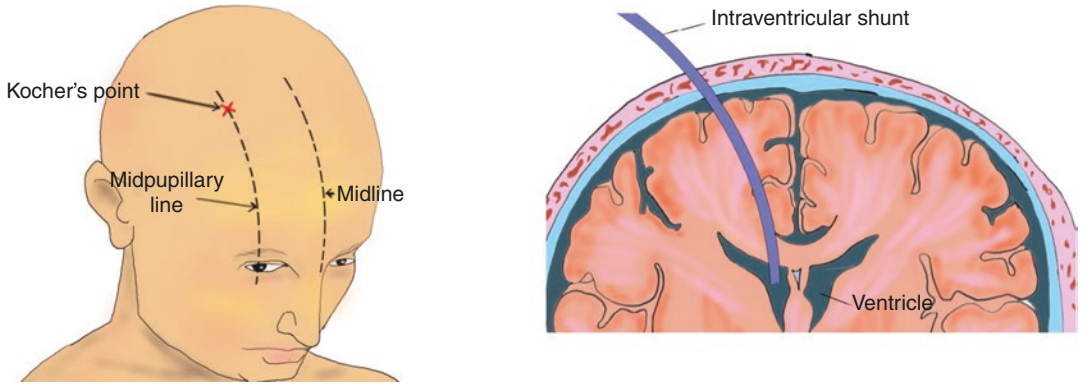

Fig. 12.5 A. Frontal site of intraventricular catheter insertion at Kocher's point (1 cm anterior to the coronal suture and 2–3 cm lateral to the midline). The Frazier point (occipito-parietal burr hole, not depicted in the image, is 6 cm above the inion and 3 cm lateral to the midline). B. In situ intraventricular catheter in the lateral ventricle

(c) **Reservoir** is the antechamber placed between the proximal catheter and the valve assembly underneath the skin in the postauricular area to allow CSF sampling, injecting drugs, and assessing the patency of the proximal and distal catheter in case of a shunt malfunction. Normally, on pushing the reservoir, it bounces back. Failure to spring back may be a sign of proximal shunt block, while a stiff reservoir may signify a distal catheter block.

(d) **Anti-siphon device**: Siphoning and over-shunting/over-drainage present a unique problem with CSF shunts as postural changes, straining, coughing, nocturnal vasogenic effects on CSF secretion all cause significant CSF sucking out of the ventricles/lumbar theca through the shunt system [39]. The majority of the shunt-related complications are due to siphoning, i.e., proximal catheter blockage, slit ventricle syndrome, subdural/extradural collections, etc. To prevent this, some kind of anti-siphon and anti-gravity devices are incorporated into the shunt system to provide progressive resistance to flow and mitigate the negative pressure exerted with standing up. Siphon control devices are either membrane type, gravitational, or flow resistor [38–40].

(e) **Distal catheter** is the distal end of the shunt assembly placed into the desired area of drainage, most commonly the peritoneal cavity. When the abdominal placement is contraindicated or technically difficult in conditions such as peritonitis, abdominal surgery, and morbidly obese, alternative sites such as the pleura or the right atrium may need to be considered.

Indian shunt systems: Considering the high cost of most internationally available shunt systems in developing countries and the need for repeated revision surgery for malfunction, indigenous valves such as Upadhyaya shunt system, Chhabra shunt system, and Sri Chitra shunt system are popular. These are conventional fixed DP types with slit and spring and Z-flow, available as low-pressure, medium-pressure, and high-pressure valves. Efficacy has been found to be comparable to the western shunt systems [4, 41, 42].

12.7 Endoscopic Third Ventriculostomy

Endoscopic third ventriculostomy (ETV) is a neuroendoscopic procedure that involves creating new CSF egress from the third ventricle into the prepontine cistern and subarachnoid spaces surrounding the brainstem, thus bypassing the obstruction downstream. It is indicated in non-communicating hydrocephalus with patent CSF pathway downstream and adequate CSF absorp-

tion [43]. It has also been efficacious in certain forms of communicating hydrocephalus such as idiopathic normal pressure hydrocephalus, posttraumatic hydrocephalus, hydrocephalus secondary to SAH, and tubercular meningitis [43].

Neuroendoscopy provides a safe, speedy, minimally invasive alternative to implanted shunts. An ideal third ventricle floor fenestration site should be in the midline to avoid the posterior communicating artery and posterior cerebral artery, in the area of tuber cinereum (prominence on the base of the hypothalamus), posterior to the infundibular recess and anterior to the mammillary bodies and tip of the basilar artery. The procedure however has its share of complications. Morbidity of 5–30% and operative mortality of <1% have been reported [44]. Serious complications occur due to injury to the structures in and around the floor of the third ventricle, i.e., posterior hypothalamus, midbrain, fornix, caudate, third, and sixth cranial nerves, and basilar artery and its perforators. These are attributed to poor surgical technique (ventriculostomy away from the midline), direct pressure from the perforating instrument or Fogarty balloon, high temperature of the cautery, or rapid distension of the third ventricle with jet irrigation.

12.8 Hydrocephalus Outcome

The outcome of hydrocephalus without treatment is grim with 50% mortality within 3 years and only 20% surviving to adulthood [45]. Depending on the follow-up period, the overall mortality with hydrocephalus and CSF diversion procedures is between 0 and 3% [4]. With surgical management, the mortality rates with nontumoral hydrocephalus are about 11% at 10 years. There is some degree of cognitive sequelae in approximately 12–50% of children and schooling difficulties affecting 20–60% of children [46]. Almost 60% of children have some motor disabilities with almost 13% requiring walking aids and another 17% requiring wheelchair for mobility. Optic nerve atrophy or cortical blindness occurs as a result of raised ICP. As a consequence, almost 83% of patients develop visual field defects, diplopia, vision loss, and visuoperceptive defects [47]. Endocrine sequels are common due to hypothalamic dysfunction with resultant hyperplasia, weight gain, and precocious puberty and reduced fertility [48]. The intellectual outcome of hydrocephalus is governed by the severity of parenchymal damage at presentation and is maximal in infantile hydrocephalus (PHH, post-meningitis) and posttraumatic hydrocephalus.

12.9 Anesthetic Management for CSF Diversion Procedures

Understanding and applying the basic neurophysiologic principles underpin the successful anesthesia in children presenting for CSF diversion procedures; a few additional concerns are paramount:

- Larger cranium and therefore larger blood volume are accounted for by the head and neck area in infants and children. Also, macrocrania predisposes the infants to hypothermia.
- In neonates with congenital hydrocephalus, enlarged head places the neck in flexion and makes the airway management difficult. Elevating the body with towels may be required to facilitate laryngoscopy.
- Hydrocephalus in infants, unlike adults, may present with nonspecific symptoms of raised ICP due to the pliant cranial sutures.
- Acute-onset intracranial hypertension requires emergent intervention to prevent serious neurologic sequelae.

12.9.1 Preoperative Assessment

Hydrocephalus may present with different perioperative scenarios (Table 12.6). A thorough preoperative evaluation should encompass baseline neurologic status, any neurologic deficits, and features of raised ICP. In shunted children, there may be subtle signs of new or worsening postural headache, new-onset seizures, and new neuro-

Table 12.6 Presentations of hydrocephalus with different perioperative scenarios

• Prenatal diagnosis: With antenatal diagnosis and advancement in the field of in utero surgery, there is a trend toward prenatal management of hydrocephalus associated with MMC (fetal neurosurgery)
• Preterm patients with post hemorrhagic hydrocephalus
• Neonate with congenital/non-tumoral hydrocephalus
• An older child with hydrocephalus
• Acute-onset intracranial hypertension in a shunted child
• Shunt malfunction with hydrocephalus
• Shunted child with fever
• Long-standing hydrocephalus with chronic headache

logic deficits suggestive of shunt malfunction or fever with meningismus and intra-abdominal infection pointing to shunt infection. Depressed sensorium may be a harbinger of aspiration, while repeated vomiting may cause dehydration and electrolyte imbalance. A focused examination is paramount to rule out raised ICP and its sequelae. In the case of multiple revisions, prolonged difficult surgery may be anticipated due to likely abdominal adhesions. In patients with VA shunt, pulmonary hypertension needs to be ruled out. In the case of a ventriculo-pleural shunt, pleural effusion on the same side may be present, and intermittent positive pressure ventilation (IPPV) may block the distal draining end. This mandates vigilant neurologic assessment and aggressive postoperative chest physiotherapy.

Laboratory studies are usually not necessary in infants and children, apart from baseline hemoglobin and total leucocyte counts. Serum electrolytes are governed by the suspicion of disturbed sodium homeostasis as in pituitary tumors with suprasellar extension, craniopharyngiomas, hypothalamic dysfunction, persistent vomiting, etc. Patients with an external ventricular drain may have excess sodium loss via the CSF necessitating preoperative serum electrolytes.

Congenital hydrocephalus may require evaluation for associated anomalies. Additionally, preemies commonly have associated anemia, coagulopathy or jaundice, bronchopulmonary dysplasia, or persistent fetal circulation that need to be borne in mind while anesthetizing these babies. Particularly, infants with vein of Galen malformation-associated hydrocephalus commonly present with high output cardiac failure making the anesthetic course tumultuous. In the case of ex premature infants, a note of the risk factors of postoperative apnea should be borne in mind while anesthetizing these babies, i.e., postconceptual age (PCA) less than 60 weeks, general anesthesia, history of apnea at home, anemia, stormy postnatal course, and presence of neurologic disease [49–53].

Seizure medication should be continued through the perioperative period. It is prudent to avoid sedation in children with an obtunded sensorium. An awake combative child may require oral/nasal midazolam. Ketamine is best avoided owing to its detrimental effects on ICP and cerebral blood flow (CBF). Systemic antibiotics are advocated at induction for all shunt surgeries.

Preoperative fasting rules as recommended should be followed (2–4-6 rule); clear fluids are allowed liberally till 2 h as prolonged fasting time in small children causes lack of cooperation, dehydration, and hypotension at the induction of anesthesia. Caution should be nevertheless exercised in children with obtunded sensorium [54].

12.9.2 Anesthetic Considerations

The ideal anesthetic is one that maintains the cerebral hemodynamics close to homeostasis; the choice of anesthetic is therefore guided by the concerns for CPP/ICP preservation. Grossly hydrocephalic children in the emergency present challenges to anesthesiologists due to associated congenital anomalies, macrocephaly, and a full stomach [55]. A difficult airway cart comes handy in tackling such scenarios. Shunt placement is an urgent procedure, so the child is fasted but an obtunded sensorium and risk of aspiration may necessitate rapid sequence intubation [56]. Rapid sequence intubation (RSI) should always be considered in emergency shunting, particularly shunt malfunction with acute intracranial hypertension. Further, the risk of RSI needs to be

weighed against the risk of an unanticipated difficult airway in infants with large heads. In children, use of succinylcholine in RSI is a dilemma with its detrimental effects on ICP and undiagnosed muscular dystrophies; rocuronium may be a safe alternative as a part of RSI regime.

In children, volatile induction with sevoflurane and securing venous access for the further conduct of anesthesia is logical to avoid ICP rising in a crying, combative child. Intravenous (IV) induction with propofol or thiopentone may be undertaken if iv access is available. Maintenance of anesthesia is done with either TIVA or volatile agents supplemented with short-acting opioids (remifentanil/fentanyl) and muscle relaxants to achieve controlled ventilation and normocapnia along with standard monitoring modalities. Volatile anesthetics below 1 MAC can be safely used. Nitrous oxide is best avoided for its effect on increasing CBF [56]. One of the most noxious stimuli during the course of surgery is at the time of distal catheter tunneling when local anesthetic infiltration could be useful to alleviate the response. The anesthetic depth may be increased briefly by increasing dialed concentration of volatile agents and administration of titrated doses of opioid to counter such response [57, 58].

For VP shunt placement, the child is positioned supine with the head turned to the contralateral side and a roll under the ipsilateral shoulder to facilitate the tunneling of the distal catheter. The extremes of neck flexion/rotation should be avoided to allow unimpeded cerebral venous outflow and undesired endotracheal tube migration. Proper securing of the endotracheal tube is quintessential as tube migration is commonplace in young children with changes in head position.

Preoperative fasting is kept to the bare minimum (2 h) so that for short procedures (<1 h), there is hardly any requirement for fluid therapy. Preoperative deficits if any should be replaced before anesthesia is induced. In children, consensus guidelines recommend using background infusion with the solution of osmolarity as close to plasma with added metabolic anions (acetate, lactate, malate) and 1–2.5% glucose to maintain volume status and tissue perfusion while avoiding hypoglycemia, hyponatremia, hyperchloremia, and lipolysis/ketoacidosis [58, 59]. The best method to assess dehydration is by subtracting the current body weight from the immediate premorbid weight; however, this is usually unavailable and one has to rely on the clinical assessment. The deficit is calculated by multiplying the degree of dehydration by body weight (in kg) multiplied by a factor of 10 (e.g., a 5 kg child with 10% dehydration will have a fluid deficit of 500 ml). A rough guide is replacing with 10 ml/kg boluses for each 1% dehydration [60]. Most pediatric patients undergoing CSF diversion procedures may have preoperative fluid deficits due to prolonged fasting in the face of the obtunded sensorium, repeated vomiting, and diuretic therapy or CSF loss from external ventricular drainage. It is difficult to reliably estimate the deficit, especially in the context of a large amount of CSF in the cranium contributing to the body weight. Therefore, an initial bolus of 10–20 ml/kg of the balanced solution with 1–2.5% glucose may be a reasonable choice before anesthesia induction.

12.9.3 Postoperative Management

Postoperative analgesia can be maintained with paracetamol and NSAIDs. In the case of pleural shunts, the initial 48 h may require opioid supplementation for the sharp pleuritic pain. The expremature infants require adequate attention for postoperative apnea for at least 12 h in a high dependency unit. Non-osmotic stimuli such as stress, fever, pain, hypovolemia, hypoglycemia, etc. cause ADH release that peaks at 6–12 h, postoperatively [59]. Therefore, oral fluid intake should be encouraged early unless the sensorium is obtunded in which case; fluid management is guided by the same principle of using the balanced salt solution with glucose guided by the Holliday-Segar formula. Special caution is advocated in endoscopic third ventriculostomy where postoperative hypokalemia, hypernatremia, and CSF acidosis are noted with saline irrigation, while hyperkalemia is reported with Ringer lactate irrigation [61]. Therefore, it is advisable to

monitor serum electrolytes postoperatively to guide the choice of fluid therapy.

12.10 Shunt Complications

Shunt malfunction impairs the cognitive function and intellect, requires multiple hospital admissions and revision surgeries, and increases the risk of death. The failure rates are substantial in pediatric age group with 38% shunts failing in the first year and 5% every year thereafter. The two most common reasons are shunt blockage and shunt infection (Table 12.7) [62].

12.10.1 Shunt Blockage/ Under-Shunting

Shunt malfunction is estimated to have a mortality rate of 1% per year during the initial years of implantation [63]. Hardware issues are commonest in the first year of shunting (≈10%). Clogging may occur in any of the shunt parts, the ventricular end being the most notorious. The ventricular end may get obstructed by the choroid plexus, scar, blood, or debris or may migrate into the brain parenchyma. Connectors at various segments or the tubing may fracture. The valve assembly may be poorly selected or get clogged by debris. The distal end may fracture, migrate, or get kinked or may form a pseudocyst.

Presentation is one of a raised ICP, and immediate evaluation of the shunt type, underlying etiology, any revisions, and presence of infection should be done. The most frequent symptoms in older children are vomiting and drowsiness, whereas infants commonly present with nausea, vomiting, irritability, and bulging fontanel. The shunt chamber must be palpated; the inability to depress the chamber may indicate distal obstruction, whereas slow, poor refilling may indicate proximal obstruction or a slit ventricle syndrome due to over-shunting. Shunt series (AP and lateral skull, chest, and abdominal radiographs) should be evaluated to rule out fractures/disconnections at any of the segments. Newer shunt systems may require CT scanning or radionuclide scintigraphy with 99 m-Tc to delineate the site of malfunction. Shunt blockage requires urgent intervention in the form of exteriorization of the ventricular end,

Table 12.7 Factors predictive of shunt failure

1. Hardware-related	• Type of valve: The incidence, however, has not been correlated with any particular valve type (DP/flow-regulated/programmable) • Material of the catheter: Antibiotic or silver-impregnated catheter tubing may reduce the chances of shunt infection
2. Patient factors	• Age of the patient: Higher failure rate in pediatric (48%) compared to the adult population (27%), more so in the preemies • Etiology of hydrocephalus: Higher chances of failure in myelomeningocele (MMC), posterior fossa neoplasms, post-hemorrhagic hydrocephalus, and aqueductal stenosis are noted • Multiple revision surgeries • Repeated shunt taps • Time since shunting: Failure rates are inversely proportional to the time since insertion with maximal chances of failure in the first 6 months • Malnutrition, craniospinal irradiation, steroid therapy, recent MMC repair, postoperative CSF fistula, and tracheostomy have all been found to predispose to shunt infections
3. Surgical factors	• Surgical expertise • Lower rate of complications is noted in high volume institutions • Operating room (OR) factors: – High operating room personnel traffic – Multiple surgeries in the OR prior to shunting in the day – Poor OR climate control • Preoperative prophylactic antibiotics reduce shunt infection • Good skin preparation and double gloving/changing gloves prior to shunt insertion • Optimal length and positioning of the proximal catheter: The tip should ideally be sited at the atria of the lateral ventricle and away from the parenchyma • Siting of distal catheter: VA shunts and VP shunts have a higher rate of revisions and morbidity compared to VP shunts

shunt revision, or abdominal end revision depending on the site of obstruction.

12.10.2 Shunt Infection

The presence of clinical symptoms in a shunted patient with a positive culture and/or pleocytosis may suffice to point toward shunt infection. It is reported in 5–15% of procedures, though the incidence may be as high as 50% in the developing countries [64–66]. There is a bimodal distribution with the first peak within 3–6 months of shunting and second peak after a year [67]. Neonates and infants have a higher incidence compared to older children and adults. Most infections are typically from the patient's skin flora. Coagulase-negative staphylococcus, *Staphylococcus epidermidis*, and *Staphylococcus aureus* (≈60%) and Gram-negative bacilli (*E. coli* and *Streptococcus* hemolytic in neonates) account for early infections, whereas almost all late infections (>6 months) are caused by *Staphylococcus epidermidis* [4].

Typically, there are signs of raised ICP with fever, meningismus, abdominal pain with peritonism, erythema around the shunt tract with leukocytosis, and raised C-reactive protein. Fever occurring soon after the intervention and irritability are good predictors of shunt infection. Once all possible causes of systemic infection are ruled out by appropriate cultures, a shunt tap under strict aseptic conditions may be indicated to confirm the diagnosis. CT scanning may reveal shunt malfunction with enlarged ventricles, brain abscess, or subcutaneous pockets of pus along the CSF shunt path, and the shunt hardware can also be checked. Ependymal enhancement along with intraventricular fluid level due to sedimented debris may be seen on CT, suggestive of ventriculitis. MRI may reveal empyema along the tract or periventricular enhancement on FLAIR. Abdominal ultrasound may show a CSF pseudocyst.

The key to management is a high degree of suspicion in a shunted child with persistent fever despite antibiotics. Antibiotic therapy needs to be instituted early, though most cases only respond once the shunt hardware is removed. Broad-spectrum antibiotic cover with vancomycin plus meropenem or cefepime is generally a reasonable choice while awaiting culture and sensitivity reports.

12.10.3 Over-Shunting

Up to 10% of patients develop symptoms related to over-drainage causing a state of intracranial hypotension in the supine position [68]. The siphoning with gravity causes the obstruction of the valve by ependymal or choroid plexus with episodes of intracranial hypertension. Over-drainage may cause a myriad of complications:

- **Slit ventricle syndrome**: A complete collapse of the ventricles occurs as a result of over-drainage in about 10–12% of shunted patients. These patients present with intermittent or complete shunt malfunction due to shunt occlusion by the ependymal scar [69, 70].
- **Intracranial hypotension** presents as a postural headache that resolves on lying supine. Serious symptoms due to downward displacement of the brainstem may be worrisome [71].
- **Subdural hematomas** are more commonly seen in adults with normal pressure hydrocephalus. There is tearing of the bridging cortical veins due to craniocerebral disproportion. Similarly, SDH may also occur in children with long-standing hydrocephalus with enlarged ventricles and a thin cerebral mantle [72].

Treatment usually mandates increasing the pressure in a programmable valve or upgrading to a higher-pressure valve, one with a siphon control device or flow-regulated valves.

12.10.4 Miscellaneous Complications

Immediate procedure-related risks are intraparenchymal/intraventricular/subdural hematomas, catheter misplacement, and stroke. At the abdom-

inal end, pseudocyst may form following indolent infection with *Propionibacterium* acnes. Case reports of hollow viscus perforation, distal catheter migration, and volvulus are abundant. VA shunts may cause thrombosis, pulmonary hypertension, right heart failure, and shunt nephritis. Pleural shunts result in pleural effusions/hydrothorax. Seizures may occur in about 6–30% with an incidence of 2% per year. Risk factors being preemies with hydrocephalus, young age at first surgery, PHH, post-infectious HCP, post-traumatic HCP, following shunt obstruction, and shunt infection [73].

12.11 Special Anesthetic Considerations

12.11.1 Shunted Patient for Incidental (Laparoscopy) Surgery

Despite concerns of pneumoperitoneum causing an increase in ICP, a well-functioning shunt does not contraindicate laparoscopy [74]. The one-way valve in the shunt can withstand pressures up to 300 mmHg, and clamping the abdominal end of the shunt is not a wise idea as it may actually raise the ICP. More so, pneumoperitoneum exceeding 15 mmHg causes only transient, small in magnitude changes in ICP; in presence of a well-functioning shunt, this is hardly a cause for concern. Other concerns are with respect to the placement of central venous lines; the shunt tunnel should be well-demarcated to avoid shunt catheter damage.

12.11.2 Shunted Patient for MRI

This is the cause of concern in the case of programmable shunts as resetting, heating, and dislodgement of the shunt magnet are all possible during imaging. The valve assembly may also cause artifacts in the images. It is recommended to do an after check of the valve settings following MRI [75].

12.11.3 Shunted Patient for Neuraxial Block

The theoretical concerns are primarily retrograde shunt infection and meningoencephalitis/ventriculitis in shunted patients. Abundant literature on obstetric patients who underwent spinal anesthesia for cesarean or labor analgesia has found similar risk as to the general population. It is safe to say that neuraxial block can be safely administered using strict asepsis and systemic antibiotics in shunted patients [76].

12.12 Conclusion

Pediatric hydrocephalus remains a menacing burdensome diagnosis for the treating physicians with its resolute course, brain parenchymal effects of raised ICP, shunt complications, and multiple revisions despite successful surgical management of the underlying pathology. The course is arduous despite CSF diversion procedures; the outcomes are dismal in terms of morbidity and economic burden. Though ETV as a CSF diversion procedure is gaining wide acceptance in pediatric non-communicating hydrocephalus, CSF shunts remain the gold standard for diversion in majority of pediatric patients with hydrocephalus. Anesthetic management of these patients is challenging due to concerns regarding airway management, intracranial hypertension, intraoperative hemodynamic and electrolyte disturbances, associated congenital anomalies, and multiple revision surgeries. A thorough understanding of the pathophysiology, clinical presentation, and early management of the underlying pathology and shunt complications therein are paramount to achieve good functional outcome in pediatric hydrocephalus.

Conflict of Interest Nil.

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Neural Tube Defects: Meningocele and Encephalocele

13

Charu Mahajan

Key Points

- Neural tube defects (NTD) are either open or closed depending upon the defect during embryogenesis.
- Generally, open defects have an overall poor prognosis as compared to closed NTD.
- Meningomyelocele (MMC) is usually associated with other cranial and spinal malformations like hydrocephalus, Arnold-Chiari malformation II, corpus callosal agenesis, tethered cord syndrome, syringomyelia, etc.
- The surgery should be done as soon as feasible on an urgent basis rather than on an emergency basis.
- Pediatric age group, associated anomalies, possible difficult airway, and positioning makes anesthesia for patients with encephalocele quite challenging.
- These children may present for repeated surgeries and have a protracted disease course, often requiring a multi-specialty medical team.

13.1 Introduction

Neural tube defects (NTD) are one of the common congenital malformations of the central nervous system (CNS) responsible for either in utero fetal loss or chronic disability among those who survive. It may occur anywhere in the midline along the neural axis extending from the brain to the sacrum resulting in cranial or spinal dysraphism. Dysraphism means defective midline fusion or closure of neural tube, resulting in defects in nerve roots, spinal cord, or vertebrae. NTD can be divided into an open (aperta) defect if the overlying skin cover is absent or closed (occulta) type if the lesion is covered with skin [1]. There is cerebrospinal fluid (CSF) leak in the open form, and the neuroepithelium protrudes externally through the defect. This loss of CSF is implicated in developing other CNS abnormalities resulting in a worse functional neurologic outcome than the closed NTD. Like cranial dysraphism, spinal dysraphism may be open or closed depending upon the presence or absence of exposed neural tissues, respectively [1]. The open spinal defects are usually associated with other brain malformations. In closed spinal dysraphism, there is congenital absence of a spinous process and part of the lamina. As a result, the neural tissue lies deep to an intact layer of skin. This type is usually not associated with brain maldevelopment, and the prognosis is also better than open defects.

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Table 13.1 Classification of neural tube defects (NTDs)

Cranial dysraphism	Spinal dysraphism
Open defects • Anencephaly • Iniencephaly • Craniorachischisis Closed defects • Encephalocele • Meningocele	• Spina bifida aperta: Myelomeningocele, myelocele, hemimyelocele, hemimyelomeningocele • Spina bifida occulta: Split cord malformations (diastematomyelia, diplomyelia), dorsal dermal sinus, meningocele, lipomyelomeningocele, terminal syringo-hydromyelocele, abnormal filum terminale, spinal lipoma, caudal agenesis

The NTD spectra can thus be classified into cranial and spinal depending upon the site of maldevelopment (Table 13.1). Common ones are spina bifida and anencephaly, while rarer types include craniorachischisis and iniencephaly.

The incidence of NTD has decreased since the mandatory folic acid prescription for all pregnant women and has remained stable for the last 20 years. The birth prevalence, live birth, and still-birth prevalence of neural tube defects in India are 4.1, 1.3, and 1.7 per 1000 births, respectively. Among the NTD, in India, the prevalence of anencephaly is highest (2.1 per 1000 births), followed by spina bifida (1.9 per 1000 births) [2]. The worldwide prevalence ranges from 1 to 3 in 1000 live births [3]. A systematic review found great variability in reporting of NTD prevalence between and also within countries ranging from 0.3 to 199.4 per 10,000 births, possibly due to variation in data collection and lack of surveillance/registry data in lower-income countries [4]. On a worldwide average, spina bifida is the most common type, followed by anencephaly and then encephalocele [4].

13.2 Embryology and Pathogenesis

The neurulation process, which occurs between 17 and 28 days post-conception, forms the brain and spinal cord. At the end of the second week after fertilization, the embryo becomes a trilaminar disc consisting of three germ layers—ectoderm, mesoderm, and endoderm. The ectoderm overlying the notochord (at the cranial end) thickens to forms neural plate. At 3 weeks after gestation, a depression appears along its midline to form neural groove. With further deepening, the two edges start fusing in the midline to form the neural tube. This process of neural plate folding to form a cylindrical neural tube is known as primary neurulation. The neural tube divides into the cranial part, forming the early brain, and the caudal part forms the early spinal cord. The closure starts dorsally around the midpart of the neural plate and proceeds in cephalad and caudal direction. The openings at the two ends of the tube are known as cranial and caudal openings. The cranial neuropore closure (approx. day 24) is followed by caudal neuropore closure (day 28). Failure of anterior neuropore closure leads to anencephaly, and non-closure of posterior (caudal) neuropore results in spinal bifida. Failure of neural tube closure along its whole length gives rise to rachischisis. The development of the neural tube, its closure, and separation from the overlying ectoderm is completed beyond 4 weeks post-conception. Failure of fusion of neural folds and closure of neural tube, anywhere from cranial to caudal part during primary neurulation, results in different types of open NTDs. The secondary neurulation process deals with the hollowing of the neural tube, and formation of medullary cord and cavities that ensues in weeks five to six thus forming the lower spinal cord segments (sacral and coccygeal). Any defect in the process of secondary neurulation results in closed dysraphism. As this process occurs beneath the ectoderm, the lesions are covered by skin, hence known as closed NTD.

The genetic, nutritional, and environmental factors are implicated in the etiopathogenesis of NTDs. The risk is increased in the sibling of the affected case, same-sex twins, and offspring of consanguineous marriage [5]. The majority of the cases are sporadic, and it has been difficult to identify genetic risk factors because of the involvement of multiple genes and gene-environment interaction. The various genes like 5,10-methylene tetrahydrofolate reductase

(MTHFR), methionine synthase (MTR), methionine synthase reductase (MTRR), and cystathionine synthase are associated with increased risk of NTDs but with variable certainty [6]. Syndromic cases of NTD have associated chromosomal disorders like trisomy 13, trisomy 18, triploidy, or partial aneuploidy. Others include Meckel-Gruber syndrome, PHAVER syndrome, VATER syndrome, and X-linked disorder. Various other factors responsible are antenatal use of anti-epileptic drugs (valproic acid and carbamazepine), maternal diabetes, obesity, advanced maternal age, alcohol consumption, hypervitaminosis A, exposure to lead, nitrates, cytochalasin, febrile illness, and micronutrient deficiency (zinc and folic acid) [7]. However, folate deficiency leading to NTD has been a topic of controversy, and some implicate it as a risk factor only in the presence of predisposing genotype [8].

13.2.1 Primary Prevention

In 1991, the British Medical Research Council (MRC) conducted a multicentric randomized control trial to study the effect of supplementing folic acid to women at high risk of having pregnancy with NTD. This study confirmed that periconceptional supplementation with 4 mg folic acid significantly reduced the risk of recurrence of NTDs [9]. Based on this evidence, it has been suggested that all women of child-bearing age capable of becoming pregnant should consume 400 μg of folic acid daily in the preconception period and early pregnancy. High-risk women (those having previous pregnancy affected with NTD, receiving valproic acid or carbamazepine) should consume a higher dose of 4 mg of folic acid per day to prevent NTD [10].

13.3 Spinal Dysraphism

13.3.1 Meningomyelocele

Defect in neural arch results in herniation of meninges or neural tissue, resulting in different types of spinal dysraphism. Meningomyelocele (MMC) is a type of open NTD with congenital defect in vertebral arches leading to the formation of protruding membranous sac containing CSF, meninges, and nerve roots. If the herniated sac contains CSF without any neural tissue, then it is known as meningocele. MMC is the most common form of spinal NTD [3]. The commonest site of occurrence is the lumbosacral area (>80%), followed by thoracic and cervical regions [11]. The higher the level of spinal defect, the poorer the prognosis of the child. Overall incidence and prevalence of MMC have decreased following folic acid supplementation, better antenatal diagnosis, and legalization of medical termination of pregnancy.

13.3.1.1 Pathophysiology

The two-hit theory of nerve damage states first hit as the defective formation of the neural tube and second hit as the damage occurring in utero environment [12]. In this open-type defect, the neuroepithelium is exposed to the amniotic fluid in utero. This leads to damage to the neuronal tissue and neurodegeneration [3]. Moreover, loss of CSF through an open defect leads to nondistension of the neurocranium and the formation of the small posterior fossa and CNS maldevelopment [13]. Thus, it is often associated with brain abnormalities.

13.3.1.2 Clinical Presentation

The child usually presents with a membrane-covered sac on the back (Fig. 13.1) at the time of birth. The lesion is usually cystic, and if the overlying membrane is disrupted, a CSF leak occurs, which might lead to meningitis. Depending on the site and age, the child may present with motor, sensory, or bowel/bladder involvement. The child may have partial or complete flaccid paralysis and loss of sensation below the level of lesion. Bowel and bladder involvement are seen in the majority of the patients. There is a loss of autonomic control below the level of the spinal lesion. Several other neurological abnormalities may coexist, like hydrocephalus (65–85%), Arnold-Chiari malformation (ACM) type II (55–60%), corpus callosal agenesis, microgyria,

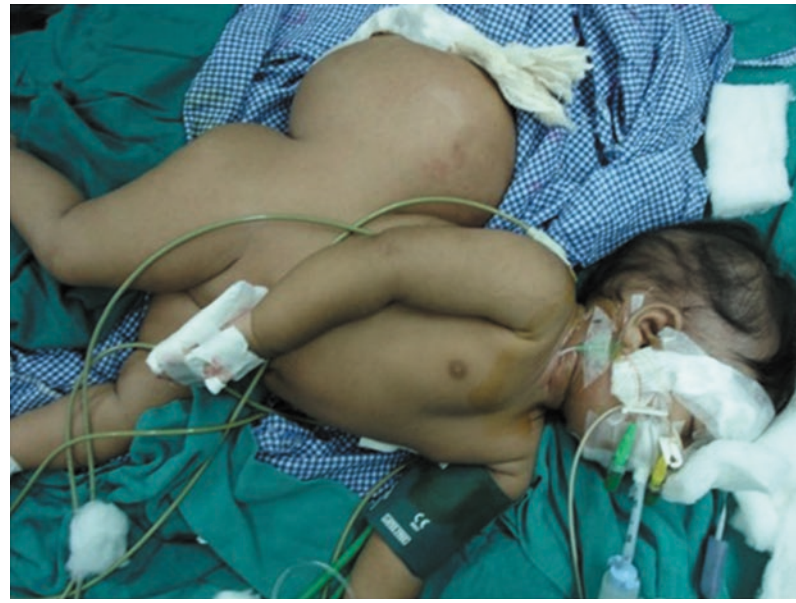

Fig. 13.1 A 10-month-old child with lumbosacral meningomyelocele

arachnoid cyst, porencephalic cyst, tethered spinal cord, and syringomyelia [14]. Hydrocephalus usually develops by the second week of birth or after repair of MMC, when the CSF egress site is closed. The child may present with features of raised intracranial features if overt hydrocephalus is present. ACM II may present as brainstem or lower cranial nerve dysfunction resulting in feeding, swallowing, and breathing problems. In infants, central apnea, stridor, and swallowing disturbances may be evident. Older children may complain of neck pain, headache, and sensory symptoms in limbs. The malformation also results in obstruction to the flow of CSF, leading to development of hydrocephalus. Lower extremities may have deformities like club feet; and various other systems like renal, cardiac, and gastrointestinal tract may also be involved. Congenital cardiac defects like atrial septal defect (ASD), ventricular septal defect (VSD), tetralogy of Fallot (TOF), bicuspid aortic valve, coarctation of aorta, and anomalous pulmonary venous return may be seen and have an important bearing during perioperative management. Older children may have associated autonomic cardiovascular disturbances due to paraplegia and associated hypomobility [15].

13.3.1.3 Diagnosis

Prenatal diagnosis can be made by ultrasonography and maternal alpha-fetoprotein (AFP) levels. An abnormally high level of AFP indicates open neural tube defects. Further evaluation by ultrasound and amniocentesis may be done. In cases with raised AFP, ultrasound helps in differentiating NTD from other non-neurologic causes. The decision for termination of pregnancy may be taken depending on the lethality of the condition, legal laws of the country, and period of gestation. Prenatal diagnosis also helps in the decision for in utero correction of MMC depending upon the severity of the lesion and availability of expertise.

Postnatal diagnosis: X-ray will define any bony spinal abnormality and coexisting skull defects. CT scan of the head and spine can help to evaluate the hydrocephalus and spinal column. Complete MRI of the head and spine helps in the assessment of the cranial as well as spinal cord abnormalities.

13.3.1.4 Management

Management of spina bifida is multidisciplinary and at times requires multiple surgeries either for primary correction or for treatment of complica-

tions thereof. In addition, the child may also require urological and orthopedic interventions. Open defects may be repaired either in utero or postnatally. Antenatal surgery for correction of the open defect is less commonly practiced and is limited to few centers.

Antenatal management: The exposure of open neural tissue to amniotic fluid worsens the neurologic function [16]. So, in utero repair of open defect may halt the secondary neural tissue destruction and improve the neurologic outcome. The results of intrauterine surgery for repair of MMC have been found to be encouraging; but it is also associated with maternal and fetal risks. In a prospective trial, 158 women were randomized to undergo either MMC repair before 26 weeks of gestation (in utero) or standard postnatal repair. In utero repair was found to reduce the incidence of hydrocephalus and the need for ventriculoperitoneal shunts significantly. There were improved motor outcomes and ACM reversal in the preterm group. However, it was also associated with an increased risk of preterm delivery and uterine dehiscence at delivery [17]. Assessment of 1-year outcome of these patients revealed that when ventricle size is 15 mm or larger, prenatal surgery does not reduce the need for shunting [18]. For this reason, ventriculomegaly more than 20 mm is considered as a contraindication for in utero repair. The details of fetal surgery are beyond the scope of this chapter.

Postnatal management: The decision about the route of delivery depends upon the presence of gross hydrocephalus and obstetric indications. After delivery, all precautions must be taken to prevent any trauma or compression of exposed neural tissue. The child should be nursed in prone or lateral position, and the sac should be covered with saline dressings to prevent desiccation. It is generally believed that early closure of the defect decreases the risk of CSF leak and infection. However, there is insufficient evidence to support that the closure of MMC within 48 h decreases the risk of wound infection. A recent retrospective review found no difference in neurological and urodynamic deficits when early repair (within first 48 h after delivery) was compared with late repair (>48 h after delivery) of MMC [19]. If the closure is delayed beyond 48 h, antibiotics should be given to reduce infection risk (level III) [20]. Timing of the surgery depends upon the child's condition, and optimization is essential before proceeding. The surgery should be done as soon as feasible on an urgent basis rather than an emergency basis. If the sac is ruptured, antibiotics need to be started immediately.

13.3.1.5 Preanesthetic Preparation

During preanesthetic evaluation, complete history (including antenatal history, birth history, premature birth) and thorough examination of CNS and other systems should be made. Laboratory investigations include hemogram, blood sugar and renal function tests, and serum electrolytes. Other additional appropriate investigations may rule out the presence of other congenital anomalies. Chest X-ray helps to see the trachea (if short in length), lung shadows (any aspirational changes), and cardiac silhouette (congenital cardiac diseases). Cardiac abnormalities are common, and ECG along with cardiac consultation usually suffices. Preoperative echocardiography has been suggested in these children to rule out congenital heart disease but is not a routine protocol at all places. History of rubber allergy should be noted, and if positive, latex avoidance protocol should be followed. These children should not be exposed to latex to prevent sensitization. Despite prophylaxis, anaphylactoid reactions may still occur. Adequate blood and blood products should be arranged beforehand. Signs of brainstem or lower cranial nerve involvement points toward a possible need for mechanical ventilation postoperatively. Thoracolumbar MMC may be associated with abdominal muscle weakness, ineffective cough, and may also require postoperative ventilation [21]. Sedative premedication is contraindicated in these small children.

13.3.1.6 Anesthetic Management

The operation room (OR) should be prepared, keeping in mind the age of the child. Essential points include maintenance of OR temperature,

availability of appropriate size equipment and airway devices, positioning aids, fluid warmers, etc. The standard monitoring includes electrocardiography, noninvasive blood pressure monitoring, pulse oximetry, capnography, temperature, and urine output. An important aspect of anesthesia management of such children is positioning, and the sac should always be free of any compression. The child may be placed either supine with a sac placed inside a doughnut or in a lateral position. Inhalational or intravenous induction may be done depending upon the availability of intravenous access. In a child who has associated ACM II, intubation should be carried out with the head in a neutral position to avoid any brainstem compression. These children may have a short trachea; hence, endobronchial intubation should be ruled out before the final fixation of the tracheal tube. Insertion of a ventriculoperitoneal shunt for hydrocephalus and repair of MMC can be done in the same sitting. For excision of MMC, the patient should be carefully placed prone. The abdomen should be free for unrestricted ventilation and unimpeded drainage by inferior vena cava. All pressure points related to the prone position should be adequately padded, and eyes should be kept free. Precautions for the prevention of hypothermia should be taken. Latex should be avoided to prevent contact sensitization. It is advisable to use non-latex gloves by all medical and paramedical staff, to avoid any known latex product in the sterile field by the surgeon; to use latex-free anesthesia face masks, reservoir bags, ECG leads, stethoscope, BP cuff, and tubing; and not to administer any intravenous injection through rubber injection port [22]. Inhalational anesthesia is preferred in children for their earlier recovery and rapid titration. In a study carried out by Singh et al., children who received sevoflurane had an earlier recovery than those maintained on isoflurane anesthesia [23]. Short-acting inhalational anesthetic agents are associated with an increased incidence of emergence delirium. In children aged 8–12 years, dexmedetomidine, when used as an anesthetic adjuvant to sevoflurane-based anesthesia, had a significant opioid-sparing effect and reduced postoperative pain and emergence agitation without adverse hemodynamic effects [24]. Similarly, on comparison of the effect of sevoflurane and desflurane, earlier tracheal extubation and emergence were seen in the desflurane group, while the incidence of emergence delirium was the same in both the groups [25, 26]. Muscle relaxants should be used sparingly for the maintenance of anesthesia. Fentanyl or remifentanil can be used for analgesia intraoperatively. In patients having large MMC, huge insensible losses and blood loss may occur, which can cause hemodynamic instability and needs to be adequately replaced. Large amounts of fluid/blood transfusion, a large area of exposed tissue, and infancy predispose these children to hypothermia. Complications related to prone positioning may also be encountered intraoperatively.

The surgical technique involves isolation of neural tissue, placing it back within the spinal canal, repair of dura mater, and closure of muscles, fascia, and overlying skin. These patients may also require untethering of cord. In cases of large MMC with large skin defects, a plastic surgeon may be required for performing flap closure of defect. This may make it a considerable long surgery, and anesthesia technique needs to be modified accordingly. At times, in children with clinically evident HCP, shunt surgery may be done in the same setting. The chances of hypothermia increase during such situations. The decision for endotracheal extubation depends upon neurological status of child, vitals, temperature, blood loss, metabolic profile, and duration of surgery.

After adequate reversal of neuromuscular blockade, trachea should be extubated only when child is awake, cough and gag reflexes return, and breathing is regular. Postoperatively, nursing should be done in supine or lateral position. Apnea or stridor may occur postoperatively and should be closely watched for in an intensive care unit. Autonomic disturbances are common in these children and require close monitoring. CSF leak, wound infection, and meningitis are the possible early postoperative complications. Other long-term complications are hydrocephalus, shunt malfunction, tethered cord, scoliosis, and worsening of features of ACM II. These children

have associated vertebral deformities like scoliosis, kyphosis, or lordosis and often require subsequent surgeries. Neurogenic bladder and related complications often require urology consultations. Anal sphincter dysfunction may result in bowel incontinence. These children often require shunt revisions, surgeries for other congenital problems, and multispeciality follow-up. They often have associated cognitive disturbances.

13.3.1.7 Latex Allergy

The reported incidence of latex allergy varies from 20 to 65% in patients with spina bifida. It is due to the sensitization to latex due to repeated bladder catheterization and exposure to latex during hospital admissions [27]. The spectra include mild non-allergic irritant contact dermatitis, allergic contact dermatitis (type IV hypersensitivity) to more severe type I Ig E-mediated hypersensitivity reactions. The most serious manifestation is the anaphylaxis, vascular collapse, and shock seen due to type I reaction. Patient may present with angioedema, hypotension, rash, and bronchospasm. Differential diagnosis is anaphylaxis to other drugs and is managed in a similar way. In the preoperative period, a careful history and pertinent risk factors indicating latex sensitization and food allergy should be evaluated. History of prior surgical procedures should also be noted. A child with confirmed type 1 allergy should be made to wear a latex allergy medical alert bracelet. Prophylactic use of antihistamines and corticosteroids is not recommended. Child should be posted first in OR list, and all equipment containing latex like BP cuffs, gloves, urinary catheters, face mask, reservoir bag, syringes, IV sets, drug vials with latex stoppers, and tourniquets should be removed from the site. Non-latex gloves, plastic airways, glass/latex-free syringes, PVC endotracheal tubes, neoprene bags, and silicon valves are safe to use. Barrier protection should be used, and latex-containing equipment should not come in contact with patients' skin.

In case of an intraoperative anaphylaxis, the exact diagnosis of latex allergy is a challenge. The first step is to check airway, breathing, and circulation (ABCs) along with removal of triggering agents. There may be delay in recognition of signs as the child is under drapes. The first presentation of anaphylaxis can be fall in blood pressure and increase in peak airway pressures (bronchospasm). Other signs may be angioedema, urticaria, rash, skin flushing, or tachycardia. This requires immediate treatment and prompt administration of 100% oxygen and intravenous fluids. Intravenous adrenaline 1–10 μg/kg bolus doses are given depending upon the severity of reaction, till blood pressure or bronchospasm improves. In case of circulatory arrest, bolus doses of adrenaline 10 μg/kg should be used as per protocol for advanced cardiac life support (ACLS). β-2 agonists via metered dose inhaler or nebulization helps in improving bronchospasm. After resuscitation, a vasopressor infusion is usually required for maintenance of blood pressure. In addition, secondary treatment includes administration of anti-histaminics like IV diphenhydramine 1–2 mg/kg (50 mg maximum) or IV ranitidine 1–2 μg/kg and corticosteroids like IV hydrocortisone 1–2 ug/kg. Arterial blood gas values should be collected and corrected accordingly. Blood sample for serum mast cell tryptase for confirmation of anaphylaxis may be sent once patient is stabilized. Skin prick test can be done later on to confirm latex allergy.

13.4 Occult Spinal Dysraphism

It is a type of congenital anomaly in which there is bony defect in spinal column and resulting structural deformities are limited to the spinal cord, which are not visible externally. The lesion is covered with an intact skin cover and CSF leak does not occur. The overall prognosis is usually better than open defects as there is no major motor/sensory involvement. During antenatal period, it is not associated with raised AFP as the dural lining is intact and neural tissue is not exposed to amniotic fluid. The child may remain asymptomatic for years and may be diagnosed incidentally on imaging studies. This type is usually associated with typical overlying cutaneous manifestations like nevus, hypopigmentation, tuft of hair, lipoma, hemangioma, telangiectasias,

dermal sinus, skin tags, or gluteal cleft. The different types of occult spinal dysraphism are enumerated in Table 13.1.

Lipomatous malformations are the most common type of closed spinal NTD. The lipomatous tissue can be present at filum, conus, and within or attached to the spinal cord. Lipomyelocele contains fat tissue only, while lipomyelomeningocele contains fat and neural tissue in the sac. The lipomatous tissue herniates through the bony defect and attaches to the spinal cord. The neurological symptoms are usually due to associated tethering of cord or due to compression by the lipomatous mass. This requires removal of lipomatous tissue and untethering of the cord.

Meningocele is a midline outpouching of fluid-filled meningeal sac without neural tissue herniation and is covered by normal skin or a membrane. The spinal cord is positioned within the spinal canal only. These are usually not associated with neurologic deficits and brain malformations. These usually occur in lumbosacral spine. The lumbar and sacral meningoceles are classified as closed spinal NTD, while posterior cervical NTD are difficult to exactly classify. The cervical meningoceles can be both open and closed and are often considered as transition between the two ends [1]. MRI helps to differentiate meningocele from MMC. Other types of associated occult dysraphism like tethered cord and split cord malformation should be ruled out. Surgical correction involves resection of herniated meninges and closure.

Congenital dermal sinus is an epithelial lined tract close to midline extending from the skin to anywhere up to the conus medullaris. It may get infected and can result in meningitis. It can cause mass effect if a dermoid cyst forms in the tract. Surgical treatment involves excision of the tract and dermoid cyst.

Split cord malformations (SCM) are the conditions in which the spinal cord is double. Type I SCM also known as diastematomyelia has two hemicords in two separate spinal canals, with each having its own meninges and a set of dorsal and ventral nerve roots. The two cords are separated from each other by an osteocartilagenous bony median septum (Fig. 13.2). It is associated with overlying skin stigmata like nevi, tuft of hair, dimple, hemangioma, and lipoma. Symptom manifestations relate to associated tethered cord or MMC. There may be coexisting orthopedic problems like scoliosis, kyphosis, and foot deformities. Motor weakness, limb atrophy, sensory deficit, and bladder dysfunction are frequently seen. Untethering of the cord is the usual treatment required. It also involves removal of bony septum and reconstitution of dura as single tube. The anesthetic concerns are same as for excision of MMC and detethering of cord. In addition, removal of bony septum can cause significant intraoperative bleeding, and consequently hypotension may occur. In type 2 SCM, also known as diplomyelia, two hemicords along with four sets of dorsal and ventral nerve roots are present within a single dural tube separated by fibrous median septum. There is no associated spinal deformity at level of split. The fibrous band is removed, and cord is untethered during surgical correction. Though the septum is fibrous, still bleeding is an important intraoperative concern.

13.4.1 Tethered Cord Syndrome

Tethered cord syndrome (TCS) is defined as an entity which presents with symptoms and signs arising from abnormal spinal cord strain [28]. Inside the spinal canal, normally the spinal cord hangs free. In TCS, there is restriction of free movement of spinal cord either due to presence of thick filum or its abnormal adherence to an adjacent structure. It is often seen in association with other congenital malformations of the spinal cord and spinal dysraphism. As the spinal cord grows, stretching of cord results in decrease in blood flow and ischemic changes. In children, this condition is usually congenital; but acquired causes like infection, scarring, tumor, and MMC closure can also cause tethering of the cord due to development of fibrotic adhesions. The most common site of involvement is the lumbosacral region. Infants who undergo prenatal MMC closure may develop TCS later in life, at a similar or even higher rate than seen after postnatal repair [29]. In majority of the patients, it is recognized

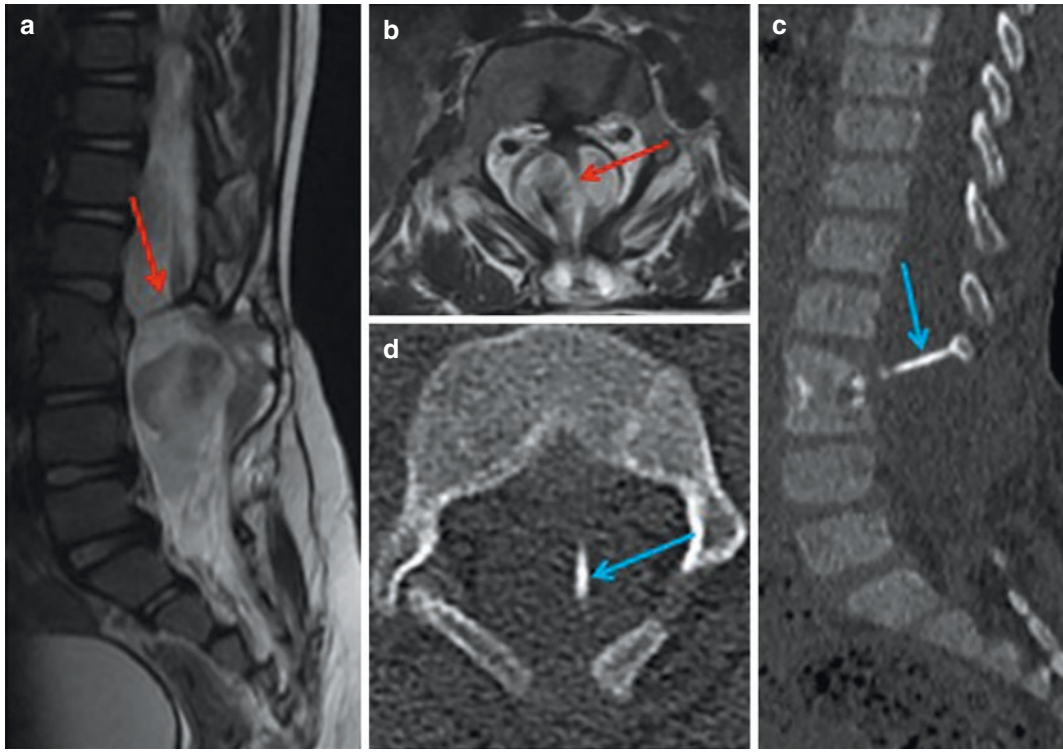

Fig. 13.2 A 7-year-old boy presented with fecal and urinary incontinence with lower limb weakness and inability to walk since birth. He has history of meningomyelocele repair on day 3 of life. (**a**) Sagittal and (**b**) axial T2 MRI shows linear hypointense structure arising from the posterior aspect of the L2 vertebral body extending up to the posterior elements, signs of spur (red arrow). # Note is made of closed meningocele defect inferior to the spur. (**c**) Sagittal and (**d**) axial NCCT show osseous spur at the level of L3 (blue arrow). # Note is made of spina bifida

by presence of associated cutaneous markers (tufts of hair, skin tags, dimples, benign fatty tumors, skin discoloration, or hemangiomas) and musculoskeletal or vertebral abnormalities. The neurological manifestations are quite subtle in children and gradual in progression. The symptoms and signs include leg and back pain especially on flexion of lower spine or vigorous physical activity, lower extremity weakness, gait impairment, hyperreflexia, sensory changes, and musculoskeletal abnormalities like clubfeet, atrophied lower leg muscles, scoliosis, kyphosis, etc. In older children, urinary incontinence, urinary tract infections, abnormal voiding, and fecal incontinence may be seen. Small children are unable to communicate, do not have bowel and bladder control, as well as are not ambulatory. This delays the recognition of TCS in small children. Diagnosis is done by detailed neurological examination and MRI (Fig. 13.3). MRI helps to identify the level of tethering, presence of other congenital conditions, and underlying cause of tethering. In addition, urodynamic assessment and electromyographic measurement of perineal floor muscles are also required. Children presenting for correction of scoliosis should undergo evaluation for TCS, and detethering should be done before orthopedic correction. The surgical technique involves detethering of the cord and dural repair in prone position. The anesthetic concerns are almost similar as during repair of MMC. Removal of associated bony spur (Fig. 13.2) may increase the risk of intraoperative bleeding. There are reports of venous air embolism during detethering of cord in prone position as the surgical site is above the level of the heart resulting in negative pressure gradient and air entrainment [30, 31]. This

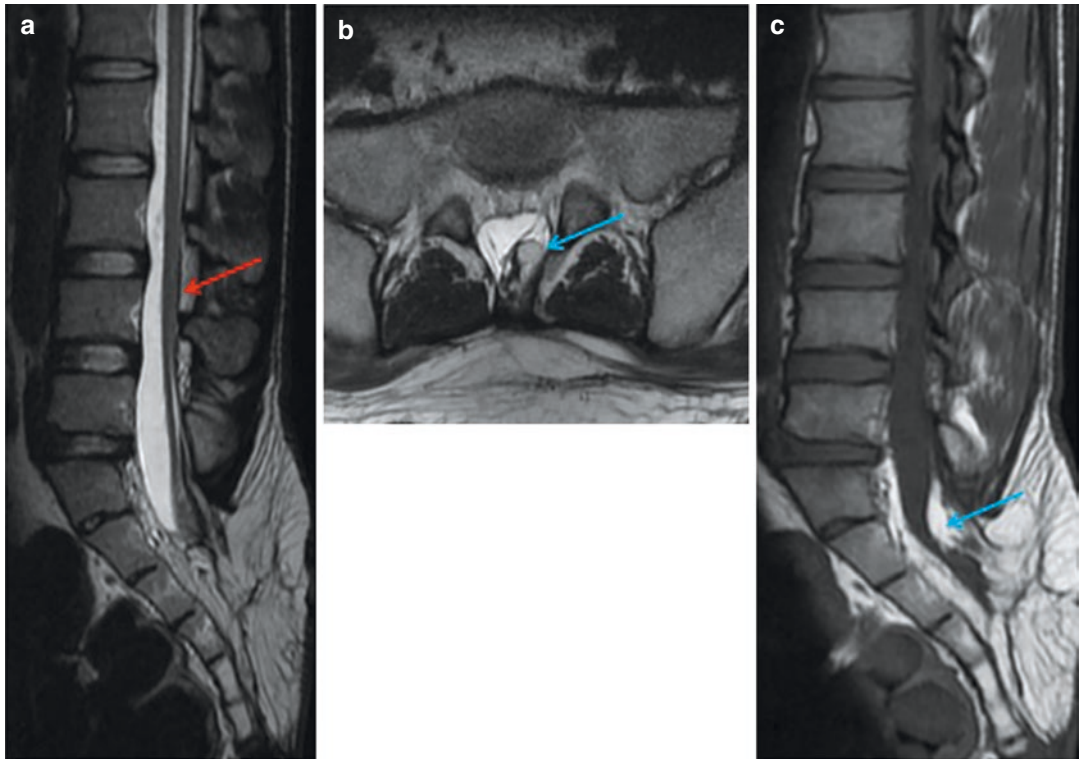

Fig. 13.3 A 16-year-old boy presented with progressive weakness in both lower limbs. MRI shows low lying conus (L4-L5) level (red arrow) with tethering of the filum terminale and a linear fat signal intensity lesion (lipoma) in the sacral spinal canal (blue arrow)

might occur from open dural sinuses or from opening of osseous venous channel during excision of bony spur. Intraoperative motor evoked potential (MEP) monitoring for identification of motor roots requires modification of anesthetic technique. It requires total intravenous anesthesia, use of halogenated agents less than 0.5 MAC, and omission of muscle relaxants. MEP can be evoked by transcranial stimulation, and recording is done from limb muscles and external anal sphincter. Somatosensory evoked potentials (SSEP) can be evoked by tibial or pudendal nerve stimulation and recorded from electrodes placed in epidural space or cortex. Electromyography (EMG) responses from muscles can be recorded by direct motor nerve root stimulation. Pudendal nerve stimulation can elicit bulbocavernous reflex which can be recorded from muscles of external anal sphincter. This is important for maintaining integrity of sphincter function. Postoperatively, children are nursed flat to minimize CSF pressure on the surgical repair site. Surgical complications include wound infection and CSF leak. Retethering is quite common after MMC repair, and child should be regularly followed thereafter.

13.5 Cranial Dysraphism

Cranial dysraphism is analogous to spinal dysraphism where a defect in development of brain or closure of skull during embryogenesis results in a spectrum of malformations. Different types of cranial NTD have been listed in Table 13.1.

Anencephaly: The NTD is limited to cephalic area, and there is absence of cerebral hemisphere and skull bones above the bony orbits. This condition is incompatible with life, and pregnancy should be terminated when diagnosed early in antenatal period.

Craniorachischisis: It is a rare and severe form of NTD involving the cephalic and spinal

zones. There is complete failure of neural tube formation because of non-closure of both cranial and caudal neural tubes. There is complete absence of skull and major defects in the vertebra and skin. This condition is also incompatible with life.

Iniencephaly: It is a rare disorder characterized by a defect in occipital bone, spina bifida at cervical vertebrae, and extreme retroflexion of the head.

Cranial meningocele: Protrusion of meninges and CSF through a defect in the skull results in formation of cranial meningocele.

Encephalocele: Here, encephalocele will be discussed in detail.

13.5.1 Encephalocele

Protrusion of intracranial tissue (meninges and brain parenchyma) through a defect in the skull leads to formation of a sac-like structure known as encephalocele (Fig. 13.4). Herniation of just meninges through a defect in the skull is termed as meningocele. As discussed earlier, its pathogenesis is a defect during neurulation in which neural folds fail to fuse anteriorly. The exact cause is not known and genetic and environmental factors also play a role. Irradiation, maternal fever, hypervitaminosis, folic acid deficiency, irradiation, viral infections, and drugs like warfarin, phenytoin, valproate, and carbamazepine are the implicated causative risk factors [32]. Encephaloceles constitute 8–19% of all craniospinal dysraphism. The worldwide incidence varies from 1/300 to −1/10,000 livebirths [33]. The prevalence is higher in Southeast Asia than in other parts of world. The different sites can be (a) posterior or occipital; (b) anterior or sincipital, also known as frontoethmoidal (e.g., nasofrontal, nasoethmoidal, nasoorbital), (c) basal (e.g., transsphenoidal, trans-ethmoidal, sphenoorbital, sphenoethmoidal); or (d) cranial vault (e.g., frontal, parietal, temporal, through anterior and posterior fontanelle) [34]. The occipital encephalocele is more common in Europe and the USA, while frontoethmoidal encephaloceles is commonly seen in Asia and African countries. Rarely, children may present with a giant encephalocele, size of which is even larger than the head [35]. These children often have difficulty in nursing because of the huge swelling. Encephalocele is often associated with other congenital cranial and extracranial anomalies. The neurologic problems include hydrocephalus, craniosynostosis, microcephaly, agenesis of the corpus callosum, Arnold-Chiari II malformation, porencephaly, cortical atrophy, Dandy-Walker malformation, developmental delay, vision problems, seizures, and mental and growth retardation. Other associated systemic abnormalities such as micrognathia, polydactyly, cleft lip/palate, spina bifida, vertebral abnormalities, renal agenesis, pulmonary hypoplasia, dextrocardia, patent ductus arteriosus, and septal defects have also been reported. Frontonasal encephalocele involves herniation of intracranial contents from foramen caecum to the junction of nasal and frontal bones presenting as a nasal mass, causing breathing difficulty. Transsphenoidal encephaloceles may present with CSF rhinorrhea, visual defect (in older children), epipharyngeal mass causing respiratory obstruction, and features of pituitary-hypothalamic insufficiency [36]. This is due to the involvement of structures like the pituitary gland, hypothalamus, and optic pathway. Patients with orbital encephaloceles have proptosis on presentation. Nasopharyngeal and transsellar transsphenoidal types have nasal mass and consequent respiratory obstruction [37]. An

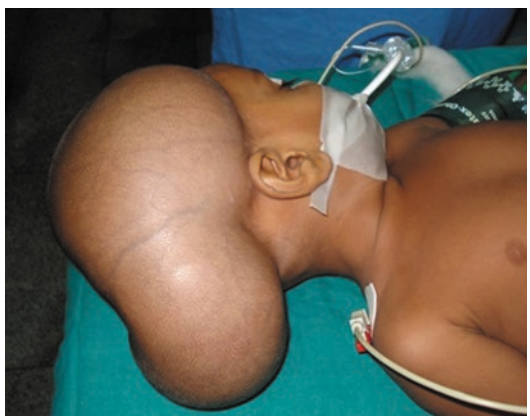

Fig. 13.4 A 1.5-year-old child with giant parieto-occipital encephalocele

enlarged head can be a result of associated hydrocephalus. On the other hand, occipital encephaloceles present with brainstem dysfunction, lower cranial nerve involvement, respiratory distress, and involvement of vital centers. Encephalocele is also recognized as a part of various syndromes like Knobloch syndrome, Meckel syndrome, Von Voss syndrome, Walker-Warburg syndrome, and aberrant tissue band syndrome [38].

Fetal ultrasonography is the main modality for antenatal detection. Serum alpha-fetoprotein is not usually raised because of the closed nature of this NTD. For postnatal diagnosis, CT scan provides information primarily about the bony defect, while MRI depicts the nature of herniated contents, details of the cranial defect, and other associated intracranial anomalies like Chiari malformation, aqueductal stenosis, corpus callosum agenesis, etc.

Surgery is done on an elective basis, as soon as feasible. An urgent repair is indicated if there is a rupture of sac or excoriation of overlying skin, which can cause CSF leak and predispose to the risk of developing meningitis. This makes it necessary for urgent repair [37]. In cases with large skull bone defects, cranioplasty may be required along with split thickness graft to restore complete closure of the defect.

Pediatric age group, associated anomalies, possible difficult airway, and positioning make anesthesia for this group quite challenging. Preanesthetic evaluation consists of complete history and examination of all systems. Other coexisting congenital anomalies, especially cardiac, pulmonary, and renal, should be completely evaluated because of the associated anesthesia risk.

Investigations include hemogram and electrolyte and renal function tests. Head CT shows the bony defect with herniation of neural tissue and the presence of hydrocephalus, if any. Brain MRI gives detailed information about other coexisting cranial malformations and hydrocephalus. An adequate amount of blood has to be arranged preoperatively.

Anesthesia technique: Sedative premedication should not be administered to these children. If fiber-optic bronchoscopy is planned, a dose of antisialagogue may be administered. Anesthesia technique must be planned according to the site and size of encephalocele, anticipated difficult mask ventilation, or intubation. Mask ventilation may be difficult in cases having large frontonasal encephalocele [39]. Compression of a frontonasal sac by face mask or of occipital sac during positioning has to be avoided in all cases. Undue pressure on the sac can increase the pressure on vital brain structures, raise ICP, and can rarely cause rupture of the sac. An occipital sac makes head extension and positioning difficult making intubation difficult. It is more difficult to attain an optimum position for intubation in a child with hydrocephalus and a large head. In children with occipital encephalocele, various positions used for induction and intubation are lateral decubitus, supine with swelling resting inside a doughnut, or head held beyond the table's edge with an assistant holding it. In children with giant encephalocele, the drainage of CSF from the sac before anesthesia induction helps make the swelling slack and makes positioning easier for mask ventilation and intubation [40]. An assortment of pediatric difficult airway equipment should always be kept ready to deal with a difficult airway. It has been experienced that laryngoscopy performed by a right-handed anesthesiologist in a patient placed in left-lateral position is easier [41]. In a retrospective study, difficult mask ventilation and intubation incidences were 5.9% and 19.5%, respectively [42]. Nasal intubation should not be attempted in intranasal encephalocele or basal encephaloceles. Inhalational induction with sevoflurane is advantageous as its rapid wash-off enables early awakening if the difficult airway is encountered. A practice of check laryngoscopy in lateral position after inhalational induction and administration of muscle relaxants only after visualization of the glottis safeguards against failed intubation [43]. For maintenance of anesthesia, short-acting volatile anesthetic agents are preferred. Intraoperative complications like hypotension, bradycardia/tachycardia, and hypothermia may be commonly seen. Rapid drainage of CSF from the encephalocele sac during surgery may result in hypotension, bradycardia, and even cardiac arrest. To avoid it, controlled drain-

age of CSF is always advocated. Other causes of refractory hypotension can be pituitary-hypothalamic insufficiency, hypothyroidism, and adrenal insufficiency, which may be seen in transsphenoidal encephalocele. Hypotension may require correction with fluids and vasopressors, even if it is secondary to loss of third space fluid. Poorly developed autonomic control may fail to retain body heat, thus accentuating hypothermia. Blood loss may occur during dissection of the large sac, cutting through suboccipital bone, damage to contents of sac like blood vessels or venous sinuses; and it requires urgent replacement. Other intraoperative complications secondary to prone position like dislodgement of tube, cannula, and catheters, increased abdominal pressure, and venous air embolism may also be encountered. Postoperatively, if all parameters are normal, the trachea is usually extubated once the child is fully awake and breathing well. In a few patients, mechanical ventilation may be required secondary to inadequate recovery, hypothermia, hemodynamic instability, respiratory complications, or other metabolic reasons. Apneic episodes in the postoperative period may occur and should be watched for in an ICU. Common postoperative complications seen are the development of hydrocephalus, cerebrospinal fluid leak, and meningitis. The prognosis of these patients depends upon the presence or absence of brain tissue within the herniated sac. If grossly herniated brain is damaged and gliotic, then the prognosis remains usually poor.

13.6 Conclusion

Neural tube defect is a worldwide common congenital anomaly affecting the most vulnerable small children. This pediatric population requires specialized anesthetic care for dealing with associated congenital anomalies, difficult airway, atypical positioning, and cardiorespiratory disturbances. These children may present for repeated surgeries and have a protracted course of the disease, often requiring a multispeciality medical team.

Conflict of Interest None.

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Anesthesia for Fetal Neurosurgery

14

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Key Points

- Meningomyelocele repair is the most commonly performed neurosurgical intervention in the fetus, which can be performed via either an open approach or minimally invasive fetoscopic approach.
- Careful consideration of fetal and maternal physiology, maternal comorbidities, anesthetic and analgesic needs of both the mother and the fetus, and adequacy of uterine relaxation are some of the important aspects of anesthetic management of fetal neurosurgical intervention.
- Fetal interventions can impart significant risks to the mother and the fetus, which should be carefully considered prior to offering fetal intervention as a treatment modality.
- Fetal neurosurgery should be carried out by a multidisciplinary team in a tertiary care center capable of managing preterm infants.

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14.1 Introduction

Prenatal diagnosis of various congenital abnormalities became feasible with the advancement in obstetric ultrasonography techniques. Fetal surgeries were developed to improve the postnatal outcome by early intervention in a very select group of prenatal defects. The first attempt at fetal surgery was performed in the early 1980s by creating bilateral ureterostomies to relieve urinary obstruction in a case of congenital hydronephrosis [1]. Widespread use of prenatal ultrasound in the 1980s led to increase in the diagnosis of prenatal hydrocephalus and various attempts to treat the hydrocephalus early by means of fetal interventions. Initial attempts to treat congenital hydrocephalus were aimed at reducing the hydrocephalus by ventriculo-amniotic shunting and repeated cephalocentesis. Multiple case reports of successful insertion of fetal ventriculo-amniotic shunt as early as 1981 have been attempted to treat congenital hydrocephalus [2]. Unfortunately, many of these fetuses had associated congenital anomalies, which led to poor postnatal outcomes despite the prenatal interventions. The first annual meeting of International Fetal Medicine and Surgery Society held in 1982 outlined the criteria for invasive fetal treatment and the creation of an international fetal treatment registry [3]. The scope of fetal neurosurgery has grown considerably since then with the advancement of diagnostic, surgical, and anes-

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thetic techniques to include more complex intrauterine interventions.

14.2 Fetal Surgeries in General

Fetal interventions are separated into three main categories: minimally invasive procedures, mid-gestation procedures, and EXIT (ex utero intrapartum treatment) procedures. Minimally invasive procedures are performed fetoscopically through the use of trocars and dependence on ultrasonography to access the fetus for endoscopic intervention. The most commonly performed minimally invasive procedure is selective fetoscopic laser photocoagulation (SFLP) for the treatment of twin-to-twin transfusion syndrome (TTTS) (Table 14.1).

14.3 Fetal Neurosurgery

Fetal neurosurgical interventions in humans have been attempted since 1981 with initial attempts at repeated percutaneous needle aspiration as a treatment for hydrocephalus [4]. This was followed by the insertion of ventriculo-amniotic shunts [2, 5]. However, the fetal outcome in either modality was not encouraging. Initial attempts at fetoscopic repair of meningomyelocele (MMC) were also met with poor outcomes. One of the important landmarks in fetal neurosurgery is the Management of Myelomeningocele Study (MOMS) trial, which was published in 2011; it showed significant benefits of fetal intervention compared to the postnatal repair of MMC [6]. This led to the widespread adoption of fetal repair of MMC and fetal centers' opening to perform these interventions. Other neurosurgical fetal interventions such as endoscopic third ventriculostomy for the management of hydrocephalus and embolization of vein of Galen malformation are presently in the experimental stage limited to very selected cases in highly experienced centers.

Table 14.1 Common fetal malformations and interventions

Fetal malformation	Intervention
Twin-to-twin transfusion syndrome (TTTS)	Serial amnio-reduction, selective fetoscopic laser photocoagulation (SFLP), selective fetal reduction by radiofrequency ablation or fetoscopic cord coagulation
Twin reverse arterial perfusion (TRAP) sequence	Selective fetal reduction by radiofrequency ablation or fetoscopic cord coagulation
Lower urinary tract obstruction/posterior urethral valves (PUV)	Vesicoamniotic shunt, fetoscopic ablation, open fetal vesicostomy
Congenital pulmonary airway malformation	Serial thoracentesis, fetoscopic thoracoamniotic shunt placement, selective lobectomy, EXIT-to-resection
Congenital diaphragmatic hernia (CDH)	Fetal endoscopic tracheal occlusion (FETO), EXIT-to-airway, EXIT-to-resection
Amniotic band syndrome	Laser release of amniotic bands
Critical aortic stenosis with hypoplastic left heart syndrome (HLHS)	Aortic balloon valvuloplasty
HLHS with restrictive or intact atrial septum	Atrial septostomy with balloon or stent, EXIT-to-ECMO
Meningomyelocele (MMC)	Open or fetoscopic MMC repair
Sacrococcygeal teratoma	Open tumor debulking

Adapted from Hoagland et al. [32]

14.4 Ventriculo-Amniotic Shunt for Hydrocephalus

The initial attempts of antenatal treatment of hydrocephalus include repeated ultrasound-guided percutaneous cephalocentesis to reduce the intracranial CSF volume. Unfortunately, other coexisting congenital abnormalities led to a poor postnatal outcome [4]. Soon after, ventriculo-amniotic shunt placement for hydrocephalus treatment was developed as a possible

treatment for hydrocephalus [5]. However, these procedures' outcomes were poor secondary to unrecognized central nervous system (CNS) anomalies or shunt failure and migration. The reported incidence of associated CNS anomalies ranged between 70 and 84%, with many of these anomalies undetected during the prenatal period. Isolated ventriculomegaly without associated CNS anomalies, with an estimated 4–14% incidence, is one example of a condition that may benefit from a ventriculo-amniotic shunt [7]. The criteria to perform a ventriculo-amniotic shunt should include isolated progressive ventriculomegaly, early diagnosis (preferably within 28 weeks of gestation to minimize the risk of irreversible brain damage), progressive ventricular dilation, and exclusion of other anomalies by fetal MRI and karyotyping. Reports of the few selected cases of isolated ventriculomegaly treated with prenatal shunts, however, continue to show poor outcomes [8]. Currently, the role of prenatal VAS in the management of hydrocephalus is in experimental stage. Endoscopic third ventriculostomy (ETV) is another experimental alternative fetal therapy for isolated ventriculomegaly [9].

14.5 Meningomyelocele Repair

Meningomyelocele (MMC) is the most common form of neural tube defect, with a reported 3.5 per 10,000 pregnancies in the United States [10]. MMC develops when the neural tube fails to close around 3–4 weeks of gestational age and can be associated with Arnold-Chiari malformation, obstructive hydrocephalus, hindbrain herniation, motor and sensory deficiency, loss of bowel and bladder control, tethered cord syndrome, and developmental delay. The concept of early fetal intervention stemmed from the hypothesis of a *two-hit hypothesis* in which neural injury stems from the failure to close the neural tube followed by the prolonged exposure of the neural tissue to the intrauterine environment worsening it [11]. Closing the neural tube defect early minimizes the neural tissue exposure to the amniotic fluid and is thought to improve neurological outcomes. Hindbrain herniation and Chiari II malformation can be reversed with fetal MMC repair [12]. The initial fetal MMC repairs were attempted in 1997 using a fetoscopic approach [13]. This approach was promptly abandoned due to poor outcomes and technical limitations [14]. Following this, standard closure of MMC repair through a maternal laparotomy and hysterotomy was adopted with encouraging results, which led to the Management of Myelomeningocele Study (MOMS), which compared the outcomes between prenatal and postnatal repair of MMC [6, 15, 16]. Pregnant women above the age of 18 years with a singleton fetus diagnosed with MMC between the T1 and S1 level, with a normal karyotype, were randomized between 19 and 26 weeks of pregnancy to undergo mid-gestation open fetal repair or postnatal repair. This MOMS trial was prematurely suspended after enrolling 183 patients (targeted for 200 patients) due to the superior efficacy of fetal surgery in reducing the need for a ventriculoperitoneal (VP) shunt by 50% and improving the motor outcomes at 30 months of age, when compared to postnatal repair in the interim analysis. Mothers in the MOMS trial who had prenatal surgery did experience a significantly greater obstetrical complication rate than noted in the postnatal surgery group, including chorioamniotic separation, pulmonary edema, oligohydramnios, placental abruption, spontaneous rupture of membranes, spontaneous labor, blood transfusion, and uterine dehiscence.

14.5.1 Open Approach

Open meningomyelocele repair involves maternal laparotomy followed by hysterotomy to deliver part of the fetus for repair. Maternal laparotomy typically involves a low transverse (modified Pfannenstiel) incision or a midline laparatomy

followed by exteriorization of the uterus. At this point, uterine relaxation is achieved with the combination of volatile anesthetic agents and intravenous magnesium sulfate bolus followed by infusion. Supplemental doses of nitroglycerin can be used as needed to aid the uterine relaxation. A small hysterotomy incision is made after confirmation of the placental location. The risk of massive hemorrhage is high at this point due to the highly vascular and atonic uterus. Surgeons use a stapling device to extend the hysterotomy incision to reduce the risk of bleeding. The lumbar region of the fetus is exposed, and the MMC repair is carried out by the neurosurgeon using a patch with a large defect or through a primary closure with a smaller defect. A continuous warm crystalloid infusion into the uterus is given to maintain normothermia and a tamponade effect on the placenta. Following the MMC repair, a multiple layer closure is performed, followed by the laparotomy incision closure. This open approach carries significant risks, including preterm labor, bleeding, uterine dehiscence and rupture, pulmonary edema, chorio-amnionic membrane separation, placental abruption, placenta accreta, and the need for cesarean sections for future deliveries.

14.5.2 Fetoscopic Approach

The major concern with open fetal surgery is the associated maternal and fetal risk secondary to preterm delivery, uterine dehiscence, and the need for life-long cesarean delivery. This reinvigorated a renewed interest among the international fetal community in the fetoscopic approach to attempt to minimize the risk of maternal complications. Currently, two different types of fetoscopic approaches are described: percutaneous fetoscopic surgery and laparotomy-assisted fetoscopic surgery (Fig. 14.1).

The trocars are placed through the abdominal and uterine wall under ultrasound guidance in the entirely percutaneous approach. The advantages include minimal postoperative pain and avoidance of routine tocolysis [17]. The average gestational age for delivery reaches 33 weeks after the percutaneous fetoscopic approach, but the risk of preterm premature rupture of the membranes (PPROM) is very high (80%) [18, 19]. In the **laparotomy-based approach**, a uterus is exteriorized after a maternal laparotomy. Fetal access to MMC repair is gained by strategically placing the trocars through the uterine wall with ultrasound guidance. The expectation of significant postop-

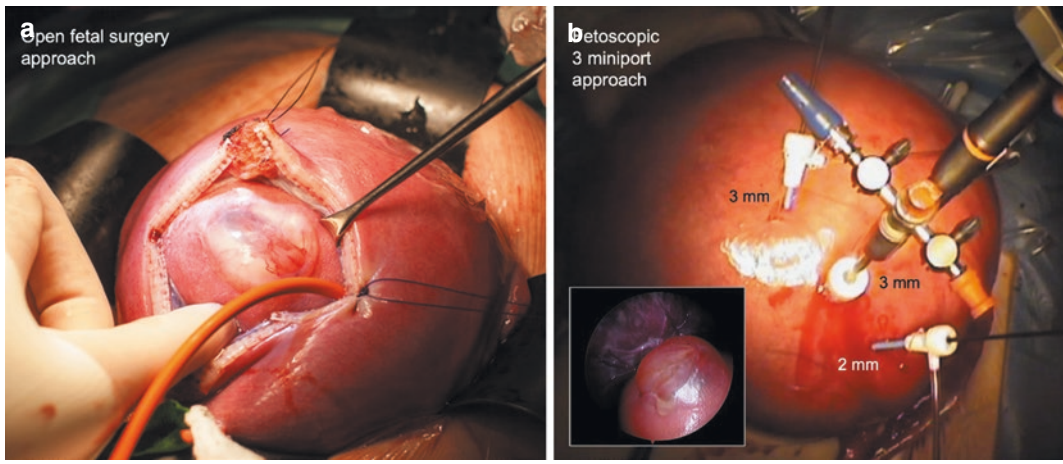

Fig. 14.1 Fetal neurosurgery with (**a**) open and (**b**) fetoscopic approaches. [Courtesy: Dr. Jose L. Peiro MD PhD MBA, Cincinnati Fetal Care Center, USA]

erative pain requires a multimodel pain management strategy that often includes a preoperative high lumbar or low thoracic epidural catheter placement. In the laparotomy approach, the risk of PPROM is low (33%) compared to the percutaneous approach, and the average gestational age at delivery is improved to 36–37 weeks [20, 21]. The risk of fetal acidemia from intrauterine CO_2 insufflation is minimal, and using humidified CO_2 for insufflation is beneficial [22].

14.5.3 Maternal and Fetal Physiology

Fetal MMC repairs are typically scheduled in the second trimester between 19 and 26 weeks of gestation. Several physiologic changes need to be considered, which can significantly affect the anesthetic management during this time [23]. While a complete description of the physiologic changes are beyond the scope of this chapter, the most relevant descriptions of maternal (Table 14.2) and fetal (Table 14.3) changes along with their anesthetic implications are enlisted.

Table 14.2 Maternal physiologic changes and anesthetic implications

Physiologic changes	Anesthetic implication
Cardiovascular system Increased in intravascular volume, cardiac output, heart rate, and stroke volume; decrease in systemic vascular resistance Aortocaval compression (caval compression as early as 16 weeks)	Exaggerated hypotension will likely need vasopressors to maintain uteroplacental perfusion Left lateral tilt by wedge under the right hip to minimize IVC compression
Respiratory system Mucosal engorgement Increased minute ventilation, decreased functional residual capacity, increased oxygen consumption Need for postoperative tocolytics compromise ability to administer generous intravenous fluids. Risk for pulmonary edema postoperatively	Potential for difficult airway, need for smaller endotracheal tubes, adequate preoxygenation necessary
Gastrointestinal system Stomach displacement, decreased lower esophageal sphincter tone	Aspiration risk
Hematology Physiologic anemia of pregnancy, gestational thrombocytopenia, hypercoagulable state	Risk of bleeding as well as deep vein thrombosis (DVT), caution with regional anesthesia

14.6 Anesthetic Management

14.6.1 Preoperative Preparation

Fetal interventions should be taken place in a specialized fetal center capable of performing emergent cesarian sections as well as taking care of extremely premature babies. The multidisciplinary team consists of providers from various fields, including maternal and fetal medicine, pediatric surgery, neurosurgery, anesthesiology, neonatology, pediatric cardiology, maternal and fetal nursing, and social workers. The patient should undergo extensive counseling regarding the risks and benefits of fetal surgery, and the same should be documented appropriately. It is also recommended that the patient should be residing close to the specialized center after the fetal intervention for close observation and to be able to reach the fetal center quickly for any emergencies such as premature labor.

14.6.2 Maternal Evaluation

Patients should be healthy ASA 1–2 status without significant comorbidities to be eligible for fetal intervention. Anesthetic management for fetal neurosurgical procedures begins with a focused maternal preoperative evaluation, including medical history and physical examination focused on the airway, cardiac, respiratory, musculoskeletal, and neurological systems. Laboratory studies, including complete blood count, electrolyte and coagulation studies, and blood typing and cross-matching, should be ordered as indicated. An electrocardiogram and an echocardiogram may be considered to evaluate patients with cardiovascular concerns. The proposed anesthetic plan along with the risks of

Table 14.3 Fetal physiology and anesthetic implications

Physiologic considerations	Anesthetic implications
Cardiovascular Uteroplacental blood flow is directly proportional to uterine perfusion pressure and inversely proportional to uterine vascular resistance	Maternal hypotension decreases uteroplacental blood flow and fetal oxygen delivery
Hematologic Higher blood volume per kg body weight and placenta accounts for 2/3 of fetoplacental blood volume Maternal coagulation factors do not cross the placenta, and the liver is immature to produce adequate coagulation factors	Need more volume to achieve euvolemia Fetus is more prone for bleeding
Thermoregulation Unable to thermoregulate, dependent on maternal temperature	Continuous infusion of warm crystalloid solution into the amniotic cavity during open fetal repairs imperative to maintain normothermia
Nervous system Parasympathetic system is dominant and plays an important role in hemodynamic stability Stress response to noxious stimuli develops as early as 18 weeks, and cortical response to pain develops between 24 and 30 weeks	Fetal bradycardia is an early warning sign of fetal distress Fetal analgesia should be considered to minimize fetal pain perception and stress response

general and regional anesthesia should be discussed by the anesthesiologist in detail.

14.6.3 Fetal Evaluation

The fetal evaluation includes the estimation of gestational age and weight, multiple or singleton pregnancy, prior procedures (e.g., amnioreduction, thoracoabdominal shunt), fetal echocardiogram findings, karyotype (if completed), and other significant ultrasound and fetal ultrafast MRI findings. Fetal blood products consisting of 15–20 ml/kg O negative PRBCs should be available.

14.6.4 Operating Room Setup and Monitoring

Room setup on the day of the surgery should include a routine anesthesia machine check and a desflurane vaporizer. In addition to the standard ASA monitors, including temperature probe, an arterial line for hemodynamic monitoring and a bispectral index (BIS) monitor to assess anesthetic depth should be available. Two intravenous (IV) line setups with filter and/or warmer appropriate for blood transfusion as needed should be ready. Difficult airway equipment, including a video laryngoscope and/or fiberoptic scope, should be available if needed. An orogastric tube should be available to decompress the stomach after intubation.

14.6.5 Fetal Supplies

A second pulse oximeter monitor should be available for the fetus. A peripheral IV line with in-line volumetric cylinder tubing such as Buretrol® primed with normal saline and 24G angiocaths should be available in the event a fetal IV line needs to be established. Tubing and filter appropriate for blood transfusion should be in the room if fetal blood transfusion is warranted. Lastly, a fetal echocardiography machine should also be available as intermittent fetal cardiac echocardiography may be needed to be performed during the case to assess the volume status and well-being of the fetus.

14.6.6 Medications

Preoperatively the mother should receive oral non-particulate antacid such as bicitra to increase the pH of stomach contents and metoclopramide to promote gastric emptying. Anxiolytics to reduce maternal anxiety can be considered in the form of short-acting benzodiazepine such as midazolam before the administration of regional anesthesia.

Table 14.4 Commonly used maternal medications for fetal neurosurgery

Medications	
Premedication	Midazolam for anxiolysis, Bicitra and metoclopramide for anti-aspiration prophylaxis
Induction agents	Propofol
Muscle relaxants	Succinylcholine for rapid sequence induction, NDMR for maintenance
Opioids	Fentanyl, Morphine (preservative-free for neuraxial use)
Maintenance	Desflurane for uterine relaxation, Propofol infusion
Local anesthetics	0.2% Ropivacaine
Uterine relaxants	Magnesium sulfate, Nitroglycerine, Terbutaline (see Table 14.5)
Vasopressors	Phenylephrine and ephedrine bolus, Phenylephrine infusion
Emergency medications	Atropine and epinephrine
Antibiotics	Per surgeon

The most commonly used maternal medications for this surgery are outlined in Table 14.4. It may be of use to have a pre-made fetal anesthesia kit available, which contains commonly used medications.

14.6.7 Intraoperative Anesthetic Management

It is imperative that before the scheduled fetal intervention, a multidisciplinary team meeting involving all the providers to be held outlining the patient's preoperative condition, planned intervention, planned anesthetic management, maternal wishes regarding fetal resuscitation in case of emergent delivery, and any other safety concerns.

Typical anesthetic management includes placement of an epidural catheter awake followed by induction of general anesthesia. The epidural catheter is placed in the low thoracic or high lumbar (between T10 and L1) region for postoperative pain control and tested with 3 cc of 1.5% lidocaine with 1:200,000 epinephrine. The epidural should not be dosed at this time to avoid exacerbated hypotension during the intraoperative period due to high-dose volatiles, magnesium, and nitroglycerine boluses. Fentanyl and/or additional midazolam may be given as needed for pain or anxiolysis related to epidural placement.

The mother is then placed in the supine position with left uterine displacement by placing a roll under the right hip. General anesthesia is induced with a rapid sequence induction technique after adequate preoxygenation to minimize the risk of aspiration. Once the airway has been secured, a second IV line, arterial line, orogastric tube, temperature probe, BIS monitor, compression boots, and Foley catheter can be placed.

During the procedure, maintenance of anesthesia is accomplished with a combination of volatile anesthetic (desflurane 4–6%) and IV anesthetic agent such as a propofol infusion (started at 50 μg/kg/min) until the uterus is exposed. At this point, the propofol infusion is turned off, and volatile anesthetic concentration is increased to aid in the uterine relaxation. As blood pressure correlates with uteroplacental perfusion and thus fetal oxygenation, the goal should be to maintain maternal systolic blood pressure (SBP) >100 mmHg or mean arterial pressure (MAP) within 10–20% of baseline. Ephedrine (5–10 mg IV) boluses and/or phenylephrine (50–100 μg IV) boluses of phenylephrine infusion may be needed to achieve this goal. Unless there is excessive blood loss, IV fluid administration should be limited to a maximum of 1–1.5 L of crystalloid fluid to minimize the risk of postoperative maternal pulmonary edema.

14.6.8 Uterine Relaxation

Inadequate uterine relaxation can lead to umbilical cord compression and abruptio placenta. Adequate uterine relaxation should be maintained throughout the procedure. Surgical palpation of the uterus is the gold standard to assess for the degree of uterine relaxation. Multiple medications in combination, such as halogenated anesthetic agents, nitroglycerin, beta-adrenergic agonists like albuterol and terbutaline, magnesium sulfate, and oxytocin antagonist atosiban, are used to minimize the adverse effects on the mother, such

as hemodynamic instability. Among the halogenated agents, desflurane seems to be the most potent uterine relaxant secondary to its potent Na^+ channel blocking effects. Magnesium sulfate 4–6 gm IV bolus is given over 20 min upon laparotomy incision, followed by a 2–4 gm/hr infusion to assist in this effort. This should allow for a decreased volatile anesthetic concentration and thus avoid large swings in hemodynamics. Adequacy of uterine relaxation and magnesium sulfate dose should be confirmed with the maternal-fetal medicine (MFM) team. Serum Magnesium level is checked 30 min after the initial bolus is given and then every 2 hours thereafter to avoid magnesium toxicity. For continued increased uterine tone, nitroglycerin boluses (30–50 μg at a time) or an infusion titrated up to 10 μg/kg/min can be started. If additional uterine relaxation is needed after the aforementioned interventions, the volatile anesthetic agent concentration may be increased as necessary (Table 14.5).

During an open laparotomy procedure, hysterotomy is performed using a stapling device to minimize blood loss. If the case is performed fetoscopically, the uterus is insufflated with CO_2, and two to three ports are placed in the uterus (Fig. 14.1). Vigilance for detecting maternal bleeding (e.g., due to placental laceration, abruption) is critical, and frequent communication with the surgical team is imperative to the success of these procedures.

14.6.9 Fetal Anesthesia and Analgesia

Even though it is difficult to predict whether fetus can perceive pain, it seems prudent to provide analgesia to minimize the stress response and ensure immobility during the surgery. Functional spinal reflexes are present in the fetus by 19 weeks of gestation, cutaneous nociceptive receptors and spinothalamic tracts are fully developed after 20 weeks, and thalamocortical tracts are developed after 26–30 weeks [24]. The fetus is shown to produce stress hormonal responses such as increased plasma cortisol and beta-endorphin to painful stimuli [25]. Fetal anesthesia is primarily provided by the transfer of maternal volatile anesthetics through placental circulation. Upon fetal exposure, a fetal intramuscular (IM) cocktail (fentanyl 20 μg/kg, atropine 20 μg/kg, and vecuronium 0.2 mg/kg) is administered by the surgeon to ensure fetal immobility and analgesia. This medication is prepared by the anesthesia team and handed to the surgical team in a sterile manner at the beginning of the procedure.

At the end of fetal procedure, the fetus is returned to the uterine cavity, and the hysterotomy is sutured. The uterine ports are closed if the procedure was performed via fetoscopic approach. The volatile agent should be decreased at this point in the procedure, and the epidural should be loaded with 0.2% ropivacaine 10–20 ml and preservative-free morphine 3–4 mg per epidural. Magnesium sulfate infusion is usually continued and adjusted as needed after a discussion with the MFM team. Other pain control and antiemetic medications including acetaminophen 15 mg/kg and ondansetron 0.1 mg/kg IV can be given at this time. Neuromuscular blockade can be reversed with neostigmine and glycopyrrolate or sugammadex. The patient is then allowed to safely emerge from anesthesia and be extubated once fully awake to reduce aspiration risk.

Table 14.5 Uterine relaxants

Drug	Dose
Volatile anesthetics	Titrate between 1.5 and 3 MAC as tolerated by hemodynamics
Magnesium sulfate	4–6 gm bolus over 30 min followed by 2 gm infusion
Nitroglycerine	10–30 μg intermittent bolus; 2–10 μg/kg/min infusion
Terbutaline	0.25 mg subcutaneously every 4 hrs
Atosiban	6.75 mg (bolus); 300 μg/min (3 h); 100 μg/min (45 h)

14.6.10 Postoperative Anesthetic Management

Postoperatively, the mother will be transferred to postanesthesia care area for routine monitoring. The epidural block should be maintained for postoperative pain control. Care in the postanesthesia care area should include monitoring and

maintenance of normal vital signs and tocodynamometry and fetal heart rate documentation. The mother should remain in the supine position with left uterine displacement. Once the patient has fully recovered from anesthesia and can tolerate clear liquids, the diet may be advanced as tolerated.

Continuous infusion of low concentration of local anesthetic medication such as 0.2% ropivacaine at a rate of 10–12 ml/hr. through the epidural catheter should be continued up to postoperative day two to ensure adequate pain control. IV acetaminophen 15 mg/kg (maximum 1 gram) every 6 hours is continued for up to 3 days or transitioned to oral acetaminophen if the pain is well controlled. Oral opioids such as oxycodone 0.1 mg/kg every 4 hours may be initiated once the patient tolerates oral intake. After discussion with the fetal surgery and MFM teams, and if postoperative pain is well controlled, the epidural catheter may be removed on the morning of postoperative day two. The timing of epidural removal should be considered in the context of pharmacologic venous thromboembolism (VTE) prophylaxis administration if applicable. Lastly, the Foley catheter can be removed 4 hours after epidural removal to help facilitate early ambulation and minimize discomfort and infection risk.

14.7 Outcome and Future Directions

The decreased need for VPS placement and improved neurological outcomes are the primary outcomes of validating prenatal MMC repairs despite the increased risk of prematurity and maternal risks. Endoscopic third ventriculostomy (ETV) is an alternative technique with comparable 1-year failure-free survival rate to VPS placement. MOMS trial final update reports that prenatal repair in fetus with ventriculomegaly of 15 mm or larger does not improve outcomes [26]. As the postnatal treatment options for ventriculomegaly improve with time, the guidelines for prenatal repairs should reflect those changes. The most common cause of death in patients with MMC is renal failure [27]. A supplementary study by MOMS trial investigators found that at 30 months follow-up, there is no significant difference in mortality or requirement of clean intermittent catheterization between the prenatal and postnatal repair groups. Long-term follow-up of prenatal MMC repair patients is needed to compare renal failure and related mortality in patients surviving into adulthood [28]. Regarding maternal complications and preterm births, minimally invasive fetoscopic repair allows for future vaginal deliveries and reduces the risk of uterine dehiscence. Meta-analysis studies report that minimally invasive repair has a higher rate of premature births and obstetrical complications, and a similar VP shunt placement rate compared to the open repair groups [29, 30]. Prospective randomized control studies are needed comparing maternal complications and preterm births between open and fetoscopic repair. Cell-based therapies utilizing mesenchymal stem cells and fibroblast growth factors to augment or replace invasive repair are currently being studied in various fetal centers and shown to improve neurological functions and ability ambulate in ovine models [31]. It is still to be determined if anesthesia affects the developing fetal brain when administered for these cases. Effects of fetal anesthesia on postnatal cognitive function are currently unknown, and underlying cognitive dysfunction in MMC patients makes it difficult to estimate the effects of anesthesia per se.

14.8 Ethical and Legal Considerations

Current data indicates that the patients undergoing fetal intervention are delivering prematurely compared to postnatal intervention, and the risks associated with prematurity must be clearly explained to the parents. Similarly, the mother undergoing the open fetal repair must be explained about the future need for cesarean sections and associated risks. MOMS trial had strict inclusion criteria for patient selection for fetal intervention. As the outcome of fetal intervention gets better, further trials are needed to include patients with comorbidities. Outcomes at centers

with limited experience may not be comparable to the high volume centers. Similarly, we still have limited data on fetoscopic repair, potentially increasing maternal complications and preterm births. Legal considerations regarding whether paternal consent is needed to operate on the fetus can vary depending on jurisdiction and country, and clear guidelines need to be established regarding the scope of maternal capacity to refuse the procedure due to increased personal risk if future studies demonstrate clear benefits of the prenatal intervention to the fetus.

14.9 Conclusion

Anesthesia for fetal surgery remains a reasonably new area within the field of anesthesiology. The MOMS trial's success provided some future direction, but additional data is needed for the fetoscopic repair. Anesthetic management of fetal surgery is currently being performed under the guidance of teams consisting of either pediatric or obstetric anesthesiologists. While there are established fetal centers globally, there has been a recent push for new centers to open and offer these services. While fetal surgery for neurosurgical defects is a promising field and has demonstrated success with MMC defects, there are complicating factors to be taken into account before considering fetal interventions. Standard guidelines for fetal anesthesia need to be constantly updated with new findings. Before any fetal intervention, careful assessment of fetal benefit should be considered against the risks to mother and fetus.

Conflict of Interest Nil.

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15 Perioperative Management of Children with Chiari Malformation

Varun Jain, Kashmiri Doley, and Sumit Sinha

Key Points

- Chiari malformation is a group of congenital malformations of the hindbrain and spinal cord associated with a constellation of symptoms due to compression of the medulla, lower cranial nerves, or flow obstruction to the cerebrospinal fluid (CSF).
- Chiari I malformation is more common and diagnosed in adolescence or young adulthood.
- Chiari II malformation is associated with an array of spinal cord deformities like tethered cord, meningomyelocele, and hydrocephalus; it is usually diagnosed in infancy or childhood.
- CSF flow obstruction around the foramen magnum may cause symptoms of raised intracranial pressure.
- Foramen magnum decompression is the primary procedure performed to improve CSF flow dynamics.
- Difficult airway, autonomic dysfunctions, and challenging neurosurgical positioning are important anesthetic concerns in these children with the goal of early emergence from anesthesia after the surgery is over.

15.1 Introduction

Chiari malformation is a condition characterized by herniation of the lower part of the brain, namely, the cerebellar tonsils through the foramen magnum into the spinal canal. The malformation was named after Austrian pathologist Prof. Hans Chiari, who described this in a 17-year-old female in 1891 [1]. Arnold-Chiari malformation was named in honor of Chiari and German pathologist Julius Arnold by the latter's pupils after they reported four meningomyelocele cases with alterations in the cerebellum and brainstem in 1907 [2]. However, Cleland was the first to describe Chiari malformation in a child with spina bifida, hydrocephalus, and anatomical variations of the cerebellum and brainstem in 1883 [2]. The prevalence of Chiari malformation is estimated at 1 per 1000 to 1 per 5000 individuals. The majority of Chiari I malformation cases are diagnosed in late childhood to early adulthood. Chiari II malformation is usually diagnosed at birth or in utero due to its association with meningomyelocele.

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15.2 Posterior Cranial Fossa and Cervicomedullary Junction

The posterior cranial fossa is the most inferior part of the cranial cavity and is located between the tentorium cerebelli superiorly and foramen magnum inferiorly. The posterior cranial fossa is occupied mainly by the cerebellum and the brainstem. The foramina present in the bones forming the boundaries of the posterior cranial fossa transmit various important structures through them, including the seventh, eighth, ninth, tenth cranial nerves, the labyrinthine, vertebral, and the anterior and posterior spinal arteries. The medulla crosses the foramen magnum to continue as the spinal cord.

At the foramen magnum level, the CSF usually flows freely around the medulla, forming a CSF cushion that functions as a shock absorber. Normally, a large amount of CSF is collected at the back of the cerebellum in a space called the cisterna magna. The CSF flow dynamics are well maintained due to an unobstructed passage of CSF within the foramen magnum. Any herniation of tissue at this level can partially or completely hamper the CSF flow.

15.3 Pathophysiology of Chiari Malformation

The initiation of Chiari malformation happens due to the underdevelopment of the fetal skull during pregnancy itself. Various theories have been suggested to explain this anomaly. One such theory is the malformation or the overgrowth theory. According to this theory, as the brain grows relatively bigger than the skull during early childhood, there is crowding of the intracranial structures leading to herniation of the cerebellar tonsils through the foramen magnum [3]. Another theory is the hydrodynamic theory, which suggests that the herniated brain tissue blocks the normal flow of CSF, causing pulsating movement through the foramen magnum displacing the tonsils in a downward direction [3, 4]. There is an accumulation of the CSF in the brain and spinal canal, leading to hydrocephalus and syringomyelia.

15.4 Types of Chiari Malformation

Chiari initially described three types of malformation (Type I, Type II, and Type III); Type IV was later added to the classification [5]. Chiari malformations represent a varying spectrum of pathology of maldevelopment of the hindbrain (Table 15.1). Chiari I malformation is the commonest of Chiari malformation due to cerebellar tonsils' descent of more than 5 mm below the foramen magnum (Fig. 15.1). This type is usually the mildest and, therefore, is diagnosed during adolescence or young adulthood. It is associated with spinal syrinx (fluid-filled cavity in the spinal cord) in approximately 50% of cases [6]. Chiari II malformation is the next most common due to cerebellar vermis and lower brainstem herniation below the foramen magnum (Fig. 15.2). This is a pathologically more severe entity and manifests in infancy or early childhood due to associated meningomyelocele, hydrocephalus, tethered cord, and other neurospinal defects. It is described as the "Classic" Chiari malformation or Arnold-Chiari malformation. Up to 98% of children with meningomyelocele can have Chiari II malformation [7]. The occurrence of spinal

Table 15.1 Types of Chiari malformations

Types	Description(s)
Type I	Herniation of cerebellar tonsils >5 mm below the foramen magnum
Type II	Caudal displacement of the cerebellar vermis and lower brainstem (medulla, pons, fourth ventricle)
Type III	Occipital or cervical encephalocele in addition to hindbrain herniation as seen in type II
Type IV	Cerebellar aplasia or hypoplasia
Type 0	Spinal syrinx with no cerebellar herniation (*zero herniation*)
Type 1.5	Tonsillar herniation, as seen in type I but with elongated brainstem and fourth ventricle (*Bulbar variant of Type I*). No neurospinal defects are present
Type V	Cerebellar agenesis with occipital lobe herniation through the foramen magnum

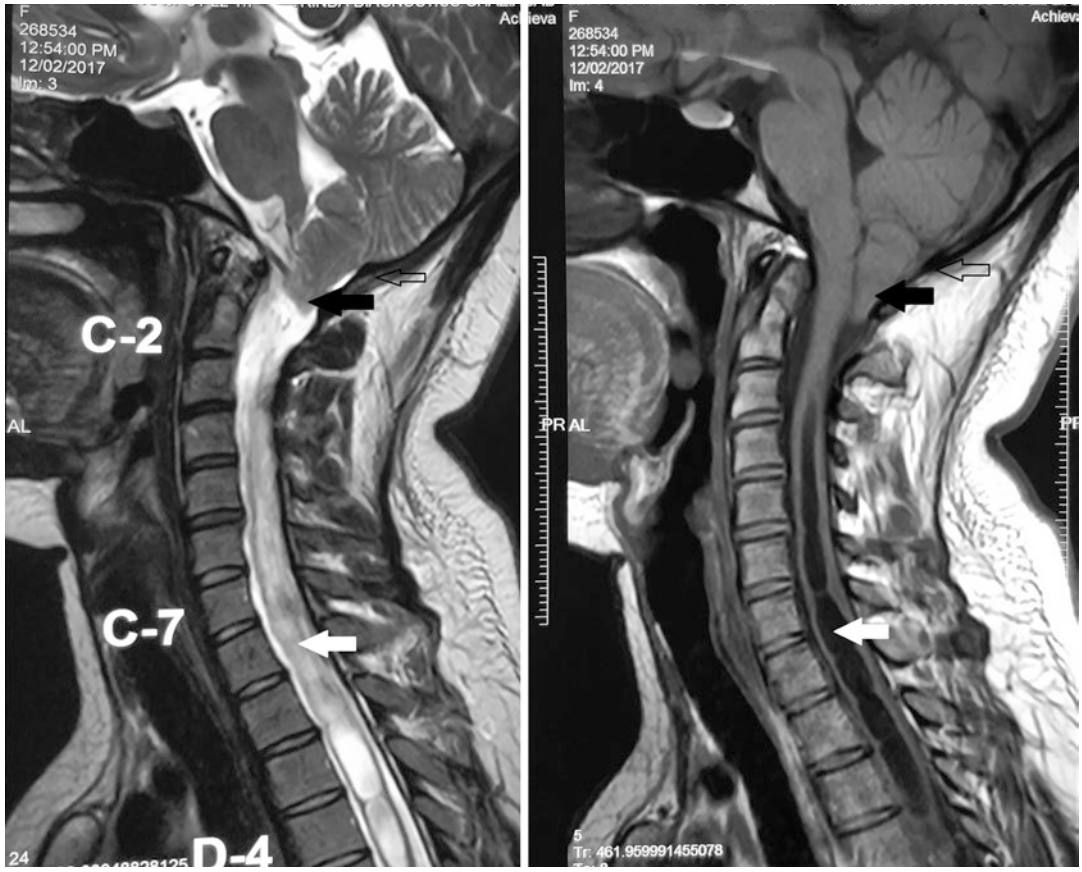

Fig. 15.1 Chiari I malformation; cranio-cervical MRI (T2 sagittal section on the left side, T1 sagittal section on the right side) shows cerebellar herniation (solid black arrow) below the foramen magnum (hollow black arrow) along with cervicothoracic syrinx (solid white arrow)

syrinx with no cerebellar tonsillar herniation is labeled as Chiari 0 malformation [8]. This is usually associated with scoliosis. Chiari Type III may present with occipital or cervical encephalocele (Fig. 15.3). Both Chiari Type III and IV are rare types and have a poor prognosis, usually not compatible with life. The Chiari Type V entity has recently been described with cerebellar agenesis and occipital lobe herniation below the foramen magnum [9].

15.5 Clinical Presentation

Children with Chiari I malformation are mostly asymptomatic and diagnosed incidentally. Symptoms may be varied due to abnormal CSF flow equalization, compression of the brainstem and cerebellar connections, and traction on the lower cranial nerves [10]. Headache (mostly occipital) and neck pain are common and exacerbated by exertion (cough and Valsalva maneuver). Dizziness, fainting, drop attacks, and sinus bradycardia are autonomic dysfunctions due to brainstem compression. Breathing disorders like central sleep apnea and obstructive sleep apnea may be in the initial presentation [11]. The loss of sensitivity to pain and temperature and weakness in the upper torso are due to syringomyelia. The problem in balance and coordination may also happen. Photosensitivity, blurred vision, nystagmus, and diplopia may be associated with visual complaints.

Chiari II presents in infants and younger children as difficulty in swallowing, slow or noisy

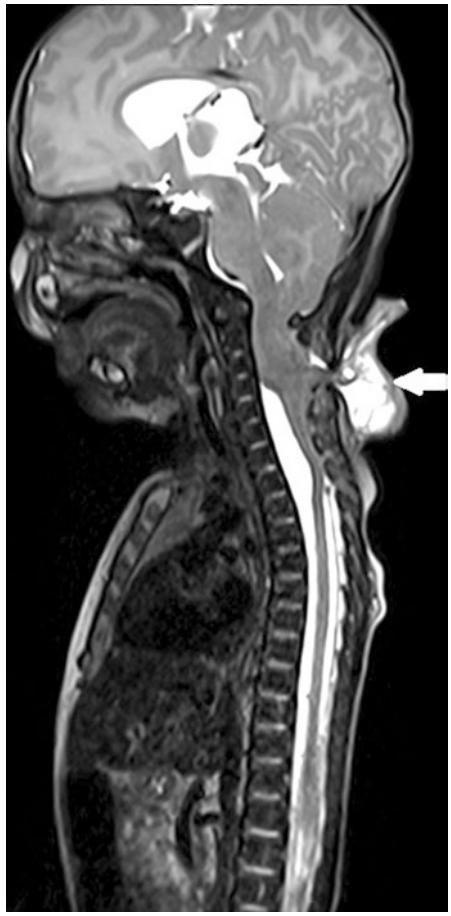

Fig. 15.2 Chiari II malformation; brainstem descent below the foramen magnum along with cervical meningomyelocele (solid white arrow) in MRI whole spine T2 sagittal section

respiration leading to feeding problems, gagging, drooling from the angle of the mouth, and vomiting. Vocal cord impairment has been reported in up to 50% of patients [12]. Compression and traction on the lower cranial nerves, especially the vagus nerve, is the most likely cause of bilateral vocal cord paralysis and stridor [13]. Similarly, sleep apnea may occur in up to 83% of patients [12]. Stridor, apnea, and bradycardia are frequent and severe by 10–12 weeks of age and decrease in severity by 6 months of age [13]. Other common signs can include irritability, headbanging, and night-time awakening. In ACM, the child may present with just a bulge or swelling over the back due to meningomyelocele. Scoliosis may develop due to the tethered cord or because of syringomyelia. Urinary tract abnormalities such as vesicoureteral reflux or hydronephrosis may be present in up to 30% of children with meningomyelocele [14]. Besides these, Chiari malformations can be associated with various syndromes and pathologies (Table 15.2).

15.6 Diagnosis of Chiari Malformations

A definitive diagnosis of Chiari malformation can be made only with a magnetic resonance imaging (MRI) of the brain, which would reveal an abnormal protrusion of the cerebellum toward the spinal canal with or without hydrocephalus [15]. Cerebellar tonsils' descent below the foramen magnum decreases with age [16]. MRI of the spine may also show syrinx within the spinal canal (Fig. 15.1). A CT may not reveal a Chiari malformation, and an X-ray has no role in diagnosing Chiari malformation.

The signs of raised intracranial pressure (ICP) may be delayed in infants due to a more compliant intracranial space attributed to the open fontanelle and cranial sutures. In a few cases, Chiari malformation diagnosis may be incidental as patients with Chiari malformation may remain asymptomatic for a long time before they develop clinical symptoms. ACM can also be detected with ultrasound during pregnancy as early as 12 weeks of gestation. Raised serum alpha-fetoprotein levels are a marker of neural tube defect [17].

15.7 Treatment Options

In asymptomatic children with Chiari malformation and those diagnosed incidentally, a regular follow-up with MRI is usually advised. Symptomatic treatment with pain medication is given for mild headaches; however, surgery remains the definitive treatment (Table 15.3). Surgery benefits children with persistent headache impacting quality of life and large or increasing size of syrinx and in presence of

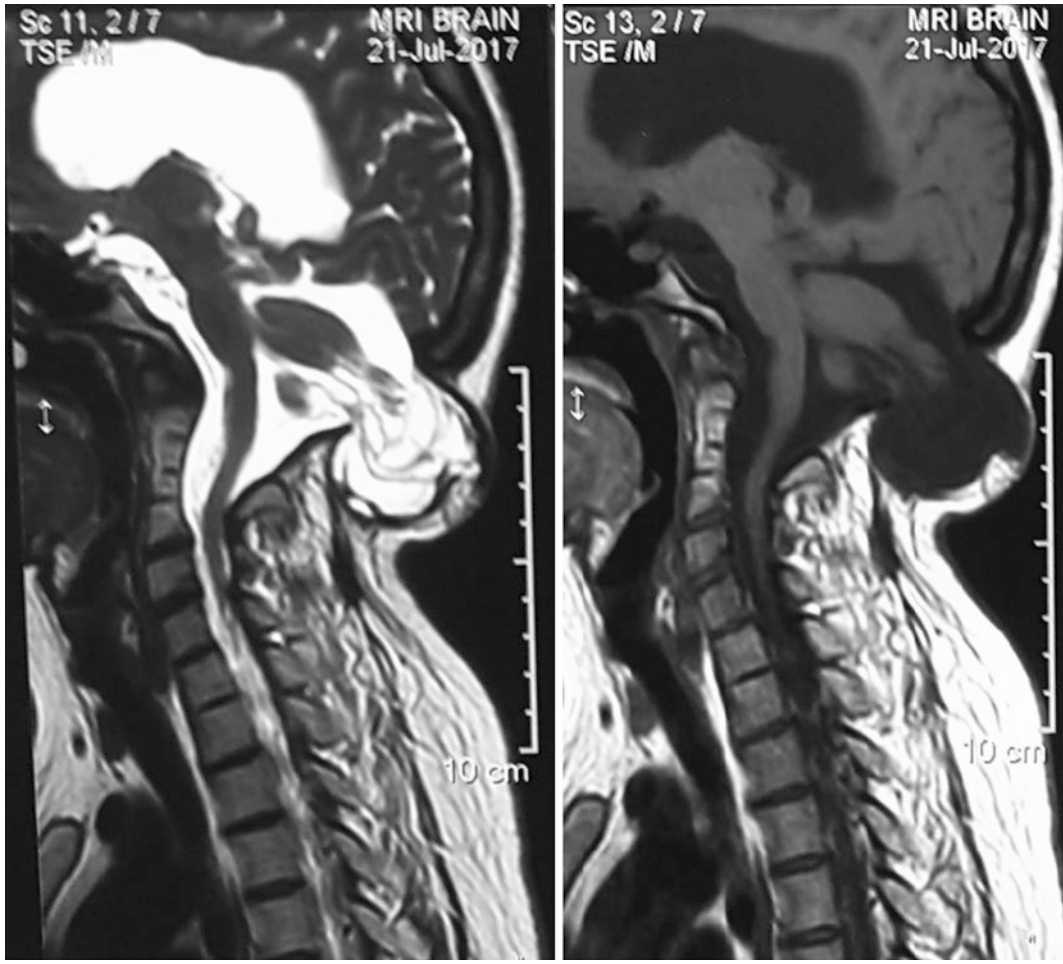

Fig. 15.3 Chiari III malformation with occipital encephalocele (cranio-cervical MRI images: T2 left side, T1 right side)

abnormal neurological findings or presence of myelopathy. The most common surgical procedure performed for Chiari malformation is foramen magnum decompression or posterior fossa decompression surgery with or without duraplasty so as to restore normal CSF dynamics at cervicomedullary junction (CMJ) and relieve pressure on the cerebellum and hindbrain [18, 19]. In the presence of disrupted CSF dynamics, different shunt types and procedures are done to restore CSF flow. Minimally invasive techniques for tonsillectomy and endoscopic decompression of posterior fossa have also been shown to be safe and effective for surgical treatment of Chiari I malformation [20, 21].

Patients with meningoencephalocele require sac removal surgery to prevent meningitis or rupture of the sac. Sometimes, a ventriculoperitoneal (VP) shunt is performed for hydrocephalus prior to the removal of the sac. Infants with mild symptoms often improve with a VP shunt procedure alone, whereas infants with moderate to severe symptoms may require decompression surgery [22, 23]. In principle, associated abnormalities like hydrocephalus, meningomyelocele, tethered filum terminale, syringomyelia, and split cord malformations are treated with the "cranial to spinal rule," i.e., the more cranial abnormality is treated first. The duration of brainstem compression also affects the functional prognosis in Chiari malformation, with better surgi-

Table 15.2 Associated anomalies and syndromes in Chiari malformations

- Diastematomyelia
- Ehlers-Danlos syndrome
- Marfan's syndrome
- Apert syndrome
- Crouzon syndrome
- Jackson-Weiss syndrome
- Achondroplasia
- Osteopetrosis
- Paget's disease
- Neurofibromatosis type I
- Waardenburg syndrome
- Atlantoaxial assimilation
- Caudal regression syndrome
- Klippel-Feil syndrome
- Beckwith-Wiedemann syndrome
- Cystic fibrosis
- Fabry disease
- Pierre-Robin syndrome

cal results seen when surgery is performed within 2 years of symptom onset [24]. However, infants and young children may recover, even if medullary dysfunction is long-standing [25].

15.8 Anesthetic Management

15.8.1 Preoperative Evaluation

Children with Chiari malformation may present for a shunt procedure, sac removal/repair, or a posterior fossa decompression surgery. Those posted for a posterior fossa surgery may have a shunt in situ. It is important to check if the shunt is functioning properly, as a functional shunt reduces the risk of intraoperative raised ICP.

Table 15.3 The surgical treatment options for Chiari malformations and associated neurosurgical problems

Type of Chiari malformation	Primary surgery	Type of foramen magnum decompression (FMD)	Various surgical approaches to dura	Various surgical approaches to arachnoid	Various surgical approaches to cerebellar tonsils
Chiari I	Foramen magnum decompression	Only suboccipital craniectomy	Dura left intact	Arachnoid left intact	Subpial resection of tonsils (*tonsillectomy*)
Chiari II		Suboccipital craniectomy with C1 arch excision	Dura opened and left open	Arachnoid dissection was done and CSF drained	Subpial resection of tonsils with pulling up of tonsils and tethering to overlying dura
			Dura opened and duroplasty done	Meticulous arachnoid dissection with freeing of tonsils	
Chiari III	Excision of the encephalocele and detethering of neural contents with the closure of the skin defect				
Chiari IV	Usually no surgical treatment for the malformation itself				
Chiari 0	Treatment similar to Chiari I if all other causes are ruled out and the patient has deficits or troublesome symptoms				
Chiari 1.5	Surgical treatment similar to Chiari I if the patient is symptomatic				
Hydrocephalus	Ventriculoperitoneal (VP) shunting is done commonly. Endoscopic third ventriculostomy (ETV) is also an option				
Syringomyelia	Usually resolves spontaneously after FMD. Syringo-subdural and syringo-peritoneal or syringo-pleural shunts are now practiced rarely				
Meningocele And tethered filum terminale	Often associated with Chiari malformations, particularly type II. Requires surgical repair with detethering of neural components				
Split cord malformations	Need surgical excision of the septum and dural closure				

CSF cerebrospinal fluid

A preanesthetic evaluation should include careful investigation of the medical history and a complete physical examination of the patient's airway and respiratory, cardiovascular, and neurologic systems to exclude possible associated comorbidity (Table 15.4). Signs and symptoms of raised ICT such as headache, vomiting, etc. should be carefully examined. Papilledema should be ruled out when raised ICP is suspected. Lumbar puncture, if needed, should be done cautiously to avoid herniation. Dehydration and deranged electrolytes should be corrected, which may be the result of vomiting due to raised ICP or following dysphagia. Pulmonary aspiration and infection may be present in children with dysphagia and impaired gag reflex, indicating lower cranial nerve dysfunction.

The importance of a thorough airway evaluation cannot be underestimated. Patients with Chiari malformation should be anticipated to have a difficult airway. Due to the altered anatomy of the skull base and upper cervical spine, there is restricted cervical mobilization. Moreover, the presence of basilar invagination makes the cervical spine extremely unstable. Since there is a risk of compression of the neural structures underneath, especially with the extreme neck flexion for surgery in the prone position, preoperative permissible neck flexion-extension must be assessed and documented. Patients with Chiari II malformation tend to have a higher incidence of airway abnormalities and other neurological dysfunctions. Sleep studies and flexible fiberoptic laryngoscopy is recommended for airway evaluation [12].

Table 15.4 Anesthetic challenges in a patient with Chiari malformation

• Airway – Vocal cord palsy – Stridor – Limitation in cervical spine mobility – Scoliosis
• Raised intracranial pressure – Papilledema
• Surgical position related – Prone—Pressure on eyes, accidental extubation – Sitting—Venous air embolism, compromised cerebral perfusion, macroglossia – Supine
• Autonomic dysfunction – Hemodynamic variations and instability – Altered thermoregulation
• Abnormal sensitivity to neuromuscular agents—Especially in patients with syringomyelia
• Latex allergy—Especially in children with meningomyelocele
• Blood loss—Especially in large meningomyelocele requiring skin grafting

Operative position needs to be discussed with the neurosurgeon; the position could be prone, sitting, or Concorde for posterior fossa decompression. The shunt is performed in a supine position with the head turned to one side. Risks of venous air embolism, systemic hypotension, pneumocephalus, paraplegia, and peripheral nerve injury (ulnar, brachial plexus, sciatic) are associated with sitting position. In contrast, the risk of accidental extubation, airway and facial edema, and postoperative blindness increases with the prone position. Excessive pressure on the abdomen during prone positioning may cause venous congestion and bleeding. Preoperative screening with 2D echo should be done to rule out the presence of patent foramen ovale as surgery in a sitting position is contraindicated in the presence of intracardiac septal defects. Alterations in cardiovascular and respiratory physiology should be taken care of during the respective positioning of the patient.

Children with meningomyelocele, tethered cord, and spina bifida undergoing multiple surgical procedures are at higher risk of latex sensitization and allergy [26]. Urological evaluation should also be performed in all children with meningomyelocele because of the increased possibility of upper urinary tract anomalies [14].

15.8.2 Premedication

Premedication is avoided in children with signs of raised ICP as they may cause respiratory depression and hypercapnia. However, it is important to allay preoperative anxiety to avoid further increases in ICP. Premedication with oral benzodiazepines like midazolam has a calming effect and should be administered if appropriate, only under supervision. Steroid-induced hyper-

glycemia and diuretic-induced electrolyte abnormalities should be ruled out.

15.8.3 Monitoring

Monitoring of a patient with Chiari malformation includes routine monitors such as pulse-oximetry, capnography, invasive arterial and noninvasive blood pressure monitoring, bispectral index (BIS), and temperature monitoring. Neuromuscular blockade may be monitored with a peripheral nerve stimulator due to undue sensitivity to the muscle relaxant. Central venous line placement is indicated in patients undergoing posterior fossa decompression due to the risk of venous air embolism, especially if the surgery is performed in a sitting position. Transesophageal echocardiography is desirable to detect the occurrence of venous air embolism. A precordial Doppler may be placed to detect even a minimal volume of a venous air embolus. Urine output monitoring should also be done in prolonged procedures. Arterial blood gas analysis is also recommended at regular intervals. Surgery near the brainstem and cranial nerves may necessitate neurophysiological monitoring to detect and revert any reversible neurological insult. Use of somatosensory evoked potential and motor evoked potential can guide about effect of positioning on spinal cord perfusion, intraoperative compression, and predict postoperative function in Chiari malformation [27, 28].

15.8.4 Induction of Anesthesia

Both inhalational and intravenous techniques can be employed for inducing anesthesia. Although inhalational induction may not be preferred in adults due to its effects on increasing intracranial pressure, sevoflurane has been widely used to induce anesthesia in the pediatric age group for the advantage of avoiding a restless and combative child in the process of securing an IV access. Neuromuscular blocking agent is administered to facilitate laryngoscopy and tracheal intubation and avoid any coughing, which may cause increases in ICP. It becomes necessary to immobilize the cervical spine in order to prevent any further neurological insult, and manual in-line stabilization is advisable. Flexible fiberoptic intubation, either awake or under sedation, decreases the extreme movement of the neck. Children with encephalocele or high meningomyelocele are intubated commonly in lateral decubitus position or with swelling supported by a doughnut or by placing the child's head beyond the edge of the table, supported by an assistant. Patients with vocal cord paralysis with stridor may even require a tracheotomy [29]. Early diagnosis and prompt airway management in these patients can be lifesaving.

In children with a high risk of aspiration, a rapid-sequence induction with thiopentone or propofol followed by rapid-acting muscle relaxants such as succinylcholine or rocuronium may be required. Succinylcholine should be avoided when there is muscle weakness due to the risk of hyperkalemia because of denervated muscles. Care should be taken to avoid extreme fluctuations in hemodynamics. Increased blood pressure during laryngoscopy can lead to raised ICP, whereas excessive blood pressure decreases can compromise cerebral perfusion pressure. Controlled hyperventilation before laryngoscopy may decrease the rise of intracranial pressure. An armored endotracheal tube is usually used to prevent kinking of the tube.

The presence of autonomic dysfunction in Chiari malformation complicates the anesthetic management further. Hemodynamic instability, altered temperature regulation, hypoxia, and hypocarbia may be observed during the perioperative period [22]. A strong vagal tone in children may cause bradycardia during laryngoscopy and intubation, which can be exaggerated by brainstem compression at the time of surgery.

15.8.5 Maintenance of Anesthesia

Anesthesia can be maintained with intravenous agents alone (TIVA) or with inhalational agents using a low MAC (less than 1). Patients with syringomyelia may show abnormal sensitiv-

ity to neuromuscular agents [21, 22]. Opioids like fentanyl are used for analgesia. Controlled mechanical ventilation with appropriate tidal volume and respiratory rate is continued to maintain normocapnia.

Dextrose-free fluids like normal saline and Ringers' lactate are usually used for fluid replacement. Blood loss should be meticulously monitored and appropriately replaced. Due to the risk of vascular injury, surgical steps should be closely monitored [18]. The vertebral artery may be injured during foramen magnum decompression and C1 laminectomy; the posterior inferior cerebellar artery may be injured during intradural exploration [25]. Blood loss should be assessed regularly and adequately replaced.

In children, the surface area of the head is comparatively large, so care should be taken to prevent hypothermia. Also, VP shunt procedure requires exposure of a large surface area and may lead to hypothermia. Warming devices such as warm air blankets and hot air mattresses should be used to maintain normal body temperature during surgery. Careful padding should be done to avoid any compression nerve injuries.

15.8.6 Awakening and Extubation

A smooth emergence from anesthesia is essential to avoid coughing or bucking on the endotracheal tube. Extubation should only be performed once the child follows commands or opens eyes and actively moves the extremities. Rapid recovery from the anesthesia allows early assessment of the neurological status. The presence of significant pneumocephalus can cause delayed awakening and can interfere with neurological function. The decision to keep the patient intubated is taken if there is extensive brainstem manipulation or suspected airway edema that interferes with adequate respiration.

15.8.7 Postoperative Management

Monitoring the child in the first 24 hrs postoperative period in the intensive care unit or a high dependency unit is necessary. Supplemental oxygen may be required for a certain period of time. Postoperative tension pneumocephalus is a known complication after surgeries are done in a sitting position. Close monitoring should be done to look for signs of brainstem dysfunction, particularly apnea, which is a rare but serious complication. Stridor may happen in postoperative period. Patients with type II CM may require a tracheostomy when extubation attempts are unsuccessful [12].

Extensive muscle dissection required during posterior fossa surgery leads to increased postoperative pain, neck muscle spasm, and nausea/vomiting [30]. Occipital nerve blocks may be useful in alleviating this pain [31]. Acetaminophen is usually started intraoperatively and continued in the postoperative period. Titrated doses of opioids may also be needed for adequate analgesia but should be given along with antiemetics to prevent opioid-induced vomiting. Complications of surgery include meningitis, wound infection, stroke, hydrocephalus, or CSF fistula.

15.9 Conclusion

Chiari malformation is a group of congenital anomalies arising because of developmental malformation of hindbrain leading to symptoms of cerebellar or brainstem dysfunction or of CSF flow obstruction leading to the symptoms of increased intracranial pressure. Chiari I malformation is more common and diagnosed in adolescence, whereas Chiari II malformation is the next common and diagnosed in infancy or young children. Chiari III and IV usually do not survive long. Chiari malformation may be associated with several neurospinal malformations like meningomyelocele or tethered cord and associated syndromes. Foramen magnum decompression is the most common procedure to relieve the pressure of cerebellar compression on the brainstem. Anesthesia workup requires a thorough assessment of the airway and the cardiorespiratory system as autonomic dysfunction and breathing difficulties are common. Operating teams must cooperate to give optimal neurosurgi-

cal positions (sitting or prone), avoiding excessive neck flexion. Anesthesia should be suitable for neurophysiological monitoring and must be titrated with the intention of early emergence. Postoperative care involves close monitoring of neurological and cardiorespiratory parameters.

Conflict of Interest None.

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16 Anesthesia for Craniovertebral Junction Anomalies in Pediatric Patients

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Key Points

- The craniovertebral junction (CVJ) represents a specialized osseo-ligamentous coupling between the cranium and the cervical vertebral column enclosing the cervico-medullary junction and bears intricate relationships between bony structures, blood vessels, and the neural elements.
- Abnormalities of the CVJ can result from bony or soft tissue pathologies which may be developmental, genetic, or acquired.
- Clinical presentation may vary, including localized pain, radiculopathy, sensory loss, vertigo, lower cranial nerve palsies, quadriparesis/quadriplegia, and respiratory distress depending upon the level and grade of neural compression and the neurological substrates involved.
- Surgical correction is the mainstay of treatment in most CVJ pathologies, with conservative management having a limited role.
- Anesthetic management involves specialized attention due to the unique pathology of the disease in addition to the usual concerns of pediatric patients; airway maintenance, meticulous assessment of blood loss, positioning, and careful extubation are the usual accompaniments of this procedure.

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16.1 Introduction

The craniovertebral junction (CVJ) or craniocervical junction is a specialized articulation, coupling the cranium and the relatively mobile cervical vertebral column that is uniquely designed to provide mobility in addition to stability. It comprises of the basi-occiput, occipital condyles, atlas, and axis vertebrae. The CVJ has two major joints: the atlanto-occipital (stable) and the atlanto-axial (mobile) joints. Both joints provide mobility in different axes such that the atlanto-axial joint is comparatively less stable with greater degrees of mobility [1]. The CVJ encloses the cervico-medullary junction (CMJ), and there exists an intricate relationship between the bony, neural, and major vascular elements in this region.

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The incidence of CVJ anomalies is higher in the Indian subcontinent as compared to the rest of the world. Various permutations and combinations of bony and soft tissue anomalies exist, and these defects are rarely found in isolation. However, the most commonly encountered anomalies in isolation are mobile atlanto axial dislocaions (AAD) followed by the non-reducible AAD along with occipitalization of the atlas (C1) and various grades of basilar invagination (BI) [2]. The Chiari malformation is also commonly associated with different complex CVJ anomalies [3, 4]. The maximum numbers of cases are in India and are reported from states like Uttar Pradesh, Bihar, Rajasthan and parts of Gujarat, with the causes of such geographical clustering remaining speculative. The CVJ anomalies can be exclusive or may present with various combinations such as AAD with BI, AAD with Chiari malformation, BI with Chiari malformation, etc.

16.2 Anatomy of the Craniovertebral Junction (CVJ)

16.2.1 Embryological Basis of CVJ Anomalies

Embryological development of this region begins in the early weeks of intrauterine life when mesodermal cells condense to form notochordal process. This process invaginates between endoderm and ectoderm to form notochord; the ectoderm fuses to form neural tube. From the mesoderm on either side of the notochord, somites are formed, and the ventromedial portion of the somites (sclerotome) forms the vertebral bodies. The first four sclerotomes form the occipital bone. Out of these, the first two form the basi-occiput, the third forms the jugular tubercles, and the fourth (pro-atlas) forms parts of the foramen magnum, atlas, and axis [4, 5]. Anomalies may result out of fault in the development of the occipital sclerotomes and adjacent cervical sclerotomes during the early embryonic weeks. A few of them are depicted in Table 16.1.

Table 16.1 Anomalies resulting from developmental defects in occipital and cervical sclerotomes

Platybasia	Dysplasia of the occipital segments causing flattening of the clivus
Basilar invagination	Underdevelopment of basi-occiput, occipital condyles, and rim of foramen magnum causing the invagination of the odontoid and arch of atlas
Occipital vertebra	Proatlas may develop into separate vertebrae
Anterior cervico-medullary compression	Hypochondral bow of proatlas may persist and gain attachment to the atlas, clivus, or the apical segment of the dens
Bipartite articular facets	Failure of fusion of proatlas with the atlas: Horizontal instability of the atlanto-occipital joint
Bicornuate dens	Dens body failing to fuse in utero resulting in a radiological V-shaped cleft
Klippel-Feil syndrome	Failure of segmentation of axis and the third vertebrae: Associated with Klippel-Feil syndrome

16.2.2 Osseo-ligamentous Anatomy

The CVJ consists of occiput, the foramen magnum, the first two cervical vertebra, and the supporting ligaments encompassing the medulla oblongata and the upper cervical spinal cord. The upper surfaces of the lateral masses of the first cervical vertebrae are concave into which fit the occipital condyles in ball and socket configuration. There are three atlanto-axial joints, one each on either side between the lateral mass of atlas and upper articular surface of axis, and a median articulation between posterior surface of the anterior arch of atlas and the anterior surface of the odontoid process. The transverse atlantal ligament and the alar ligaments are the principal ligaments in the structural integrity of the atlanto-axial articulation. Other ligaments in order of decreasing importance include the capsular ligaments at each joint, the membrana tectoria, the apical ligament of the dens, and the anterior and posterior atlanto-occipital membranes. The atlanto-occipital and atlanto-axial joints are all synovial joints. The median joint between the atlas and the axis is of pivot type, while the two lateral atlanto-axial joints are of plane joint variety.

16.2.3 Neurovascular Structures of the CVJ

The neural contents of the CVJ include the caudal portion of the brainstem (medulla), CMJ, rostral spinal cord, obex of the fourth ventricle, lower cranial (IX, X, XI) nerves, and upper cervical nerves (C1, C2 nerve roots). In small posterior fossae, the cerebellar tonsils and biventral lobules of the cerebellum herniate downward and occupy the region of foramen magnum and the CVJ. The biventral lobules are located above the lateral part of the foramen magnum, while the tonsils overlie the posterior edge. Major arteries traversing the CVJ include bilateral vertebral arteries (VAs), posterior inferior cerebellar arteries (PICAs), and meningeal branches of the VA. Bilateral internal carotid arteries also remain anterior to and within 1–2 cms of the anterior end of the atlanto-occipital articulation. Major veins in relation to CVJ are the peri-vertebral venous plexus, extradural veins (extraspinal and intraspinal part), intradural (neural) veins, and dural venous sinuses (basilar venous plexus, circular sinus, and the occipital sinus). These veins anastomose through bridging and emissary veins.

16.3 Classification of CVJ Anomalies

Several classification systems of the CVJ anomalies have been proposed. A classification by Menezes categorizes the CVJ anomalies into "congenital" and "developmental (acquired)." [6] Another classification by Pang et al. is based on embryogenesis and includes "malformation of central pillar" and "malformation of surrounding rings." The central pillar malformations may result in instability and neural compression, as observed in BI and a retroflexed odontoid process [4]. However, for the ease of understanding, these abnormalities can be classified as per **anatomical anomaly**, bony or soft tissue related (Table 16.2). Soft tissue anomalies are also known as Chiari malformations, which are discussed in detail elsewhere [3].

Etiological classification is broadly based on congenital and acquired causes (Table 16.3).

Table 16.2 Anatomical classification of craniovertebral junction (CVJ) anomalies

A. Bony craniovertebral junction (CVJ) anomalies	
Major anomalies	Minor anomalies
• Platybasia • Occipitalization • Basilar invagination • Dens dysplasia • Atlantoaxial dislocation	• Dysplasia of atlas • Dysplasia of occipital condyles, clivus, etc.
B. Soft tissue or cervico-medullary junction (CMJ) anomalies: Chiari malformations	
Types	Features
Chiari I malformation	Cerebellar tonsillar descent into the foramen magnum, with peg-shaped tonsils, usually with associated syringomyelia
Chiari II malformation	Downward descent of the medulla, fourth ventricle, and caudal vermis; often with tectal beaking, in addition to syringomyelia/syringobulbia Commonly associated with lumbar meningomyelocele
Chiari III malformation	Similar to Chiari II malformation, but associated with high cervical meningomyelocele, often incompatible with life
Chiari IV malformation	Severe cerebellar hypoplasia, with no downward descent of cerebellar tonsil

Table 16.3 Etiological classification of craniovertebral junction (CVJ) anomalies

Congenital (common in children)	Acquired (common in adults)
• Basilar invagination • Atlantoaxial dislocation (AAD) • Odontoid dysplasia • Os odontoideum • Atlas assimilation • Congenital malformations or syndromes (Marfan's, Down's, Klippel-Feil, and Morquio's syndrome, achondroplasia, osteogenesis imperfecta)	• Injuries • Infections (tuberculosis) • Rheumatoid arthritis • Metastatic diseases

Congenital anomalies are usually due to bony anomalies and are associated with anomalies of neural tissue, meninges, vascular anatomy, or any combination [7].

16.4 Syndromic Associations with CVJ Anomalies

Certain clinical syndromes have CVJ anomalies as the associated feature; the common syndromes with associated CVJ anomalies are listed in Table 16.4.

16.5 Pathophysiology of CVJ Anomalies

The pathophysiology of these disorders usually involves pressure over the neuraxis and alterations in the blood supply and CSF flow. In BI, the odontoid prolapses into the limited space of the

Table 16.4 Syndromic associations of craniovertebral junction (CVJ) anomalies

Syndrome	Clinical features	CVJ anomaly
Marfan's syndrome	• Genetic disorder affecting the connective tissues • Mutation in a gene (FBN1) on chromosome 15 • Patients are tall and thin, with long arms, legs, fingers, and toes, arachnodactyly • Aortic root dilatation/dissection, mitral valve prolapse • Overly flexible joints, scoliosis, sternal deformities • Lens dislocation, myopia	• Atlantoaxial dislocation • Features of dysfunction of the brainstem, cerebellum, spinal cord, and cranial nerves
Down's syndrome (trisomy 21)	• Down's facies: Flattened face, small head, short neck, protruding tongue, upward slanting palpebral fissures, unusually shaped or small ears • Intellectual and developmental problems • Congenital heart defects • Poor muscle tone • Excessive flexibility • Short stature	• Atlantoaxial instability (AAI) occurs in 14–24% of patients
Klippel-Feil syndrome	• Abnormal fusion of at least two vertebrae in the neck • Short neck • Low hairline • Restricted movement of the upper spine	• C1-C2 hypermobility and instability • Basilar invagination • Chiari I malformation • Diastematomyelia, Syringomyelia.
Morquio's syndrome (mucopolysaccharidosis type IV)	• Large head, coarse facial features (prominent scalp veins, flat-bridged nose, and bulging forehead), widely spaced teeth • Hepatosplenomegaly • Short stature • Heart and vision problems • Hypermobile joints, scoliosis or kyphosis, bell-shaped chest with ribs flared out at the bottom, knock knees	• Atlanto-axial subluxatio • Odontoid hypoplasia, peri-odontoid soft tissue masse • Spinal canal narrowing and spinal cord compression • Communicating hydrocephalus
Achondroplasia	• Fibroblast growth factor receptor-3 gene mutation • Short limbed dwarfism • Limited range of motion at the elbows • Large head size • Small fingers • Normal intelligence	• Underdeveloped skull base, facial bones • Salient morphometric feature of foramen magnum stenosis causing CVJ compression • On the sagittal view of imaging: "Teardrop configuration"
Osteogenesis imperfecta	• Collagen-encoding gene defects • Reduction in either the quality or the quantity of type I collagen	• Platybasia, basilar impression, and basilar invagination • Compression of the brainstem • Aqueductal stenosis • Hydrocephalus • Spinal cord edema and syrinx

foramen magnum and causes ventral compression at the CMJ. This has often been associated with a hypoplastic clivus, which is deviated upward, giving an impression of the cephalad migration of cervical spine into the posterior skull base [4]. Often there is associated foramen magnum stenosis, further accentuating neural compression. BI is a primary developmental (congenital) anomaly; it is seen in association with Klippel-Feil syndrome, Down's syndrome, etc. Secondary (acquired) BI due to softening of bones at the skull base is termed as "basilar impression"; it is seen in association with osteomalacia, Paget's disease, hyperparathyroidism, osteogenesis imperfecta, Hurler's syndrome, and rickets. The basilar impression may be associated with rheumatoid arthiritis, which is also known as "cranial settling." In platybasia (flattening of the skull base), there is a reduced volume of the posterior cranial fossa and resultant Chiari malformation (cerebellar herniation), syringomyelia with or without syringobulbia formation. The CVJ anomalies are often accompanied by anomalous fusion of the cervical vertebrae (e.g., Klippel-Feil syndrome) [8]. An increasingly recognized group is the complex Chiari malformation, which includes herniation of brainstem through the foramen magnum, kinking of medulla, retroflexion of odontoid, occipitalization of the atlas, BI, and syringomyelia. These patients require more aggressive bony decompression and fixation, unlike patients with pure Chiari malformation who can usually be managed with foramen magnum decompression alone [9].

16.6 Clinical Features of CVJ Anomalies

The clinical presentations due to the anatomical disorders include the following:

- **Neck Pain:** It may occur due to muscular contracture, bony instabilities, or compression of C2 root and greater occipital nerve. There may be associated torticollis. The primary event appears to be the cord compression due to the posterior displacement of the odontoid process. The physical manifestations and bony deformities, including the short neck and torticollis, may be the secondary protective responses to reduce the over-stretching of the spinal cord. A significant CVJ instability may incite neck pain, restricted neck movements, and cervical hyperlordosis [3]. History of pain in the neck or occiput with neurological symptoms suggests lower brainstem, upper cervical, or cerebellar involvement that should prompt investigations with neuroimaging.
- **Weakness:** Limb weakness, spastic paresis, hyporeflexia, and impaired vibration, pain, and temperature sensations may be present due to compression of the spinal cord. Pyramidal symptoms are predominantly affected, while spinothalamic dysfunctions are less frequent [3]. The different characteristic (cruciform, Elsberg phenomenon, U-shaped, and reverse U-shaped) patterns of weakness are explained based on the site of compression of the decussating pyramidal tract.
- **Respiratory Dysfunction:** Respiratory system is involved due to two major causes. One is the involvement due to weakness of muscles of respiration, and another one is central compression by odontoid. The weakness and dysfunction of respiratory muscles, including the diaphragm, results in poor coughing ability, decreased vital capacity, and increased atelectasis. This predisposes the patient to pneumonitis and type II respiratory failure. Compression of the brainstem and respiratory center disturbs the autonomic control, such as ninth and tenth cranial nerve dysfunction leading to decreased functional chemoreceptor afferents due to carotid body denervation insensitivity of peripheral chemoreceptor [10, 11]. These patients present with obstructive sleep apnea (OSA) with symptoms of daytime somnolence, respiratory symptoms, focal brainstem signs, or myelopathy. Additionally, syringomyelia, which extends into the lower brainstem (syringobulbia), is a common finding with complex Chiari malformations, which further compromises the lower cranial nerves and respiration, necessitating prolonged postoperative ventilatory support.

- Vertigo, intermittent syncope, and visual disturbances may occur due to disturbance in cerebrospinal fluid (CSF) flow dynamics and altered blood supply of the spinal cord [12]. There may be sphincter disturbances, the incidence of which is more in irreducible abnormalities [7].

16.7 Diagnosis of CVJ Anomaly

Diagnosis is usually made based on clinical history, symptoms, and neurological examinations. There may be difficulty in establishing the diagnosis in a pediatric patient as the manifestations are usually subtle and can easily be missed [13–15]. Moreover, the radiological pictures may be confusing due to the incomplete ossification of bones until 9 years [16].

16.7.1 Imaging Studies

The imaging modalities include plain X-rays (lateral, anteroposterior, or oblique views), computed tomographic (CT) scan, magnetic resonance imaging (MRI), and CT or MR angiography. Diagnosis of CVJ anomalies requires understanding and analysis of certain radiological lines whose variations signify abnormalities. These radiological lines were initially described on standard radiographs, and later CT scans were used (Table 16.5**,** Figs. 16.1, 16.2, and 16.3) [17]. The study of these imaginary lines is known as "craniometry," where the different lines, planes, and angles are studied in relation to each other concerning their different components [18]. There exist limitations for these measurements individually, and no single measurement is independently helpful. This is attributed to the variations in anatomical structures and planes [18]. Although dynamic X-rays may be useful in making the diagnosis, a three-dimensional (3D) CT scan is preferred as it allows better anatomic orientation, and MRI helps further ascertain the extent of neuronal compression. **Atlanto-dental interval (ADI)** represents the distance between the posterior surface of anterior arch of atlas and the anterior surface of the odontoid process at that level. Increased ADI more than 3 mm in adults or more than 5 mm in children suggests AAD (Fig. 16.2d).

If MRI and CT scan are unavailable, dynamic X-rays, lateral view, AP view, or oblique view may help make the diagnosis. Dynamic X-ray of the cervical spine is taken in full flexion and full extension to the extent tolerated by the patient without aggravating the symptoms (Fig. 16.4). Advanced modalities like CT or MR angiography may also help anatomic variations in the course of VAs to prevent intraoperative injuries. Assessment CT or MR angiograms superimposed on 3D reconstruction helps evaluate the dominance of VAs (Fig. 16.5) [19–21]. It helps the neurosurgeons understand the exact relationship of the VAs to the osseous CVJ structure dynamics with possibility of changes in location of the artery during the neck movements [22].

16.7.2 Acquired CVJ Pathologies

CVJ tuberculosis is indicated by the presence of prevertebral collection, odontoid erosion, and granulation tissues. Extensive ligamentous infiltration and hyperemic decalcification are also seen. Radiologically, in tuberculosis, three distinct stages are observed: Stage I includes retropharyngeal abscess and ligamentous laxity, while the bony architecture of C1-C2 is preserved. In stage II, there is the disruption of ligaments along with AAD, minimal bony destruction, and retropharyngeal mass. Stage III presents with marked bony destruction, complete obliteration of anterior arch of C1 and loss of odontoid process, significant AAD, and OA instability.

A specialized entity called **Grisel syndrome** involves subluxation of the atlanto-axial joint due to inflammatory ligamentous laxity following infections in the region of the head and neck (e.g., pharyngeal infection) [23].

Table 16.5 Craniometry (radiological lines, angles, and distances to diagnose) of basilar invasion (BI)

Description	Clinical presentation
Lateral projection	
• Foramen magnum line, McRae line (1, Fig. 16.1a) • Line joining the basion and opisthion	• Odontoid process should not cross this line • In BI: Dens lies above this line • Normal foramen magnum: 40 mm • Stenosis: <20 mm • Chiari malformation: >50 mm
• Palato-occipital line: Chamberlain's line (2, Fig. 16.1a) • Joins the posterior tip of the hard palate with the opisthion (posterior margin of the foramen magnum)	• The tip of the odontoid process should not be >5 mm above this line (range 0–5 mm)
• Palato-suboccipital line: McGregor line (3, Fig. 16.1a) • Modification of Chamberlain's line which extends between the posterior pole of the hard palate and the lowest point of the occipital basi-squamous surface • Used when the opisthion could not be identified	• The tip of odontoid process should be no higher than 7 mm above this line (range 1–7 mm).
• Wackenheim's clival canal line • Line along the surface of clivus (**1,** Fig. 16.1b) and its extrapolation inferiorly into the upper cervical spinal canal	• Line should fall tangent to the posterior aspect of the tip of the odontoid process • In BI: Intersecting the odontoid process
• *Craniovertebral or clivus-canal angle* (2, Fig. 16.1b) formed at the intersection of Wackenheim's line with a line constructed along the posterior surface of the axis body and odontoid process	• Normally ranges: 150° in flexion to 180° in extension • At less than 150°: Ventral spinal cord compression may occur
• Basal angle, also known as Welcher's angle (Fig. 16.2c) formed at the intersection of the nasion with tuberculum sellae line (1) and the tuberculum-sellae with basion line (2)	• Average value: 132° • Platybasia: >140°
• Klaus index**:** (5**,** Fig. 16.1c) • Vertical line joining the Twining's line (3, from tuberculum sellae to the internal occipital protuberance) and McRae's line (4)	• Normal height: 40–41 mm • Small posterior fossa (platybasia/BI): Less than 30 mm
• Boogard's angle (Fig. 16.1d) is measured by drawing a line along the plane of the clivus (1) and another line from basion to opisthion intersecting the first line	• Normal angle: 126° +/− 6° • Platybasia: >136°
• Bull's angle (Atlanto-palatal angle, Fig. 16.2a) • Measured by the angle between the palatal line (1) and the line along the plane of atlas (2)	• Normal: Less than 10° • Presence of BI: >13°
• Ranawat's line (Fig. 16.2b) is the perpendicular distance between the center of the sclerotic ring of C2 and the line drawn along the axis of C1	• Normal value: 15–17 mm • Presence of BI: <15 mm
• Clark's stations (Fig. 16.2c) represent the zones made by vertically dividing the odontoid process into three equal parts • They are named zones I, II, and III cranio-caudally	• Normally the anterior arch of atlas should be in the zone I • If anterior arch in the zones II or III, it is suggestive of BI
• Atlanto-dental Interval (Fig. 16.2d)**:** From posterior surface to C1 arch to anterior surface to dens at the same level	• Normal <5 mm in children and < 3 mm in adults • Atlanto-axial dislocation: >5 mm and > 3 mm
Frontal projection	
• Condylar angle/atlanto-occipital joint axis angle (Fig. 16.3a)	• Average angle is 125^0 ($124–127^0$) • Becomes more obtuse in occipital condyle hypoplasia
• Bi-digastric line (Fischgold & Metzer, 1, Fig. 16.3b) • Line drawn between right and left digastric grooves	• Also known as **biventer line** • This line is situated 10 mm above the bi-mastoid line • Odontoid tip normally should not project above this line
• Bi-mastoid line (Fischgold & Metzer, 2, Fig. 16.3b) • Line connecting the tip of two mastoid processes	• The tip of the odontoid process of C2 normally projects less than or equal to **10 mm** above this line • In BI, this distance decreases

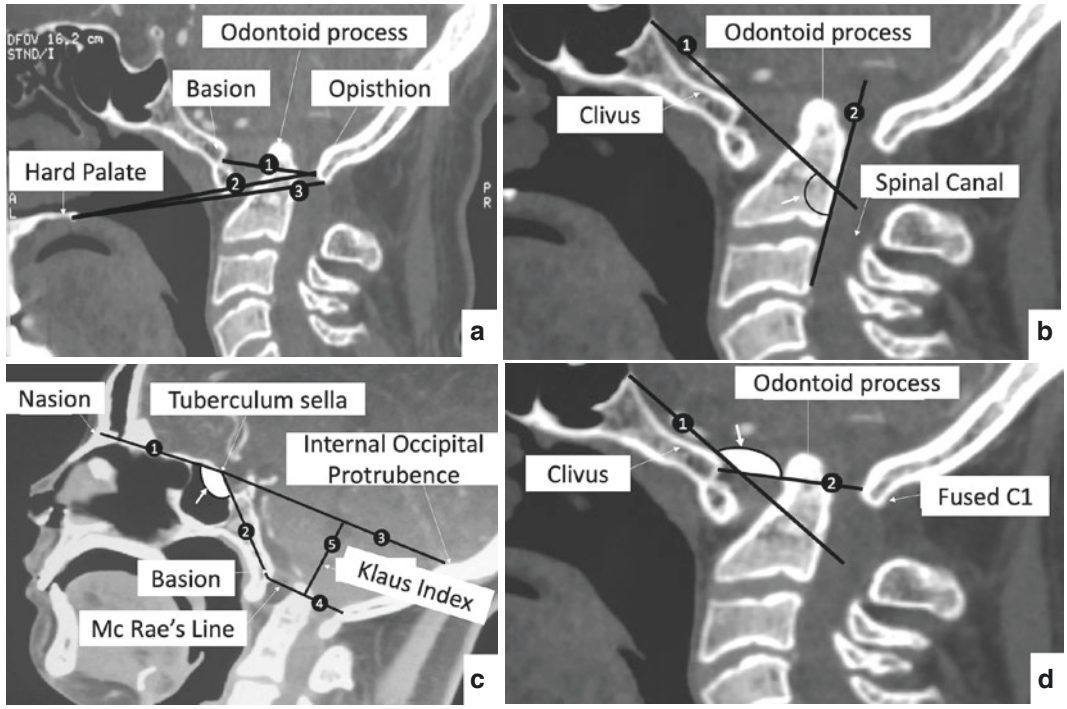

Fig. 16.1 Computed tomography scan of the head and neck in sagittal view. **(a)** *McRae's* line represents a line joining the basion and opisthion (1). *Chamberlain's line* (palate-occipital line) joins the posterior tip of the hard palate with the opisthion (2). *McGregor's* line (palato-suboccipital line) extends between the posterior pole of the hard palate and the lowest point of the occipital basi-squamous surface (3). **(b)** *Wackenheim's clivus line (1)* represents a line along the surface of clivus and its extrapolation inferiorly into the upper cervical spinal canal. *Clivus-canal angle (2):* formed at the intersection of Wackenheim's line with a line constructed along the posterior surface of the axis body and odontoid process. **(c)** *Welcher's basal angle* is formed at the intersection of the nasion to tuberculum sellae (1) line and the tuberculum sellae to basion (2) line. *Twining's line* represents a line joining the tuberculum sellae to the internal occipital protuberance (3). The vertical distance of Twinning's line and McRae's line represents Klaus index (4). **(d)** *Boogard's angle* represents the angle between the line along the plane of clivus to the basion (1) and basion to opisthion line (2), intersecting the former

16.8 Management of CVJ Anomalies

Management of these anomalies is mainly surgical; a conservative approach is rarely offered to the congenital subset compared to post-traumatic patients. Intermittent cervical traction has been identified to be symptom-relieving therapy for years [24, 25]. As reducibility is an important consideration in surgical management of these patients, preoperative traction is a valuable tool to assess the degree of reducibility and neurological status. Hard cervical collars and halo brace can be applied for a duration of 8–12 weeks. Gardner-Wells tong traction is also applied in selected patients under local anesthesia to reduce the AAD prior to definitive surgery [26]. A weight of 2.5 kg is used for traction at head and CVJ; thereafter, 0.5 kg is added for each cervical vertebra. However, it is not used in children less than 3 years of age.

In pediatric patients, the management of this anatomical complexity offers specialized surgical challenges. These difficulties are due to the separation and re-segmentation of the spinal column at the CVJ as part of the development process. It requires an understanding of the age-dependent ossification process of the cartilaginous part of C1 and C2. To make a surgical plan, the stability of the CVJ must be assessed

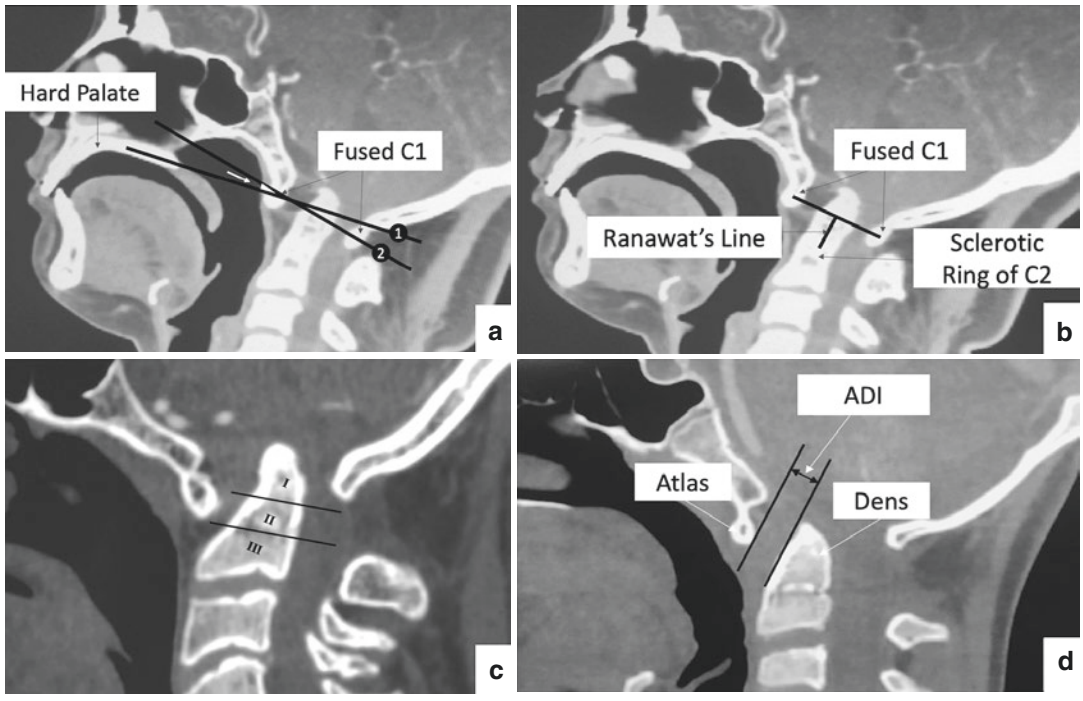

Fig. 16.2 Computed tomography scan of the head and neck in sagittal view. **(a)** *Bull's angle* (atlanto-palatal angle) is measured by the angle between the palatal line (1) and the line along the plane of atlas (2). **(b)** *Ranawat's line* is the perpendicular distance between the center of the sclerotic ring of C2 and the line drawn along the axis of C1. **(c)** Clark's stations represent the zones made by vertically dividing the odontoid process into one-thirds. They are named zones I, II, and III cranio-caudally. **(d)** Atlanto-dental interval (ADI) represents the distance between the posterior surface of the anterior arch of the atlas and the anterior surface of the odontoid process at that level

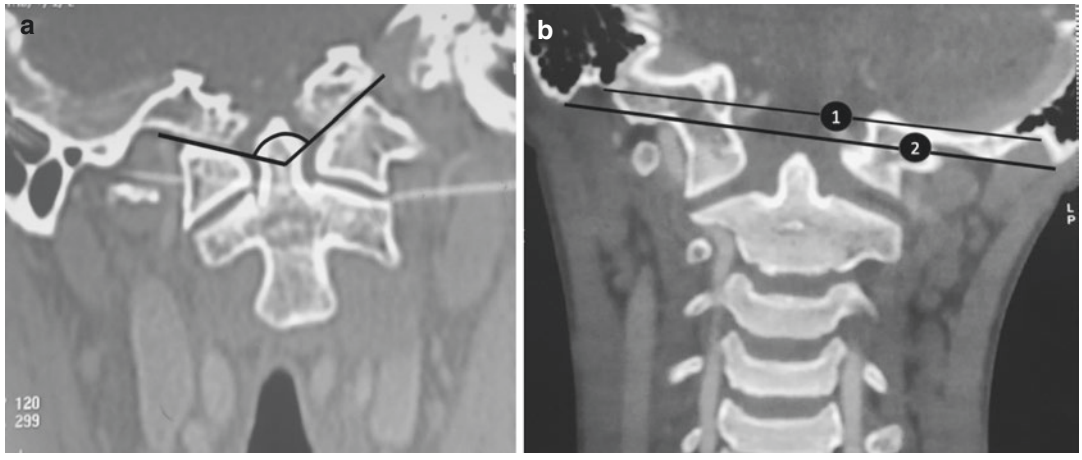

Fig. 16.3 Computed tomography scan of the head and neck in coronal view. **(a)** Atlanto-occipital joint axis angle is formed by a line drawn parallel to the atlanto-occipital joint. **(b)** Bi-digastric line: line drawn between right and left digastric grooves (1). Bi-mastoid line: line drawn between the inferior tips of the mastoid processes bilaterally (2)

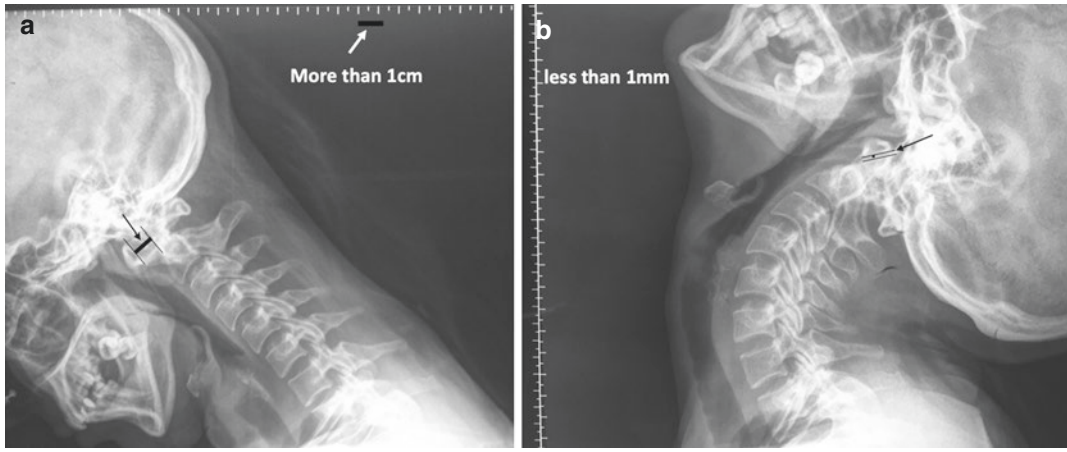

Fig. 16.4 Dynamic X-ray of the neck: **(a)** in full flexion position. Dens moving posteriorly increases the atlanto-dental interval (ADI) (marked by black line) and causes narrowing of spinal space. White arrow shows the measurement of the distance using the scale (ADI > 1 cm). **(b)** In full extension: showing reduction in the ADI to <1 mm, indicating mobile AAD with reducibility on extension

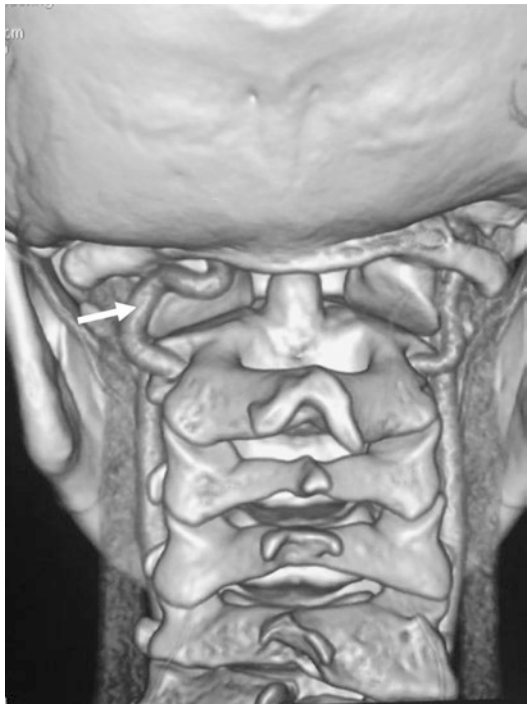

Fig. 16.5 Three-dimensional reconstruction of computed tomography angiography showing abnormal vertebral artery loop (white arrow)

using a dynamic X-ray [1]. The atlanto-axial joint is called mobile when it reduces during extension and aggravates during flexion (Fig. 16.4). AAD is called reducible when BI is corrected on traction application and irreducible if it does not. In reducible AAD, posterior fixation is practiced, while in fixed AAD, anterior transoral decompression (transoral odontoidectomy, TOO) and posterior fixation are planned.

16.9 Surgical Procedures

The surgical intervention aims to alleviate neural compression and correct the instability if any. The surgical procedures can be divided into three categories: (a) decompression, (b) fusion, and (c) a combination of both [5], a simplistic algorithm of which is shown in Fig. 16.6. The commonly undertaken anterior decompression procedures could be a transoral (microscopic- or endoscopic-assisted) decompression, endoscopic trans-nasal odontoidectomy, or transcervical approach (open or endoscopic). Similarly, the posterior fusion is commonly achieved with C1-C2 fusion (Goel and Harm's approach) [27], C1-C2 trans-articular screw placement (Magerl's technique) [28], occipito-cervical fusion [29, 30], or distraction, compression, extension, and reduction (DCER) and universal distraction technique (Fig. 16.7) [31, 32].

- **Anterior decompression** consists of removing the C1 body, the odontoid process, and

part of the C2 vertebra body to remove the ventral compression on the CMJ due to BI or the irreducible odontoid displacement. A midline approach through the posterior pharyngeal wall is employed. Using a high-speed drill, the anterior arch of the atlas and the odontoid process are drilled. Depending upon the situation, sometimes, the lower portion of the clivus and part of the C2 body is also removed. The alar, apical, cruciform, and tectorial membranes are also excised to decompress the dura mater. After achieving hemostasis, the posterior pharyngeal wall is closed in layers with interrupted sutures. This procedure produces gross instability in CVJ; hence, posterior fixation must be done to stabilize it.

- **Posterior Fixation** involves fusing the occipito-cervical joint. The fusion is achieved using several types of instrumentation based on articular mass morphology, C1-C2 joint orientation, course of VA, and procedural preference of the neurosurgeon. The age-old contoured steel rods and sublaminar wires are replaced with either titanium rods and wire or lateral mass screws and plates (Goel and Harm's technique) [27]. Several new techniques have been introduced by different authors, such as DCER technique having the universal goal of alleviating compression from the neuraxis and achieving robust fusion at CVJ [33, 34].

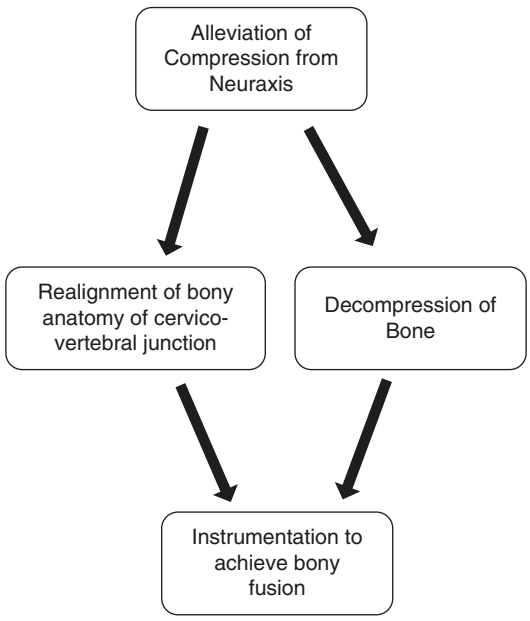

Fig. 16.6 Flowchart depicting the principle of surgical procedure

Both of these procedures, i.e., anterior decompression followed by the posterior fusion, can be done in the same sitting or in isolation with either of the approaches undertaken first followed by the second or vice versa [10].

16.10 Anesthetic Management

The anesthetic goals of the management of CVJ anomalies involve the adherence to the general anesthetic management principles for children and certain pertinent concerns specific to the underlying pathology.

16.10.1 Preoperative Evaluation and Optimization

A thorough preoperative evaluation is a must to assess associated other anomalies and the effect of CVJ anomaly on the patient's physiology. As the respiratory system is most affected, optimization should be initiated preoperatively. The respiratory insufficiency is assessed by pulmonary function tests (PFTs), laboratory or bedside. Predominantly, a restrictive pattern is seen; however, an obstructive pattern may be observed in some children [10, 33–36]. The pediatric patients may not be able to perform the PFTs, especially when traction is applied. In those children, bedside PFTs, such as respiratory rate, breathing pattern (abdominothoracic, predominantly abdominal, or paradoxical), breath-holding time, chest expansion, and single-breath count, may be the useful tools for assessment of the respiratory reserve. In children with respiratory insufficiency, preoperative chest physiotherapy and incentive spirometry are initiated to get acclimatized for the postoperative period. In patients with weak or absent gag and cough

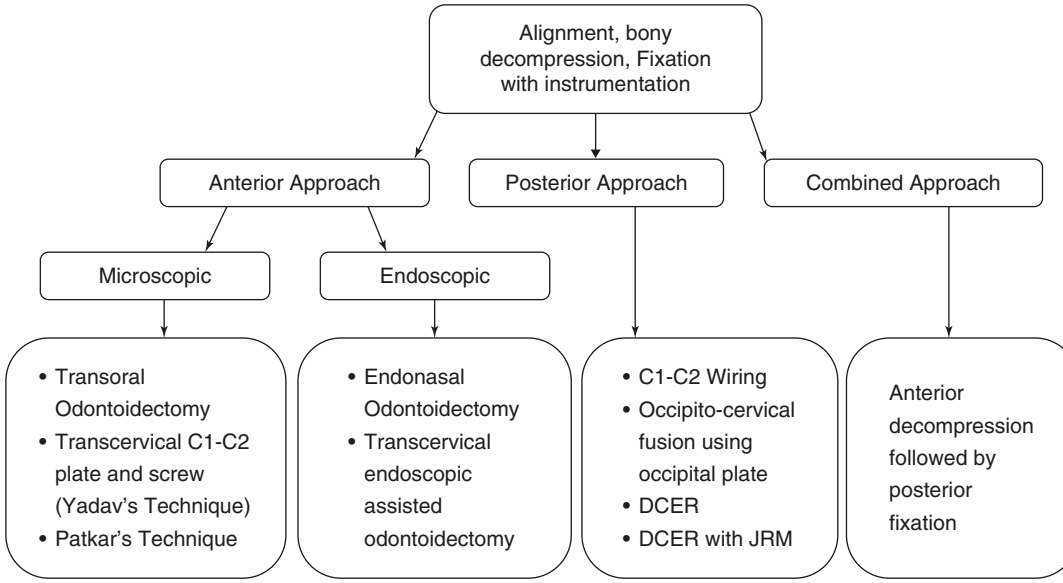

Fig. 16.7 Various surgical procedures for the craniovertebral junction. C1, first cervical vertebra; C2, second cervical vertebra; DCER, distraction, compression, extension, and reduction; JRM, joint remodeling

reflexes, elective tracheostomy may protect the airway. For children who show the signs of OSA, polysomnography is required for confirmation [37]. As various syndromes are associated with CVJ anomalies, the advanced cardiac assessment may be indicated if there is any finding on auscultation or electrocardiography [38]. Preoperative somatosensory evoked potentials (SSEPs) from the extremities and neurodevelopmental assessment of muscle function along with proper documentation of prior limb weaknesses and neurologic deficits are necessary to assess postoperative improvement [5]. Evaluation of the airway should be done meticulously. Restriction of neck extension and presence of rigid collar complicate conventional method of airway control and, hence, call for a planned modified or alternate approach. Concurrent medications like baclofen (centrally acting muscle relaxant) are often administered in these children, which might have anesthetic drug interactions such as increased sensitivity to muscle relaxants [39, 40]. The potential complications should be explained, and appropriate consent should be taken from the parents [41]. Sedative premedication should, thus, be avoided or cautiously administered.

16.10.2 Monitoring

Basic monitoring involves electrocardiography (ECG), noninvasive blood pressure (NIBP), pulse oximetry, temperature, and end-tidal carbon dioxide; bladder catheterization aids in urine output monitoring. Beat-to-beat monitoring arterial blood pressure monitoring is usually indicated as surgery is conducted in the brainstem vicinity may elicit abrupt hemodynamic fluctuations [26]. Additionally, neurophysiological monitoring like motor evoked potential (MEP) or SSEPs allows prompt identification of changes at a reversible stage, thereby permitting immediate correction of the cause and avoidance of permanent neurologic deficits [38].

16.10.3 Induction of Anesthesia and Endotracheal Intubation

Control of the airway in these patients is fraught with the risks of increasing the neurologic compromise due to the movement of the unstable CVJ. Simultaneously, anomalous CVJ is a potentially difficult airway due to bony defects or the presence of inline traction and hard collar.

Decreased oxygen reserve in pediatric patients makes them prone to rapid desaturation once spontaneous ventilation is abolished. Anesthesia can be induced using either intravenous (IV) or inhalational techniques, as the situation demands. Due to the varying degrees of preexisting paresis, succinylcholine is avoided though some authors advocate its usage [41]. Various maneuvers may be required to facilitate ventilation after anesthesia induction, such as jaw thrust, airway (oral or nasopharyngeal), and supraglottic device. Airway control should be done in a manner that causes the least movement of the neck. Awake fiberoptic intubation (FOB) is preferred as it causes minimal movement at the cervical region, and neurological status can be assessed simultaneously. However, the feasibility of the procedure in a conscious uncooperative child is questionable; in a cooperative child, titrated sedation and anesthesia of the airway may help secure the airway. In pediatric patients, various techniques can be used to secure the airway, including FOB under anesthesia (with or without paralysis), videolaryngoscope, and intubating laryngeal mask airway [38]. Manual inline stabilization (MILS) should be maintained during intubation attempts. A reinforced flexometallic tube may be used, which prevents kinking of the lumen during both the transoral and posterior fixation [36]. However, the probability of postoperative ventilation is high in children undergoing a combined approach where PVC tracheal tube could be a better choice and, hence, practiced frequently [26]. Usually, oral intubation is undertaken; however, sometimes, the nasal approach is chosen [42]. The laterality of fixing the endotracheal tube should be decided in consultation with the operating neurosurgeon, most commonly at the left angle of mouth. Peri-laryngeal packing may be done during transoral surgeries to prevent aspiration or ingestion of blood; however, it should be removed methodically at the conclusion of the surgery. During positioning of the child from supine to prone and vice versa, the head should be held carefully, and twisting or turning is avoided as much as possible. The head movements with respect to the rest of the body may cause excessive neurological compression leading to neurologic deficits, severe bradycardia, or even asystole. Hence, it is recommended to keep at least one vital monitor connected while turning the patient under anesthesia, such as ECG, pulse oximeter, or arterial BP. The head should be elevated to decrease bleeding, the eyes should be pressure-free, and the pressure points should be well-padded. Excessive abdominal compression impedes venous return and may contribute to bleeding from the operative site due to engorgement of the venous epidural plexus [43]. Extreme degrees of neck flexion may cause endobronchial intubation and intraoral kinking of the endotracheal tube (ETT) or brainstem compression in patients having Chiari malformation [38].

16.10.4 Maintenance of Anesthesia

Anesthesia can be maintained either with volatile agents or IV agents. In addition, oxygen, either air or nitrous oxide, can be used. Ventilatory strategies should ensure normocarbia; both hypo- and hypercarbia are avoided. Intermittent boluses of nondepolarizing muscle relaxants and additional doses of opioids can be administered based on clinical requirements and responses. Crystalloid solutions, preferably balanced salt solutions, are infused to replenish the fasting period, hourly maintenance, and blood losses.

16.10.5 Intraoperative Complications

Significant blood losses may be encountered during dissection due to bleeding from the epidural vertebral venous plexuses during posterior fusion or anterior decompression in Transoral Odontoidectomy [43]. Depending upon the clinical needs and allowable blood loss, blood transfusion may be required. Vascular injuries (e.g., vertebral artery injury) should be anticipated with catastrophic consequences, and accordingly, resuscitative measures should be prepared beforehand if such an eventuality occurs [43]. Vascular injuries are usually observed during the dissection of the C2 ganglion, drilling during

transoral odontoidectomy, or during the insertion of the screw in the axis [44]. The control of bleeding due to the bone hole is achieved with the use of bone wax. If vessels overlie the screw insertion site, an alternative site or method should be considered to fix the atlantoaxial joint [45]. Some authors advocate placing the construct screws on the side of the nondominant vertebral artery first [21].

During surgery via a transcervical approach, stimulation of the ansa cervicalis and sympathetic plexus can give rise to hemodynamic disturbances. Here, cessation of the stimulus and deepening the level of anesthesia can mitigate the disturbances. Abrupt hemodynamic changes like bradycardia or asystole are frequently observed when instrumentation is being done due to excessive pressures at the CVJ. During such events, the neurosurgeon should be notified for the prompt removal of the surgical stimulus. Anticholinergics should be avoided as these events are transient and may mask the surgical damage to vital areas of brain stem; the events resolve soon after the removal of the stimulus.

Pediatric patients being extremely vulnerable to hypothermia require vigilant temperature monitoring, covering of exposed parts, use of warming devices, warm IV fluids, and scrubbing and irrigating solutions. Hypotension should be avoided in these patients, as even temporary hypotension may lead to cord ischemia resulting in worsening of neurological outcome [44]. Autonomic dysfunction may be encountered that manifests as hypotension or bradycardia, which requires correction using volume expanders and shorter-acting vasopressors [36].

16.10.6 Electrophysiological Monitoring

Intraoperative neurophysiological monitoring (IONM) has increasingly been used to avoid neurological complications during surgery. During CVJ surgeries, the risk of neurological injuries exists both during both patient positioning and the surgical procedure. IONM, during the positioning, allows prompt recognition of impending neurologic injury, and real-time continuous IONM assesses the functional integrity of the spinal tracts [46]. The use of IONM is mainly described in relation to the intradural procedures; however, its wider application has also been described during spinal cord degenerative diseases. It helps in a better understanding of the pathophysiology of spinal cord injuries. In patients with severe myelopathy, SSEP and/or MEP monitoring should be considered. While using neuromonitoring, baseline preoperative values should be obtained prior to incision [44].

16.10.7 Extubation

Extubation should be attempted only with prior planning and preparation. Prolonged postoperative ventilation may lead to the occurrence of various complications; hence, early extubation is preferred [47]. In children with preexisting respiratory insufficiency or weak gag or cough reflexes, the tracheal extubation is usually delayed. Pronged surgery in a prone position may result in upper airway edema and obstruction. A cuff leak test may help in assessing the extent of airway edema before extubation. The use of intraoperative steroids and placement of a nasopharyngeal airway may help to reduce upper airway obstruction. However, it may not be effective for dependent edema [22]. Preoperative steroid administration may reduce the severity of oral and tracheal mucosal edema facilitating early extubation and avoidance of the need for tracheostomy [48]. As reintubation is difficult in these children due to airway edema and fixed cervical spine, difficult airway gadgets must be kept ready before tracheal extubation. Tube exchanger introduced through the ETT may also be used; however, it may aggravate obstruction and causes airway irritation.

16.11 Postoperative Management

Postoperatively, a wide variety of complications may be encountered for which the treating physician should be observant (Table 16.6). The majority of these cases require elective ventilation in

Table 16.6 Postoperative complications following surgical correction of craniovertebral junction (CVJ) anomalies

Specific to anterior approach (transoral odontoidectomy)	Specific to posterior approach (occipito-cervical fusion) surgery
• Damage to Eustachian tube and hypoglossal nerve • Severe tongue swelling • Palatal and pharyngeal dehiscence • Retropharyngeal abscess • Neurological worsening • Aspiration • Cerebrospinal fluid leak • Meningitis • Delayed pharyngeal bleeding • Craniovertebral junction instability	• Neurological worsening • Craniovertebral junction instability • Cord edema • Cerebrospinal fluid leak • Meningitis • Non-union • Hardware failure • Sudden death

view of oral edema. Also, central causes like medullary control of breathing, respiratory motor function, or sensory inputs may be affected, necessitating assisted ventilation. Children with congenital abnormalities of CVJ may have decreased preoperative pulmonary reserve. The postoperative complications after awakening from anesthesia include apnea, cyanosis, bronchospasm, and respiratory failure. These complications may be exaggerated due to oral secretions related to the prone position, preexisting stiffness of thoracic cage, and development of respiratory and cardiac problems due to intraoperative fluid overload. Some children may require ventilatory assistance in an ICU for 24–48 hours. Intraoperatively, resection of the uvula and soft or hard palate may cause postoperative palatal insufficiency. In rare cases, delay in the resumption of respiratory efforts may be due to excessively tight instrumentation exerting pressure over the respiratory centers, thereby requiring urgent decompression. In patients receiving blood transfusions, the incidence of postoperative pulmonary complications (POPCs) is higher along with the development of immune suppression and immune tolerance, thereby increasing the chances of nosocomial and postoperative infection. Monitoring the respiratory functions along with physiotherapy and phrenic nerve stimulation (diaphragmatic pacemakers) has been advocated to prevent POPCs [49, 50]. Regular limb mobilization, compression stockings, and intermittent pneumatic compression devices should be used to prevent the development of deep vein thrombosis. The use of anticoagulants (heparin/LMWH) should be considered for these patients who remain non-ambulatory for a significant duration. Heparin may be administered as a loading dose of 75 U/kg IV given over 10 min, followed by an initial maintenance dose of 20 U/kg/h (children), and the dose is adjusted to maintain aPTT between 55 and 85 sec; it must be measured daily once the therapeutic level is achieved [51, 52]. LMWHs (enoxaparin) are administered at the dose of 0.5 mg/kg every 12 hours, and doses are adjusted to achieve an anti-Xa activity in the range of 0.5–1 unit/ml 4–6 h after injection or a range of 0.5–0.8 unit/ml 2–6 h after injection [53, 54]. Judicious use of supportive measures like frequent postural change, nutritional support, chest physiotherapy, suctioning, spirometry, etc. improves the overall outcome of these children. The resumption of oral feeding should begin as early as possible through Ryle's tube. However, due to the presence of a suture line over the nasopharynx and oropharynx, placement of the same may be complicated, and an orogastric tube may be needed to be placed with the help of a laryngoscope.

16.11.1 Tracheostomy

Tracheostomy allows the prevention of POPCs and is a safeguard against airway obstruction from postoperative lingual edema [55]. Usual indications in these patients include the need for prolonged intubation, lower cranial nerve palsies, and development of POPCs and, in rare cases, as an emergency rescue measure due to extubation failure [55].

16.11.2 Post-discharge Care

Irrespective of the type of surgery, some rehabilitation is required in most children. The combined

specialized expertise of physical therapists, speech, and occupational therapists may be required to regain muscular function for overall improvement in the quality of life. Maintenance of a safe environment and adequate support system at home are necessary for proper recovery and rehabilitation of these children.

16.12 Conclusion

Surgery for pediatric CVJ lesions can be challenging and risky. Technological progress (like 3D reconstruction) has aided CVJ surgery to achieve a new, higher efficacy and ease of performance. However, children with CVJ anomalies continue to provide a distinct set of challenges for the attending anesthesiologists due to the immature age of the patient coupled with the basic pathology and its associated comorbidities such as complex airway syndromic associations, intraoperative adverse events, need for postoperative prolonged ventilation, etc. To ensure safe conduct and successful outcomes in these children, a thorough understanding of the pathophysiology, as well as cautious and vigilant perioperative management, is necessary.

Conflict of Interest Nil.

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Anesthetic Concerns During Pediatric Spine Surgery

17

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Key Points

- Surgeons and anesthesiologists planning for pediatric spine surgery should be fully aware of the characteristics of the target condition, such as the age of onset and commonly affected sites, which influence treatment approaches and anesthetic management.
- Preoperative assessment for congenital vertebral anomalies should focus on cardiac, pulmonary, or neurological comorbidities.
- Myelomeningocele repair is often performed in neonates; attention should be paid to prevent compressing the sac during anesthesia induction.
- The aim of surgery for spinal lipomas and cord detethering (infants and toddlers) should be functional recovery and preventing delayed neurological decline due to retethering than complete excision.
- Surgical correction of idiopathic scoliosis, commonly performed in school-age children, involves the risk of major bleeding.
- Although intraoperative neurophysiological monitoring is increasingly used in children, there is considerable doubt on the immaturity of the neural networks in infants and the risk of anesthetic overdose due to underdeveloped metabolizing systems, requiring careful monitoring titration.

17.1 Introduction

The most common surgical procedures for the spine by age group are as follows: myelomeningocele (MMC) repair in neonates, spinal lipoma resection in infants and toddlers, and correction of idiopathic spinal scoliosis in school-age children. Less frequent surgeries include the procedures for congenital spinal deformities, tumors, or vascular anomalies such as spinal arteriovenous malformation (AVM), cavernous malformation, dural arteriovenous fistula (AVF), and capillary telangiectasia. For safe and effective anesthetic management during spine surgery, the child should be placed in a comfortable prone position. An appropriate anesthetic protocol suitable for intraoperative neural monitoring should be chosen to minimize the risk of spinal nerve injury. It is not practical to make a "one size fits all" statement about anesthetic management for pediatric spine surgery since different types of such surgeries have different anesthetic considerations. For example, in patients undergoing MMC repair, attention should be paid to protecting the exposed neural tissue when introducing anesthesia. In patients undergoing spinal lipoma

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removal and tethered cord release, anesthetic management suitable for intraoperative neurophysiological monitoring (IONM) should be implemented to preserve function. For patients undergoing idiopathic scoliosis correction, the focus should be on appropriate anesthetic management for IONM, preparation for the possibility of bleeding, and postoperative pain management. The following sections will discuss the perioperative management for pediatric patients with common spine diseases like MMC, spinal lipoma, and idiopathic scoliosis and less common conditions like spinal tumors, vascular malformations, and neurofibromatosis.

17.2 Overview of Anesthetic Management

For safe and effective anesthetic management during spine surgery, the patient should be appropriately evaluated preoperatively and placed in a comfortable prone position during surgery, and an appropriate anesthetic agent that maximizes the effectiveness of IONM should be chosen to minimize the risk of spinal nerve injury during surgery. The types and doses of anesthetic agents should be carefully determined because they significantly impact the effectiveness of IONM.

17.2.1 Preoperative Evaluation and Preparation

Preoperative evaluation of the child posted for spine surgery should be individualized based on the pathology and the associated presenting features requiring further evaluation. All patients scheduled for elective surgeries must undergo basic investigations like complete blood counts (CBC) to look for baseline hemoglobin levels. Coagulation profile is warranted in cases with major anticipated losses, especially in associated neuromuscular diseases (NMDs). Further blood investigations are recommended based on the clinical condition of the child. Specific to spinal pathologies, a urinalysis must be done in cases of sphincter disturbances to look for asymptomatic urinary tract infection (UTI) as it may contribute to perioperative morbidity. A chest roentgenogram, electrocardiograph (ECG), and echocardiography are indicated in NMDs with suspected cardiac involvement. Pulmonary function testing may be done in an older child with kyphoscoliotic spine deformity. If the response to bronchodilator therapy be found (though a restrictive lung disease is more commonly observed), relevant therapy is initiated preoperatively. Airway management can be complicated by the involvement of the cervical spine necessitating imaging. Although less common, the anesthesiologist may face a situation where the child has been tracheostomized in the face of a difficult airway, commonly due to Klippel-Feil syndrome, Goldenhar syndrome, or Treacher Collins syndrome. It is essential to replace the tracheostomy with an endotracheal tube (ETT), especially in the prone position, to avoid traction due to the airway circuit and displacement of the tube (1). The risk of malignant hyperthermia (MH), though rare, should not be forgotten while anesthetizing children with NMDs (2).

17.2.2 Patient Positioning

Patients undergoing spine surgery are typically placed in the prone position. If the head of a child undergoing thoracic, lumbar, or sacral spine surgery does not fit in prone head support such as ProneView® (Dupaco Inc., Oceanside, CA), the surgeon should turn the head safely on one side to avoid kinking and obstruction of the ETT, eyeball compression, and facial pressure ulcers. Excessive head turning can lead to compression of the carotid artery, which may compromise cerebral perfusion, increase intracranial pressure (ICP), and cause venous hemorrhage resulting from poor venous return. Postoperative visual loss (POVL) is a rare complication of prone spine surgery, but with a devastating and irreversible outcome. The incidence of POVL after spine surgery is approximately 0.2% (3). For adults undergoing cervical spine surgery, the Mayfield skull clamp is used to stabilize the neck. However, the skull clamp is not suitable for infants because of

Table 17.1 Specific measures for positioning

- Optimize the head position
  - Avoid eyeball compression
  - Avoid excessive head-turning
- Prevent elongation and compression of the nerves and vessels of the extremities. In particular, the nerves of the ulnar and brachial plexus in the upper extremities and the femoral and peroneal nerves in the lower extremities are prone to paralysis
- Prevent skin lesions (e.g., blisters, exfoliation, pressure ulcers)
- Avoid abdominal compression

the risk of cranial fracture or epidural hemorrhage due to their thinner skull bones.

The specific measures should not be overlooked and are enumerated (Table 17.1). Optimal positioning can also be aided by the use of neurophysiological monitoring like in superman position; monitoring for upper extremity injuries can be done with the help of somatosensory evoked potentials (SSEPs).

17.2.3 Intraoperative Neurophysiological Monitoring (IONM)

Spine surgery involves a risk of physical damage to the nervous system by inadvertent compression or traction during maneuvers and postoperative spinal dysfunction due to the compromised blood supply. To prevent those outcomes, IONM should identify neural structures and evaluate their function during surgery. The purpose of neurophysiological mapping is to identify neural network structures. Evoked potentials (EPs) are monitored to evaluate motor, somatosensory, urinary, or bowel function. Thirumala et al. carried out a systematic review of the diagnostic accuracy of intraoperative transcranial MEP monitoring to detect neurological deficits during corrective spine surgery in patients with idiopathic scoliosis (4). Neurological deficits were observed at an incidence of 1.38% (29/2102). The sensitivity and specificity of MEP monitoring were 91% and 96%, respectively. Significant MEP decreases were 250 times more likely to be observed in patients with a new-onset motor deficit immediately after idiopathic scoliosis correction surgery than in those without.

IONM was long considered infeasible in young children, particularly infants and toddlers, because of their immature myelin sheaths and synapses and difficulty adjusting anesthetic doses. In recent years, however, remifentanil has facilitated intraoperative evoked potential monitoring in infants and young children because it can reduce the dose of hypnotics used and eliminate the use of muscle relaxants during maintenance anesthesia (5–9).

(a) **Neurophysiological Mapping.**

Neurophysiological mapping is performed to localize neural networks and differentiate spinal nerves from other tissues. Technically, the spinal nerve is electrically stimulated in the surgical field, and the corresponding muscle potentials are recorded from the lower extremity or external anal sphincter muscles. This mapping technique is particularly effective for differentiating nerves from fibrous or other connective tissues in a spinal lipoma during resection.

(b) **Motor Evoked Potential (MEP) Monitoring.**

MEP monitoring is conducted to evaluate the function of the descending motor pathways. Two different techniques of MEP monitoring following transcranial stimulation of the motor cortex described are (**1**) D-wave monitoring and (**2**) muscle MEP monitoring. Transcranial electrical stimulation is applied to the motor cortex, and the resulting compound muscle action potentials are recorded in all four extremities (Fig. 17.1). Intraoperative MEP monitoring can be successfully performed in babies as young as 1 month old. However, since their neural pathways are still growing, results may be unstable in younger children. The transcranial electrical stimulation required to elicit MEP responses should be stronger in younger children. Although no safety limit has been officially recommended for electrical stimulation in pediatric patients, the maximum intensity and voltage should be 200 mA and

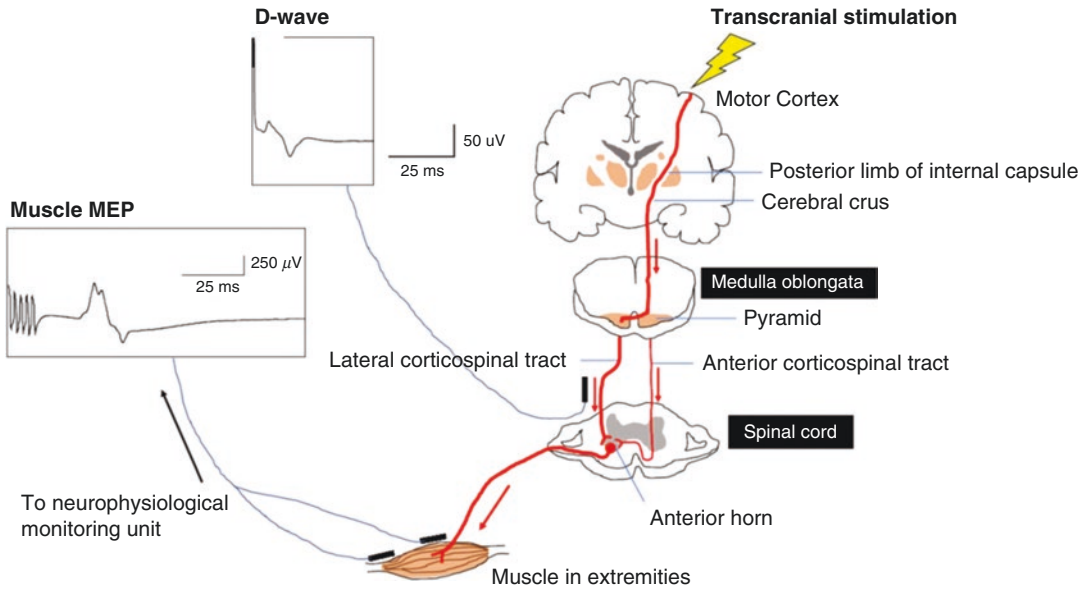

Fig. 17.1 Motor evoked potential (MEP) monitoring. Schematic diagram shows the motor pathways involved in two types of MEP monitoring. D-wave monitoring is done by placing electrodes proximal and distal to the spinal cord lesion and following a single wave stimulus. Muscle MEP monitoring is done from the peripheral muscle following multiple wave stimuli

500 V, respectively, considering their impact on the central nervous system (CNS). Propofol does not suppress MEP responses to the same extent as inhaled anesthetics. Nitrous oxide should not be used for maintenance anesthesia because it strongly suppresses MEP responses. Since opioids do not suppress MEP responses, there are no particular restrictions on their use as far as MEP monitoring is concerned.

(c) **Somatosensory Evoked Potential (SSEP) Monitoring.**

Somatosensory evoked potential (SSEP) monitoring evaluates the function of the ascending somatosensory pathways. The sensory nerve of the upper extremities (typically the median nerve) or lower extremities (typically the tibial nerve) is electrically stimulated, and the resultant SSEP waveforms are recorded over the scalp. SSEP waveforms reflect the joint position, vibration, and discriminatory tactile senses mediated by the posterior column-medial lemniscus pathway, but no pain or temperature sensation transmitted by the spinothalamic tract. The posterior column pathway is immature in children before 5 or 6 years of age and conducts at a lower velocity than in adults. Consequently, small children have more variation in latency.

(d) **Bulbocavernosus Reflex (BCR) Monitoring.**

BCR monitoring records the external anal sphincter muscle potentials elicited via the spinal reflex arc following pudendal nerve stimulation (Fig. 17.2). This technique allows for direct surveillance of the integrity of the sacral nerves that regulate urination, defecation, and sexual function. This technique is particularly useful for tethered cord release surgery in patients with spinal lipoma or patients undergoing other types of lumbosacral spine surgery (10). The incidence of postoperative voiding dysfunction is estimated at 10–20% for pediatric patients who undergo the release of tethered cord (11).

(e) **Intraoperative Wake-up Test.**

Intraoperative wake-up test in pediatric spine surgeries has been described in the literature (12, 13). For this test, the level of anesthesia is reduced

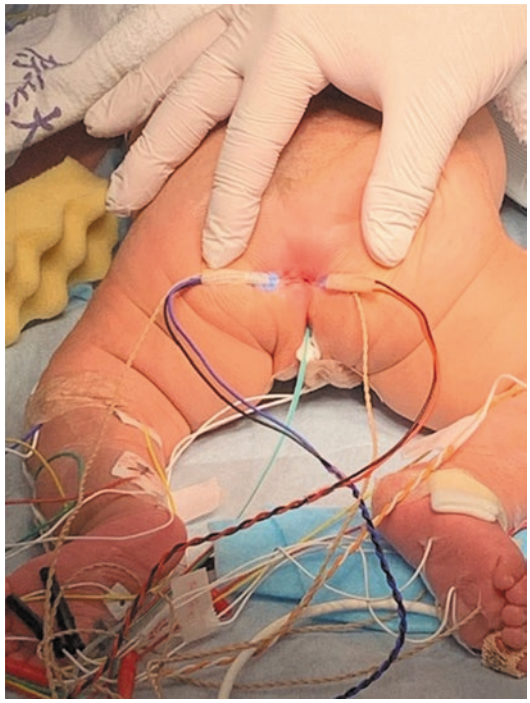

Fig. 17.2 Bulbocavernosus reflex (BCR) monitoring. BCR monitoring was performed in an infant with spinal lipoma during surgery. BCR is recorded from bilateral external anal sphincter muscles after electrical stimulation to the sensory branches of the pudendal nerve (the dorsal penile or clitoral nerve). For BCR recording, the needle electrodes are placed into the external anal sphincters on both sides (right and left). For stimulation of the dorsal penile or clitoral nerve, a single cathode on the dorsal surface and a single anode on the ventral surface of the penis have been placed. For stimulation of the bilateral dorsal clitoral nerves, a single cathode is placed on the clitoris and a single anode in the adjacent labia. Surface electrodes are used to stimulate the dorsal penile or clitoral nerve

until the patient is conscious enough to respond to the anesthesiologist's request to move the ankle or knee. Since this test necessitates the patient's full understanding and cooperation, it is not always viable for small children. If a patient undergoing scoliosis surgery is not securely fixed to the table and makes a forceful body movement upon emergence from anesthesia, it may cause spinal injury. In addition, the patient is at risk of air embolization resulting from active inspiratory effort upon awakening. Currently, propofol and remifentanil availability has enabled stable MEP monitoring, eliminating the need for the wake-up test. Exceptional cases may involve patients with motor nerve injury who do not respond to MEP stimulation.

17.2.3.1 Anesthetic Management for IONM During Pediatric Spine Surgery

Benzodiazepines and clonidine must be avoided because they have long half-lives and strongly suppress MEP responses (14, 15). If no intravenous (IV) line has been established, the anesthesiologist should perform slow induction with sevoflurane. Rapid induction with propofol is advised if an IV line is available. In addition to less airway irritation, sevoflurane has low solubility (blood-gas partition coefficient), which allows for rapid induction and elimination and causes little interference with subsequent MEP monitoring (16, 17). Since children have a larger central compartment volume than adults, children undergoing propofol anesthesia require higher bolus doses and higher early-stage injection rates to maintain the same steady-state concentrations (18, 19). Although nitrous oxide strongly suppresses MEP responses, it can be used for anesthesia induction.

For maintenance of anesthesia, propofol or inhaled anesthetics (sevoflurane or desflurane) are administered. Small children are at significant risk of propofol accumulation due to low clearance. Neonates have poor propofol clearance with substantial inter-individual variability. Infants from 3 to 12 months of age have immature liver enzyme systems (20, 21). These facts suggest the benefit of adjusting the maintenance anesthetic dose based on the exhaled drug concentration. Propofol accumulation in pediatric patients may be prevented by combining low-dose propofol and a low dose ($\leq$0.5 minimal alveolar concentration, MAC) of inhalational anesthetic (22–24). Anesthesiologists administering propofol to children should be aware of propofol-related infusion syndrome (PRIS), which often presents a fatal complication. In patients undergoing continuous propofol infusion, the infusion rate should be minimized by concurrent administration of remifentanil (25). The various drugs used to maintain anesthesia

Table 17.2 Effects of anesthetic agents on evoked potentials

	SSEP amplitude	MEP amplitude
Intravenous anesthetics		
Barbiturates (low dose)	→	↓↓
Benzodiazepine	↓	↓↓
Dexmedetomidine	→	→
≤0.6 ng/mL	↓	↓↓
>0.6 ng/mL	↓	→
Opioids	↓	↓
Propofol	↑	→
Ketamine		
Inhalation anesthetics		
Desflurane	↓	↓↓
Sevoflurane	↓	↓↓
Isoflurane	↓↓	↓↓
Nitrous oxide	↓↓	↓↓
Muscle relaxant		
Rocuronium bromide	→	↓↓

SSEP: somatosensory evoked potential. MEP: motor evoked potential
↓: suppression, ↓↓: severe suppression, →: no change, ↑: increase

and their effects on neurophysiological monitoring are enlisted in Table 17.2.

17.3 Tethered Cord Syndrome (TCS)

Owing to its tapered shape, the lower end of the spinal cord is called the medullary cone. The spinal cord is anchored to the coccyx by a filament known as the terminal filum. At birth, the medullary cone is located at the third lumbar (L3) vertebra level. It gradually moves upward to the cranial side over time until it reaches the level of the L1 or L2 vertebra in adulthood. TCS is a stretch-induced neurological disorder caused by the fixation (tethering) of the medullary cone, often leading to progressive lower-limb sensorimotor deficits and neurogenic bladder and bowel dysfunction. Tethered cord release is the only definitive treatment option.

Pediatric patients with TCS typically have spina bifida, a congenital morphological abnormality of the neural tube that results from a failure of the vertebral arch to fuse early in development. Spina bifida has two clinical forms: open and occult. Open spina bifida represents an externally visible defect of the spine, whereas occult spina bifida does not have outward signs. One of the most common types of congenital neurological anomaly is classified as a type of open spina bifida. The occult spina bifida includes spinal cord lipoma, terminal filum lipoma, and congenital dermal sinus. Patients with spina bifida are at extremely high risk for latex sensitization and allergy due to long-term urethral catheterization and multiple surgeries. Therefore, patients with spina bifida must be treated in a latex-free environment.

17.4 Spina Bifida and Latex Allergy

Latex anaphylaxis may lead to significant morbidity. Deaths have been reported. Compared with adults, children are generally at a higher risk of latex sensitization due to long-term urethral catheter use and multiple surgeries. The condition of spina bifida per se might be an independent risk factor for latex sensitization, irrespective of the number of previous surgeries (26). Approximately 70% of patients with myelomeningocele have allergic reactions to latex (27). Latex-free precautions should be exercised starting at birth for patients with spina bifida (28).

17.5 Myelomeningocele (MMC)

MMCs predominantly occur in the lumbosacral region. These lesions occur when the spinal cord and meninges are contained in a saccular herniation that protrudes through a vertebral arch defect (29). MMCs that occur at the sacral level mainly cause bladder and bowel problems, whereas those at the lumbar level cause lower limb sensorimotor dysfunction.

If a neonate has incomplete closure of the spinal column that involves exposure of the spinal cord or leakage of cerebrospinal fluid (CSF), there is a high risk of immediate infection, and the neonate should undergo closure within 24–48 h of life. After birth, the neonate should be

maintained in the prone position to prevent injury to the exposed nerve tissues. The surgeon makes a circumferential incision around the exposed neural placode to detach the arachnoid membrane; the dura, fascia, and skin are sutured in a water-tight manner to cover the spinal cord.

Children with MMC often develop hydrocephalus and Chiari type II malformation. More than 80% of patients with MMC have hydrocephalus that requires surgical treatment, such as ventriculoperitoneal shunt placement and foramen magnum decompression. The symptoms of Chiari type II malformation include wheezing, apnea, and dysphagia, which require airway management in the patient. Cervical MMCs occur very infrequently, constituting 4–8% of all cases of spina bifida; these lesions are distinctly different from lumbosacral MMCs. In the absence of hydrocephalus and Chiari type II malformations, cervical MMCs are not associated with neurological disorders. Elective surgery is indicated in typical cases where the spinal cord is covered, and its risk is small.

The recent development of maternal serum marker screening and fetal ultrasound imaging has enabled prenatal diagnosis of MMC, allowing for adequate planning of closure surgery at a very early stage of life. In this context, social attitudes and laws concerning prenatal screening and abortion may differ considerably from one country to another.

The anesthetic management for infants undergoing MMC surgery will be similar to that for neonates in general. In routine cases, lumbosacral MMCs are closed surgically within 24 to 48 hours after birth. The multidisciplinary surgical team members must share a common understanding of the operating risks through clinical conferences in advance. Optimal anesthetic management protocols should be selected to mitigate stress reactions to surgical intervention while maintaining sufficient cardiac function in neonates, who are very sensitive to inhalational and intravenous anesthetics. Opioid-based anesthetics are the agents of choice for neonates because they can stabilize hemodynamics most effectively. The anesthesiologist should bear in mind that neonates require a significantly longer time to recover from anesthesia than older patients because of their immature hepatic and renal function; artificial ventilation may occasionally be needed postoperatively.

A latex-free environment is prepared during the preoperative period. The surgeon should take utmost care to prevent spinal injury and elevation of ICP due to the meningeal sac's compression. For this purpose, endotracheal intubation in the prone position may be helpful (30), but this technique is not widely accepted. Doughnut-shaped support or elastic pad can be inserted beneath the patient to maintain a secure position and protect the meningeal sac from direct contact with the table or other solid materials. In children with cervical MMC, cervical spine extension may occur during intubation, possibly leading to the displacement of the support pad placed to protect the sac from injury. For this reason, intubation may be performed while the neonate is held (31). In most cases, however, patients are transferred from the neonatal ICU to the operating room. Consequently, intubation is generally performed under intravenous anesthesia. Thiopental (3–4 mg/kg) or propofol (1.5–2 mg/kg) is used in combination with opioids. The anesthesiologist should carefully check the breathing status of neonates undergoing anesthesia, given the possibility that spontaneous breathing may stop. Mask ventilation may be used to supplement the oxygen supply. The use of high-dose muscle relaxants in neonates deserves careful consideration because they may have a delayed onset of action.

Intraoperative Management: Inhalational anesthetics are commonly used for general maintenance anesthesia. Propofol may be used for general IV anesthesia in patients suspected of having malignant hyperthermia or myotonic dystrophy and patients undergoing MEP or BCR monitoring (Fig. 17.3). In intubated neonates, tube tip position may vary by the length of one vertebral body along the trachea due to neck flexion and extension. Ventilation problems should be detected early using a chest or esophageal stethoscope and end-tidal carbon dioxide measurement. Accidental intraoperative extubation can easily result in serious hypoxemia and cardiopulmonary arrest in small children with a low

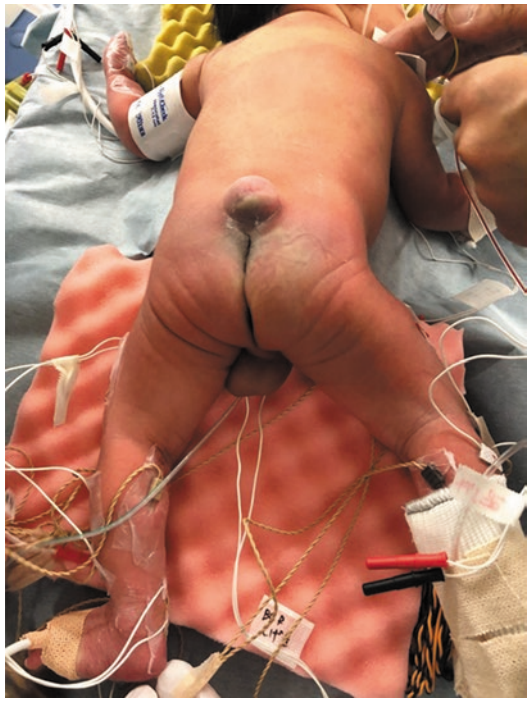

Fig. 17.3 A neonate with lumber myelomeningocele positioned prone for surgical excision with neurophysiologic monitoring electrodes in place. This neonate with lumber myelomeningocele underwent a closure operation within 48 h of birth. He was placed in a prone position after endotracheal intubation. The operation was accomplished by intraoperative monitoring of motor evoked potential (MEP) and bulbocavernosus reflex (BCR). The electrodes to record BCR were still not set to the bilateral external anal sphincter muscles in this picture. No significant change in MEP and BCR monitoring were observed through the operation. There was no postoperative neurological deterioration

functional residual capacity. Neonates cannot be placed on prone head support devices designed for adults. Therefore, the head should be turned safely to one side to prevent compression of the eyeballs and the ETT when the neonate is maintained in the prone position. Generally, neonatal MMC repair does not involve much bleeding. Fluid infusions may be considered to compensate for CSF loss at the operative site, especially during prolonged procedures. Body temperature control is more difficult in patients with greater exposure to neural tissue. The OR should be maintained at a temperature higher than usual using a forced-air warming apparatus or another appropriate heating system. If the patient is a termed infant with no major comorbidities, the patient may be extubated in the operating room. Extubation should be performed in the prone or lateral position. The child should be nursed in the prone position; if associated with hydrocephalus or a Chiari malformation, the child should be monitored for postoperative apnea. Transfer of the child to the postanesthetic unit also should be done in a prone position. A continuous infusion of fentanyl (0.2–0.3 μg/kg/h) may be used for postoperative analgesia.

17.6 Spinal Lipoma

Occult spina bifida includes two major conditions: congenital dermal sinus and spinal lipoma. Lumbosacral skin stigmata are frequently observed in patients with occult spina bifida. Spinal lipoma in younger children is suspected based on the presence of a subcutaneous mass, dimple, hypertrichosis, tail-like skin appendage, and other forms of skin stigmata. In contrast, diagnosis in older children is triggered by neurologic signs and symptoms such as lower limb sensorimotor dysfunction, bladder and bowel problems, and foot deformities (32). Since spinal lipomas are not malignant neoplasms, greater attention is directed to functional recovery and preventing delayed neurological decline due to retethering than to complete lipoma removal. Specifically, the basic objectives of surgical intervention include (1) untethering of the spinal cord, (2) debulking of the lipoma, and (3) re-establishing normal anatomical structures (33). Before the onset of neurologic symptoms, prophylactic surgery is recommended for patients with spinal lipoma since neurologic manifestations are unlikely to respond to surgical treatment adequately. Surgical interventions are typically performed during infancy. IONM is effective for preventing surgically induced nerve injury in these children (34, 35). The modalities of choice include neurophysiological mapping to locate neurological structures through direct stimulation in the surgical field, MEP monitoring of the descending motor pathways, and BCR monitoring

of bladder and bowel function. Since these techniques rely on muscle contraction, they should be started after the effects of any muscle relaxants administered for induction anesthesia have cleared. The use of muscle relaxants for maintenance anesthesia should, therefore, be avoided.

Preoperatively, a latex-free surgical environment may be ensured. For IONM, the anesthesiologist should carefully determine the optimal anesthetic protocol that avoids muscle relaxants. Since muscle relaxants strongly suppress neurophysiological mapping, MEP, and BCR responses, they should be administered at the minimum dose necessary for facilitating endotracheal intubation and subsequent positioning. The anesthesiologist must ensure that the anesthetic protocol will not interfere with the planned IONM. IV propofol is the first choice for surgeries that involve MEP or BCR monitoring. Inhalational anesthetics may be used for surgical procedures, but neurophysiologic monitoring performance is less satisfactory with inhalational anesthetics than with propofol. While the opioids do not interfere with neurophysiological monitoring, the use of muscle relaxants must be avoided in patients undergoing neurophysiological mapping, MEP monitoring, or BCR monitoring. A continuous infusion of fentanyl infusion at 0.5 μg/kg/h may be needed for postoperative sedation, depending on the extent of the surgical incision and the stress reaction.

17.7 Spinal Deformity

Pediatric patients with spinal deformity have a wide variety of congenital or idiopathic conditions involving abnormal spinal curvatures in the coronal or sagittal plane (Table 17.3). Abnormal spinal curvature may also develop as a result of NMDs acquired after spinal cord injury. In neonates and infants, severe spinal deformities can affect the thoracic cage and lung growth, thereby decreasing chest volume and respiratory function and ultimately leading to chronic respiratory failure. Spinal fixation surgery may be performed to prevent the progression of spinal deformity. In school-age and older individuals, spinal deformity most commonly manifests as idiopathic scoliosis and kyphosis. Lateral curves of more than 45° and potentially progressive deformity are indications for surgery. Children with juvenile or adolescent idiopathic scoliosis are generally healthy and have no life-threatening pulmonary conditions. However, they may have psychological problems due to their effect on physical appearance.

Table 17.3 Syndromes and neuromuscular conditions associated with abnormal spinal curvature

- Cerebral palsy
- Charcot-Marie-tooth disease
- Poliomyelitis
- Spinal muscular atrophy
- Arthrogryposis multiplex congenita
- Duchenne muscular dystrophy
- Congenital hypotonia
- Neurofibromatosis
- Marfan syndrome
- Ehlers-Danlos syndrome
- Myelomeningocele
- Osteogenesis imperfecta congenita
- Achondroplasia

17.7.1 Congenital Spinal Deformity

Pediatric patients who undergo fixation or other spinal deformity surgeries may have underlying congenital diseases, which could specifically impact their respiratory, cardiovascular, neurological, or other functions. These possibilities underscore the importance of comprehensive preoperative assessment. Jarcho-Levin syndrome and Jeune syndrome are congenital disabilities that cause the severe malformation of the spine and ribs, which result in severe respiratory dysfunction. Achondroplasia very frequently manifests as thoracolumbar kyphosis in infants, though most cases spontaneously improve once ambulation starts. It may progress to a fixed kyphotic deformity, seen in 15–30% of adults (36). Early sitting in infancy is considered a major risk factor for kyphosis (37, 38). It is recommended that infants with achondroplasia be restricted from unsupported sitting until they can independently achieve a sitting posture. Since children with achondroplasia are at a high risk of upper airway

obstruction, careful perioperative respiratory management is needed. Ellis-van Creveld syndrome is a genetic disorder characterized by thoracic hypoplasia, vertebral anomalies, and cardiac malformations. Approximately 60% of patients with this syndrome have an atrial septal defect (ASD) or an endocardial cushion defect.

Congenital scoliosis is frequently associated with cardiovascular anomalies such as mitral valve prolapses, ASD, and patent ductus arteriosus, as well as horseshoe kidney, muscular dystrophy, Ehlers-Danlos syndrome, and Marfan syndrome (39). When infants with congenital scoliosis are scheduled for spine surgery, the preoperative assessment should include overall physical appearance, skin condition, and neuromuscular function. Measurement of the infant's height (or length) is important for evaluating skeletal growth. If a patient has disproportionately long arms, fingers, and toes, Marfan syndrome should be suspected. This syndrome is frequently complicated by cardiovascular conditions such as aortic root enlargement, aortic valve incompetence, aortic aneurysm, aortic dissection, and mitral valve prolapse. Therefore, they should undergo preoperative echocardiography and other cardiovascular evaluations. Surgery for scoliosis correction in the case of Marfan syndrome should not be undertaken before 4 years of age, considering the high risk of mortality due to cardiac and other comorbid conditions (40). If a patient has unstable joints and fragile skin combined with scoliosis, Ehlers-Danlos syndrome or other connective tissue disorders may be suspected. Common syndromic conditions manifesting with congenital scoliosis (40–44) and their comorbid presentations requiring the attention of the neuroanesthesiologist are listed in Table 17.4.

Anesthetic management needs to be optimized by considering the child's age and respiratory and cardiovascular comorbidities. Ensure that the anesthetic protocol will not interfere with any planned IONM, and plan for a wake-up test if the patient is old enough to cooperate. One invasive arterial line and two venous lines are to be maintained; central venous access or pulmonary arterial line may be required depending on the cardiac function of the patient. Suxamethonium and inhalational anesthetics are to be avoided if muscular dystrophy is present. Early tracheal extubation is usually encouraged, whenever possible. However, extubation at the end of surgery may not be a practical goal for children with moderate to severe respiratory problems. Intravenous patient-controlled analgesia (IV-PCA) for following extensive surgery is a reasonable option for postoperative pain management.

Table 17.4 Common syndromes associated with scoliosis and their anesthetic risks (40–44)

Syndrome(s)	Anesthetic risks
Down's syndrome	Cardiac involvement, cognitive disturbances, thyroid disorders
Klippel-Feil syndrome	Cervical spine involvement and difficult airway
Neurofibromatosis	Multiple tumors, complications like renal artery stenosis, pheochromocytomas
Marfan syndrome	Cardiac
Muscular dystrophy	Malignant hyperthermia

17.7.2 Idiopathic Scoliosis

Idiopathic scoliosis accounts for approximately 80% of all cases of scoliosis. Although it can be detected in infants and toddlers, it manifests most frequently in the pre-teen and teenage years and is more common in females. Typically, patients with idiopathic scoliosis are otherwise healthy. The key challenges for the anesthesiologist in surgery for this condition include preparing for a risk of major bleeding and ensuring that the anesthetic protocol does not interfere with any planned IONM. The children would experience severe postoperative pain due to extensive thoracic intervention. IV-PCA may be considered for postoperative pain control.

Preoperative Preparations: It is important to identify the risk factors for bleeding based on a preoperative assessment of the patient's medical history and family history. History of bleeding events like epistaxis, easy bruisability, bleeding instances following dental treatment, and menorrhagia in adolescent girls are relevant in the pediatric population. Tests for coagulation and

plans for autologous blood transfusion, wherever possible, to avoid the risk of infection from allogeneic blood transfusions may be ensured preoperatively. Pre-donated autologous blood significantly reduces the need for allogeneic blood transfusion in scoliosis surgery (45). The benefits of an intraoperative cell salvage system remain a matter of debate (46, 47). IONM should include combined MEP and SEP monitoring; the intraoperative wake-up test for patients with preoperative motor nerve injury may be considered if the children are intellectually capable and old enough to cooperate with the examination.

Intraoperative Management: Administer short-acting muscle relaxants at the lowest dose necessary for facilitating endotracheal intubation and subsequent positioning. Recognize that these agents strongly suppress MEP responses. Place the patient in the prone position carefully to prevent pressure on the face and eyes. Use appropriate prone head positioning devices (e.g., ProneView®). If a long surgery that involves a risk of major bleeding is expected, place an invasive arterial pressure line to monitor blood pressure continuously and analyze arterial blood gas parameters at appropriate intervals. Secure two intravenous lines; a 20G or wider-bore line should be reserved for blood transfusion, while the other line is used for continuous anesthetic administration. Surgery for scoliosis correction involves a risk of major bleeding due to the fixation of multiple spinal segments. Use a warming device to prevent hypothermia. General anesthesia with intravenous propofol is the first choice for operations that include MEP monitoring. Inhaled anesthetics can also be used along with opioids, which do not interfere with IONM. In children undergoing MEP monitoring, do not use muscle relaxants. Alternatively, administer minimal doses of muscle relaxants continuously with neuromuscular monitoring. Perform the wake-up test if MEP measurements continually show a significant decrease or no response.

Risk of Major Bleeding: Scoliosis correction involves a risk of major bleeding, which increases the likelihood of allogeneic transfusion. Allogeneic transfusions have potential complications such as infection, fever, transfusion-associated circulatory overload, immunologic reactions, and allergic reactions. Allogeneic transfusions are also associated with a higher incidence of postoperative complications, longer hospital stay, and higher 30-day readmission rates (48). Use of the anti-fibrinolytic agent tranexamic acid may help reduce surgical blood loss (49).

Postoperative Management: Pain management is crucial after posterior spinal fusion in an adolescent with idiopathic scoliosis. This type of surgery may cause severe postoperative pain involving multiple vertebral bodies. Adolescents may have high levels of frustration and dissatisfaction when they are confined to bed with pain. Effective postoperative pain control can facilitate early out-of-bed activities, early postoperative feeding, and shorter hospital stay, thereby increasing patient satisfaction. IV-PCA with fentanyl and morphine is very effective for postoperative pain control.

17.8 Spinal Tumor Surgeries

Spinal cord tumors are classified into intradural (intra and extramedullary) and extradural tumors (Fig. 17.4). Intramedullary spinal cord tumors are the most common and contribute to 35–40% of intraspinal tumors in the pediatric population, including astrocytomas (60%) and ependymomas (30%), the major subtypes. The most common clinical presentation is that of pain along the spinal axis, which, if left unattended, can progress to sensory problems (dysesthesia/paresthesia), motor weakness, and autonomic disturbances (bladder/bowel involvement) depending on the level of the lesion. Young infants may manifest with crying (due to pain) and motor regression (loss of achieved motor milestones). Extramedullary tumors include schwannoma and neurofibroma (benign and generally avascular), meningiomas (usually not involving the nerve roots and rarely occur except in neurofibromatosis), and metastasis. The treatment of spinal tumors is surgical excision. Certain unique characteristics of spinal tumors and the corresponding implications for the neuroanesthesiologists are enlisted in Table 17.5.

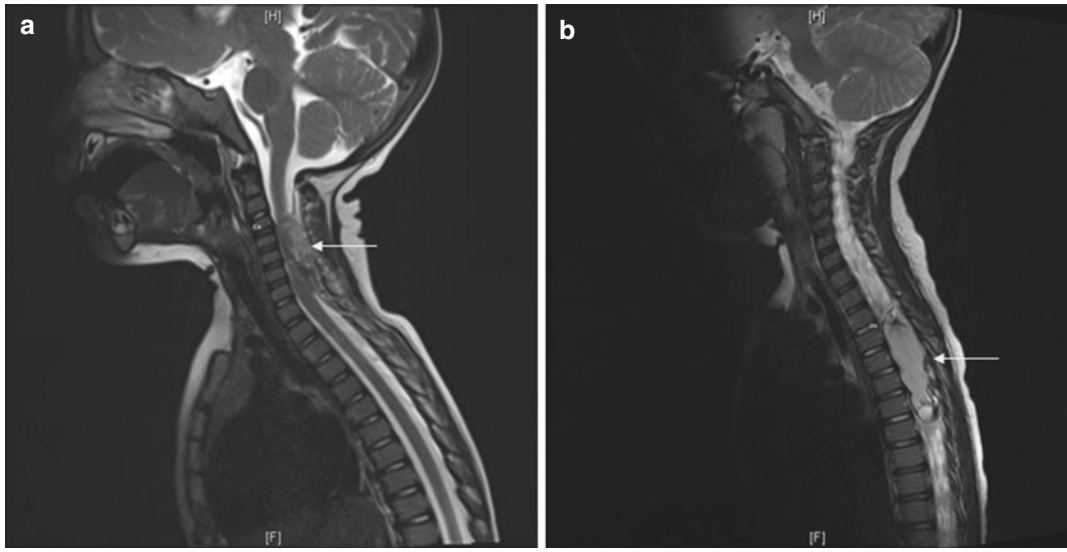

Fig. 17.4 Magnetic resonance imaging (MRI) of spinal tumors. (**a**): Mid-sagittal T2-weighted image of a 2-year-old female child who presented with quadriparesis showing intradural extramedullary (IDEM) mixed signal intensity lesion (white arrow) extending from C3 to C6 with a dural tail with severe spinal cord compression. The lesion was resected successfully and histopathological examination revealed an atypical teratoid rhabdoid tumor. (**b**): Sagittal T2-weighted image of a 10-year-old male child who presented with back pain and progressive lower limb weakness demonstrated a hyperintense extradural lesion (white arrow) with lateral displacement of the cord extending from D3 to D7 levels which was successfully resected without any neurological deficits

Table 17.5 Characteristics of spinal tumors and anesthetic implications

Lesion	Characteristics	Anesthetic implications
Astrocytoma	1. Compress and displace white matter tracts with a distinguished plane making their excision easier 2. High-grade malignant tumors (rare) have high vascularity and no definite plane	1. Neuromonitoring during retraction of the cord 2. Bleeding with malignant tumors
Ependymoma	Central location within the cord with symmetric expansion	Gross total excision is possible without high morbidity with the use of neuromonitoring
Lipoma	Involvement of multiple segments with no clear plane. The goal of surgery: Decompression of the cord rather than complete excision	Chances of recurrence requiring multiple surgeries
Teratoma	Associated with congenital malformations like diastematomyelia, meningomyelocele	1. Chances of recurrence and requirement of redo surgeries with immature teratomas 2. Associated with neurofibromatosis and may require systemic evaluation preoperatively
Oligodendroglioma	Preference for the meningeal spread	Component of intracranial hypertension and fluctuation of symptoms need documentation preoperatively
Hemangioblastoma	Associated with von Hippel Lindau syndrome	1. Evaluation for pheochromocytomas and intracranial tumors 2. Risk of torrential intraoperative bleeding – Preoperative embolization has a role

Surgical Considerations in Spine Tumors: Surgery for removal of spine tumors is considered with progressive symptomatology. The major goal of surgery is to remove the lesion with minimal traction on the spinal cord (50). Advances in surgical techniques and the advent of neuromonitoring have resulted in reduced postoperative morbidity. Intraoperative tools like ultrasonography assist the surgeon in localizing solid and cystic components, drainage of cysts, and confirmation of complete removal of the lesion (51). The major considerations in pediatric spine surgeries are:

1. Need for spinal fusion: The requirement of multiple-level laminectomies disrupts the spinal sagittal alignment and results in kyphoscoliosis, which is undesirable in growing children. Hence, it is imperative to do laminoplasty or spinal fusion (instrumentation), which results in increased operative time, increased bleeding, and an overall chance of increased morbidity. It is important to note here that there is a class of intramedullary tumors called holocord tumors, extending from the cervicomedullary junction to the conus medullaris. The establishment of spinal stability in such cases may be difficult with the high morbidity rates, as mentioned above. It also compounds the management of postoperative pain due to increased musculoskeletal manipulations.
2. Tumors that present caudally (T10–T12 and below) tend to infiltrate the gray matter tracts, usually not seen with rostral tumors, and can result in postoperative neuro-deficits.
3. Prior irradiation and multiple surgeries increase the chances of wound dehiscence, adding to the morbidity.
4. For IONM in spinal tumors, it is recommended that both SSEP and MEP are used together to increase the sensitivity of the results. However, there are high chances of SSEPs being lost with initial myelotomy and, hence, more dependence on MEP. Several factors like level of lesion (conus: no possibility of distal monitoring as the corticospinal tracts have ended there), dural adhesions, or desynchronization from previous surgery or irradiation hinder successful monitoring of MEP as well.

17.9 Spinal Vascular Malformations

Spinal vascular malformations encompass cavernous malformations (CM), arteriovenous malformations (AVM), and arteriovenous fistulas (AVF) (52–54)**.** From a surgical perspective, they may be classified as neoplastic, aneurysms, AVM, and AVF, further divided based on the locations: extradural, intradural ventral, and intradural dorsal (55). Their presentation differs from spinal tumors in that acute neurological deficit due to hemorrhage from the lesion is more common compared to the chronic progressive deficit and pain with tumors. Diagnosis is established by magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA) and digital subtraction angiography (DSA). DSA serves for both diagnostic and therapeutic (embolization) purposes. Treatment is usually by surgery, after preoperative embolization in some suitable cases, or by endovascular embolization. Considerations for surgery and anesthesia in these cases are the facilitation of neuromonitoring to detect neurological deficits and control bleeding. In these cases, the unique feature of neuromonitoring is that feedback from monitoring should not compromise the complete resection, considering the possibility of bleeding from residual lesions and the worsening of or development of new neurological deficits. The characteristics of spinal vascular lesions are described in Table 17.6**.**

17.10 Spinal Surgery for Neurofibromatosis

Neurofibromatosis (NF) covers a wide spectrum of manifestations ranging from neurocutaneous, neurologic, osseous, and soft tissue involvement (56, 57). Spinal deformities (scoliosis being the most common) and bone growth disorders are seen more commonly in NF-1 and intraspinal

Table 17.6 Characteristic features of spinal vascular malformations

Cavernous malformation	1. Confined to 1–2 spinal levels 2. Low risk of intraoperative bleeding 3. Iatrogenic bleed – Slow venous bleed, easily controlled with pressure and surface hemostatic agents
Arteriovenous malformation	1. Rare in children 2. Supplied by medullary branches of anterior/posterior spinal arteries 3. Significant risk of hemorrhage 4. Angiography to identify and possibly embolize ventral feeders 5. Surgery: Larger levels of exposure are required to identify the feeders reliably
Arteriovenous fistula	1. Seen in neurofibromatosis type 1 and teratomas 2. High risk of hemorrhage with high flow intradural ventral AVF

lesions in either NF-1 or NF-2. Among the two types, manifestations in the pediatric age group are seen mainly in NF-1. Children diagnosed with NF may undergo spine surgeries for scoliosis and spinal tumors like neurofibromas. Manifestations that can hinder the smooth conduct of surgery and anesthesia in these patients include mental retardation, epilepsy, pheochromocytomas, and renal artery stenosis. Plexiform neurofibromas found in NF can have high vascularity due to the plexiform venous channels resulting in increased blood loss during surgery. Increased ligamentous laxity can result in atlantoaxial subluxation and hinder airway management in these patients. Meningiomas, spinal schwannomas, and ependymomas are different tumor types observed in association with NF-2.

17.11 Conclusion

Pediatric patients undergo spine surgeries for several reasons. In-depth knowledge of the pathological condition, the type of procedure to be undertaken, thorough preoperative evaluation, and a detailed discussion with the operating team members, including the surgeon and the neurophysiologist, are essential for the proper conduct of spinal surgery in children. Modifying the anesthetic plan, including airway management, maintenance of anesthesia in the intraoperative period to facilitate neurophysiological monitoring, managing complications, a decision regarding emergence and extubation, and managing postoperative pain are all crucial steps in such cases requiring the expertise of a neuroanesthesiologist.

Conflict of Interest None.

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Craniosynostosis and Anesthetic Concerns

18

Karen Ruby Lionel, Ajay Prasad Hrishi, and Neeraja Ajayan

Key Points

- Craniosynostosis is a developmental anomaly attributed to the abnormal, non-physiologic, and premature fusion of one or more cranial sutures resulting in an abnormally shaped skull.
- This cranial deformity gradually progresses resulting in restricted brain growth and raised intracranial pressure leading to a neurocognitive decline.
- Surgical correction aims to restore an "acceptable" normal appearance of the skull and increase the intracranial volume to allow space for the rapidly growing brain.
- Syndromic craniosynostosis is associated with other system involvement, such as cardiac septal defects or skeletal abnormalities, which need to be evaluated before anesthesia.
- Since invasive and open surgeries are associated with hemodynamic changes attributed to massive blood loss, fluid shifts, and risk for venous air embolism, it is essential to be vigilant and maintain cardiovascular stability throughout the entire procedure.
- Meticulous care during the perioperative period with regard to airway management, positioning and optimal intraoperative complication management plays a significant role in ascertaining good postoperative outcomes.

18.1 Introduction

Craniosynostosis is a developmental anomaly attributed to the abnormal, non-physiologic, and premature fusion of one or more cranial sutures resulting in an abnormally shaped skull. Apart from the cranial dysmorphism, children with craniosynostosis have associated craniofacial anomalies such as mid-face hypoplasia, proptosis, and hypertelorism [1]. Virchow (1851) stated that when a cranial suture is fused, the bone growth at right angles to the affected suture is restricted, resulting in a compensatory growth that occurs parallel to this suture, allowing for continued brain growth, but attributing to the abnormal head shape [2]. The prevalence of craniosynostosis ranges from 3 to 5 per 10,000 births [3–5]. Dr. Paul Tessier, the father of modern craniofacial surgery, pioneered the surgical treatment of craniofacial dysmorphism associated with craniosynostosis. Advances in surgical techniques and neuroanesthetic refinements over the past century have resulted in dramatic

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decreases in perioperative complications with significant improvements in cosmetic, neurodevelopmental, and psychosocial outcomes in children with craniosynostosis.

The children usually present with complaints of an abnormally shaped head, protruding eyes, and abnormal facies. Uncorrected craniosynostosis results in progression of the cranial deformity giving rise to the following complications:

- Cranial growth restriction leads to decreased intracranial volume resulting in increased intracranial pressure (ICP). ICP may be further increased due to associated abnormalities in cerebral venous drainage, obstructive sleep apnea (OSA) with elevated central venous pressures, and hydrocephalus, especially when multiple sutures are affected [6, 7].
- Psychosocial implications due to the deformity as the child interacts with peers.
- Neurodevelopmental issues attributed to cognitive impairment due to impeded brain growth and development as well as a consequence of increased ICP [8].

18.2 Embryology and Anatomical Variations of Craniosynostosis

The development of the skull starts from the 23rd day of intrauterine gestation [9]. Adjacent bones of the skull are separated by designated spaces called sutures. These sutures serve to allow molding of the skull, which plays an essential role during normal childbirth and helps accommodate the rapid growth of the infant's brain. Embryologically, the skull develops from the neurocranium, which has a membranous part that forms the skull vault and the cartilaginous part that forms the skull base. The normal anatomy of the sutures and fontanelles is illustrated in Fig. 18.1.

The closure of the posterior fontanelle occurs at 2–3 months of age, the sphenoidal fontanelle at 6 months, the mastoid fontanelle at 6–18 months, and the anterior fontanelle is the last to close between 12 and 18 months after birth. The metopic suture typically starts to close at the age of 2 years. The sagittal suture begins to close after 22 years, the coronal suture after 24 years, and the lambdoid after 26 years. It is within the normal range for them not to fully close until the age of 40 years.

There is premature closure of sutures in children with craniosynostosis, leading to restriction of growth of skull bones along the suture lines attributing to various skull deformities (Table 18.1), schematically described in Fig. 18.2.

18.3 Classification of Craniosynostosis

The etiologic classification and the common causes are illustrated in Fig. 18.3.

(a) **Non-syndromic Craniosynostosis.**

When premature fusion of calvarial sutures occurs as an isolated condition not associated with any syndrome, it is termed non-syndromic craniosynostosis, seen in 80% of cases [10]. Non-syndromic craniosynostosis commonly affects only one suture. The most common type of craniosynostosis, scaphocephaly, involves only the sagittal suture (50% of cases) [11, 12]. The second most common type is plagiocephaly, attributed to the fusion of only the coronal suture (20% of cases). The premature fusion of only metopic suture results in trigonocephaly, contributing to 10% of the cases. These non-syndromic craniosynostoses have an autosomal dominant inheritance in 6–14% of cases [11].

(b) **Syndromic Craniosynostosis.**

Syndromic craniosynostosis accounts for 20% of craniosynostosis cases and has been described as part of over 150 syndromes [13, 14]. Muenke, Crouzon's, and Apert's syndrome are the most commonly associated syndromes (Fig. 18.4); while, Pfeiffer, Saethre-Chotzen, and Carpenter are worth the mention. These syndromes are commonly associated with other facial anomalies such as micrognathia and midfacial hypoplasia leading to obstructive sleep apnea (OSA) attributing to anesthetic concerns

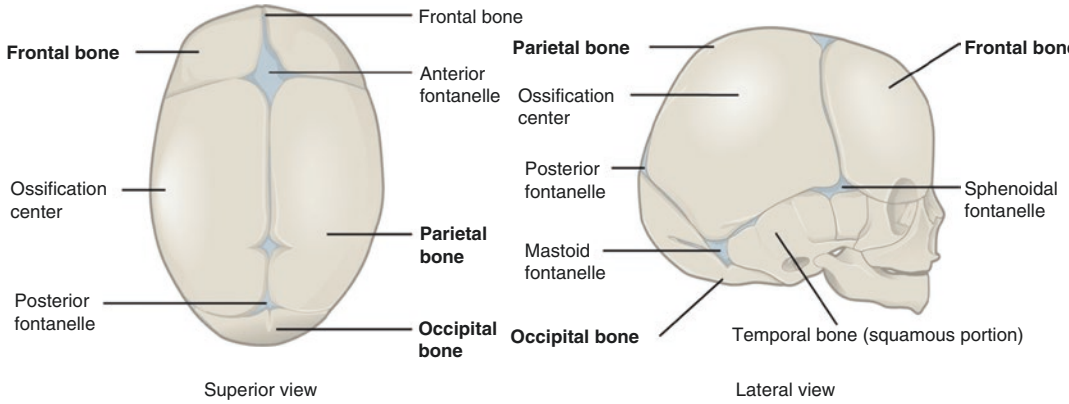

Fig. 18.1 Anatomy of sutures and fontanelles. Source: Wikimedia; permission was obtained for use the picture. Visit link: https://creativecommons.org/licenses/by/3.0/deed.en

Table 18.1 Types of craniosynostosis

Deformity (meanings from Greek)	Suture(s) involved
Dolichocephaly (dolikhos meaning long)	Sagittal
Scaphocephaly (scaphe meaning boat)	Sagittal
Brachycephaly (braku meaning short)	Bicoronal
Anterior plagiocephaly (plagios meaning oblique)	Unicoronal
Turricephaly (turri meaning tower)	Bilateral lambdoid
Turribrachycephaly ("tower" + brachycephaly)	Coronal+ sagittal+ lambdoid
Posterior plagiocephaly/ pachycephaly	Unilateral lambdoid
Trigonocephaly (trigonos meaning three angles)	Metopic
Oxycephaly (oxys meaning sharp)	Sagittal + coronal + metopic
Kleeblattschädel (Kleeblatt meaning cloverleaf; schadel meaning skull)[a]	Sagittal + coronal + lambdoid pansynostosis

[a]*In German*

of difficult mask ventilation, difficult intubation, as well as the need for postoperative care in an intensive care unit (ICU) to monitor for apneic episodes. Children with syndromic craniosynostosis have other associated systemic involvements (Table 18.2). This warrants careful evaluation and optimization during the perioperative period.

18.4 Diagnosis of Craniosynostosis

The diagnosis is usually made based on the phenotype of skull deformation (Fig. 18.2). For further evaluation, a computed tomographic (CT) scan and 3D bone reconstruction is done, allowing accurate diagnosis of specific suture involvement; facilitating surgical planning. Careful screening for systemic pathologies should also be done, particularly in children with syndromic craniosynostosis (Table 18.2).

18.5 Surgical Management of Craniosynostosis

18.5.1 Indications for Surgery

If left untreated, the cranial deformity in craniosynostosis gradually progresses, resulting in restricted brain growth and the dreadful consequences of raised ICP. Surgical correction aims to restore an "acceptable" normal appearance of the skull and increase the intracranial volume to allow space for the rapidly growing brain. Surgical interventions have attributed to a better cosmetic, neurodevelopmental, and psychosocial outcome in these children [15, 16].

It is essential to operate on these children for the following indications:

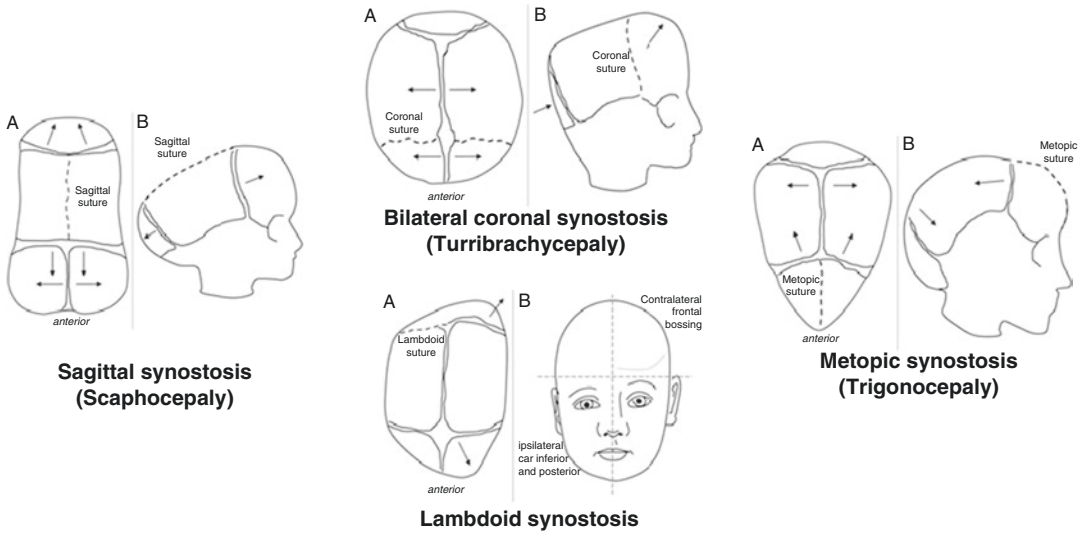

Fig. 18.2 Schematic diagram showing the commonly encountered craniofacial deformities. Source: Senarath-Yapa K, Chung MT, McArdle A, et al. (2012). Available via license: CC BY 4.0

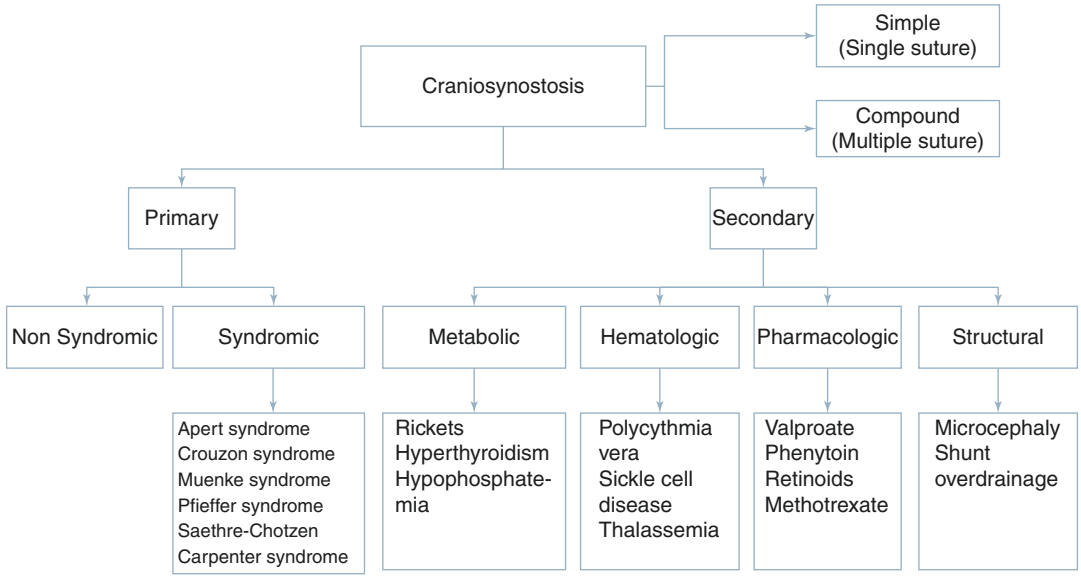

Fig. 18.3 Etiological classification of craniosynostosis

- *Functional:* Restriction of brain growth leads to developmental delay and features of raised ICP and progressive visual loss.
- *Cosmetic:* As the child matures, the abnormally shaped skull will be a source of low self-esteem and body image, leading to psychological stress.
- *Emergency surgery* is indicated when children present with an imminent threat to vision, airway, or an acute and symptomatic increase in ICP.

18.5.2 Surgical Options

Surgical correction is directed at reshaping the cranial vault and thus, increasing the cranial volume allowing for normal brain development.

The surgical procedure can be classified into invasive or open surgery and minimally invasive or endoscopic surgery.

(a) **Open Surgery for Craniosynostosis.**

Fig. 18.4 (**a**) Apert's syndrome facies: front-on (**a1**) and lateral view (**a2**). (**b**) Crouzon's syndrome: front-on (**b1**) and lateral view (**b2**) (with permission from the parents of the children for publication of the images)

- **Total Calvarial Reconstruction, Fronto-orbital Advancement, and Remodeling:** This is the traditional method of surgical treatment where a bicoronal craniotomy is performed and the malleable skull bone is removed, reshaped, and replaced on the deformed portions of the bony convexity, including the fused suture. Surgery is carried out by a team of neurosurgeons aided by craniofacial surgeons (Fig. 18.5).
- **Cranial Distraction**: This is indicated in children with a normal skull shape but with pansynostosis. A biparietal-occipital craniotomy is performed, and distractors are implanted in the cut bone. The screws placed are turned at 1 mm per day for 30 days over a three month period. This results in a distraction of 3 cm, an adequate increase in intracranial volume. After this period of 3 months, distractors are removed, and skin is closed as an office procedure.

(b) **Minimally Invasive Surgery or Endoscopic surgery.**

- **Strip Craniectomy with Use of Postoperative Molding Helmet**: The fused sutures are excised in order to unlock the bone, and reshaping is carried out with a cranial molding helmet. This requires the child to wear the helmet for 23 h/day up to the age of 1 [17, 18].
- **Strip Craniectomy with Spring Implantation:** The fused sutures are excised to unlock the bone, and reshaping is carried out with the assistance of implanted custom-made springs. A second surgery is done after 3 months for spring removal [19, 20].

18.5.3 Timing of Surgery

The timing of surgical intervention is controversial. The decision to operate between the age of 6

Table 18.2 Common syndromic craniosynostosis and its associated systemic features

Syndrome	Genetic mutation locus	Inheritance pattern	Incidence	Associated features
Apert's syndrome (acrocephalosyndactyly)	FGFR2 (chromosome 10)	Mostly sporadic de novo mutations and autosomal dominant	1 in 65,000	Midface hypoplasia, cleft palate, maxillary retrusion, proptosis, syndactyly, hypertelorism
Crouzon syndrome	FGFR2 (chromosome 10)	Mostly sporadic and autosomal dominant	1 in 60,000	Midface hypoplasia, hypertelorism, strabismus, proptosis, maxillary retrusion, beaked nose, cervical spine abnormalities (present in 1/3)
Muenke syndrome	FGFR3 (chromosome 4)	Autosomal dominant, 61% de novo mutations	0.8–1 in 10,000	Ptosis, unicoronal or bicoronal synostosis, hypertelorism, high-arched palate, abnormalities of phalanges without syndactyly, facial asymmetry
Pfeiffer syndrome	FGFR 1 (chromosome 8), FGFR2 (chromosome 10)	Autosomal dominant, de novo mutations	1 in 100,000	Maxillary retrusion, midface hypoplasia, nasopharyngeal stenosis, hypertelorism, proptosis, strabismus, partial syndactyly, cartilaginous tracheal sleeve, beaked nose, hearing loss, broad thumbs and great toes, radiohumeral synostosis of elbow, hydrocephalus, imperforate anus may occur
Saethre-Chotzen syndrome	TWIST (chromosome 7)	Familial and autosomal dominant	1 in 25,000–50,000	Short stature, hypertelorism, hearing loss, facial asymmetry, low frontal hairline, mild partial syndactyly, ptosis, usually normal intelligence
Carpenter syndrome	RAB23 (RAS-associated protein)	Autosomal recessive	1 in 1,000,000	Midface hypoplasia low set ears, high-arched palate, flat nasal bridge, shallow orbital ridges, limb defects (pre-axial polydactyly), hypogonadism, omphalocele. Up to 50% have cardiac defects (ASD, VSD, PDA, PS, TOF, TGA)

and 12 months is based on the fact that rapid brain growth occurs during this time when the brain weight doubles by the sixth month of life and head circumference is halfway to full growth at about 8 months of age [21]. Minimally invasive surgical techniques such as extended strip craniectomy and, subsequent, helmet molding therapy, which relies on early rapid brain growth to drive remodeling, are sometimes considered from 3 to 6 months of age. Early surgery is advocated since the skull is more malleable with softer bone, and the ongoing brain growth is not compromised. The disadvantages of an early presentation (<6 months of age) for surgery are the increased inherent risks of anesthesia, reduced physiological blood reserve, increased incidence of restenosis rate, and poorer resolution of the cephalic index. Surgery at a later day assures a safer clinical course during anesthesia and surgery, as well as a lower requirement for a re-surgery. The disadvantages of delayed surgery are that the bone is less malleable, deformities may be more severe, and the skull has a reduced ability to ossify defects, thus requiring bone grafts [22]. Invasive surgeries are more complex procedures with an increased risk of complications such as massive blood loss, venous air embolism (VAE) along with the perils associated with

a prolonged duration of surgery. These children also require postoperative admission to the ICU. Thus, invasive surgeries are ideally recommended for children after 6 months of age [23].

18.6 Anesthetic Management

18.6.1 Preoperative Concerns

(a) **Preoperative Multidisciplinary Evaluation.**

Since the cosmetic and functional prerequisites vary widely between each child affected by craniosynostosis, treatment has to be individualized. The team involves an anesthesiologist, neurosurgeon, a plastic and reconstructive surgeon, pediatric neurologist, child psychologist, otolaryngologist, a pediatric cardiologist, and an intensive care physician. Apart from these, the craniofacial team requires an audiologist, orthodontist, ophthalmologist, genetic experts and counselors, occupational and physical therapists, and pediatric nurses to make the treatment holistic [24, 25].

(b) **Airway Assessment and Risk Evaluation for Need for Surgical Airway and Postoperative Ventilation.**

Careful preoperative airway assessment is vital to the successful management of a difficult airway. This allows adequate time for forethought and stepwise execution of the plan for induction and intubation. Syndromic craniosynostosis is associated with difficult mask ventilation and intubation. Pre-anesthetic assessment must focus on features such as proptosis, mid-facial hypoplasia, and choanal atresia, which could contribute to difficult mask ventilation. Features such as adeno-tonsillar hypertrophy, laryngo-tracheo-bronchomalacia subglottic stenosis, laryngeal cleft, and vocal fold paresis are commonly associated with OSA and difficult intubation. Syndromic craniosynostosis, especially Crouzon's syndrome, is associated with cervical spine abnormalities and atlantoaxial dislocation (AAD); therefore, care should be taken to avoid excessive cervical spine movements during intubation and positioning. Similar concerns exist in Apert's syndrome, wherein the cervical vertebrae are fused, thereby restricting cervical spine movements. In patients presenting for midface advancement and reconstruction surgeries, a preoperatively planned tracheostomy is recommended. Other options are the submental or the retromolar intubation with reinforced flexometallic tubes.

Children with facial anomalies may present for cranial reconstruction surgery post-frontofacial advancement procedures. In such children, intubation will be difficult as a result of the altered relationships between the maxilla and mandible and reduced temporomandibular joint movement. An elective tracheostomy or fiber-

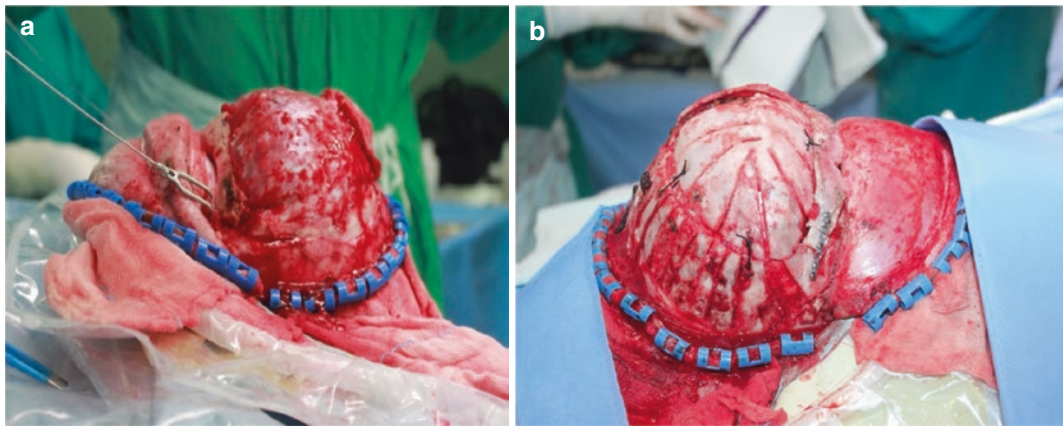

Fig. 18.5 Total calvarial reconstruction and fronto-orbital advancement (**a**), and remodeling (**b**)

optic intubation (FOI) needs to be considered in such scenarios.

Children with syndromic craniosynostosis are at risk for OSA syndrome (OSAS) [13]. OSA is associated with adenotonsillar hypertrophy, laryngo-tracheo-bronchomalacia, subglottic stenosis, laryngeal cleft, and vocal fold paresis. Various screening methods, such as the Brouillette questionnaire and scoring system, have been used as screening questionnaires for OSA [26]. However, polysomnography remains the gold standard for diagnosis [27]. Depending on the severity of OSAS as shown by the apnea-hypopnea index (AHI) and an oxygenation desaturation index (ODI), noninvasive methods of ventilatory support such as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) or invasive methods such as a tracheostomy may be planned, for appropriate postoperative airway management. The risks and plans made must be communicated with the parents and the rest of the caregiving team. As per the craniosynostosis guidelines, it is strongly recommended to postpone surgery if there is a recent upper respiratory tract infection (URTI) as airway infections are associated with complications [28].

(c) **Systemic Evaluation and Preoperative Concerns.**

Syndromic craniosynostosis is associated with other systems involvement, such as cardiac septal defects or skeletal abnormalities, which need to be evaluated before anesthesia. Preoperative echocardiography is warranted to evaluate the cardiac status and screen for patent foramen ovale (PFO) and other congenital defects. Apert's syndrome is characterized by fused digits of the hands and feet, making intravenous (IV) access challenging (Fig. 18. 6). Children with syndromic craniosynostosis are highly prone to recurrent lower respiratory tract infections (LRTI) and bronchospasm in the perioperative period. This is due to the lower airway compromise caused by stiff or vertically fused tracheal rings and the accumulation of secretions.

Raised ICP is seen in syndromic children with multiple suture involvement; 50% of children with compound craniosynostosis and 15–20% of children with simple craniosynostosis present with features of raised ICP [17, 21]. These features of raised ICP, can be attributed to multiple factors such as malunion of the skull bones resulting in a rigid skull box, OSA causing hypercapnia leading to increased cerebral blood flow (CBF), abnormal cerebrospinal fluid (CSF) circulation, and hydrocephalus.

(d) **Baseline Hematological Evaluation and Optimization.**

Hematological, biochemical, and coagulation profiles have to be done routinely during the preoperative period for adequate planning. Optimization of preoperative anemia is recommended by iron supplement and erythropoietin administration (EPO). The dose of EPO recommended is 600–200–100 U/kg, once to thrice a week, encouraged during 3 weeks preceding the elective surgery [29, 30].

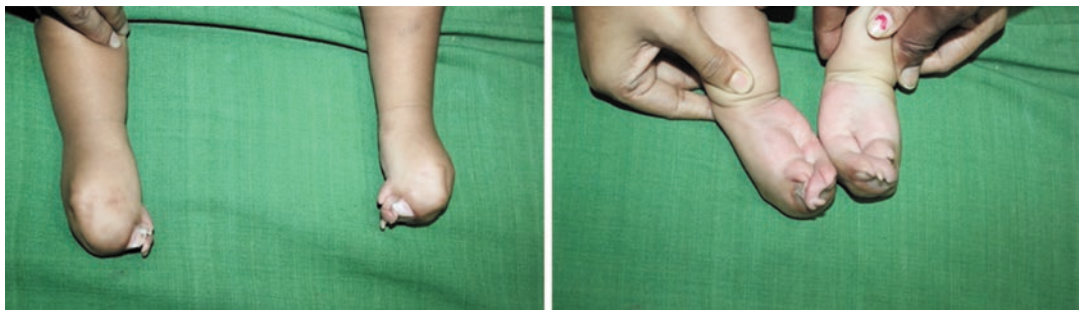

Fig. 18. 6 Limb defects seen in Apert's syndrome

18.6.2 Intraoperative Management of Craniosynostosis

(a) **Mandatory Precautions.**

The following things are mandatory before initiating the procedure:

- *Checklists*: The use of pre- and postoperative checklists and the time-out procedure before the start of surgery add to the safety of the entire perioperative process.
- Adequate blood and blood products must be cross-matched and readily available. The blood bank duty doctor must be intimated about the surgery and the possibility of activation of massive transfusion protocols.
- Availability of the pediatric intensive care unit (PICU) bed and mechanical ventilator should be ensured. Due to the increased complexity and duration of the procedure planned in a relatively small child, certain patients may require elective postoperative ventilation. Even if the child is fit for tracheal extubation, it is safer to monitor the patient in the PICU during the postoperative period.

(b) **Intraoperative Concerns.**

- Pediatric patient presenting for a prolonged and complex neurosurgical procedure.
- Difficult airway management in a syndromic child.
- Intraoperative patient positioning.
- Prevention and management of increases in ICP and preservation of the uninjured brain by providing brain relaxation during surgery.
- Maintenance of cerebral homeostasis with adequate cerebral perfusion and appropriate ventilation.

The anesthesiologist is faced with the multiple challenges of managing an infant with a developing central nervous system (CNS), an immature liver, and renal systems with altered response to drugs and impaired thermoregulation. Conventionally, neurosurgical operating rooms (ORs) have temperatures of 18–21 °C; However, in these cases, the theater's ambient temperature should be maintained at 24–27 °C before induction of anesthesia to prevent hypothermia. Drugs must be diluted and kept ready according to the weight of the child and equipment required for securing a difficult airway as well as difficult venous access must be available. Smooth induction and careful anesthesia maintenance are mandatory to prevent a further rise in ICP in children with reduced intracranial volume. IV or inhalational induction can be chosen subjectively based on the difficulty of mask ventilation and the ease of securing venous access.

(c) **Airway Management.**

Airway management in this subgroup of patients should preferably be dealt with by an experienced anesthesiologist. Non-syndromic children with craniosynostosis usually present with no difficulties in mask ventilation or tracheal intubation, whereas the syndromic children may present with difficulties. A surgical team is kept on standby if the need arises for a front of neck airway access in case of a failed intubation. Due to the difficulty in mask ventilation and associated congenital systemic anomalies, these children tend to desaturate faster than the normal population. Mask ventilation is a challenge due to the presence of proptosis, mid-facial hypoplasia, and choanal atresia. Small nares and a degree of choanal stenosis cause high resistance to airflow through the nasal route. Since most of these children are obligate mouth-breathers, after induction of anesthesia with a mouth closed and increased resistance offered by the choanal atresia, mask ventilation may become very difficult. To overcome this, the mouth is kept open with an oral airway, and the mask is held inversely to overcome the mid-facial hypoplasia, thus enabling mask ventilation. Associated structural abnormalities of the airway such as adenotonsillar hypertrophy, laryngo-tracheo-bronchomalacia, subglottic stenosis, laryngeal cleft, and vocal fold paresis make tracheal intubation difficult. In children with tracheomalacia, a smaller-size endotracheal tube is preferred. Children with syndromic craniosynostosis may have associated spine abnormalities, restricting the neck extension, further contributing to difficult intubation.

A planned fiber-optic intubation is optimal in children with craniofacial and cervical spine abnormalities. A pediatric D-blade CMAC videolaryngoscope may also be beneficial in establishing the airway in children with limited neck

extension and in the presence of an anteriorly placed larynx [31]. In children in whom mid-face advancement (LeFort III and monobloc procedures) is considered, a planned preoperative tracheostomy is done, or other options such as the submental or the retromolar intubation with reinforced flexometallic tubes need to be considered after consultation with the surgical team. After tracheal intubation, the tube position should be checked with the head flexed and extended to prevent accidental endobronchial intubation or extubation during positioning.

(d) **Monitoring and Anesthetic Management.**

Apart from the routine monitors such as pulse oximetry, ECG, noninvasive blood pressure (BP), end-tidal carbon dioxide ($EtCO_2$), temperature, precordial Doppler and urine output, invasive monitoring is advocated. Invasive monitors include central venous access and an invasive arterial line to monitor beat-to-beat variations in the BP. These invasive monitors play an essential role in the early detection and management of intraoperative complications such as massive blood loss, VAE, as well as electrolyte and acid-base abnormalities.

A balanced anesthetic technique, which ensures cardiovascular stability with inhalational anesthetic (preferably sevoflurane), opioids (fentanyl and morphine), and intermediate-acting muscle relaxants (atracurium and cis-atracurium), is advocated. Remifentanil infusion (0.25–0.5μg/kg/min) has also been well described [32, 33]. Scalp block with 0.2% ropivacaine or 0.25% levobupivacaine provides good intraoperative pain relief and has the advantage of providing postoperative analgesia as well [34].

(e) **Patient Positioning.**

Careful positioning allows for good surgical access as well as avoidance of related complications. Depending on the fused suture site, the child may be positioned supine with a reverse-Trendelenburg tilt or prone or in a modified prone position (sphinx position) [35]. In the "sphinx position," the child is positioned prone with the neck extended so that the chin rests on a support. Owing to the higher rate of perioperative complications such as VAE and hyperextension of the cervical spine, this position has fallen out of vogue in the recent past. Figure 18. 7 shows the precautionary measures taken prior to positioning for surgery. Care must be taken to prevent hyperextension of the neck, which may result in spinal cord injury and quadriplegia. In any position adopted, the eyes must be well protected. In cases of fronto-orbital advancement where there is an extensive dissection of the orbit, the eyes must be covered with a waterproof transparent dressing. In the prone position, care should be taken to avoid pressure on the eyes, and they must be well-padded and protected. The head should be kept, as much as possible, in the neutral position without hyperflexion or rotation to facilitate venous drainage from the brain.

(f) **Intraoperative Complications.**

Since invasive and open surgeries are associated with hemodynamic changes attributed to massive blood loss, fluid shifts and VAE, it is essential to maintain cardiovascular stability throughout the whole procedure. This can be achieved with adequate replacement of fluids and timely administration of blood and blood products. Complications like VAE leading to hemodynamic compromise must be detected early and treated appropriately, thus maintaining cerebral homeostasis.

- **ICP Management.**

Care should be taken to detect and manage scenarios resulting in an increase in ICP, such as light plane of anesthesia, inadequate analgesia, coughing on the endotracheal tube, full bladder, hypercarbia, and hyperthermia. During open surgeries such as strip cranioplasty and fronto-orbital advancement, it is crucial to provide adequate brain relaxation to prevent retraction injury. This is usually facilitated by using a single dose of an osmotic diuretic such as mannitol at a dose of 0.5 mg/kg given at the time of the craniotomy.

- **Massive Blood Loss and Transfusion.**

Invasive correction surgeries for craniosynostosis are associated with massive blood loss (Fig. 18.8), often exceeding 20–500% of the blood volume requiring massive transfusion; attributing to significant transfusion-related morbidity and mortality [36, 37]. The apposite management of massive blood loss in a patient with an age-related small circulating volume within a short period of time poses an anesthetic challenge [10]. Estimation of blood loss with adequate and appropriate

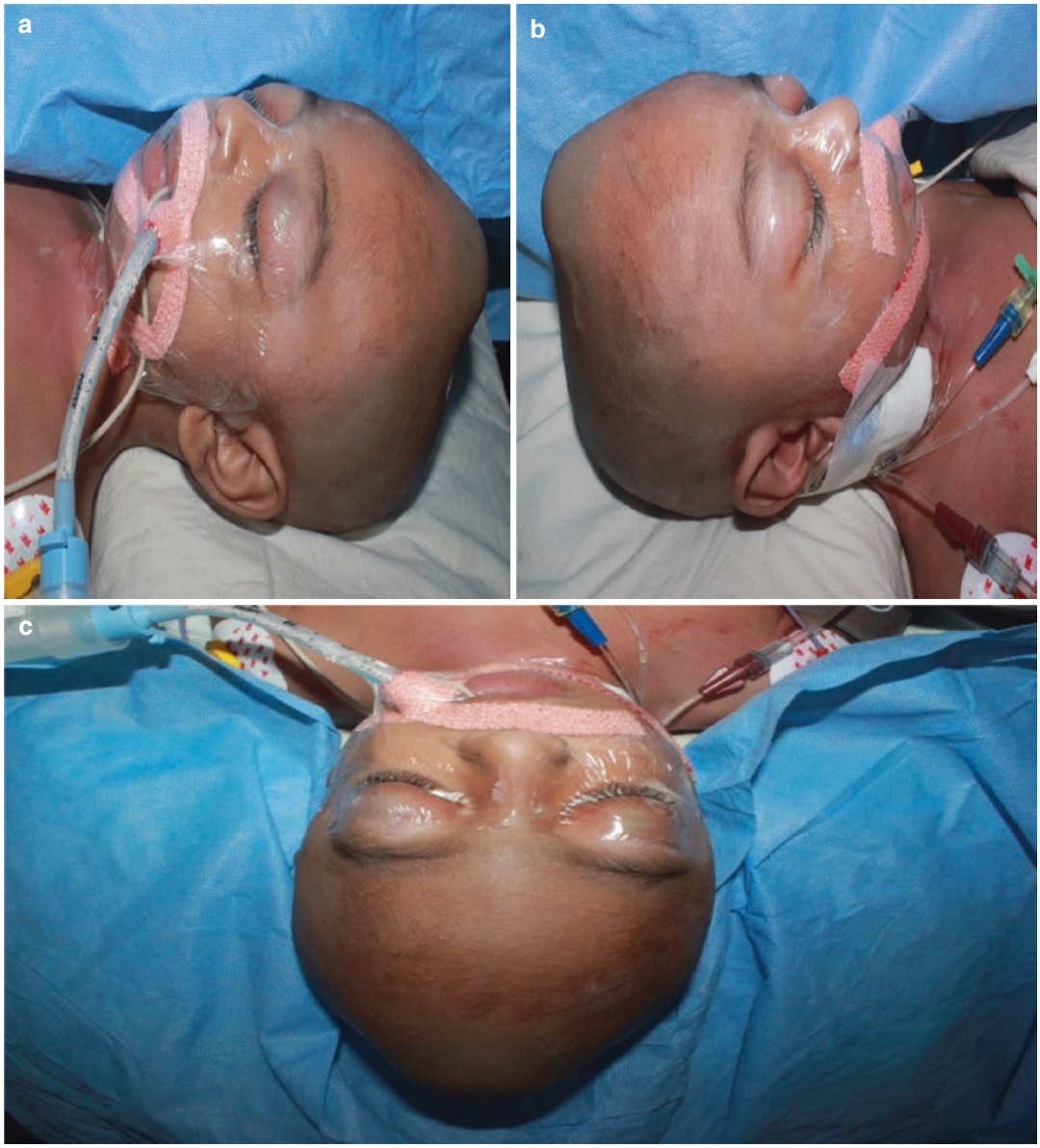

Fig. 18.7 Shows precautionary steps before positioning for craniosynostosis repair. (**a**) Securing the endotracheal tube, oral temperature probe, and eye covers with transparent adhesive plasters. (**b**) The central venous line has been secured with the lumens facing caudal to facilitate access. (**c**) Final position for surgery on a head ring (with permission from the parents for the publication of images)

replacement is vital for good perioperative outcomes. Each institution has its protocols for cross-matching and transfusion of blood and blood products. Coagulation profile and platelet counts need to be monitored during the intraoperative period in the event of massive blood loss. Often the estimation of blood loss is inaccurate due to concealed bleeding under the surgical drapes [38, 39]. The methods by which blood loss and replacement calculations are made in the intraoperative period are explained in Table 18.3 [40].

Various blood conservation strategies have been tried in perioperative settings [Table 18.4]. Intraoperative strategies to minimize blood loss

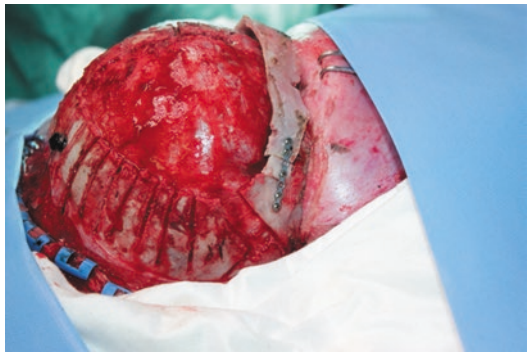

Fig. 18. 8 Continuous oozing of the blood from the surgical field during reconstructive cranioplasty

Table 18.3 Intraoperative blood loss and replacement calculations in craniosynostosis [40]

Estimated blood volume (EBV) = • 80 ml/kg for infants younger than 12 months • 75 ml/kg for children older than 12 months
Estimated Red Cell Volume (ERCV) = Estimated Blood Volume (EBV) × Hematocrit/100
EBV_{lost} (ml/kg) = $ERCV_{lost}$ (ml)/[wt (kg) × Preoperative hematocrit/100]
ERCV lost = ERCV preoperative + ERCV transfused − ERCV postoperative
ERCV transfused = PRBC (ml) transfused × Hematocrit of transfused PRBC/100 Hematocrit for packed cells = 0.65

Table 18.4 Blood conservation strategies in craniosynostosis

Blood conservation strategies
• Perioperative recombinant erythropoietin • Acute normovolemic haemodilution • Intraoperative cell salvage • Antifibrinolytic drugs: Tranexamic acid, epsilon-aminocaproic acid (EACA) • Fibrin sealants or fibrin glue • Postoperative cell salvage

are appropriate positioning of the head, reverse-Trendelenburg to facilitate venous drainage from the scalp, infiltration of the skin with vasoconstrictors before incision, and use of antifibrinolytics. Tranexamic acid administration has been shown to significantly decrease the amount of blood loss and blood transfusion in children undergoing corrective surgery for craniosynostosis. The dose of tranexamic acid used is 20 mg/kg bolus over 15 min, followed by an infusion at 1–2 mg/kg/h or 5 mg/kg every 3 h [40]. A bolus of epsilon-aminocaproic acid (EACA), 100 mg/kg followed by 20–40 mg/kg/h, has been advocated as an alternative to tranexamic acid [41]. The use of continuous autotransfusion system (CATS) has also been shown to reduce homologous transfusion during the repair of craniosynostosis [42].

Risk factors for massive blood loss are syndromic craniosynostosis, pansynostosis, age < 18 months, and long duration procedures (>4 h) [36]. Point-of-care (POC) tests such as thromboelastography (TEG) or thromboelastometry (ROTEM) have been advocated for the precise management of massive blood transfusion and the titration of blood products [41]. Massive blood loss predisposes to depletion of coagulation factors and platelets, resulting in a consumptive and dilutional coagulopathy, which may need to be treated with cryoprecipitate, fresh frozen plasma, or platelets as guided by POC tests [43, 44]. Administration of cold blood results in hypothermia, which further contributes to the coagulopathy by causing a 10% decrease in the coagulation factor levels for every degree of fall in the temperature. Furthermore, hypocalcemia due to citrate overload and acidosis resulting from massive blood transfusion may worsen the coagulopathy. Since massive blood transfusion is expected in such children, it is wise to secure two peripheral venous accesses to administer blood rather than use central venous access for this purpose. This allows the high potassium content and the citrate to mix and get diluted before it returns to the heart.

- **Venous Air Embolism.**

The incidence of VAE is 2.6 to 86%, based on the monitoring modality; clinically significant VAE is encountered in 1–2% of patients [12, 45, 46]. VAE is common due to the open diploic veins of the skull, the reverse-Trendelenburg position, which facilitates the sucking in of air since the head is at a higher level as compared to the heart, massive bleeding with continuous ooze from the operative site, and the proximity to the venous sinuses.

- **Hypothermia.**

Intraoperatively, a large surface area of the infant scalp, with its high perfusion is exposed to the ambient temperature. The effects of anesthesia, OR environment, and transfusion of large volumes of fluids, blood, and blood products put the infant at risk for hypothermia. Blood is stored at a temperature between 2 and 6 °C, whereas FFP is stored at −40 °C. These products should be administered through a warmer to prevent hypothermia. In addition, measures such as the use of fluid warmers, overhead radiant lights, forced air convection blankets, and circulating warm water mattresses are different methods utilized to prevent hypothermia.

- **Electrolyte Abnormalities.**

Intraoperative electrolyte abnormalities such as hypocalcemia (due to citrate toxicity), hyponatremia, hyperkalemia, and metabolic acidosis are attributed to the massive blood transfusion and fluid shifts. These abnormalities need to be corrected with care; it is important to remember that an infant is not just a "small adult". Hyponatremia may also occur due to the cerebral salt wasting syndrome (CSWS) [47]. It has to be differentiated from the syndrome of inappropriate antidiuretic hormone secretion (SIADH) before the commencement of appropriate treatment measures.

18.6.3 Postoperative Concerns

(a) **Emergence Plan** [10]**.**

Smooth emergence is targeted to prevent a rise in ICP and systemic hypertension resulting in excessive postoperative blood loss into the drain. After this complex surgery, the anesthesiologist may consider early extubation of the trachea or plan for elective ventilation based on different criteria (Table 18.5).

(b) **Monitoring in a High Dependency Unit (HDU) or ICU.**

Postoperative monitoring in an ICU is advocated for all children undergoing correction surgeries for craniosynostosis as they may encounter various postoperative complications.

Table 18.5 Extubation criteria for craniosynostosis patients undergoing surgery

Early emergence and extubation	Postoperative ventilation and delayed extubation
• Short duration surgery (<4 h)	• Prolonged procedure (>4 h) • Prone position
• Noninvasive surgical techniques	• Invasive surgical techniques
• Minimal blood loss and blood transfusion	• Massive blood loss and transfusion • Coagulation abnormalities
• Hemodynamically stable	• Marked fluid shifts and on vasopressor support
• Normothermia	• Hypothermia
• Normal electrolytes	• Dyselectrolytemia
• Rapid recovery of spontaneous and stable breathing	• History of obstructive sleep apnea (OSA) • History of difficult airway

- **Airway Obstruction and Respiratory Distress.**

If a child has undergone a cranial distraction procedure, tracheal extubation has to be planned gradually; it is advisable to allow the child to be completely awake with the return of airway reflexes. Re-intubation in these children is impossible due to the distraction screws placed over the maxilla and mandible and rods placed across the face. Hence, cutting pliers and screwdrivers should always be available to aid in the quick removal of the distracting screws and rods to gain access to the airway. In some cases, fiber-optic intubation has been described. Children who have been on a cranial distraction chronically may develop trismus making mouth opening difficult, and direct laryngoscopy is almost a non-viable option.

- **Hypovolemia and Dyselectrolytemia.**

Cardiovascular status must be continuously monitored to detect any further blood loss/fluid shifts, which may continue into the immediate postoperative period attributing to hemodynamic instability. These children are prone to large fluid shifts and dyselectrolytemia.

- **Coagulopathy and Bleeding.**

Coagulopathy could occur due to massive transfusion, hypothermia, and, in rare cases, dis-

seminated intravascular coagulopathy (DIC). Optimization of coagulation parameters is of paramount importance during the perioperative period. Bleeding may continue into the postoperative period via the drains if there is uncorrected coagulopathy. Thus, the hemoglobin, as well as coagulation profile, will have to be closely monitored.

- **Postoperative Pain and Analgesia.**

Postoperative pain is managed with rectal or IV paracetamol (15 mg/kg). If the pain is not controlled by paracetamol in children older than 1 year of age, tramadol may be used. The role of non-steroidal anti-inflammatory drugs (NSAIDs) is controversial as they may increase the risk of bleeding due to derangements of the coagulation profile. Opioids are avoided in syndromic children who have a history of difficult airway management or OSA. Short-acting opioids such as fentanyl are used as an infusion in children who are on elective postoperative ventilation and planned for delayed extubation. Preoperative scalp block with 0.2% ropivacaine or 0.25% levobupivacaine has been beneficial in providing pre-emptive analgesia and reducing acute postoperative pain. It is very effective in reducing immediate postoperative pain, especially in children less than 2 years [48].

18.7 Conclusion

Providing safe anesthesia for this unique group of children with craniosynostosis is a challenge. Surgery aims to promote normal brain development and achieve a cosmetic effect to avoid psychological trauma later in life. A well-coordinated multidisciplinary team is required to ensure a good outcome. Careful pre-anesthetic evaluation with particular attention to possible difficult airway and massive intraoperative bleeding is vital. Meticulous care concerning the difficult airway, intra-operative positioning, management of complications such as massive blood loss and transfusion, VAE, fluid, and electrolyte imbalance play a significant role in ascertaining good postoperative outcomes.

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Anesthesia for Craniopagus Separation Surgery

19

Girija Prasad Rath, Siddharth Chavali, Ritesh Lamsal, and Deepak Gupta

Key Points Craniopagus twins (CPTs) are rare forms of the very uncommon conjoined twins; surgical separation of CPTs is one of the most complex neurosurgery procedures.

- The surgery includes the multi-staged separation of shared vasculature, interdigitating brain parenchyma, and reconstructive plastic surgery; the procedures are meticulously planned with a multidisciplinary team's participation.
- Multiple anesthesia episodes are required, such as for neuroimaging, tissue expander placement, multi-staged separation, and reconstructive surgeries.
- Neuroimaging procedures for CPTs can be carried out under sedation as well as general anesthesia.
- For separation surgery, clear communication is required among the anesthesia team members with specific attention to possible difficult airway, careful positioning, appropriate management of massive blood loss and fluid shifts, and anticipation of complications.
- With advances in medical technologies and surgical expertise, more separation attempts are expected despite the associated high cost and procedural complexities.

19.1 Introduction

Joined in utero, the conjoined twins are known as "Siamese twins." There are different theories related to aberrant embryogenesis proposing why conjoining occurs [1]. One such theory suggests that a single fertilized egg may not split fully during the process of formation of identical twins, and the zygotic division occurs 2 weeks after the development of the embryonic disc, resulting in the formation of conjoined twins (*fission theory*). The other theory suggests that two fertilized eggs fuse in the early part of the development process (*fusion theory*); subsequent splitting of primitive nodes and streak partially may lead to this rare phenomenon. Conjoined twins occur in not more than 1:50,000 to 1:200,000 births [2].

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The conjoined twins are typically classified based on the part of the body where they join (Table 19.1). The incidence of different types also varies [3]. The most common types encountered are thoraco-omphalopagus, thoracopagus, omphalopagus, parasitic twins, and craniopagus; thoraco-omphalopagus is considered as the commonest type. Forty percent of the conjoined twins are still-born, and 60% are live-born; one-third of the live-born may die within 24 hours after birth due to congenital anomalies. Hence, the actual occurrence of conjoined twins is very rare, and only about 25% of these twins survive long enough to be candidates for surgical separation. Additionally, conjoined twins are genetically identical and are of the same sex. Conjoining is more common in females with a male/female ratio of 1:3 [4]. No association with heredity, race, maternal age, or environmental factors is established.

Table 19.1 Classification of conjoined twins

Types of conjoined twins	Description(s)
Common types	
Thoraco-omphalopagus	Fused bodies from the upper to the lower chest Heart is shared; may share liver or partly the digestive system
Thoracopagus	Bodies fused at the chest Heart is invariably shared
Omphalopagus	Fused bodies at the lower abdomen May share a liver, digestive system, and diaphragm; but never share a heart
Parasitic twins	Asymmetrically conjoined twins; one twin is small and less formed and is dependent on the other (larger twin) for survival
Craniopagus	Joined at the head, but not on the face or the base of skull
Rare types	
Xiphopagus	Fused at xiphoid process; no other organ involved except the liver
Ischiopagus	Joined at the ischium; the lower half of the two bodies are fused with spines
Pygopagus or iliopagus	Bodies fused at the pelvis (buttock)
Rachipagus	Fused at the back of their bodies with the fusion of the vertebral arches

When such twins are fused at the skull, they are known as craniopagus conjoined twins. Craniopagus twins (CPTs) are one of the rarest forms of conjoined twins and account for 2–6% of all conjoined twins, with an incidence of approximately 1 in 2.5 million live births [4, 5]. In these twins, cephalic fusion may occur at any part of the calvarium except the face, foramen magnum, skull base, and vertebrae.

19.2 Historical Aspects of Conjoined Twins

The uniqueness and uncertain origin of conjoined twins have inspired many myths and legends in ancient literature for centuries. Art forms of different examples of conjoined twinning can be seen in museums throughout the world. They were feared as bad omens and, hence, were abandoned or even killed. Later, they were viewed with curiosity; they became sideshow acts, performed in circuses, or even became stage performers. They were also worshipped as gods due to their unusual appearances.

The Biddenden Maids (Mary and Eliza Chulkhurst), conjoined pygopagus twins, were born in the year 1100 in the Kentish village of Biddenden, England, and they lived as long as 34 years. They are considered the first documented case of conjoined twins [6]. Similarly, the first documented case of craniopagus twins (CPTs) of Bavaria, Germany, was mentioned as a monster (Ein monstrum) and was considered as a warning signal from God [6]. The twins born in 1491 were frontal CPTs and remained alive for 10 years. The other historical aspects of CPTs were well documented by the famous French surgeon Ambroise Paré in the sixteenth century, and his works were reprinted in 1840 (*On Monsters and Marvels*) as monsters who were a "warning from God" [6, 7]. In the eighteenth century, Sir Everard Home (1756–1832) reported a case of craniopagus parasiticus known as "Two-Headed Boy of Bengal," the CPTs born in India in the 1770s and whose skull is preserved at the Hunterian Museum at the Royal Society of Surgeons [6, 8]. Until the late 1800s, the CPTs

were considered "monsters." However, in the nineteenth century, August Förster (1822–1865) defined the twins joined at the head and introduced the term "craniopagus" in his works on the science of teratology [6]. Thenceforth, the adjective of "monster" was gradually replaced with different types of conjoined twins.

Chang and Eng Bunker, the original "Siamese twins" who were synonymous with conjoined twins during the early nineteenth century, participated in "freak shows" and became financially successful. Together, they fathered 21 children and died at the age of 62. Yvonne and Yvette McCarther, the American CPTs (born in 1949), were considered inoperable and lived up to 43 years. Despite their rarity, several CPTs lived into adulthood; nevertheless, more than 90% died by the age of 10 [6].

Surgery is considered successful when both twins survive more than 30 days after separation [6, 9]. The first craniopagus separation surgery was attempted unsuccessfully in 1928 [10]. Until 1950, several CPTs underwent urgent yet unsuccessful separation surgeries. The first successful surgery (Roger and Rodney Brodie) was carried out in stages by Oscar Sugar (1952–1953). In this case, one of the twins died after 1 month of craniopagus separation, while the other survived until 11 years of age [9]. During the last 50 years, advancements in medical science, surgical strategies, anesthesia, and intensive care have encouraged approaching craniopagus cases with renewed interest. In this context, the contributions of renowned pediatric neurosurgeons like Dr. Ben Carson and Dr. James T. Goodrich are worth mentioning. Dr. Goodrich was the single most experienced surgeon for this complex craniofacial disorder and performed seven cases of craniopagus separation [7].

19.3 Classification of Craniopagus Twins

Various classifications have been proposed for describing CPTs; the most common is the O'Connell classification (1976). O'Connell broadly divided CPTs based on the extent of the union as well as extracranial versus intracranial involvements [11]. CPTs could be partial with smaller extracranial union limited to the dura mater or total with the large intracranial union and extensively shared cranial cavities. Bucholz et al. subclassified the total craniopagus into four types: frontal, parietal, temporoparietal, and occipital [12]. O'Connell further subclassified the total (vertical or parietal) craniopagus into three types (I, II, III) based on the orientations of faces of the twins due to the long axis of one head that is rotated over the other through different angles (Table 19.2). Winston proposed another classification based on the "deepest shared structures" [13]. In the same year, Gaist and colleagues expanded the O'Connell classification with the inclusion of a transitional category apart from partial and total categories; deformities of the brain and cerebral venous connections were also described [14]. Stone and Goodrich proposed a simple classification [9], reviewing 64 cases based on *shared venous sinuses* and the extent of brain compression as either partial or total craniopagus. There were two subtypes, angular or vertical, for each category. The vertical craniopagi, like O'Connell classification, are

Table 19.2 Common classifications of craniopagus twins

Classifications	
Partial craniopagus	Total craniopagus
O'Connell classification	
Extracranial, usually frontal Sharing of minimal surface area	Intracranial Extensive surface area with wide connectivity of the cranial cavity • Type I: Facing same direction (<40°) • Type II: Facing opposite direction (140–180°) • Type III: Intermediate (40–140°)
Stone and Goodrich classification	
Less significant shared dural venous sinus • Angular • Vertical	Significant shared dural venous sinus Pronounced brain compression • Angular: <140° intertwined longitudinal axis • Vertical: I, II, III based on O'Connell classification

subclassified into three types based on intertwined axial facial rotations (Table 19.2). Browd et al. proposed a comprehensive grading system based on the issues related to separation surgery to evaluate the CPTs for surgical risks and possible success in separation [6].

19.4 Shared Vascular System in Craniopagus Twins

Cerebral venous system abnormalities are common in CPTs [11, 13]. Their complex nature may affect the separation surgery outcome due to significant intraoperative blood loss and postoperative venous infarcts. The superior sagittal sinus (SSS) may be absent in both the twins to be replaced by a single-shared SSS or circumferential venous sinus (CVS) (Fig. 19.1). Other than CVS, venous sinus lakes and separate SSS with interconnections between them have also been described [15]. These abnormalities may cause significant mixing of the venous circulation, and blood may drain to one twin preferentially. That leads to high blood pressure and cardiac output in one twin and low in the other [16, 17].

The cerebral arterial supply is usually separate in CPTs. Less commonly, there may be shared arterial supplies such as branches of one middle cerebral artery feeding both twins [18]; and large arteries may cross from one twin to another.

19.5 Management of Craniopagus Twins

Conjoined twins can be diagnosed during mid-pregnancy with a standard ultrasound examination; diagnosis also can be made by fetal magnetic resonance imaging (MRI). Delivery of these twins is commonly performed by a cesarean section a couple of weeks before the expected date; some twins have been reported to be delivered with normal vaginal delivery [19]. Proper evaluation needs to be carried out after delivery since CPTs may be associated with systemic comorbidities such as cardiovascular (hypo/hypertension, coarctation of the aorta, and patent ductus arteriosus), neurologic (hemiparesis, delayed milestones of development), and craniofacial (cleft lip and palate), genitourinary abnormalities, and anorectal agenesis. Cerebral blood flow (CBF) constitutes 15–20% of the cardiac output and in CPTs may present with unidirectional shunting of blood flow. Hence, the twins could present with features of cardiac straining as well as hypo/hypertensive episodes [6]. One of the twins may develop left ventricular hypertrophy secondary to chronic hypertension [20].

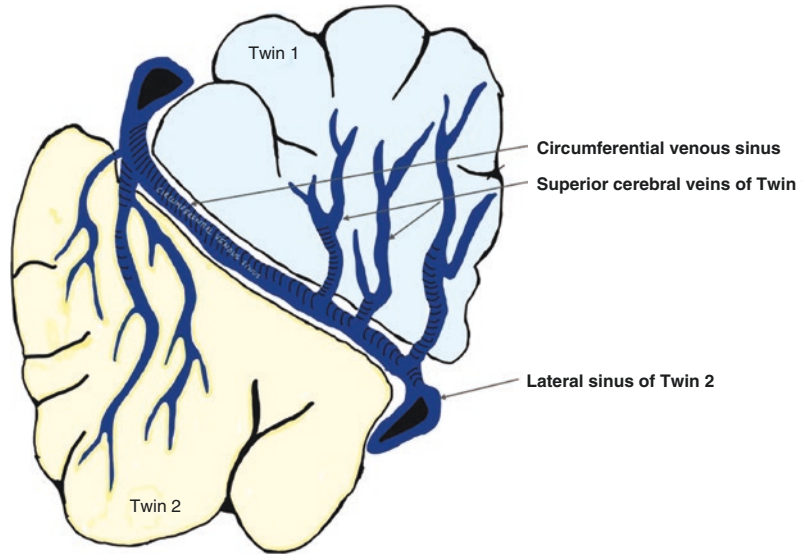

Fig. 19.1 Schematic diagram of a variant of shared venous architecture in craniopagus twins. A common venous sinus may drain the twins' cerebral cortices (Twin 1 and Twin 2)

Separation surgery for craniopagus twins is a very complex procedure. It requires appropriate planning before separation and reconstruction of different layers of tissue such as the skin, skull bone, dura mater, brain parenchyma, and vasculature. The separation surgery can be carried out as a routine procedure to allow the twins an independent life. Their separability is determined based on the extent of sharing of intracranial structures. Separation at a younger age (~1–2 years) is recommended; it is presumed the brain plasticity may help the early recovery of brain insult after separation surgery [9, 12, 21]. It is also reported that mortality is higher with such an extensive surgery at a younger age [22]. Besides this, CPTs are separated on an emergent basis due to one child's death, increasing the other's risk of death. Anesthetic and surgical concerns remain the same whether separation is planned as a routine or emergency procedure. Multiple procedures are carried out to achieve a successful separation. Neurosurgical separation includes the separation of shared vasculature, interdigitating brain parenchyma, white matter connections between the thalamic regions [23], and other structures [16]. Reconstructive surgery includes cranial and soft tissue coverage, plans for duroplasty, cranioplasty, and tissue flaps.

The final tissue defect in cases of total vertical CPTs is expected to be quite large in surface area. It is challenging to cover, exposing the twins to further complications despite a successful separation of brain tissue and vasculature. Much before the final separation surgery, tissue expanders can be placed to create the extra amount of skin required for coverage. The skin expanders are placed anteriorly followed by posteriorly and expanded with aliquots of 10 mL of saline at regular intervals [24]. Saline injection for expansion into the expanders is usually associated with severe pain and requires analgesic supplementation. At times, thinning of the skin following rapid expansion may lead to implant extrusion due to skin ulceration, commonly seen posteriorly. The total time taken for adequate expansion of the scalp may range from a few months to 1.5 years. The tissue expander use may be deferred until the final separation surgery (expanders kept for 4–6 weeks) to reduce infection risk [6]. However, the use of microvascular skin flaps obviates the need for skin expanders.

19.5.1 Staged vs. Non-staged Separation

The staged concept of surgery is based on the risk of massive blood loss and the twins' ability to tolerate the surgery. The presence of a shared SSS or CVS is the most challenging aspect of craniopagus separation surgery. In a single-stage separation surgery, the CVS is given to one twin, while the sinus is reconstructed in the other. It increases cerebral venous pressure during the separation; hence, it may lead to a cascade of events favoring failure of the procedure rather than success [25]. In a multi-stage approach, one twin (dominant) receives the CVS. Simultaneously, the other (non-dominant) develops the venous drainage system over a period during which serial surgical ligation and detachments of draining veins are carried out [26]. Staged separation offers a more graded approach to change the venous drainage in both twins. It improves venous collateral circulation and, hence, venous drainage, thereby preventing increased venous pressure and the possibility of brain edema. During final venous separation, the channels in each brain are adequate to allow complete separation. This process also favors the integrity of dura and flap repair that would reduce the risk of cerebrospinal fluid (CSF) leak. The staged approach is also intended to minimize intraoperative hemorrhage and transfusion of blood products. It may allow the twins to recover from each stage before progressing to the next stage with a gap of 4–6 weeks or more while continuing supportive therapy. Nevertheless, the other potential advantages of the staged separation surgery are the reduced duration of general anesthesia (GA), less bleeding, fewer transfusion requirements of fluids and blood, less probability of brain edema and infarction, and lesser fatigue of the operating team [24]. Technological advances in endovascular therapy also help prevent the draining/bridging

veins with coil embolization and avoid open surgery and associated complications [23]. Such procedures may play an essential role for staged surgeries in CPTs in the future.

After separation, the dominant twin may have robust vitals, whereas the non-dominant twin may present with low cardiac output, hypotension, oliguria, low weight, or failure to thrive. The staged approach is not required for partial CPTs.

19.6 Preoperative Evaluation and Preparation

There should be adequate preparations for manpower, equipment, and monitoring tools apart from a prior mock-drill before the CPTs are planned for separation. Multiple team meetings are necessary for appropriate planning and preparation.

19.6.1 Multidisciplinary Team (MDT)

A well-equipped multidisciplinary team (MDT) of surgical, anesthesia, and medical specialties, comprehensive radiological (anatomical) evaluation, addressing ethical concerns for separation, and parental participation are important prerequisites for the separation surgery of CPTs. MDT should ideally be formed under the leadership of a senior pediatric neurosurgeon, comprising of two pediatric neuroanesthesia leads (one for each twin), specialists from neuroradiology and imaging, pediatric intensive care, pediatric surgical specialties including plastic and reconstructive surgery, pediatric medicine specialties including cardiology and nephrology, and many other professionals [20]. The rarity of this complex, expensive, and lengthy yet technically challenging surgery for separation encourages international collaborations, particularly when planned in a developing country [23]. Moreover, multidisciplinary teleconferences are recommended in countries without extensive separation experiences in conjoined twins [27].

19.6.2 Neuroradiology and Imaging

Neuroimaging modalities such as computed tomography (CT), MRI, and digital subtraction angiography (DSA) contribute a very important role in diagnosing shared vasculature, interdigitating brain parenchyma, dura mater, and skull in the CPTs [26]. A comprehensive evaluation of the shared venous and arterial anatomy helps anticipate perioperative complications such as hemorrhage, air embolism, thrombosis, and infarction. Digital and 3D modeling of CT and MRI data is very useful for surgical planning and intraoperative guidance for the neurosurgeon. CT angiography (CTA) and venography (CTV) provide information on vascularity. CT venography is particularly utilized for planning at every stage of separation. MRI gives a detailed anatomical and developmental assessment of the shared cerebral cortex, ventricles, venous sinuses, and other anomalies. CTA and CTV are superior for studying the vasculature, whereas magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) are superior in studying soft tissues, including brain parenchyma. In older or adult CPTs, functional MRI (fMRI) is used to define the hemispheric dominance of the language function and surgical planning [28].

DSA is used preoperatively for anatomical clarity of the vasculature, and venography helps to identify the twin with fully formed sinuses. A temporary balloon occlusion test may be carried out at the shared vinous sinus to test changes in the venous drainage and collaterals, hemodynamics, and requirements of a bypass [24, 29, 30]. Venous rerouting and promotion of collateralization can be achieved by using endovascular venous coil embolization [30, 31]. Full segment endovascular occlusion of the shared venous system has been utilized for successful separation [23]. The endovascular approach and separation could be a preferred procedure, since preoperative and intraoperative clipping and/or bypass creation are associated with very high risks. Coil embolization of shared arterial supply has also been utilized as a part of endovascular therapy in CPTs [18].

3D reconstruction of CT data helps in evaluating the extent of bone fusions in CPTs, which can be further reconstructed to create a life-sized 3D model of transparent acrylic and ceramic types as well as holograms for depicting vasculature in relation to the other tissues [26]. The 3D models better depict the surgical anatomy and are used for surgical reference at various steps along with intraoperative neuronavigation. It is also used to plan scalp tissue expanders' placement for adequate coverage and craniotomy and to design bone grafts for subsequent cranial reconstruction. Newer techniques such as computer-aided design and modeling, custom-made devices that used distraction osteogenesis and soft tissue molding, and intraoperative neuronavigation help successful separation among young twins [32].

19.7 Anesthetic Management

The CPTs may undergo many procedures under GA before the final separation surgery. Since most patients are young, GA is a prerequisite even for diagnostic imaging. Broadly, techniques may include (1) neuroradiologic imaging for planning and prognostication, (2) tissue expander placement at least in two stages, (3) single or staged separation, and (4) reconstructive plastic surgeries. Sometimes, an attempt to obtain central venous access for any reason other than surgery may also require GA.

During the preanesthetic evaluation, IV access and airway should be properly assessed along with a thorough general and systemic examination of the twins. It is advisable to restrict **vascular access** only to peripheral lines for minor procedures so that central veins could be utilized for the separation surgery. CPTs could likely present with **difficult airways** owing to distorted necks, conjoined heads with restricted mobility of head and neck, and congenital oropharyngeal anomalies. Possible problems with mask ventilation and endotracheal intubation should be anticipated. The signs of an increased airway obstruction would need nasopharyngeal airway in certain situations; a planned tracheostomy prior to separation surgery would prevent loss of airway under challenging conditions.

Anesthetic concerns depend on the procedure planned (Table 19.3). Prior confirmation of logistic support, MDT meetings, as well as mock-drill at different anesthetic areas are mandatory to prevent confusion and possible mismanagement. While all imaging and surgical procedures would focus simultaneously on both twins, anesthetic management would require their management as different individuals since they are physiologically different [20]. Hence, there should be **two anesthesia teams** led by two pediatric neuroanesthesiologists. They should be supported by human resources (assistants and staff), equipment (anesthetic workstations with monitors, infusion pumps, and other equipment), and materials (drugs with specific color code for each twin, blood, and products), all in duplication.

The anesthetic management for CPTs can be broadly described under two headings: (a) anesthesia for neuroimaging procedures and (b) anesthesia for separation surgery. However, there are possibilities that CPTs could present for other procedures on an elective or emergency basis [33, 34]. In such a CPT case, one twin (dominant) successfully underwent adenoidectomy for obstructive sleep apnea under anesthesia [34]. Such types of emergency surgeries in CPTs, imaging and neurointerventional procedures, and different staging surgeries before the final separation may be described under *nonseparation anesthesia* (Table 19.4). The detailed discussion on this topic is beyond the scope of this chapter.

19.7.1 Anesthesia for Neuroimaging Procedures

The nil per oral (NPO) status and normal routine blood and urine need to be ascertained beforehand [35]. Sedative **premedication** should ideally be avoided in the twins; however, oral anxiolytics in the presence of parents help alleviate apprehension before subsequent activities. Induction should be carried out preferably in a place with appropriate arrangements, if not the operating room (OR), before neuroimaging. The

Table 19.3 Anesthetic concerns during the different procedure for craniopagus separation

Procedure(s)	Anesthetic concern(s)
Neuroimaging (CT, MRI, angiography)	1. Non-operating room anesthesia and other logistical issues 2. Effective communication between two anesthesia team members and other supporting staffs 3. Difficult airway and vascular access 4. Positioning patient, personnel, and equipment in different neuroimaging setups with less optimal conditions for the twins 5. Cross-transfer of administered drugs and fluids 6. Hemodynamic disturbances 7. Prolonged anesthesia time 8. Hypothermia 9. Contrast-related issues 10. Anesthetic neurotoxicity at younger age group 11. Issues with transportation to different neuroimaging suites
Tissue expander placements[a]	All concerns as above except 1, 4, 7, 9, 11 12. Surgical positioning for placement of expanders first anteriorly, and then posteriorly, in two stages
Separation surgery	All concerns as above except 1, 4, 7, 9, 11 13. Surgical positioning; preferably prone separation in the first stage followed by supine separation 14. Severe bleeding and massive transfusion 15. Massive fluid shift 16. Intraoperative tight brain 17. Venous air embolism (VAE) 18. Intraoperative cardiac arrest in one or both the twins and resuscitation 19. Long-duration surgery 20. Shifting of one twin immediately to the adjacent OR, kept ready, after separation, along with man, monitor, and machine 21. Infection control
Reconstructive surgery (duroplasty, cranioplasty, skin and tissue flaps/rotational flaps)	• Massive fluid shift • Hemorrhage and exsanguination of blood • Brain bulge during the cranioplasty • Infection control
Follow-up surgeries (ventriculoperitoneal shunt surgery for hydrocephalus and CSF leak, skin grafting)	• The absence of skull bone may lead to accidental pressure on the brain during the surgical manipulation causing hemodynamic perturbations (e.g., bradycardia) • Infection • Wound dehiscence

[a]This procedure may be combined with neuroimaging to reduce the number of anesthetics.

Table 19.4 Anesthesia encounters in craniopagus twins

Anesthesia for nonseparation surgery	Anesthesia for separation surgery	Anesthesia for reconstructive surgery and additional follow-up procedures
1. Neuroimaging procedures: • CT, MRI, angiography • Endovascular separation 2. Placement of tissue expanders to increase skin area necessary for coverage after final separation surgery 3. Multi-staged separation procedures before the final separation • Number of procedures depends on the separation planning 4. Emergency surgical procedures not related to separation: For example, adenoidectomy, colostomy, etc.	1. Surgery during the final separation • Occurs in the last and single planned attempt	1. Plastic and reconstructive procedures • For example, duroplasty, cranioplasty, skin grafting, etc. • Number of anesthetics depends on the requirements for individual twins 2. Additional procedures: • Ventriculoperitoneal (VP) shunt surgery for hydrocephalus • Placement of lumbar drains

difference in hemodynamic parameters (heart rate and blood pressure) gives a rough idea about the presence of physiological interdependence (cross circulation) in CPTs before neuroimaging. Cross-circulation between the twins may also be ascertained with IV injections of anticholinergic agents (atropine or glycopyrrolate) if an IV access is present. The variations observed in hemodynamics (heart rate) at different time points suggest the presence of cross-circulation [16, 17, 35]. Premedication with anticholinergics also helps reduce oropharyngeal secretion and may be useful, particularly when intramuscular ketamine is used for induction before IV access is secured [36]. Anesthesia may preferably be induced with sevoflurane if IV access is not secured in both the twins, else propofol may also be used. However, the procedure such as MRI can be carried out under sedation with oral triclofos, intermittent boluses of propofol along with O_2 supplementation [35].

The anesthetic **induction** may be carried out simultaneously in both twins or one after another at an interval of few minutes. Crossover of the anesthetic agents may induce anesthesia in the other twin simultaneously. Hence, oxygenation with mask ventilation should be carried out in both accordingly. Ideally, two anesthesia machines are utilized for anesthetizing CPTs. The anesthetic locations outside the OR are unlikely to have spacious accommodation for two sets of equipment and professionals. Hence, it requires adaptation to the available facility, which could be ensured during mock-drills prior to the procedures. In this context, the use of a single anesthetic machine with two breathing circuits attached to the common gas outlet with a Y-connection may be useful [37, 38]. In fact, arrangements of MRI-compatible anesthesia machines in duplication could be of logistic issue. Nevertheless, all other gadgets used in duplication should be MRI safe [38]. Heart rate, blood pressure (noninvasive and/invasive), oxygen saturation (SpO_2), ECG, and end-tidal carbon dioxide ($EtCO_2$) are to be monitored continuously from two monitors.

Many anesthesiologists prefer induction of the twin with hypertension and antihypertensive therapy first. However, anesthesia-induced hypotension may cause a further decrease in blood pressure in the other (hypotensive) twin. Pharmacologic measures utilized to control hypo/hypertensive episodes in these twins might not yield optimal results in the presence of crossover [37]. Hence, physiological control by placing the hypertensive twin higher up than the other twin with a pillow's help has been attempted. It helps to counter gravity-dependent shunting of the blood between the twins.

Transportation of the anesthetized twins to different locations outside the OR is required for preoperative neuroimaging. The twins under GA may have to be transported in a trolley with ventilatory and monitoring support. An optimal communication among supporting staff is desirable to prevent disconnection and kinking of breathing circuits, catheters, and lines. The twins could be at increased risk of adverse cardiac and respiratory events. The majority of them are preventable; if they occur, they may adversely affect the outcome [39]. Similarly, positioning during the procedures is problematic as none of the neuroimaging patient tables are specifically made for CPTs with conjoined heads. Combining all neuroimaging procedures as a single procedure may reduce the number of anesthetic attempts and, possibly, anesthesia toxicities, but it would increase the anesthesia time. The twins are prone to hypothermia due to prolonged anesthesia time and the low temperature of MRI and DSA suites. Appropriate precautions such as the use of warm crystalloid infusion and convection warmers and wrapping twins with warm blankets throughout the process may help prevent significant hypothermia.

Simultaneous **mask ventilation** after anesthetic induction of the twins might be difficult due to the paucity of space between them; the angular CPTs may lead to further difficulties in terms of mask ventilation as well as intubation. In the case of difficult mask ventilation, muscle relaxants should be avoided, and a check laryngoscopy (preferably videolaryngoscope) helps assess the situation. Supraglottic airways can be used in older CPTs undergoing neuroimaging under GA [38], whereas very small twins need tracheal intubation.

19.7.2 Anesthesia for the Separation Surgery

It is desirable to have multiple meetings of MDTs apart from few separate meetings among the team members for anesthetics. All proper investigations, including the imaging studies, are to be reviewed thoroughly. The anesthesia team should have a thorough understanding of the sequence of planned surgical steps and perioperative care. Such surgeries should be carried out in a referral medical center where the facilities can carry out such a complex procedure. The major concerns of separation include massive intraoperative hemorrhage, cerebral edema, venous infarcts, swelling of the skin flaps, and dehiscence of the repairs with CSF leak, meningitis, and exposed brain [25].

The basic **preanesthetic preparation** is more or less similar to neuroimaging procedures. One twin may be physiologically dominant, and the calculated anesthetic drug doses can be unpredictable. The planning should be done individually for each twin; drugs should be prepared in duplications in a dose appropriate for each twin. The body weight may be calculated by dividing the twins' total weight into two parts, assuming both are of similar weight. Each twin can handle a particular drug dose differently from the other. It would depend on the crossover of the circulation and hepatorenal function; the changes would be unpredictable after separation [40].

The laboratory investigations should include a complete hemogram, fasting blood sugar, hepatic and renal function tests, coagulation studies, blood grouping, and cross-matching for each twin individually. A chest X-ray and echocardiography for each twin should also be done.

The OR should be prepared beforehand, and all necessary drugs and equipment should be arranged meticulously with drugs labeled with color coding for each twin. The OR personnel should be counseled about their specific roles for this procedure. Two tables may be joined to create a single operating table considering the possible positioning of the CPTs (Fig. 19.2). A prior **simulation or rehearsal (mock-drill)** helps organize the OR and procedural planning [41], such as identifying space for the teams involved, anesthesia equipment, ventilator, and monitor in duplication. It also decides optimal patient positioning. Simulations on common intraoperative scenarios and emergencies are also suggested [42].

Both IV and inhalational induction with sevoflurane are considered suitable for the CPTs depending on the presence of an IV access [20]. Anesthesia for both twins may be induced simultaneously; however, one may take a longer time for the induction. Opioids such as fentanyl or remifentanil and muscle relaxants are to be given at a dose appropriate for each twin. Both nasotracheal and orotracheal intubation can be done [38]. While nasotracheal helps during continued postoperative mechanical ventilation after the separation, however, the possible increase in infection and meningitis incidence prevents its practice in neurosurgical patients. Hence, the orotracheal method is preferred as the endotracheal tube (ETT) can be secured relatively away from the surgical site. There may be difficulties in securing the airway when intubation is attempted in both twins simultaneously [35], or when there is restricted neck movement owing to conjoined and fixed heads. Twins with prolonged conjoining may develop cervical lordosis that inhibits mandibular growth causing further difficulties [43, 44]. The difficult airway cart should be kept ready in each case of conjoined twins. Direct laryngoscopy, as well as videolaryngoscope, are preferred during intubation. While appropriately sized cuffed PVC tubes may be used for anesthesia during neuroimaging procedures, it is preferable to use reinforced ETTs for separation surgery. There could be considerable manipulation of the head and neck during the intraoperative period leading to kinking of the ETT. In some of the CPTs, it may be necessary to lift and rotate one twin during laryngoscopy and intubation in the other and vice versa.

Vascular access may be difficult in younger CPTs; it may be complicated by a prolonged pre-separation period with multiple punctures of peripheral veins for different procedures. Central venous access for each twin with a triple-lumen catheter may be planned under ultrasound guidance. The access is needed for fluid management,

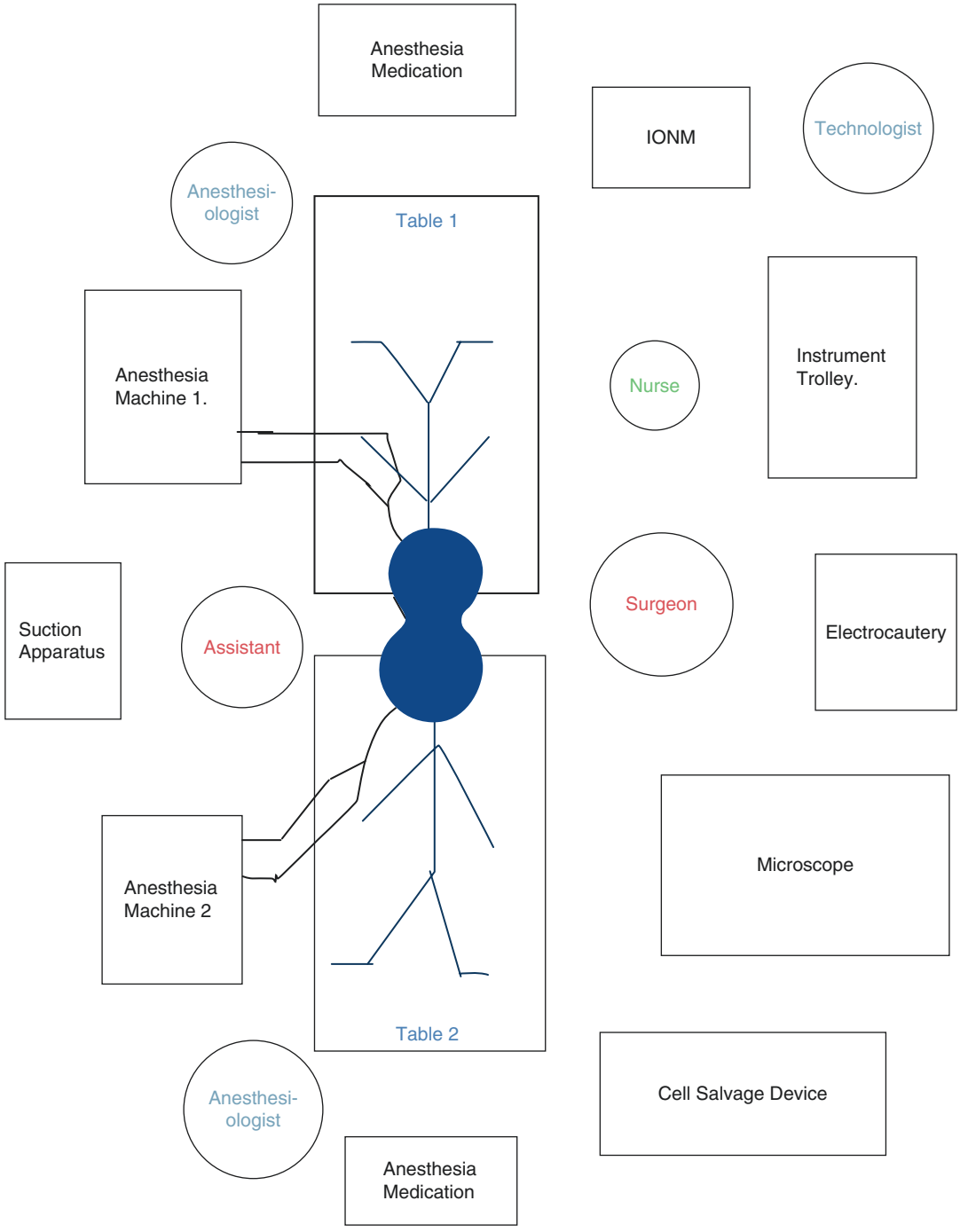

Fig. 19.2 Proposed operating room (OR) arrangements during craniopagus separation surgery

drug infusions, and measuring trend of central venous pressure (CVP) and as part of treatment in case of intraoperative venous air embolism (VAE) to aspirate air [17]. The site of preference for central venous catheter placement may vary among the clinicians. The authors would prefer

femoral or subclavian veins; however, an internal jugular vein can also be utilized after separation surgery whenever indicated. The goal is not to allow any of the central lines to come into the surgical field. The peripheral venous catheters can be placed in the limbs, preferably in the upper limbs. Arterial catheters should be placed in both the twins for continuous monitoring of blood pressure and arterial blood gas (ABG) analysis.

Monitoring should include all the routine parameters such as ECG, SpO_2, $EtCO_2$, arterial pressure, CVP, airway gases, blood loss, blood and fluid transfusion, and urine output [38]. Temperature can be recorded both from the core (esophageal and rectal temperature) and peripheral sites. Apart from these, neuromuscular monitoring (NMT), neurophysiologic monitoring (somatosensory and motor evoked potentials), and regional cerebral oxygenation (NIRS) may be measured.

Maintenance of anesthesia is done with inhalational agents (isoflurane/sevoflurane/desflurane) in oxygen and air. The use of nitrous oxide may be avoided in view of its effects on intracranial pressure and the possible occurrence of VAE [38]. Opioid supplementation at regular increments or as infusions can be given also help to achieve immediate postoperative analgesia. Total intravenous anesthesia (TIVA) with or without muscle relaxant may be utilized in case of intraoperative tight brain and neurophysiologic monitoring, respectively. However, continuous infusion of propofol for a prolonged period should be avoided because of its potential adverse effects.

The positioning of the CPTs requires careful consideration and appropriate planning based on the available gadgets. The upper ends of two OR tables are joined together to the conjoined heads on a headpin or a specially prepared headrest [17]. Precautions must be taken to keep the twins surgically accessible while ensuring that the lines and circuits are not dislodged, twins are accessible to anesthesia teams, and the pressure points are well-padded. There is no particular recommendation available regarding the twins' surgical position for the initiation and completion of separation surgery. It may be started with the twins in prone; final separation should be carried out with the twins in a supine position. It could be beneficial for last-minute turning (supine) of the twins after separation. On the contrary, if separated in prone, the twins may have to be transferred to separate tables in the prone position with fully exposed brains [38].

Management of fluid and blood loss needs utmost attention. Crystalloids and colloids are administered in a titrated manner to both children. During this prolonged surgical period, 1–2% dextrose solution may be preferred in younger twins to avoid intraoperative hypoglycemia. The insensible losses from the surgical site are unmeasurable. The near-ideal replacement of fluid and blood loss is difficult to achieve but should be guided by arterial waveform analysis, CVP trends, urine output, electrolytes, point-of-care determinations of ABGs, and thromboelastography. Blood loss estimation is complicated during the separation surgery. Even a moderate loss would have significant clinical problems, particularly in young twins. The bleeding from the common surgical would is different for each twin and is usually estimated from blood collected from the suction chamber, amount and weight of gauze pieces used, and hemoglobin and hematocrit values measured at regular intervals. Half of the estimated volume should be transfused to each twin [45]. Close monitoring of the hematological and coagulation status of each patient needs to be ensured throughout. The blood loss also could be managed with staged separation and preserving the cleavage plane between the separated brains with silicone sheets.

Complications such as hemodynamic perturbations, massive blood loss, brain edema, and hypothermia may occur during the perioperative period. **Hemodynamic disturbances** in the twins may occur due to blood loss and massive fluid shifts, and persistent differences in blood pressures throughout the surgery due to cross-circulation and a unidirectional vascular flow or unopposed shunting [20, 36, 38]. Therefore, one twin may remain hypotensive, whereas the other may present with hypertension; supplementation of fluids and inotropes in the hypotensive child

can worsen hypertension in the other twin without any obvious benefits [36]. The fluid volume requirements could be more significant in one twin, whereas the urine output is significantly more in the other [20], suggestive of a unidirectional intracranial flow pattern. The twin may become hypervolemic enough to develop cardiac failure. In contrast, the other twin might be oliguric/anuric, leading to renal failure and requiring continuous renal replacement therapy (CRRT) and possibly renal transplantation [16]. This complication of unopposed shunting may occur at any time during the multi-staged separation during intraoperative or postoperative period requiring vasoactive managements and even withdrawal of blood in the twin with impending cardiac failure; it generally resolves after final separation [38]. **Massive blood loss** should be anticipated during the stage of venous separation. The loss has to be replaced with blood and products. It is unclear which twin is more affected by the blood loss. It is also not uncommon for one twin to present with more significant clinical symptoms of hemorrhage or volume overload following transfusion, despite the blood loss shared by both [40]. The loss can be extensive and may lead to hypovolemic shock, bradycardia, and even cardiac arrest requiring resuscitation [36]. **VAE** is a strong possibility at every stage of the separation surgery. **Hypothermia** may be attributed to the extensive surgical wound as well as prolonged surgical time, which causes heat loss by evaporation, radiation, and convection. All available measures should be utilized to prevent it and to maintain normothermia as intraoperative hypothermia affects the surgical outcome [43, 45]. Post-separation, the twins may develop brain edema due to the formation of venous infarct and deranged cerebral autoregulation after surgical manipulations. **Infection** at the surgical sites, meningitis, CSF leak, and ventriculitis may occur, requiring constant vigilance and preventive measures. The high potential for infection in such cases is due to the presence of an indwelling catheter, shunts, tissue expanders, and drains. Hence, antibiotics are used during the different periprocedural periods.

After final separation, one twin has to be transported to the adjacent OR with the anesthesia team assigned. The ventilator, monitor, and infusion of drugs accompany the twin to further reconstruct the dura, calvarium, and scalp with artificial dura, absorbable plates, and split skin grafts. Both the twins at this stage develop physiological changes manifested mainly with hemodynamic perturbations.

19.8 Postoperative Intensive Care

After separation, the twins develop a lot of physiological changes, develop hypotension, and often need inotropes to maintain blood pressure. One (non-dominant) twin may develop seizures due to venous infarcts' formation and require prophylactic antiepileptic drugs (AEDs). Continued ventilation with optimization of hemostasis, hypoxia, hypercarbia, hypotension, hypothermia, hypotension, and electrolyte abnormalities is mandatory. Seizures may also occur in any of the twins due to postoperative complications such as meningitis, hydrocephalus, and metabolic derangements [17]. Fluid shift and blood loss during the perioperative period need intensive fluid management and blood component therapy. Extensive venous infarcts may cause cerebral edema and brain bulge. Many exposed areas are prone to develop severe infection and septicemia; aggressive antimicrobial treatment helps to attain a better outcome.

The twins may need multiple wound dressing episodes, skin grafting in case of wound dehiscence, lumbar drainage for CSF leaks, and VP shunt insertion for hydrocephalus under sedation or GA as and when indicated. The individual status of the twins needs consideration for anesthetics. The surgical outcome is significantly better with the separation of partial CPTs, whereas with total CPTs, both mortality and morbidity are more [9]. One or both of the twins may have to undergo rehabilitation for neurologic and cognitive disabilities due to developmental reasons and surgical complications. The twins may have a prolonged hospital course even after the final separation surgery.

19.9 Legal and Ethical Concerns

Legal and ethical questions are always raised concerning the separation of conjoined twins irrespective of phenotypes. The issues encountered with CPTs are based on principles of autonomy (respect decision of patient), informed consent in young children, principles of beneficence, and nonmaleficence (act in the benefits of the patient and not harm the patient), and justice [46]. The ethics are made even more complex when one twin is dependent on the other for survival as the latter twin may have to be sacrificed for the former's survival. In this context, a review by the hospital ethics committee opinion may help. It has also been suggested to have a prior legal opinion before separation [42].

19.10 Conclusion

The separation surgery for CPTs is one of the most complex procedures undertaken in neurosurgery. Of late, successful separation has become more common with the advances in neuroimaging, neuroanesthesia, and neurosurgical techniques. Experience and expertise with this surgical procedure are limited. Hence, the MDT may prefer having interinstitutional or international collaborations, if required, to close the learning gap. The success of surgery depends on early separation (less than 1 year), the shared vasculature nature, and multi-staged surgery. Anesthetic management requires meticulous planning and clear communication among the team members with particular attention to the difficult airway, adequate intravascular access, careful positioning, appropriate intraoperative fluid and blood management, maintenance of normothermia, and effective management of the perioperative complications.

Conflict of Interest The authors were part of 'AIIMS Craniopagus Team' responsible for the first successful craniopagus separation surgery in India.

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Anesthesia for Minimally Invasive Neurosurgical Procedures in Children

20

Sethuraman Manikandan and Prakash Nair

Key Points

- Minimally invasive neurosurgery (MIN) is gradually becoming popular among children for many neurosurgical conditions.
- Technological advancements in neuroendoscopes, image guidance systems, and availability of modalities like intraoperative computed tomographic (CT) scan, magnetic resonance imaging (iMRI), and robotic neurosurgery have revolutionized MIN.
- MIN has the potential to significantly reduce the occurrence of complications as well as hospital stay.
- Conditions that are amenable for MIN are hydrocephalus, biopsies for intracranial lesions, craniosynostosis repair, epilepsy surgeries, sellar and suprasellar tumors, and spinal surgeries.
- MIN with robotic assistance may help for more accurate resection of lesions, less blood loss, and faster recovery.
- Minimally invasive techniques for spine surgeries in children include decompressive surgeries as well as instrumentation for correction of different deformities.
- Anesthesia concerns vary based on the procedure carried out apart from the usual implications of a pediatric patient.

20.1 Introduction

Since the inception of the specialty of neurosurgery, conventional teaching was that "bigger opening is better." This statement was based on the principle that a larger opening could allow room for the swollen brain to expand adequately, resulting in lower intracranial pressure (ICP) and reducing the potential for retractor-induced ischemia to normal brain tissue. Adverse brain conditions could also be encountered due to inhalational anesthesia, vasodilatory effects of medications used to regulate blood pressure, and awkward patient positioning leading to brain swelling. Imaging techniques were not available during the early years of neurosurgery, and a large craniectomy allowed for easier localization of the lesion, easier control of bleeding, and room to perform resective surgery in cases of refractory brain bulge [1, 2]. Morbidity and mortality of traditional neurosurgery due to large craniotomies and subsequent brain damage during surgery were well-recognized a century ago [3, 4]. Over the last three decades, advancements in tech-

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nology have eliminated most difficulties encountered by earlier generations of neurosurgeons. Recent imaging modalities provide accuracy within a few millimeters, and stereotactic guidance has increased the accuracy to the submillimeter level. Neuronavigation tools allow the surgeon to map the perfect trajectory to precisely target lesions while causing minimal damage to eloquent areas of the brain [5]. Advanced micro-equipment and endoscopes allow access to deeper tissues with minimal handling of adjacent brain tissues. Advancement in anesthesia techniques and a better understanding of neurophysiology and neuropharmacology have led to improved control over ICP in the perioperative setting. Facilitation of minimally invasive neurosurgery (MIN) requires preoperative planning with investigations such as computed tomography (CT), magnetic resonance imaging (MRI), and intraoperative aids like neuroendoscope (using small burr hole/craniotomy), neuronavigation (image guidance system), or the use of robotic aided surgery [6].

Pediatric patients presenting with various neurological conditions such as a tumor, obstruction of cerebrospinal fluid (CSF) pathways, congenital and developmental anomalies of the skull and vertebral column, intractable epilepsies, and vascular anomalies may need neurosurgical procedures for their management. It has been well-recognized that major neurosurgical procedures in pediatric patients carry lots of morbidities [7, 8]. The use of MIN procedures has been shown to reduce complications associated with some neurosurgical conditions and also reduce hospital stay and cost [9, 10]. However, MIN procedures may pose unique challenges to the anesthesiologist in the perioperative management of pediatric patients [11]. This chapter describes various neurosurgical conditions where minimally invasive techniques and their anesthetic management have been established (Table 20.1), and in the subsequent sections, the technology involved with MIN for cranial and spinal conditions has been discussed.

Table 20.1 Different techniques and the procedures performed as minimally invasive neurosurgery (MIN)

Techniques	Indication	Procedure
Endoscopic transcranial procedures	Aqueduct stenosis, Hydrocephalus [12]	Endoscopic third ventriculostomy + ventriculoperitoneal shunt
	Craniosynostosis [13, 14]	Endoscopic strip craniectomy or spring cranioplasty
	Arachnoid cysts, tumors, biopsy [15]	Fenestration, Biopsy, decompression
	Hematoma/vascular malformation [16]	Evacuation
Endoscopic transnasal procedures	Sellar, suprasellar lesion [17]	Decompression of tumor
	CSF leak [18]	Repair
	Mucocele [19]	Resection, repair of defect
Image guidance surgery	Sellar lesion, tumors [20]	decompression
	Epilepsy [21]	Strip and depth electrode insertion
	Hydrocephalus [22]	Fenestration
Robot-guided surgery	Tumors [23]	Biopsy, decompression
	Epilepsy [24]	Depth electrode insertion
	Hydrocephalus [25]	Fenestration, septostomy
Minimally invasive spine surgery and VATS	Spinal trauma [26]	Decompression, fusion
	Scoliosis/kyphosis [27]	Correction of deformity, fusion
	Vertebroplasty/kyphoplasty [28]	Bone cement deposition
	Disc prolapse [29]	Discectomy

20.2 Technology Aids to Minimally Invasive Neurosurgery

Three major technologies that led to advancement in MIN are neuroendoscopes, image guidance systems, and robotic neurosurgery. Understanding the technical aspects of these advanced procedures is relevant for anesthesiologists for efficient perioperative management.

20.2.1 Neuroendoscopy

Neuroendoscopy dramatically changed the approach from open craniotomies to minimally invasive techniques to manage different pathological entities. The first neuroendoscopic procedure was performed in 1910 by L'Espinasse, using a cystoscope [30]. Since then, the interest in endoscopy and the advancement of science has led to the development of special neuroendoscopes with varying viewing angles and instruments of different sizes that can pass through them. The instrument consists of a xenon-light source, which allows clear visualization of anatomical details, and a trocar with working channels for atraumatic insertion into the brain. Through the trocar, the endoscopes (sizes: 6 mm, 4.6 mm, and 3 mm diameter) can be inserted for further visualization of intracranial structures and the passage of irrigating fluids and instruments (Fig. 20.1).

Neuroendoscopic procedures have a wide variety of applications in pediatric neurosurgery. These procedures utilize the cavity of the lateral as well as the third ventricle and may be used to manage a spectrum of lesions that obstruct the CSF pathway. Many technological advances like the development of high-definition cameras, flexible scopes, rod lens telescopes and image guidance have made neuroendoscopic procedures safer and have improved surgical outcomes. During the initial days, the neuroendoscopes were primarily used for third ventriculostomy for obstructive hydrocephalus. Currently, neuroendoscopy is indicated for the management of (a) hydrocephalus, (b) intraventricular tumors, (c) intraventricular hemorrhage, (d) intracranial arachnoid cysts, (e) pineal region cysts, (f) colloid cysts, and intraparenchymal cysts [31, 12] (Table 20.1).

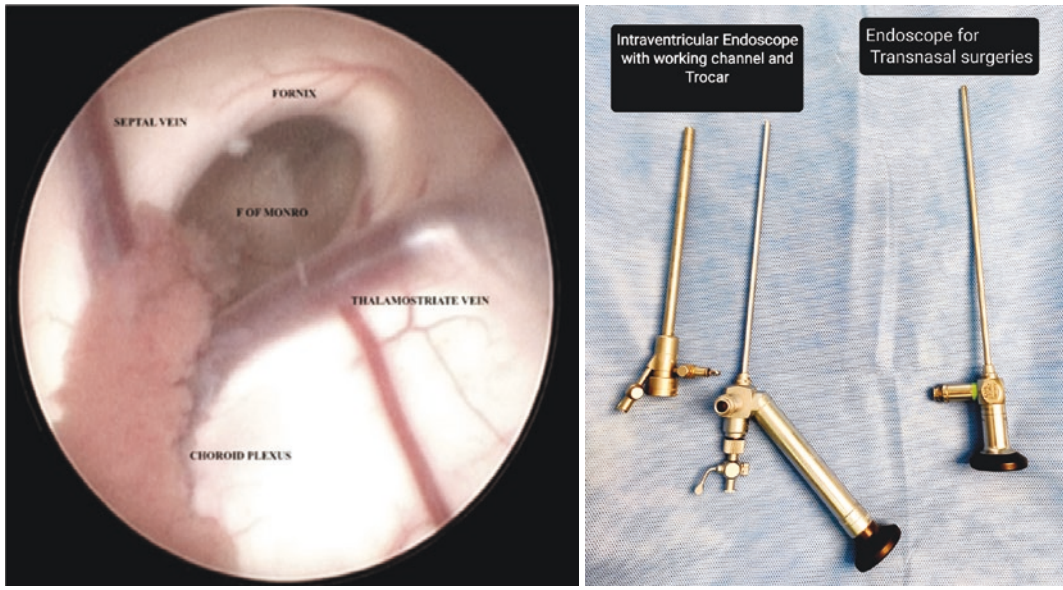

Fig. 20.1 Endoscopic view of the third ventricle and the neuroendoscopes-intraventricular with trocar and transnasal scopes

20.2.1.1 Neuroendoscopy for CSF Pathway Obstruction

Neuroendoscopy is performed in various conditions with obstruction to the CSF pathway, causing both communicating and non-communicating hydrocephalus. Some of these clinical scenarios where this procedure is employed include congenital hydrocephalus, aqueduct stenosis, entrapped lateral ventricle, fourth ventricular outlet obstruction (tumor, cyst) hydrocephalus, multi-loculated hydrocephalus, hydrocephalus with meningomyelocele, and failed ventriculoperitoneal (VP) shunts.

The presence of dilated ventricles serves as a natural cavity for neuroendoscopic procedures. The use of the ventriculoscope permits the neurosurgeon to inspect the lateral and third ventricle anatomy. In cases of obstruction to CSF outflow in the posterior third ventricle (e.g., pineal region tumors or aqueductal stenosis), an endoscopic third ventriculostomy (ETV) may be performed. In anterior third ventricular lesions (e.g., craniopharyngioma), the foramen of Monro may be occluded, and the lateral ventricles are dilated in isolation; the ventricular dilation may be asymmetrical if the outflow of only one of the ventricles is obstructed. In such a scenario, a VP shunt may be performed following an endoscopic septostomy through the septum pellucidum to establish CSF outflow from the entrapped ventricle (Fig. 20.2a, b). In multi-loculated hydrocephalus,

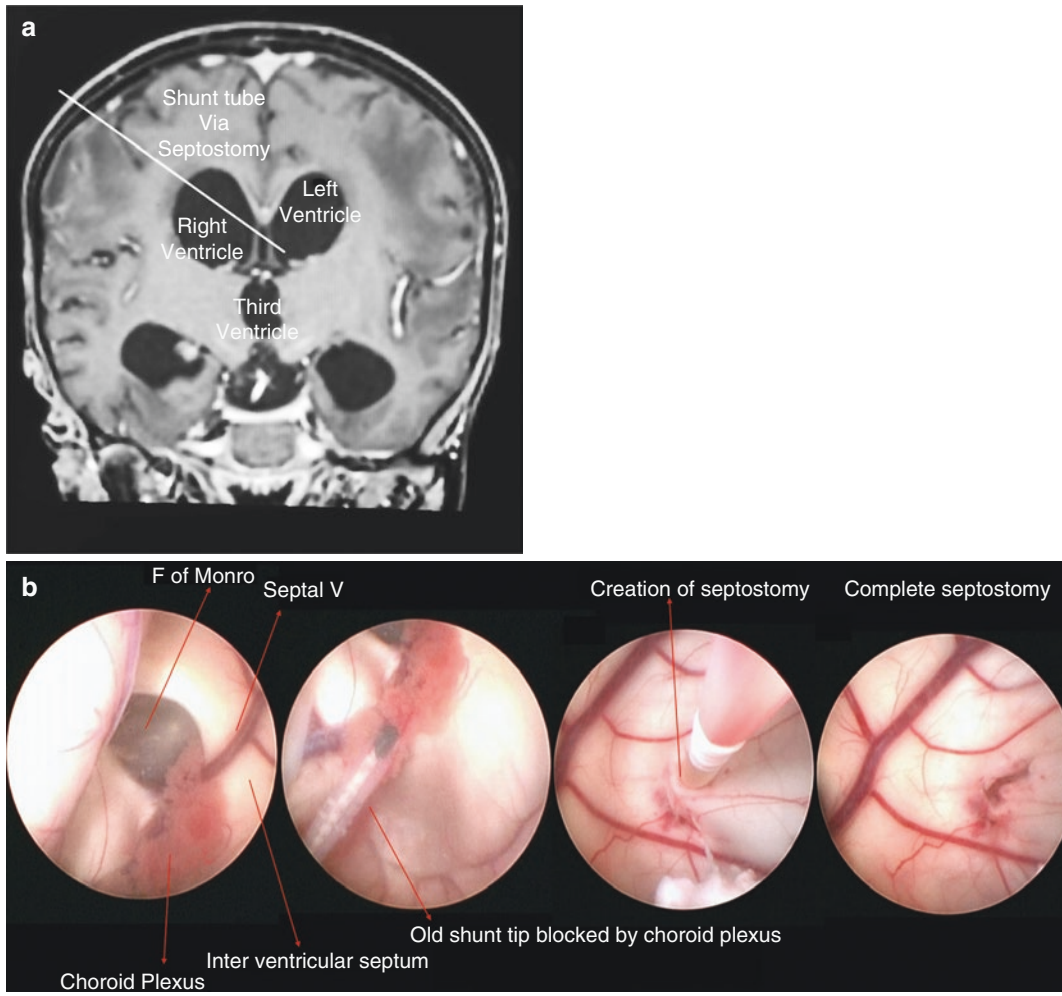

Fig. 20.2 (**a**) MRI image with shunt trajectory for endoscopic septostomy. (**b**) Endoscopic view of septostomy procedure in a patient with a failed ventriculoperitoneal shunt (shunt tube in situ)

the ventriculoscope is used to break the septations within the ventricle to create a single cavity that can be drained with a single shunt. The technique has been utilized for creating alternative channels of CSF outflow. This can be further augmented by performing foraminoplasty, aqueductoplasty, or aqueductal stenting. In patients having intraventricular tumors and concomitant hydrocephalus, neuroendoscopy may be used to treat hydrocephalus and performing a tumor biopsy in the same setting. Colloid cysts can be resected using neuroendoscopy. Certain tumors, especially craniopharyngiomas with a prominent cystic component, may be drained using a neuroendoscope, and a catheter connected to an Ommaya reservoir may be placed into the cyst cavity for repeated aspirations. This modality provides temporary relief to increased ICP before a definitive procedure in patients with acute hydrocephalus or those with poor general conditions who need preoperative optimization.

The traditional treatment of intracranial arachnoid cysts is to fenestrate the cysts into the subarachnoid space. The neuroendoscope introduced through a burr hole may be used for performing the fenestration while avoiding a craniotomy. Arachnoid cysts in the suprasellar and quadrigeminal cisterns may lead to hydrocephalus. In this setting, the cyst may be fenestrated into the ventricle.

20.2.1.2 Surgical Technique of ETV

The commonest indication for ETV is aqueductal stenosis. In this procedure, the patient is positioned supine, with the head placed on a head ring to minimize movement. In cases where image guidance is needed, the head may be fixed in a Mayfield head clamp. A burr hole is created at *Kocher's point*, which is located 2–3 cm lateral to the midline and just anterior to the coronal suture (Fig. 20.3). The dura is opened in a cruciate fashion after adequate hemostasis of

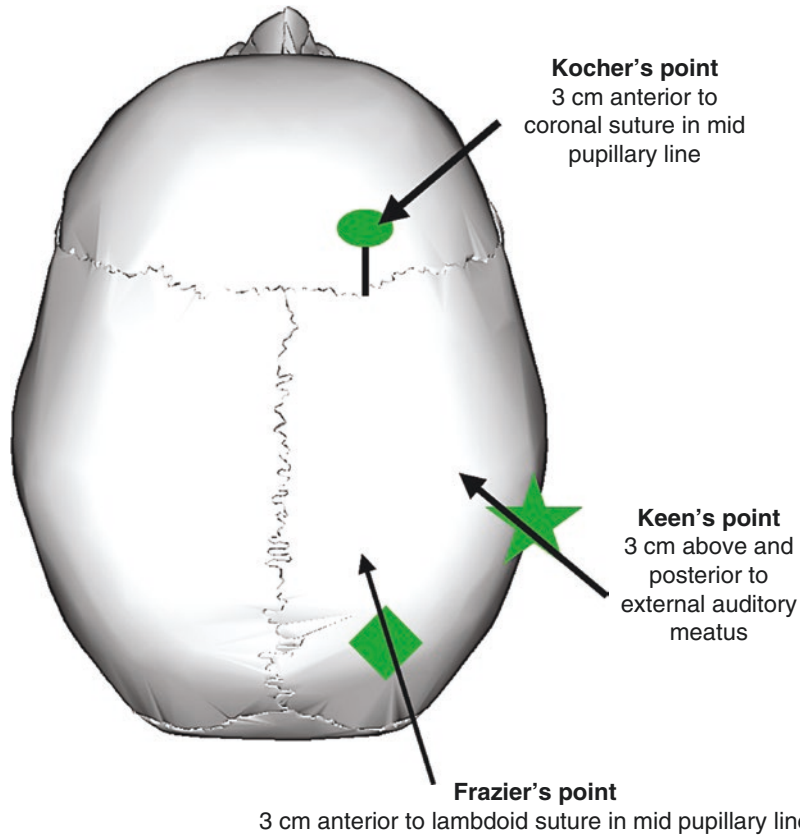

Fig. 20.3 Surface markings of endoscopic approach to ventricles

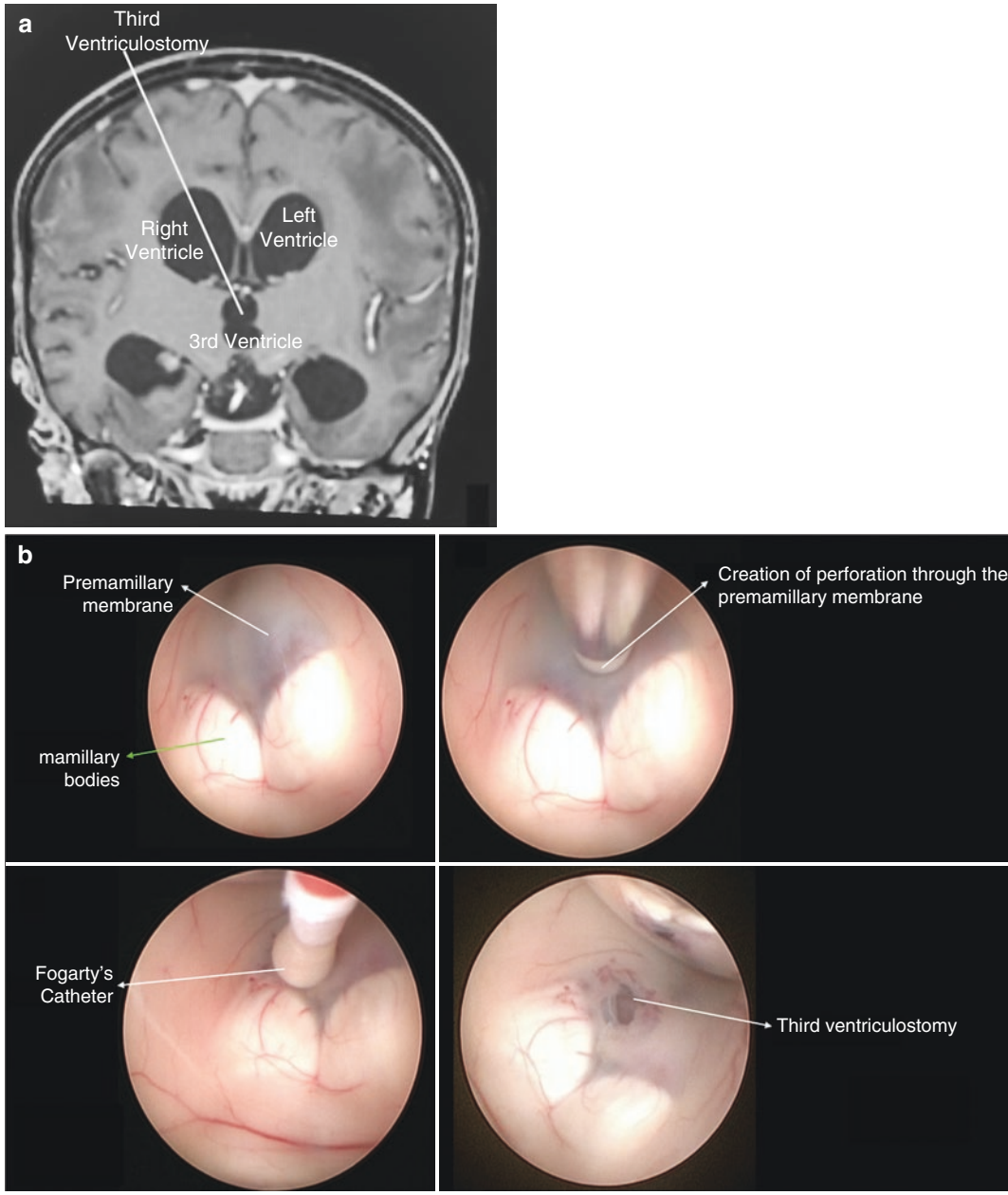

Fig. 20.4 (**a**) MRI image with endoscopic trajectory of the third ventricle. (**b**) Endoscopic view of steps of third ventriculostomy procedure

bleeding bone and soft tissue. After the ventricle is cannulated with the obturator mounted in the endoscope sheath, CSF is collected for biochemical analysis. The obturator is removed, and the ventriculoscope is introduced through the sheath, after which it is locked in place. The choroid plexus, thalamostriate vein, and septal vein are identified, and the scope is followed toward the foramen of Monro to enter into the third ventricle (Fig. 20.4a, b). The pre-mamillary membrane and the dorsum sellae are identified, and the membrane is perforated close to the dorsum sel-

lae. This perforation must be carried all the way into the prepontine cistern. All arachnoid bands and membranes are released; the perforation is further dilated using a Fogarty catheter. Adequate precautions should be taken to protect the basilar artery and its bifurcation along with the perforators that arise from the bifurcation in order to avoid neurological deterioration due to a stroke. The ventricle is irrigated to remove blood present inside, and the scope is slowly removed, visualizing the cortical track for the presence of bleeding.

20.2.1.3 Advantages of ETV

ETV restores CSF circulation by diverting its flow into the prepontine cistern. This avoids the use of a permanent shunt system for the CSF diversion. The shunt systems are associated with long-term risks of hardware infection, obstruction, over-drainage of CSF, migration into other body cavities, and extrusion through the skin. The success rate of ETV in the treatment of hydrocephalus depends on its etiology; greater success is seen in older patients and obstructive hydrocephalus due to tumors, whereas premature and newborn children, children with myelomeningocele and post-infective hydrocephalus are poor candidates for this procedure.

20.2.1.4 Disadvantages of ETV

Despite ETV being a common procedure, the costs of the equipment are very high. However, a comparative study suggested ETV as a cost-effective procedure compared to VP shunt insertion [32]. There are other disadvantages such as lack of widespread availability of endoscopes, minimal space available for the procedure, hand fatigue for the neurosurgeon holding the scopes for a prolonged time period, difficulty in controlling major vascular injury, and compromised visualization owing to the presence of blood and other tissues [33]. Procedural failure may occur if performed in patients without proper indications such as in normal pressure hydrocephalus, neonates, hydrocephalus due to subarachnoid hemorrhage, meningitis, and post-shunt ETV [34]. The procedure may fail if the stoma is not wide enough or the stoma re-occludes due to inflammation, bleeding, tumor growth, etc. Despite the procedure, the symptoms of raised ICP may not resolve if coexisting defect in CSF absorption occurs. The success of ETV in pediatric patients can be predicted by using Endoscopic Third Ventriculostomy Success Score (ETVSS), based on patients' age, etiology of hydrocephalus, and previous history of the shunt [35].

20.2.1.5 Anesthetic Challenges for ETV

The anesthetic concerns may include the concerns associated with anesthesia for the pediatric age group, emaciated children due to poor dietary intake, chronically raised ICP and enlarged head circumference, the presence of congenital anomalies, and electrolyte abnormalities due to frequent vomiting [36]. The intraoperative concerns may include difficulty positioning the child, anticipated difficult intubation, and increased sensitivity to anesthetic agents, opioids, and neuromuscular blocking agents. Preoperative fasting status may be inadequate due to the emergency nature of the surgery and delayed gastric emptying caused by raised ICP. A rapid sequence or modified rapid sequence induction may be planned for induction of anesthesia.

ASA standard monitors (ECG, pulse oximetry, blood pressure, temperature, $EtCO_2$, and urine output) are recommended for the procedure. Despite the term MIN, neuroendoscopy may last for a prolonged period. It may be associated with severe blood loss or hemodynamic fluctuations. An invasive arterial line may help to monitor beat-to-beat hemodynamic monitoring. It may also help early detection of cerebral ischemia due to an increase in ICP during the procedure and a fall in Cerebral perfusion Pressure (CPP) below threshold even before the onset of acute symptoms of raised ICP like bradycardia [15]. Additional monitoring may include transduction of endoscopic opening or CSF pressure (it represents ICP), depth of anesthesia monitoring, and blood biochemistry.

Short-acting anesthetic agents are preferred to facilitate early emergence as the procedure is usually short. Mild hyperventilation ($PaCO_2$ 32–35 mmHg) may help the control of ICP as well as ease the passage of the endoscope. The use of nitrous oxide is controversial and

is better avoided in the presence of raised ICP, risks of intraoperative hemodynamic fluctuations and cerebral ischemia due to irrigating fluids, reduced CPP, and occurrence of tension pneumocephalus postoperatively [15]. Patients are extubated at the end of surgery unless the recovery is delayed, which requires further evaluation.

20.2.1.6 Choice of Irrigating Fluid

The choice of fluid, its temperature, and the irrigation rate through the endoscope can impact the procedure. Irrigation of the ventricular cavity with warm saline or Ringer's lactate (RL), for the clear endoscopic view as well as washout of the blood along its track, is usually carried out. Irrigating with warm fluids (37 °C) is necessary to prevent fogging of the scope and control bleeding. Cold fluids may cause stimulation of the hypothalamus and bradycardia or arrhythmias [37]. The speed of irrigation must be restricted to 10 mL/min, and the time of blockage of the outflow of endoscope must be restricted to 4 min or less to prevent a dangerous increase in ICP and fall in CPP. Various experimental studies evaluated CSF composition changes following irrigation with 0.9% normal saline (NS), RL, and artificial CSF. An infusion of 500 mL of NS causes a decrease in CSF pH by 0.2, cerebral temperature by 0.6 °C, and a decrease in other constituents of CSF like carbon dioxide, calcium, potassium, and bicarbonate; sodium and chloride levels may increase. These changes can cause postoperative vomiting, agitation, and transient neurological deficits, which are unrelated to the surgical procedure [38]. The use of large volumes of NS for irrigation may cause hyperchloremic metabolic acidosis. Moreover, NS has been implicated with cellular injury and apoptosis in experimental animals [39, 45]. Artificial CSF lacks widespread availability and is expensive. RL has better optical clarity. Both artificial CSF and RL are considered better choices for irrigation than NS [40, 46]. During prolonged surgeries, serum electrolyte measurement may help identify the electrolyte changes due to irrigating fluids, especially in neonates and infants.

20.2.1.7 Hemodynamic and Biochemical Changes During ETV

The passage of scope can lead to various intraoperative hemodynamic changes. There may be varied reasons for such changes: (a) the third ventricle is close to important structures such as the thalamus, hypothalamus, choroid plexus, basilar artery, and mamillary bodies; (b) rapid or cold infusion of irrigating fluids through the scope can lead to a sudden increase in the ICP and decreased in CPP; and (c) an ongoing blood loss due to vascular injury may be difficult to quantify, at times.

Significant intraoperative hemodynamic disturbances may include tachyarrhythmias, severe bradycardia, hypertension, and even cardiac arrest [41]. Tachycardia is the most frequent occurrence during ETV, which may be associated with hypertension [42]. Tachycardia is seen during high-speed irrigation and manipulation of scope in the ventricular cavity, while bradycardia usually occurs during the fenestration of the third ventricular floor [42, 43]. The hemodynamic changes may forewarn the anesthesiologist of changes in ICP and CPP. A rise in blood pressure occurs initially when CPP falls; the classical Cushing's response of bradycardia with hypertension is more common with an acute and sudden rise in ICP. An atypical Cushing's response consisting of tachycardia and hypertension may be observed when the ICP increased and CPP falls below 15 mmHg [44, 45]. In some cases, asystole has been reported possibly due to direct hypothalamic stimulation, whereas tachycardia is presumed to be due to impaired CPP [42].

Electrolyte disturbances may also be seen during the perioperative period in children undergoing ETV. Postoperative hypokalemia has been observed when NS is used as the irrigating fluid [46], whereas hyperkalemia has been observed following the use of RL [47]. Other causes of electrolyte disturbances include hypothalamic injury-causing diabetes insipidus (DI) or syndrome of inappropriate antidiuretic hormone (SIADH) secretion. A prospective study suggested using NS as maintenance fluid and warm

RL as irrigation fluid to prevent electrolyte disturbances [48].

20.2.1.8 Pressure Inside the Neuroendoscope (PIN) and CPP

Although neuroendoscopy is considered minimally invasive, a sudden severe increase in pressure in the neuroendoscope (sometimes above systemic pressure) can occur without any major systemic hemodynamics changes. This may be related to low intracranial compliance and infusion of a rapidly large volume of irrigating fluid without release or blockade of egress of irrigating fluids due to the snug fitting of the endoscope in small children. Intermittent draining of the irrigating fluid is necessary. The increase in pressure inside the neuroendoscope (PIN) has been associated with severe fall in cerebral perfusion as monitored by transcranial Doppler [49]. A high PIN may be associated with delayed recovery. Although a safe value of PIN is not established, it is important to measure it routinely, avoiding any sudden increase [50]. A cutoff pressure of PIN more than 30 mmHg has been associated with increased complications [15].

20.2.1.9 Complications During the ETV

Neuroendoscopic procedures are considered safe, with low rates of complication (8%) [51]. Hypothermia and hemodynamic changes (45%) are more common during the intraoperative period [42]. There may be intraoperative bleeding (3.7%), which could be significant, especially following an injury to the basilar artery. Often, the bleeding occurs due to venous injury, usually thalamostriate vein, and can be treated with continuous irrigation of fluids [52]. Blood loss may be significant for a small child, and at times, it is difficult to estimate the loss and the irrigation fluids. The hemodynamic changes alone may not always be useful to guide therapy; the point of care hemoglobin estimation may be helpful. VAE is a rare occurrence but should be considered for unexplained hemodynamic changes [53]. Care must be taken to protect the eyes and face with adequate padding, which are vulnerable to inadvertent injuries. Neurological injury to the surrounding structures like the thalamus, hypothalamus, and midbrain and cranial nerve dysfunction may occur (0.24%) and present with postoperative hematoma or infarct on computed tomographic (CT) scan or with clinical signs. The majority of these neurological injuries are transient and resolve spontaneously. Excessive drainage of CSF is another issue in these patients, which may present with acute subdural hemorrhage in the immediate postoperative period or delayed chronic subdural collections [54]. Reverse herniation of the brain has been reported due to sudden excessive release of CSF [55]. Pneumocephalus may occur and may manifest with seizure and delayed awakening at the end of the surgery [56]. Delayed awakening may also be seen due to intraoperative hypothermia, neurological injury, failed ETV, excessive PIN (>30 mmHg), cerebral edema, prolonged low CPP, increased sensitivity to anesthetic agents especially in infants, seizures, etc. Postoperative complications are infrequent following neuroendoscopy and may include fever, electrolyte imbalances (commonly hypokalemia), nausea and vomiting, CSF leaks, failure of ETV, hydrocephalus, infections, and postoperative cognitive decline due to damage to surrounding limbic structures like mamillary bodies, fornix, etc.

20.2.2 Image-Guided Neurosurgery

The need to integrate imaging modalities like CT scan and MRI to the operation theater during neurosurgery is well-recognized. The integration will help in the precise location of the pathological lesion, identify the vital structures nearby, reach the especially deep-seated lesion, minimize the damage to the surrounding normal brain, and help complete resection of the lesion [57]. Improvement in the image guidance system has helped in the conduct of minimally invasive spine surgeries (MISs). The procedure consists of preoperative imaging (CT/MRI) of the patient to diagnose and plan the surgery. The image sequences are loaded in the computerized image guidance system, which provides

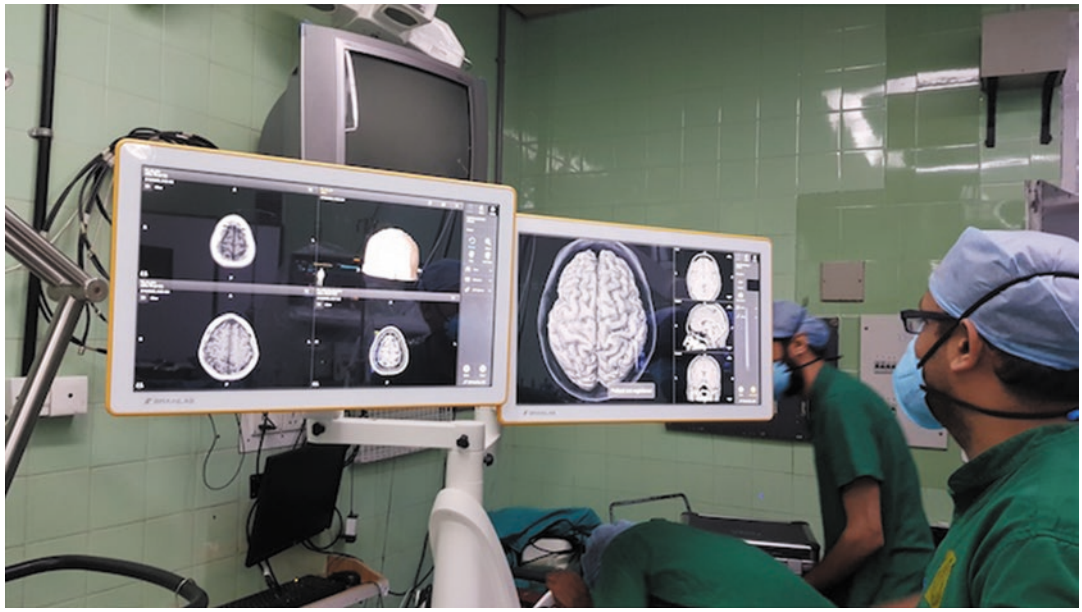

Fig. 20.5 Image guidance system in neuro-operation theater

the three-dimensional view of the brain and lesion (Fig. 20.5). In the operating room (OR), after induction of anesthesia, the head frame is fixed. In cooperative children, frame fixation and procedure may be done in an awake state (e.g., deep brain stimulation surgery). The newer generation system uses a frameless guidance system. The trajectory is marked, the accurate depth of the lesion is measured, and complete resection is made using the system.

There is always a constrained OR space and difficulty accessing the airway of the child during the procedure. Hence, monitoring lines, ventilators, and other tubings should have an adequate length and need to be secured well [58]. The choice of anesthetic drugs depends on the neurosurgical procedure. If intraoperative neuromonitoring is planned, drugs affecting these modalities are avoided or administered at lesser doses. For example, the use of benzodiazepines, high MAC of inhalation agents during ECoG recording, and muscle relaxants during MEP recording should be avoided. Since the precision of trajectory is important, the use of osmotic diuretics, hyperventilation that causes brain shift, and hemodynamic fluctuations, especially hypertension, may increase bleeding in the operative site and should be avoided. Possible complications related to airway compromise and hemodynamic instabilities may arise in the intraoperative MRI environment, which need appropriate attention. All the connections and patient ventilatory circuit must be rechecked before intraoperative scanning of the patient. Long length of ventilatory tubings and IV infusion lines are required to maintain anesthesia in such circumstances. It may cause delayed delivery of anesthetics to the patient. The MRI environment requires a low temperature to optimize the magnetic field; children may develop hypothermia and, hence, delayed recovery from anesthesia.

20.2.3 Minimally Invasive Robotic Neurosurgery

Robotic neurosurgery is one of the recent modalities increasingly being utilized for various pathologies. Despite the high costs involved, robotic surgeries are considered advantageous with accuracy, lesser blood loss, and faster recovery. Robotic neurosurgery also uses an advanced

Fig. 20.6 Ongoing epilepsy surgery with robotic neurosurgery guidance system (ROSA® Zimmer Biomet)

image guidance system; its use has been extended to the pediatric population. Robotic stereotactic assistance, also known as ROSA® (Zimmer Biomet/Medtech Surgical Montpellier, France) is a commonly used robotic device for neurosurgery. It consists of a robotic arm for precise positioning of the instruments in a predetermined trajectory using the preoperative MRI or CT scan of the patient toward the area of interest. Once the trajectory is registered, the robotic arm is aligned to the trajectory by the computer of the ROSA®, which allows the neurosurgeon to pass the instruments to the location of the lesion (Fig. 20.6). The robotic-assisted techniques in children are employed for neurosurgical procedures involving minimally invasive and stereotactic procedures like pediatric epilepsy, endoscopic transnasal surgeries, tumor removal, and ventriculostomy procedures. ROSA® is used in depth electrode placement unilaterally or bilaterally in stereoelectroencephalography (SEEG), deep brain stimulation (DBS), and laser thermal ablation of lesion or biopsy. The procedure has been seen to be associated with minimal complication rates [23, 59]. Robotic neurosurgery is usually carried out in supine position; it requires the fixation of headframes and strict immobility. Although a popular frameless system is also being used, the use of frame was found to increase surgery accuracy [60]. Anesthetic concerns are similar to image guidance surgery, like space constraints, longer duration of surgeries, and difficult patient access. General endotracheal anesthesia is commonly employed as the procedure may be prolonged, which requires strict immobility to prevent patient injury due to docking of robotic instruments [25]. In the event of a major intraoperative complication, emergency undocking of the robotic device must be readily available to resuscitate the child [25].

20.2.4 Specific Neurosurgical Procedures

20.2.4.1 Craniosynostosis

Craniosynostosis is characterized by the premature fusion of one or more cranial sutures resulting in the prevention of growth of the underlying brain. This results in abnormal expansion of other unaffected bones leading to the abnormal shape of the head and face. Uncorrected children may present with the features of raised ICP, craniofacial abnormalities, and neurocognitive defects. Surgical correction is the mainstay of treatment to prevent complications and cosmetic benefits. It is fraught with severe morbidity as well as major anesthetic challenges [61]. Advances in neuroendoscopy have led to radical changes in the management from open surgery to endoscopic treatment, reducing morbidity and mortality [13]. Surgical methods (Table 20.2) currently employed include open craniotomies, endoscopic strip craniectomy, or spring-assisted corrections (Fig. 20.7). The MIN approach is associated with reduced intraoperative blood loss, transfusion requirement, procedure times, and length of hospital stay compared to open surgery for craniosynostosis. However, there are no differences in the incidence of other complications related to the airway, pulmonary system, and hemodynamics, coagulopathy, and infections between the two groups [14, 62]. The incidence of VAE is also lower in endoscopic surgery compared to open repair [63].

20.2.4.2 Endoscopic Strip Craniectomy

Under general anesthesia, children are usually positioned prone on a head holder. If the metopic suture is involved, for combined surgery, a supine position is also utilized. Two linear incisions of 2 cm each are placed over the anterior fontanel and lambdoid suture, and a subcutaneous tunnel is created between the two incisions. Endoscope is inserted, and dissection is carried out, separating the fused subgaleal bone from the underlying dura mater. Scissors are used to cut strips of fused bone (8–10 cm length, 3–4 mm width) which is removed via the anterior fontanelle incision. Sometimes wedge is taken from the parietal bone to improve the space for the growth of the brain. The bony margins are refashioned appropriately, and hemostasis is achieved. Following surgery, appropriately customized helmets are placed, which should be worn 21 hours a day until 12 months or more to allow remodeling of the calvarium and brain growth [64].

Table 20.2 Showing different approaches to craniosynostosis management

Surgery	Indications	Timing	Advantages	Disadvantages
Open suturectomy with or without craniofacial advancement	Multiple suture involvement Syndromic children Associated facial and orbital correction Late presentation	After 6 months of age as the bone will become thicker and hold the screws	Multiple sutures can be handled	Prolonged surgery and hospital and ICU stay Venous air embolism Severe blood loss and transfusion needs Increased complications
Endoscopic strip craniectomy	Usually involving single or two sutures	Less than 6 months (usually done at 2–3 months	Early correction Less morbidity	Need for re surgeries Wearing of helmet mold for up to 12–24 months. Cannot be used in all types Redo-surgery
Endoscopic spring-assisted cranioplasty	Usually single but multiple sutures can be treated	Early surgery (<6 months)	Good outcome	Redo-surgery Cannot be used in all types

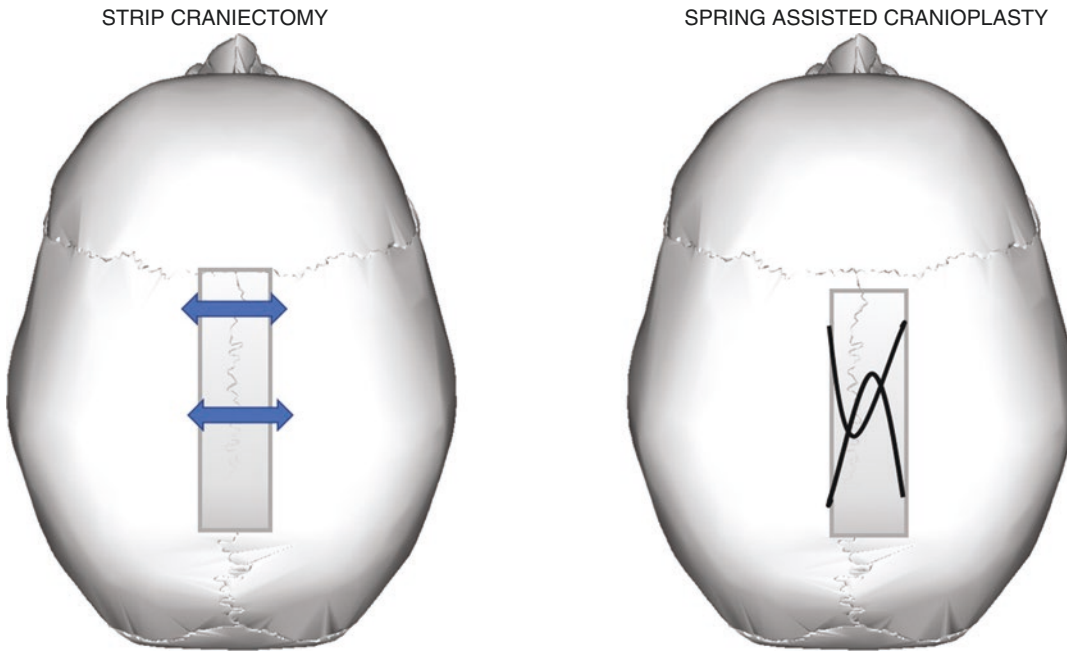

Fig. 20.7 Diagrammatic representation of endoscopic strip craniectomy and spring-assisted cranioplasty of the sagittal suture

20.2.4.3 Spring-Assisted Cranioplasty

After a strip of bone is removed for spring-assisted cranioplasty, two springs are kept between the bony edges, one anteriorly and another posteriorly, and sutured to maintain the bony separation. The force applied by the spring usually ranges between 6 and 11 N [65]. The surgery may also be performed for multiple cranial sutures. The advantage of the spring-assisted cranioplasty over endoscopic strip craniectomy is that it avoids the use of a postoperative helmet. Comparison between the two procedures has shown similar outcomes [63].

20.2.4.4 Intraoperative Monitoring and Anesthetic Management

Important anesthetic concerns in children undergoing endoscopic surgery for craniosynostosis are very young age (<6 months), associated anomalies, and blood loss. Endoscopic procedures have significantly reduced surgical time and blood loss. Children with preoperative anemia may be treated with erythropoietin. Two wide-bore IV cannula are inserted. The single suture surgeries usually do not require invasive arterial and central venous lines, but they may be warranted in complex surgeries [63]. General endotracheal anesthesia is routinely employed with muscle paralysis. Syndromic children with facial dysmorphism may cause difficult mask ventilation and intubation. Significant manipulation of the head and neck is anticipated during the surgery; hence, the risk of migration and kinking of the endotracheal tube (ETT) must be kept in mind, and reinforced ETT is preferred. Precordial Doppler is used in some centers for the detection of VAE [66]. These children may have increased ICP. Hence, a subdural ICP monitor may help assess the efficacy of the repair; ICP decreases following cranioplasty [67]. The use of antifibrinolytics (e.g., tranexamic acid) reduces blood loss and is found to be safe [68, 69]. During endoscopic surgery, the mean blood loss has been found to be 13 mL/kg; less than 4% children require blood transfusion. Severe bleeding may also occur due to injury to the sagittal sinus or other vessels [70].

Unlike open suturectomy, postoperative complications are minimal with neuroendoscopy, and the children require a shorter stay in the intensive

care unit (ICU) and may be discharged within 48 h. ICU care may be required in children with comorbidities, syndromic association, and preoperative elevated ICP and those undergoing cranial vault reconstruction. Others can be managed in the postoperative wards [71]. Postoperative pain is managed with a combination of scalp block and systemic analgesics; usually, acetaminophen or morphine either alone or in combination is used [71].

20.2.4.5 Sellar and Suprasellar Tumors

In children, 18% of the CNS tumors are present in the sellar and suprasellar region, the common ones being craniopharyngioma (58%), pituitary adenoma (30%), germinoma (5.5%), and tumors related to the optic pathway [72]. In contrast to predominant nonfunctioning tumors seen in adults, functioning tumors (80–97%) are frequently associated with pediatric patients. Adrenocorticotropin (ACTH)-secreting adenoma is the most common one, which occurs during early childhood, followed by prolactin (PRL)- and growth hormone (GH)-secreting adenomas. Excision by endoscopic transnasal approach has been carried out in children for sellar-suprasellar tumors despite being considered anatomically challenging than in adults [73]. The use of smaller scopes (2.7 mm and 3 mm in diameter) and "binostril four hand" approach allows the surgeon to decompress the tumors successfully, despite the fact that the pneumatization of sphenoid sinus in children is partial [17]. This approach better preserves visual function with gross total resection as compared to the transcranial approach.

20.2.4.6 Anesthetic Management

Anesthetic challenges are related to endocrine abnormalities, airway issues, and postoperative pain. A thorough preoperative assessment should be carried out. The endocrine functions, especially hypothyroidism and hypoadrenalism, may affect the perioperative outcomes, which need to be optimized during the preoperative period. Children with craniopharyngioma and functioning pituitary adenoma may be obese with a history of obstructive sleep apnea (OSA) with a large tongue and a difficult airway. After anesthetic induction, videolaryngoscopic intubation may be useful for endotracheal intubation with a flexometallic tube. Oropharyngeal packing is normally carried out to prevent the trickling of blood inside the stomach and lower airway. The gauze-soaked epinephrine may be packed, or a relatively higher dose of epinephrine is injected intranasally, leading to hypertension and arrhythmias. Care should be taken to limit the dose of epinephrine; the anesthesiologist should be watchful for the occurrence of hemodynamic disturbances. It is important to provide a bloodless operating field during transnasal dissection, which can be achieved by avoiding precipitating factors like a lighter plane of anesthesia, hypercarbia, and hypertension. Induced hypotension with moderate blood pressure reduction using a higher concentration of inhalational anesthetic agents, dexmedetomidine, or vasodilators is employed if troublesome bleeding precludes the surgical access. Normocarbia for resection of the infra-diaphragmatic part of the tumor and mild hypercarbia to facilitate the suprasellar part may be ensured during the intraoperative period. Besides routine monitoring, visual evoked potential (VEP) may be useful for assessing the integrity of the optic pathway [74]. There may be intraoperative complications in the forms of hemodynamic fluctuation and arrhythmia. Bleeding may be severe following injury to the cavernous sinus or carotid artery located adjacent to the surgical site. Other complications include hyperglycemia, diabetes insipidus (DI), and electrolyte disturbances. These children tend to have an increased sensitivity to opioids and benzodiazepines and are prone to postoperative respiratory complications. The postoperative period may be associated with complications such as pain, DI, CSF leaks, epistaxis, endocrine dysfunctions, meningitis, and loss of vision that requires aggressive management [75].

20.2.4.7 Minimally Invasive Epilepsy Surgery

The use of MIN in epileptic children is increasingly being carried out. A low incidence of permanent neurological deficits, shorter hospital

stays, and better outcomes have been observed with MIN techniques involving resection of focal cortical dysplasia, corpus callosotomy, hemispherotomy, and excision/lesioning of hypothalamic hamartoma [76, 77]. In some children with epilepsy, a preoperative surface EEG may be inconclusive and require bilateral intracranial electrode insertion (strips for surface or needle for depth placement). The electrodes are placed through a burr hole, or it may include stereotaxy- or endoscope-assisted depth electrode placement. These procedures require a still child and are carried out under general anesthesia. Depth electrode placement may be required in multiple areas of the brain in some children. The child may be operated in a semi-sitting position; hence, appropriate precautions must be taken for the prevention of position related complications. The anesthetic concerns include the occurrence of perioperative seizures, drug interactions involving antiepileptic and anesthetic drugs, adverse effects of antiepileptic medications such as anemia, coagulation abnormalities, and thrombocytopenia due to bone marrow suppression. Intraoperative blood loss, delayed awakening, and convulsions may add to the perioperative concerns. The children may have to undergo another surgery to remove the intracranial electrodes placed and excise the localized epileptic focus.

20.2.4.8 Movement Disorders

MIN is used in the pediatric population to treat movement disorders like tremor, dystonia, and chorea, athetosis, hemiballismus, etc. These children usually present with involuntary and sustained muscle contractions, causing abnormal twisting and posturing; if left untreated, they may lead to permanent disabilities. Hence, early DBS surgery involving stimulation of globus pallidus internus (Gpi) nuclei is performed. DBS plays an established role in providing durable symptomatic relief and improving life quality with minimal morbidity [78]. In contrast to adults, where the procedure is done in an awake state along with neurological testing, children are psychologically unprepared and usually require general anesthesia (GA). Moreover, dystonia is the most common indication for DBS in children that presents with severe involuntary movements; these patients require GA with muscle relaxation. These procedures may be complicated by the occurrence of intraoperative seizures, bleeding, and neurological deficits. Anesthetic care should focus on intraoperative microelectrode recording (MER), autonomic dysfunction, and various drug interactions [79]. Propofol inhibits the firing of Gpi, reduces dystonia, and may interfere with monitoring [80]. Dexmedetomidine has been used for MER [81] with satisfactory results. Vasoactive medications like epinephrine and ephedrine may cause severe hemodynamic disturbances in children on L-dopa and selegiline, which need to be avoided [82].

As the DBS procedure requires preoperative planning MRI for location of neuclei, the child may require anesthesia to undergo the procedure. Adolescents and cooperative children can be managed with monitored anesthesia care like in adults.

20.2.5 Minimally Invasive Spine (MIS) Surgery

The major drawback of open spine surgery is the need for large incisions, damage to paraspinal muscles and ligaments due to dissection and retraction, and thermal injury by use of cautery. This may lead to muscle weakness, instability, severe pain, pulmonary dysfunction, and scar formation in the postoperative period. Complications like prolonged surgery, severe blood loss, wound infections, neurological deficits, and redo surgeries are common (36%) [83]. Various methods are used to reduce such complications and enhance recovery by applying minimally invasive spine surgery (MIS) and modified anesthesia protocols [84–86]. The use of MIS has also been associated with reduced pain and the need for analgesics.

20.2.5.1 Indications for MIS

MIS in pediatric patients has evolved for both decompression and instrumentation. It has been utilized for lumbar, thoracic, and cervical spine; both anterior and posterior approaches have been described in relation to it. Various spinal patholo-

gies where MIS is used include spinal trauma, neoplasms, infections, and developmental disorders. Degenerative spine disease and intervertebral disc prolapses are commonly seen in adults and are relatively rare in children. Spinal deformities are another broad group affecting the children, including scoliosis, kyphosis, and lordosis of varying degrees [27]. The most common and challenging pediatric problem is scoliosis. In severe cases, if Cobb's angle is more than 45°, in a growing child, or in those with progressive disease, surgery is warranted [87]. The surgical approaches include posterior fusion surgery, anterior fusion, vertebral body wedge osteotomies, and stapling.

20.2.5.2 Surgical Approach

MIS was performed initially using a tubular retraction system where the surgeon used a microscope through the tube retractor to visualize the structures of interest. Newer developments include an endoscopic tube and extensible retractor system, which allows the endoscopic surgery (Fig. 20.8). In this technique, a 1.5 cm incision is made in the paramedian position, and a needle is first inserted through the incision to reach the junction of the pedicle and traverse the process of the respective vertebrae. Serial dilators are threaded over the needle with the advantage of minimal muscle damage by this technique. After dilatation, the desired size of the tube is inserted to reach the pedicle. Bony decompression and soft tissue release can be done through this tube via either microscopic or endoscopic approach, and finally, the spine is stabilized by interbody fusion using pins, nails, and/or rods.

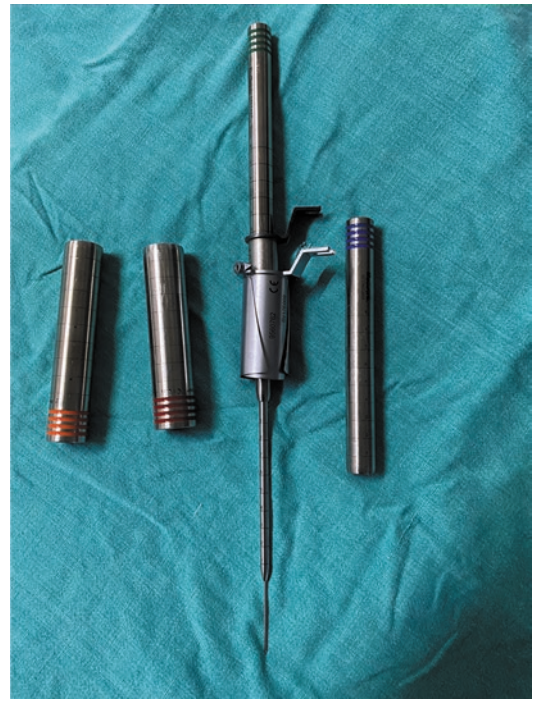

Fig. 20.8 Endoscopic tubular spine assembly with scope holder, guidewire, serial dilator for paraspinal muscle splitting

20.2.5.3 Anesthetic Management

The salient anesthetic management of MIS in children is similar to open spine surgeries. Patients with congenital anomalies may have coexisting cardiopulmonary and neuromuscular problems and recurrent surgeries; hence, a thorough preoperative evaluation and planning should be done. Careful positioning during anesthetic induction and surgery is important as structural deformities can lead to difficulty in positioning with possible neurological injuries [88]. Anesthetic plan to facilitate intraoperative neuromonitoring monitoring (IONM) may be required [89]; factors affecting evoked potentials such as anemia, hypotension, and hypothermia should be taken care of [90]. Adequate spinal cord perfusion is important to prevent neurological damage, and, hence, induced hypotension is discouraged during MIS and is contraindicated in children with preexisting neurological deficits [88]. Children may be taking analgesics for pain control in the preoperative period and may suffer from severe perioperative pain. Multimodal analgesia in the form of acetaminophen, morphine, gabapentin, and continuous epidural local anesthetic injection may have to be administered.

MIS for posterior cervical spine pathology is done either in the prone or sitting position. Sitting position helps in reducing intraoperative blood

loss. However, it can be associated with a lot of complications that require appropriate attention. Neurovascular injuries may occur during instrumentation, fixation with wires and screws, and may result in dural tear, CSF leaks, nerve injuries, and vascular injuries (e.g., vertebral artery injury). At the thoracic level, MIS may lead to injury to the inferior vena cava, thoracic aorta, and viscera. Various postoperative complications like cardiopulmonary, visual loss, and airway edema may occur similar to that during the open surgeries [88], which anesthesiologists should know [91].

20.2.5.4 Video-Assisted Thoracoscopic Surgery (VATS)

For anterior decompression of vertebral body, instrumentation intervertebral discectomy, and soft tissue release, especially kyphoscoliosis in the thoracolumbar spine, open thoracotomy or thoracoscopy is used. The use of video-assisted thoracoscopic surgery (VATS) has reduced the morbidity associated with thoracotomy by ensuring the preservation of postoperative pulmonary functions, relieved pain, enhanced recovery, and reduced hospital stay [92].

20.2.5.5 Indications for VATS

VATS is indicated in children undergoing spine surgery for the prolapsed thoracic disc, decompression of vertebral osteomyelitis decompression, corpectomy, thoracic vertebral fracture, and anterior spinal release. VATS is also indicated for the fusion of vertebral body fusion with or without spinal instrumentation in case of scoliosis or kyphosis. For children undergoing scoliosis correction, the body weight should be more than 30 kg and Cobb angle less than 80°, with a Lenke type 1 or King 3 classification.

20.2.5.6 Contraindications for VATS

Children with poor forced expiratory volume in 1 min (FEV1) (FEV1 <50% of expected), presence of emphysema/bulla, inability to achieve lung separation or one-lung ventilation, and body weight <20 kg should not undergo VATS.

20.2.5.7 Perioperative Management of VATS

Surgery is carried out via right thoracotomy in the lateral position (Table 20.3). In multilevel release cases, the procedure may be prolonged, and one-lung ventilation may be continued for a longer duration. If both anterior release and posterior fusion are planned, the double-lumen tube (DLT) should be changed to a single lumen while turning the child prone. Another alternative is to withdraw the DLT so that the bronchial lumen is in the trachea before turning the child prone. Still, there are the chances of tube malposition and injury to the bronchus. There is a

Table 20.3 Anesthetic concerns in VATS for spine surgery

Timings of procedure	Implications
Preoperative	Pulmonary function assessment and optimization (bronchodilators, chest physiotherapy, control of infections) Optimize hemoglobin levels (erythropoietin weekly injection) Evaluation of neuromuscular and cardiac functions
Intraoperative	Need for one lung ventilation using double lumen tube or bronchial blockers Control of bleeding Optimize hemodynamics Blood conservation methods (autologous donation, antifibrinolytics, cell salvage) Coagulation testing and management. (point of care testing) Intraoperative neuromonitoring Prevent hypothermia Management of hypoxemia during OLV (increasing FiO_2, application of PEEP to dependent lung and if needed CPAP to non-dependent lung)
Postoperative concerns	Watch for postoperative complications, including atelectasis, Horner's syndrome, intercostal neuralgia, and pneumothorax Assess: functioning of chest tube and monitor pulmonary functions Analgesia (patient-controlled analgesic epidural/paravertebral continuous infusion) Early mobilization and prevention of infections

risk of injury to the major vascular structures. Hence, adequate venous access and an arterial line for beat-to-beat monitoring of hemodynamics should be in place.

20.2.5.8 Vertebroplasty and Kyphoplasty

Pathological fractures of the vertebral body can occur in children and adolescents due to lytic lesions such as giant cell tumor, bone cysts, hemangioblastoma, and eosinophilic granuloma [93]. Patients usually present with localized pain and deformity; the diagnosis is confirmed by radiology. Bony decompression of the tumor with stabilization of the body is associated with longer operating time, severe blood loss, and increased morbidity. Alternatively, percutaneous procedures like vertebroplasty and/or kyphoplasty are available, where bone cement is injected into the vertebra body for stabilization in patients who cannot undergo major surgery or do not wish to undergo an open procedure. It minimizes major surgery complications and is normally carried out in a radiology suite as a daycare procedure [28]. The procedure is carried out in prone position. While in adolescents it can be carried out under MAC or sedation, uncooperative small children will need GA to undergo such a procedure. Short-acting anesthetics are administered during the procedure to facilitate rapid recovery. Due to the lytic nature of lesions, adequate padding and positioning are essential. Systemic embolization of bone cement has been reported as a complication and needs vigilance [94]. Monitoring oxygen saturation and end-tidal carbon dioxide may help identify hypoxia due to sedation, positioning, or pulmonary embolism.

20.3 Conclusion

Minimally invasive neurosurgery (MIN) is one of the most rapidly evolving techniques in the neurosurgical armamentarium of pediatric patients with the primary aim of improving the outcome and reducing complications. With advancements in imaging techniques, biomedical engineering, hardware and software, and robots, the indications will likely continue to expand in the future. The upcoming developments may include the use of micro-robots to minimize the space and to reach deeper brain structures, continuous-wave near-infrared spectroscopy (CW-NIRS) to differentiate gray and white matter based on blood flow and metabolism, 3D models of the brain with lesion using 3D printing techniques, preoperative surgical planning also known as "operation before operation" to reduce intraoperative complications, laser interstitial thermal therapy (LITT) for ablation of malignant lesions, focused ultrasound for epilepsy and movement disorders, etc. It is anticipated that more medically complex patients may undergo MIN in the future due to its benefits; the anesthetic management would be likely to be even more challenging in difficult environments. Hence it is important for the anesthesiologists to understand the needs of these advanced surgical procedures, to keep up to the challenges, and to develop and modify the anesthetic and monitoring techniques suitably to achieve the benefits of minimally invasive procedures, namely, rapid recovery, reduced morbidity, hospital stay, improved outcomes, and financial savings.

Conflict of Interest Nil.

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21 Anesthetic Concerns During Surgical Excision of Intracranial Arteriovenous Malformations

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Key Points

- AVMs are the abnormal tangle of vasculature consisting of the feeding artery, draining vein, and central nidus.
- These grow in size with age, and low-flow AVMs are turned to high-flow and high-pressure AVMs as the age progresses, leading to the dilation of arteries and arterialization of veins.
- Most of the AVMs are asymptomatic in the pediatric age group, but various presentations include intracerebral hemorrhage, seizures, mass effects, ischemia, and congestive heart failure.
- Anesthetic management of AVMs follows the general principles of neuroanesthesia, including maintenance of adequate cerebral perfusion pressure, prevention of increase in intracranial pressure, and prevention and management of serious perioperative complications such as intracranial bleeding and normal perfusion pressure breakthrough (NPPB).
- The unique feature of anesthetic management for stereotactic radiosurgery is the requirement of anesthesia at multiple different locations including transport.

21.1 Introduction

Arteriovenous malformations (AVMs) are defined as an abnormal collection of dysplastic blood vessels wherein the arterial blood flows directly into the draining veins without any intervening neural parenchyma or capillary beds. These are usually congenital lesions with a lifelong risk of hemorrhage of about 2–4% per year [1]. These lesions tend to enlarge with age and may progress from low-flow AVMs at birth to medium- or high-flow and high-pressure AVMs in adulthood [2]. Grossly, it appears as a "tangle" of vessels with a well-circumscribed center called nidus (Fig. 21.1). Intracranial AVMs are classified as parenchymal and dural depending upon the location of AVMs. Intracranial AVMs in pediatric patients might present with congestive heart failure (CHF) in neonates, seizures or hemorrhage, and varying degree of ischemic symptoms. Anesthetic management in this group of patients is quite challenging as surgical interventions are associated with massive blood loss. The pediatric population has a low cardiopulmonary reserve and poorly tolerates such losses. This chapter describes the anesthetic management of

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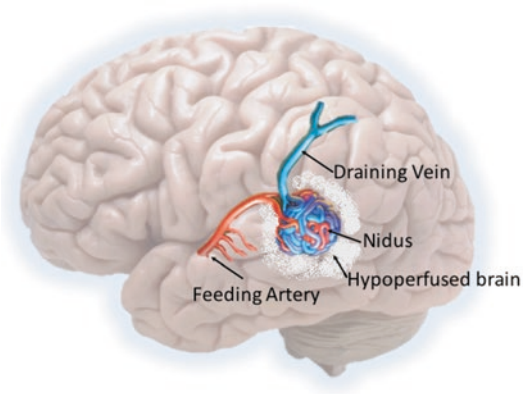

Fig. 21.1 Structure of arteriovenous malformation consists of feeding artery, nidus, and draining vain. The faded area surrounding the AVM is the hypoperfused brain

patients with intracranial AVMs posted for various interventions.

21.2 Epidemiology

The exact incidence of AVMs is unknown, but a large autopsy study estimates it to be approximately 1.4–4.3% [3, 4]. AVMs constitute about 2% of all the strokes [5, 6] and 38% of all intracerebral hemorrhages (ICHs) in the age group of 15 and 45 years [7]. The prevalence of AVMs may be slightly higher in Asian populations with an equal or slight male preponderance [8–12]. AVMs are categorized as sporadic or syndromic in origin. The sporadic AVMs have a global prevalence of 0.04–0.52% [13, 14]. In children, 3–20% of AVMs are sporadic. Intracranial AVMs are located at the supratentorial site in the majority of the cases (70–97%), followed by infratentorial (3–30%) or deeper brain structures (5–18%) [15].

21.3 Etiopathogenesis

The etiology for the formation of AVM is not very clear. The molecular studies have demonstrated the upregulation and downregulation of various homeobox genes, such as Hox D3 and B3 [16, 17]. Various congenital diseases have also been associated with a higher incidence of AVMs, such as Osler-Weber-Rendu syndrome, hereditary hemorrhagic telangiectasia, and Wyburn-Mason syndrome. Children with hereditary hemorrhagic telangiectasia (HHT) present with multiple familial AVMs [18]. Syndromic AVMs occur in approximately 2% of cases.

AVMs are usually believed to occur before the embryo is 44 mm in length. Till that time, the adult-type arterial wall structure was not formed. De novo formation may also occur rarely [19]. AVMs are composed of feeding arteries, draining veins, and an intervening dysplastic vascular "nidus," which is a tangle of abnormal vessels, which shunts the blood from the arterial to the venous system (Fig. 21.1). The absence of a capillary bed in the nidus results in the formation of low-resistance flow across the AV connections, which are devoid of gas exchange [20]. That consequence in high-flow circuitry leads to the dilation of arteries and arterialization of veins [20]. In long-standing cases, high flow leads to aneurysm formation in arteries and rupture of veins. Finally, the whole of the venous system of the brain and skull gets involved.

Shunting of blood through AVMs leads to arterial hypotension along the path of the shunt and venous hypertension in the downstream [21, 22]. There are the normal brain regions surrounding the AVMs in which cerebral perfusion pressure (CPP) is below the range of normal autoregulation (Fig. 21.1). Despite this, ischemic symptoms are usually absent due to adaptive microcirculatory changes secondary to hypoperfusion, such as a decrease in vascular resistance [23, 24]. Brain matter surrounding the AVM might show calcifications and hemosiderin-laden macrophages.

21.4 Criteria for Classification

AVMs are classified according to the Spetzler-Martin scale (SM) that includes the size of AVM, location in relation to the eloquent cortex, and type of venous drainage (Table 21.1) [25]. This grading system was established to estimate the

Table 21.1 Spetzler-Martin scale and Lawton grading scale for intracranial arteriovenous malformations (AVMs)

Spetzler-Martin scale		Lawton scale
Size of AVM (S)		**Age**
Small (<3 cm)	1	<20 years
Medium (3–6 cm)	2	20–40 years
Large (>6 cm)	3	>40 years
Location (E)		**Bleeding**
Non-eloquent site	0	Ruptured
Eloquent site*	1	Unruptured
Venous drainage (V)		**Compactness**
Superficial	0	Compact
Deep	1	Diffuse

*Sensorimotor, language, visual cortex, hypothalamus, thalamus, brain stem, cerebellar nuclei, or areas directly adjacent to these structures.

Table 21.2 Spetzler-Martin grading of arteriovenous malformations (AVMs)

Grade	Features
I	S1 E0 V0
II	S1 E0 V1 S1 E1 V0 S2 E0 V0
III	S1 E1 V1 S2 E0 V1 S2 E1 V0 S3 E0 V0
IV	S2 E1 V1 S3 E0 V1 S3 E1 V0
V	S3 E1 V1

S size of the AVM; *E* eloquent area location; *V* venous drainage of AVM

risk associated with surgery. The AVM is categorized as small (<3 cm), medium (3–6 cm), or large (>6 cm) and is scored accordingly (Table 21.2). The larger the AVM, the higher is the magnitude of adjacent healthy brain exposed during surgery. The operating time is longer in resecting the larger-size AVM, thus increasing the anesthesia-induced complications. The AVM size determines the amount of blood flow through the AVM, the number and size of feeding arteries, and the area of steal.

The eloquent brain regions are those regions that harbor the sensory, motor, or language functions, and removal of such areas leads to a significant neurological deficit. Such areas include sensorimotor, visual, language, hypothalamus, thalamus, internal capsule, brain stem, cerebellar peduncles, and deep cerebellar nuclei [25].

The deep venous drainage pattern includes the drainage in any one or all of the deep veins, including basal veins, precentral cerebellar veins, and internal cerebral veins. The venous drainage pattern determines the ease of surgical resection of an AVM. Deeper venous drainage complicates the AVM excision, even if it is small.

A supplementary grading scale was proposed in 2010 by Lawton et al. (Table 21.1) [26]. The authors included other parameters, such as patient's age, bleeding at presentation, and AVM compactness. These points were abbreviated as ABCs.

21.4.1 Applications of the Grading Scheme

The predictive value of this grading system was evaluated by analyzing 100 consecutive AVMs following resection [25]. The complications following surgery were categorized as minor deficits, major deficits, and mortality. In Grade-I AVMs, the complete surgical was possible with minor technical difficulties and was associated with a lesser risk of severe morbidity or mortality. In contrast, the Grade-V AVMs were difficult to resect and were associated with significantly higher surgical morbidity and mortality.

The sum of the SM and Lawton grading scale is known as the "supplemented Spetzler-Martin scale" (SM-Supp). This combination score has the highest predictive accuracy for AVM operability. The SM-Supp score of 6 has been validated as the boundary to operate an AVM [27].

21.5 Clinical Presentations

The pediatric age group (<20 years of age) constitutes approximately 15–33% of all patients with AVMs [6, 28, 29]. Most of the patients with AVMs are asymptomatic (18–20%), but if symptoms appear, then ICH is the most common symptom [30, 31]. This is followed by seizures in

Table 21.3 Clinical presentations of cerebral arteriovenous malformation (AVM)

• Asymptomatic
• Hemorrhage
• Seizures
• Mass effects due to: – Hematoma – Edema – Gradually expanding abnormal vascular structures such as venous aneurysms
• Ischemia
• Raised intracranial pressure (ICP)
• Metabolic depression (diaschisis)
• Hydrocephalus with macrocephaly[a]
• Congestive heart failure with cardiomegaly[a]
• The prominence of forehead veins (due to increased venous pressure)[a]

[a]Seen only in pediatric patients

8–25% [32, 33] and CHF in 18% of patients [34, 35]. Various presentations of AVMs are enumerated in Table 21.3 and described in detail vide infra.

- **Hemorrhage**

  The most common presentation of AVMs is spontaneous ICH, which is seen in about 50–79% of all patients with AVM [32, 33]. After initial hemorrhage, there may be a heightened risk of rebleeding during the first 12 months (2–4% per year) [1]. Depending upon the presence of risk factors [36, 37] (Table 21.4), the incidence of rebleeding varies from 1 to 30% in a year [37]. The various causes of bleeding include rupture of nidal vessels, associated aneurysmal bleed, or venous outflow obstruction. Patients with AVM may have an associated intracranial aneurysm, in 10% of cases. Aneurysmal rupture remains the most common cause of spontaneous subarachnoid hemorrhage (SAH) both in adults and in pediatric patients; AVM bleed is the second common cause of SAH in children [38]. This might explain the lower incidence of vasospasm after AVM bleed. The "buffering" effect of the fistula protects the AVMs from rupture due to variations in systemic blood pressure during the perioperative period [39].

- **Seizures**

  Almost 15–35% of AVMs present with seizure as the first symptom [6, 28, 40]. Seizures occur due to local effects of AVM, including cortical irritation, ischemia caused by the steal phenomenon, neuronal damage, associated hemorrhage, and gliosis [42]. In most cases, seizures are focal but can also be generalized. Various risk factors for seizure occurrence in these children are enumerated in Table 21.5 [43–45].

- **Headache**

  Headache is another common complaint in patients with AVM. It can occur even in the absence of AVM rupture [46]. The typical locations of headaches are hemicrania (either ipsilateral or contralateral) and the occipital region. The hypothesis for the origin of headache is the involvement of the meningeal artery that results in an increased blood supply of AVM [41].

- **Neurological Deficit**

  Isolated neurological deficit without underlying hemorrhage is seen in around 10% of the

Table 21.4 Risk factors for rebleeding

• Presentation with ICH (strong) (best-studied)
• Deep location and venous drainage (best-studied)
• Advanced age and small size AVMs (less robust)
• Related aneurysm (harder to define)
• High intranidal pressure (measured by direct puncture of feeding artery or during angiography)

ICH intracerebral hemorrhage; *AVM* arteriovenous malformation

Table 21.5 Predictors for the occurrence of seizures in patients with arteriovenous malformation (AVM)

Location
Supratentorial
Frontal or temporal location
Large (>6 cm), superficial, and cortical location
Angioarchitectural
Feeding by the middle cerebral artery
Cortical feeding artery
Absence of aneurysms
Presence of varices in the venous drainage
Association of a varix in the absence of an intranidal aneurysm

patients with AVM [10, 40, 46, 47]. The causes of neurological deficits might be recurrent hemorrhages, the local mass effect of the AVM, ischemia due to the steal phenomenon, and hydrocephalus. Factors predicting the increased risk of neurological deficits include the large size of AVM and low flow in the surrounding brain due to a large amount of shunting [48, 49]. However, a few studies refute this hypothesis as decreased blood is compensated by increased oxygen extraction [47, 50]. The clinical manifestations of the local mass effect vary as per the location of AVM. The involvement of eloquent areas may present as limb weakness, vision disturbances, hearing, and speech problems are also seen [51].

- **Congestive Heart Failure (CHF)**

  CHF presents in 18% of children less than two years of age [34, 35]. It can be the sole presenting symptom in neonates. AVMs constitute the low-resistance pathways for blood that rapidly returns to the heart. This rapid return of blood increases the venous inflow to the heart resulting in failure. The CHF causes a reduction in output to the other organ systems resulting in multi-organ failure that complicates the anesthetic management. Preoperative CHF thus carries a very poor prognosis [52].

21.6 Diagnosis

A variety of diagnostic modalities are used to diagnose AVMs. Non-contrast computed tomography (CT) has low sensitivity, but serpiginous isointense or slightly hyperintense vessels, intracerebral hemorrhage, mass effect, calcification, and hypodensities can be visualized. Post-contrast strong enhancement is seen on CT scan (Fig. 21.2) [53, 54]. Tightly packed "honeycomb" appearance of flow voids is a characteristic feature on T1- (Fig. 21.3a) and T2-weighted (Fig. 21.3b) sequences of magnetic resonance imaging (MRI). MRI is more sensitive and also provides information regarding the localization and topography of an AVM. Magnetic resonance angiography (MRA) is a non-invasive modal-

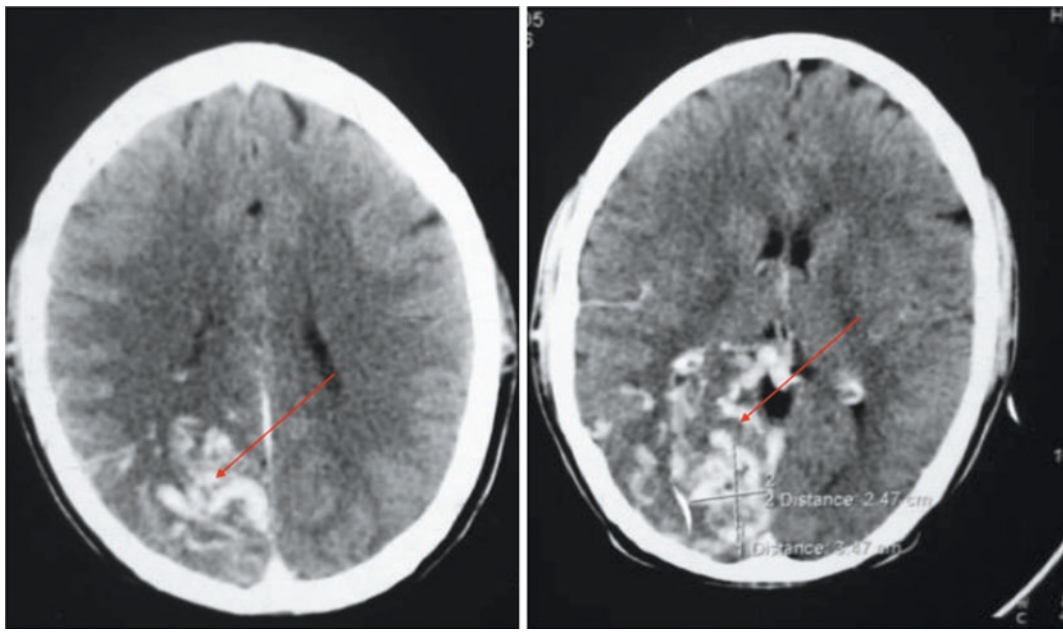

Fig. 21.2 Post-contrast computed tomography shows strongly enhancing serpiginous (arrow) arteriovenous malformation

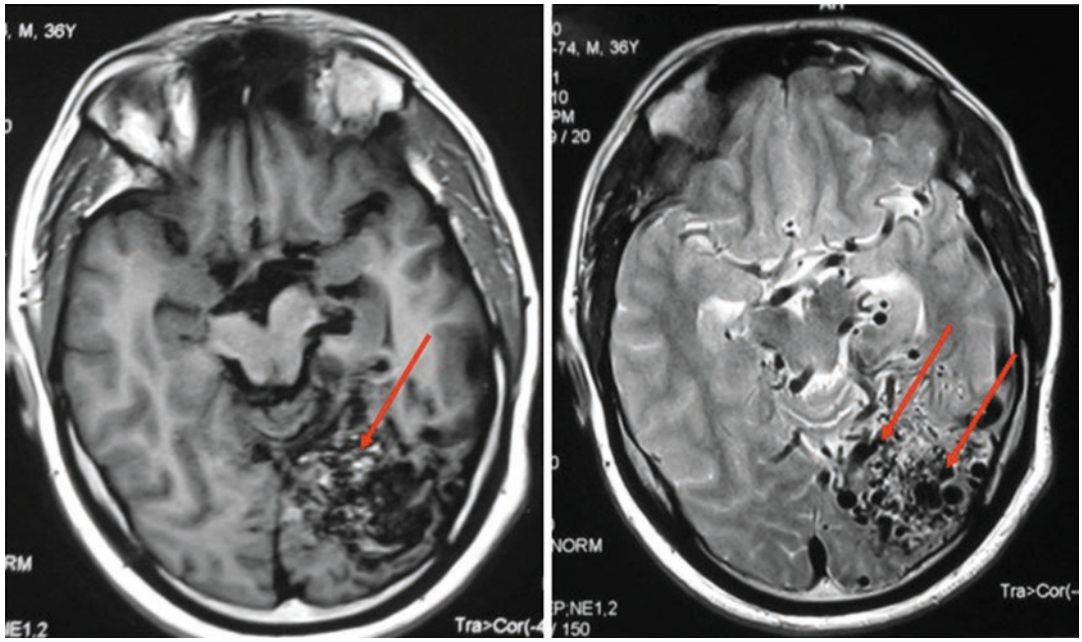

Fig. 21.3 Magnetic resonance imaging (T1, right side, and T2, left side-weighted image) of parieto-occipital region shows arteriovenous malformation with multiple flow voids created by high flow of blood (arrows)

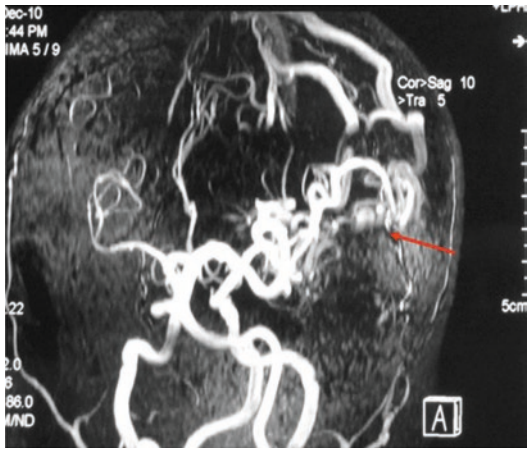

Fig. 21.4 Magnetic resonance angiography shows complete anatomical architecture of arteriovenous malformation (arrow)

ity and provides some data without detailed information about feeding arteries or venous anatomy (Fig. 21.4). Arteriography is considered the "gold standard" for providing detailed information such as the presence of intranidal or feeding artery aneurysms, venous drainage pattern, and nidus characterization (Fig. 21.5). Superselective angiography provides physiological and functional data. Currently, it is strongly recommended to get an MRI study and four-vessel angiography to delineate the complete anatomy of AVM [55].

21.7 Treatment of AVM

Various treatment modalities are available for children with AVMs. It ranges from conservative management with regular follow-ups to microsurgical resection, endovascular embolization, and stereotactic radiosurgery. These children with AVM may present to the anesthesiologists for diagnostic procedures, emergency decompressions, or definitive surgeries such as resection, coiling, or embolization.

21.8 Anesthetic Management

The anesthetic goals in children with AVMs follow the general goals of neuroanesthesia, including maintenance of adequate CPP, prevention of

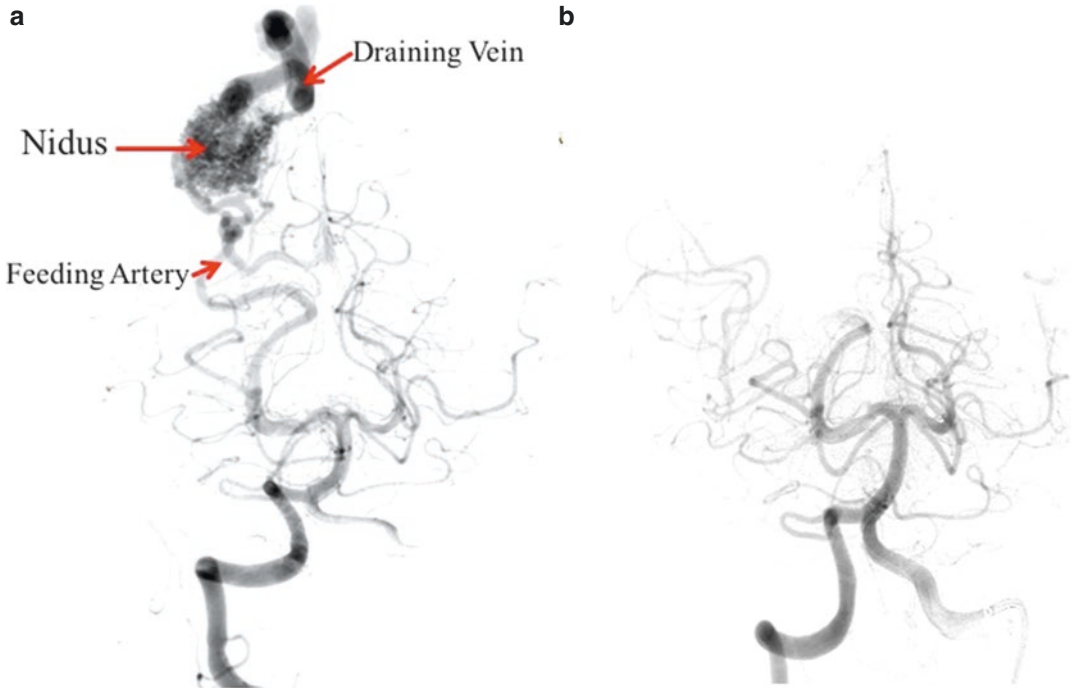

Fig. 21.5 Super selective angiography of a 12-year-old male child shows complete angioarchitecture of arteriovenous malformation; (**a**) (Left side) shows feeding artery, nidus, and draining vein angiography, (**b**) Angiography of following glue embolization shows complete occlusion

increase in intracranial pressure (ICP), and prevention and management of serious perioperative complications such as intracerebral bleeding and normal perfusion pressure breakthrough (NPPB). Anesthetic management may vary depending on the available treatment modality and has been discussed under five broad categories: (1) anesthetic management for diagnostic interventions (CT, MRI, and angiography), (2) for emergency craniotomy, (3) for microsurgical resection of AVM, (4) for endovascular embolization, and (5) for stereotactic radiosurgery.

21.8.1 Anesthetic Management for Diagnostic Interventions

Preoperative Preparation and Premedication: A thorough preoperative evaluation is needed, including the airway patency, respiratory compromise, cardiovascular instability, neurological status (including signs and symptoms of raised ICP), fasting state, and any therapeutic measures already undertaken [56]. A good rapport must be established with the child as well as the parents. Investigations including complete hemogram, serum electrolytes, coagulation profile, and liver function tests (if the child is under long-term anticonvulsant therapy) should be obtained.

Infants or younger children rarely require premedication, but it is indicated for older and uncooperative children. Midazolam, a short-acting benzodiazepine agent, is highly effective in allaying anxiety and producing amnesia [57]. Sedation should be given in the preoperative area under direct supervision. Narcotics are usually avoided in patients with raised ICP because of their inciting nausea and respiratory depression [58].

Specific Management: CT scan is usually done under appropriate sedation and monitoring if the child is cooperative and contrast is not required, but, in a few cases, GA may be needed. The choice of anesthetic agents depends on the signs and symptoms of the patients and availability and familiarity with sedative agents.

Various choices available are oral or intravenous (IV) midazolam, propofol, ketofol, triclofos, and dexmedetomidine [58]. If the procedure is prolonged, sedation can be supplemented with IV midazolam or an infusion of propofol and dexmedetomidine.

Angiography might be done as a semi-emergency or on an elective basis. The child might need either conscious sedation or GA. Among the IV agents, both thiopentone and propofol can be used safely, and rocuronium or succinylcholine can facilitate the intubation [59]. During angiography, radiopaque dye injections are frequently used to visualize the lesion that may contribute to the significant fluid loading in the small and compromised infant [60].

21.8.2 Anesthetic Management for Emergency Craniotomy

Intracranial hematomas following AVM rupture may lead to neurological dysfunction, coma, and even death due to a sudden massive rise in ICP. In such scenarios, emergency decompressive craniotomy is done with or without evacuation of the hematoma. Twenty percent of AVMs manifest in the pediatric age group, and 60–80% of these patients present with hemorrhage [61–64]. Acute onset of severe headache and rapid deterioration of consciousness with or without a focal neurologic deficit in a previously healthy child indicate "stroke" due to hemorrhage. If the hematoma is small and the child is conscious and alert, further evaluation is carried out in the form of angiography; and conservative management follows until definitive treatment for AVM is planned. Massive hematoma inside the brain causes an acute rise in ICP, leading to cerebral herniation syndromes [65].

Immediate management in such cases includes supportive care such as securing the airway (Glasgow coma scale score is less than 8), ventilation, and hemodynamic stabilization. Measures must be taken to decrease ICP, including the use of mannitol or hypertonic saline. In the cases of IVH, an external ventricular drain (EVD) may be considered. However, EVD placement acutely decreases the ventricular size and might aggravate intraparenchymal hemorrhage leading to brain herniation [65]. Hyperventilation should be instituted with care as it can decrease the perfusion of the normal brain. After initial stabilization urgent non-contrast CT (NCCT) scan should be done, and decompression should be planned as soon as possible. Delay in emergency decompression after massive intraparenchymal hematoma is associated with a high risk of early mortality [65]. In these children, emergency angiography increases the risk of rebleeding, neurological deterioration, and cardiovascular complications.

Definitive treatment in the form of emergency endovascular therapy is not recommended in these children as life-threatening brain compression caused by hematoma cannot be relieved by this modality of treatment. Hematoma can distort the angioarchitecture and alter the flow dynamics within the AVM, rendering selective catheterization difficult [65]. After initial stabilization and evacuation of the hematoma, delayed angiography is done, and the endovascular procedure can be planned for the residual lesion.

Complete surgical excision of the AVM at the time of hematoma evacuation is controversial. It will prevent the risk of rebleeding, but it increases the risk of torrential blood loss due to difficulty in controlling feeding pedicles which cannot be identified by prior neuroradiological evaluation [65]. There is a higher risk of permanent neurological deficit if the hematoma overlies the eloquent areas.

Anesthetic Goals: During anesthetic management of AVM surgery or emergency craniotomy, the goals are to maintain hemodynamic stability, CPP, control of ICP, management of fluid and blood losses, rapid and smooth emergence, and early neurological assessment. Major anesthetic concerns during these surgeries are massive blood loss and brain swelling after removal of hematoma. Hence, large-bore IV access should be secured, and invasive BP monitoring is recommended. An adequate amount of blood and blood products should be made available before the procedure.

Induction and Tracheal Intubation: The child posted for decompressive hemicraniectomy is usually intubated in the preoperative period in

the emergency department. Those who are not intubated before should undergo rapid-sequence induction and intubation. Both propofol and thiopentone are comparable in attenuating the cardiovascular and ICP changes to the manipulation of the airway [66]. Propofol is being increasingly used in neurosurgery in children. The benefits of its use include the ability to titrate the level of anesthesia rapidly, lack of accumulation despite prolonged anesthesia resulting in rapid recovery, easy maintenance in remote locations and during transport, antiemetic properties, and decreased OR pollution [67, 68]. Although ketamine raises ICP by increasing CBF and remains contraindicated in the poorly compliant brain, its favorable actions on the cardiovascular system make it beneficial in children presenting with CHF. Before tracheal intubation, IV lidocaine, an additional bolus of anesthetic agents, or shorter-acting opioids may be used to prevent or treat pressor reflexes. Mild hyperventilation using a bag and mask may be tried in children with increased ICP [34]. Nitrous oxide in oxygen with an inhalational agent appropriate to the patient's clinical condition is commonly used [56].

Vecuronium or atracurium may be used as muscle relaxants. Since these children are often on anticonvulsive therapy, increased dose requirement of narcotics and muscle relaxants must be kept in mind [69]. There is no single best anesthetic agent, and both inhalation and IV agents can be used safely in these children. Mild hypocapnia with arterial CO_2 <35 mmHg is considered to be useful in controlling the ICP [56]. The children with CHF are treated with digoxin, diuretics, dopamine, or other inotropic drugs; the drugs should be continued perioperatively.

Monitoring: Besides the standard American Society of Anesthesiologists (ASA) monitors, invasive BP should be monitored. It aids in continuous blood pressure monitoring, sampling for serial blood gases, hematocrit, electrolytes, and glucose levels. Central venous line insertion is controversial as smaller lumen and long length precludes its use for fluid resuscitation or aspiration of air during venous air embolism [54, 70].

If the hematoma is situated closer to the eloquent areas, neurophysiological monitoring such as somatosensory-evoked potential (SSEP), motor-evoked potentials (MEP), brain auditory-evoked potential (BAEP), visual-evoked potential (VEP), and electroencephalographic (EEG) monitoring may be considered. SSEP has been useful in recognizing cerebral ischemia, MEP is useful for the AVM near the motor tracts, and BAEP evaluates brainstem status in posterior fossa and AVMs [71–75]. If hyperventilation is instituted for brain edema in the postoperative period, jugular venous oximetry or cerebral tissue oxygenation should be monitored.

Fluid Balance and Blood Loss: Intravenous fluid administration governs the movement of water across the blood-brain barrier. Edema fluid in the brain can be reduced by using osmotic diuretics and fluid restriction. It should be aimed to achieve a balance between cerebral dehydration therapy and adequate circulatory volume to ensure adequate cerebral blood perfusion [56]. Normal saline is most widely used as a maintenance fluid in neurosurgeries because of its mild hyperosmolarity and ability to reduce brain edema [57]. There is no exact formula to calculate the maintenance fluid requirement; however, a formula to guide the volume has been suggested [76]. Hypotonic solutions should be avoided as maintenance fluid. The use of hydroxyethyl starch is controversial as it may cause coagulopathy or acute kidney injuries.

During a craniotomy, the intraoperative blood loss should be managed by rapidly optimizing the circulating blood volume, oxygen-carrying capacity, colloid osmotic pressure, hemostatic capability, and biochemical balance. Blood replacement should be started before reaching the maximum allowable blood loss as small-bore cannulas may not allow infusion matching the ongoing losses. Controlled hypotension is also advocated to minimize perioperative losses in selective cases [77]. Transfusion of stored blood can precipitate hyperkalemia in small children, and if combined hypocalcemia and hypothermia, it might cause cardiac arrhythmias [78].

Postoperative Care: Patients with massive hematoma usually have poor preoperative neurological status and invariably need postoperative mechanical ventilation. Close monitoring of any

further deterioration in neurological status should be monitored. Besides this, edema expansion after decompression should be masnaged with cerebral decongestants and controlled ventilation to avoid hypoxia and hypercapnia. Hemodynamics should be maintained within the normal range to maintain adequate perfusion pressure.

21.8.3 Anesthetic Management for Microsurgical Resection of AVM

General anesthesia goals, preoperative assessment, premedication, and monitoring are the same as those scheduled for investigational procedures or emergency craniotomy. The anesthetic concerns specific to microsurgical resection are highlighted here. In most cases, AVM resection is done electively. Hence, there is adequate time to evaluate and optimize patients with comorbidities.

Goals of Anesthesia: The primary anesthetic goal during AVM resection is to provide a relaxed brain to minimize retractor-induced brain ischemia [79]. Brain relaxation can be achieved by burst suppression using barbiturates, but it causes delayed awakening and does not found to the outcome. There are various pharmacological (e.g., decongestants, sedatives, or hypnotics) and non-pharmacological interventions (e.g., the position of the head, airway pressures, euthermia, euglycemia, and normal electrolytes) to provide a relaxed brain. Systemic hypotension reduces the cerebral perfusion pressure and acts synergistically with retractor pressure to cause cerebral ischemia.

The other goal is to prevent secondary brain insults with avoidance of hypotension, hyperthermia, hypoxia, hypercapnia, hyperglycemia, hyper-/hyponatremia, and hypo- or hypercapnia. It is recommended to maintain euvolemia, normotension, isotonicity, normoglycemia, and mild hypocapnia.

Anesthesia Technique: The choice of an anesthetic, narcotic, or muscle relaxant does not affect the outcome [80]. The goal of smooth induction with the maintenance of hemodynamics and rapid emergence must be followed in choosing the anesthetic agent. Even though raised ICP is not a problem in patients for elective surgery, these patients might have poor intracranial compliance. It is advisable to avoid anesthetics and vasoactive agents that can produce cerebral vasodilation, such as a high dosage of inhalational agents [57]. The incidence of AVM rupture is very low during induction and intubation, but 10% of these patients might have an associated aneurysm that can rupture with fluctuation in blood pressure [81]. If the AVMs lie near the eloquent areas, awake craniotomy with neurophysiological monitoring may be used in cooperative children to avoid postoperative neurological deficits.

Hemodynamic Control: Adequate precautions should be taken to deal with the excessive intraoperative bleeding as well as perioperative brain swelling. Controlled hypotension might be useful in a few patients with large AVMs and deep arterial supply. As small and deep-seated feeders are difficult to control, controlled hypotension might help achieve hemostasis [82]. If there is torrential bleeding, the surgeon might apply a temporary clip. In such scenarios, lowering the blood pressure might assist the surgeons in visualizing the bleeding vessel. The choice of agent to induce hypotension varies as per the patient's underlying medical conditions and the discretion of the treating anesthesiologist. In cases where massive blood loss is expected, rapid ventricular pacing can be used to provide controlled hypotension [83].

Emergence and Extubation: Blood pressure should approach near normal or slightly higher after bleeding is stopped to check whether hemostasis is complete or not. If the brain is relaxed and homeostasis is achieved, extubation should be planned as an awake patient is the best neurological monitor. Emergence hypertension should be prevented and treated as fast as possible to avoid brain swelling and tumor bed hematoma [60]. If awakening is delayed or new onset of neurological deficits appears, an urgent CT scan should be done to rule out brain edema and hemorrhage.

Children who had massive hemorrhage intraoperatively, longer duration of surgery, inadequate

hemostasis, and brain bulge after AVM resection should undergo elective mechanical ventilation in the postoperative period. Optimum sedation that keeps the child calm and allows neurological assessment should be given. Dexmedetomidine is currently gaining popularity in this field [84].

Postoperative Care: Postoperative CT scan should be performed to look for immediate complications, including hematoma formation and cerebral edema. An angiogram can also be planned once the child is stabilized to confirm complete resection of the AVM during the immediate postoperative period. Antibiotics, steroids, and seizure medications must be continued, and optimal analgesia is to be managed by using multimodal techniques such as scalp block, short-acting opioids, acetaminophen, etc.

Complications: The most common complication is the sudden occurrence of brain swelling after AVM resection, known as "hyperperfusion syndrome." There are two hypotheses proposed for brain swelling after AVM resection (Fig. 21.6). One hypothesis suggests that the chronic hypoperfusion of the normal brain surrounding the AVM causes maximum vasodilation in the blood vessels. These dilated vessels do not undergo constriction when the flow is restored after resection of AVM and leads to cerebral edema and hemorrhage even if perfusion pressure is normal [85]. This hypothesis is known as "normal perfusion pressure breakthrough" (NPPB), where cerebral hyperemia occurs due to increased flow through the dilated vessels, but perfusion pressure remains within the normal limits. According to this theory, cerebral edema and hemorrhage can be reduced by staged resection of feeders of AVM or by combining the procedure with endovascular procedures [15]. It is recommended to resect the AVM within a few days after embolizing the feeding artery to avoid the formation of collaterals. Immediate supportive care includes burst suppression using propofol or thiopentone, the use of cerebral decongestants, and controlled ventilation to prevent hypoxia and hypercapnia. Along with the supportive and resuscitative measures to decrease ICP, control of systemic blood pressure with shorter-acting antihypertensive agents, like esmolol or nicardipine, might reduce cerebral edema.

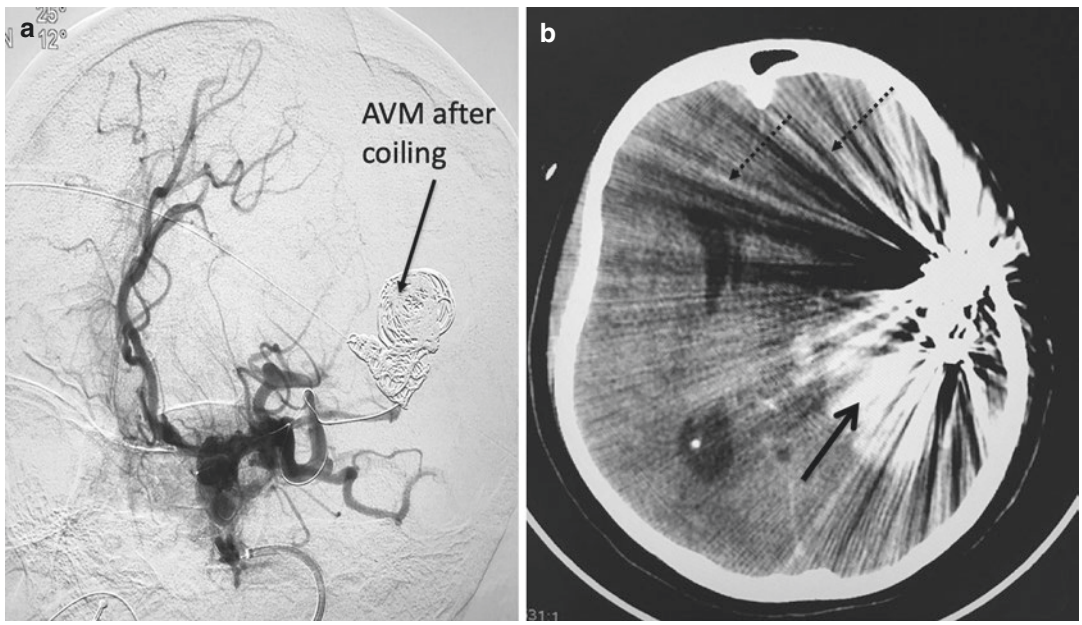

Fig. 21.6 Depicts the post-coiling hemorrhagic complication secondary to normal perfusion pressure breakthrough. (**a**) Digital subtraction angiography shows the coiling of arteriovenous malformation (coils indicated by arrow). (**b**) Non-contrast computed tomography scan showing intracranial hematoma formation post-coiling (thick arrow indicates hematoma; doted arrow indicates coil artifacts)

This hypothesis is challenged by a few pieces of evidence from observational studies. One study concludes that cerebral edema is a global phenomenon and is not restricted to the hypoperfused brain surrounding the AVM [7]. The other evidence states that there is no relationship between the degree of hypotension produced by shunt preoperatively and postoperative cerebral flow changes [7]. Literature also reports that autoregulation is shifted to the left but not impaired, and CO_2 reactivity is also preserved, suggesting that vessels are not paralyzed [86]. With these pieces of evidence, it appears that the NPPB is an exception rather than a rule for cerebral edema [79, 84].

There is an alternate hypothesis proposed known as "occlusive hyperemia." It occurs due to either arterial stagnation or venous occlusion before the ligation of the feeding artery [87–90]. Various mechanisms of arterial stagnation, include increased resistance to flow, endothelial abnormalities, and reflex vasoconstriction to normal or increased perfusion pressures. Venous occlusion might occur due to stenosis, agenesis, or major venous sinus occlusion and compression of AVM with hematoma. Controlled hypotension is deleterious if the mechanism of cerebral edema is venous occlusion. The evidence regarding one particular hypothesis is weak, and their impact on the management of AVM moderate. A few authors suggest that both these theories coexist and are termed "arteriocapillary-venous hypertensive syndrome" [91]. One more hypothesis proposes that cerebral edema is caused by the breach in the blood-brain barrier due to excessive protease activity and growth hormone abundance, as seen in the patients with ischemic stroke after the restoration of blood [92]. As there is a lack of strong evidence on optimum hemodynamics, tight control of blood pressure is recommended postoperatively.

A stroke might also occur after AVM resection due to accidental injury to the arteries of the normal brain or due to en passage arteries supplying both AVM and distal normal brain. It also presents unexpected brain swelling postoperatively. In this situation, blood pressure is augmented to increase the collateral circulation along with other measures to reduce cerebral edema. Steal phenomenon, as well as, NPPB can coexist in the same patient.

Intraoperative moderate to severe *hypothermia* might occur in the setting of massive hemorrhage and affect the coagulation cascade leading to a "lethal triad" of acidosis, hypothermia, and coagulopathy. Strict temperature monitoring is recommended. Mild hypothermia can protect the brain, but its effect on improving outcomes is not yet proven. Postoperative hyperthermia must be avoided, especially if intraoperative mild hypothermia is instituted.

21.8.4 Anesthetic Management for Endovascular Procedures

Embolization is indicated for large AVMs that are not amenable to surgical resection or radiosurgery. In such situations, the goal of embolization is to decrease the flow through AVM to decrease the symptoms or halt the progression. Other indications for this procedure include presurgical embolization, embolization before radiosurgery, and residual lesion after surgery may be required as a part of the multimodal approach. The advantages of presurgical embolization include lesser blood loss and shorter surgical time, obliteration of surgically inaccessible vessels, and theoretically staged reduction in the flow of nidus [82]. Embolization before radiosurgery has the advantage of reducing the size of AVM, thereby increasing the cure rate. It eliminates the predictors of hemorrhage during radiosurgery, such as intranidal aneurysms and venous aneurysms, and also reduces the symptoms of venous hypertension [82]. For small lesions, intravascular embolization can be used as a sole technique, but long-term follow-ups are required in such cases as there is a risk of recanalization [93].

Embolization is particularly useful in high-risk patients, e.g., patients with coagulopathy and CHF, as it reduces the size and complications of AVMs. The embolic materials available currently can be divided into solid and liquid agents. The former category includes polyvinyl alcohol particles, fibers, micro-coils, and micro balloons

[94–97], while liquid agents include cyanoacrylate monomers such as I-butyl cyanoacrylate and N-butyl cyanoacrylate (NBCA), ethylene vinyl alcohol polymers, and absolute alcohol [98–103]. The Food and Drug Administration has approved NBCA for intracranial AVMs.

General anesthesia with endotracheal intubation is usually required for AVM embolization in pediatric patients. Anesthesia goals are mostly similar to what has been discussed in the previous section, where a few additional concerns are mentioned here.

Besides neurological status, preoperative evaluation should also include a history of protamine and contrast allergy (including insulin use, fish allergy), coagulopathy, CCF, and recent steroid use. Past and present ischemic symptoms must be kept in mind while using controlled hypotension during embolization. There is no single choice of anesthetic agents. Both IV and inhalational agents can be used safely for induction and maintenance. Besides the routine monitors recommended by ASA, an arterial line must be secured following induction as there is a need for hemodynamic manipulation with vasoactive drugs. Microcatheter coaxial sheath can also be used to get arterial pressure. A pulse oximeter should preferably be placed on the lower limb cannulated with a femoral sheath to detect femoral artery occlusion during the procedure and postoperative compression for hemostasis. The patient should be catheterized as the osmotic effect of contrast agents induces diuresis.

Heparin should be titrated to keep the activated clotting time one and half times normal. During glue injection, blood pressure should be decreased to avoid glue migration to the systemic circulation. Hypotension decreases the flow through the AVM feeding artery and provides the time for the glue to occlude the AVM. Patients with prior history of ischemic symptoms can develop infarct during hypotension, especially if combined with hyperventilation. Sodium nitroprusside, being a cerebral vasodilator, is considered the best agent to induce hypotension [104]. Theoretically, it maintains CPP by its cerebral vasodilating action. In high-flow AVM, a cardiac standstill might be required during the glue injection [105]. Deliberate hypertension may be required in special situations such as cerebral ischemia secondary to arterial vasospasm or inadvertent occlusion of the major vessels due to glue displacement.

The incidence of hemorrhagic complications is 2–4% after the embolization of AVMs [23]. During hemorrhagic complications, heparin should be reversed, and blood pressure should be reduced. Efforts should be made to decrease blood pressure and ICP with various maneuvers. These include increasing the depth of anesthesia using propofol or thiopentone boluses, use of cerebral decongestants (mannitol and furosemide), transient hyperventilation, head-up position, and burr hole drainage of CSF in the intervention suite. Postoperatively, children might present with symptoms of cerebral edema and as seen after surgical resection. They should be observed in the ICU for at least 24 h. In severe cases, postoperative mechanical ventilation may be continued till ICP stabilizes or patients start improving.

21.8.5 Anesthetic Management for Stereotactic Radiosurgery

Stereotactic radiosurgery is a technique of irradiating the blood vessels of AVM that results in progressive luminal obliteration. These vessels finally undergo involution over time, and AVM volume is reduced [106]. The ionizing sources used for radiosurgery are photon beams using cobalt-60 gamma-ray or linear accelerator x-ray and proton or heavy ion particle beam. The technical steps of SR are shown in Fig. 21.7.

Radiosurgery is most useful in patients with small AVMs (size <3 cm and volume <10 cm^3), and AVMs located near the eloquent areas as radiations are focused and cause less damage to the surrounding brain [107–109]. Other indications include AVMs inaccessible to surgery or embolization and if coexisting medical diseases precludes the surgical resection.

The goals of radiosurgery are to control the symptoms like headache, seizures, minimizing the risk of hemorrhage, and obliteration of AVM

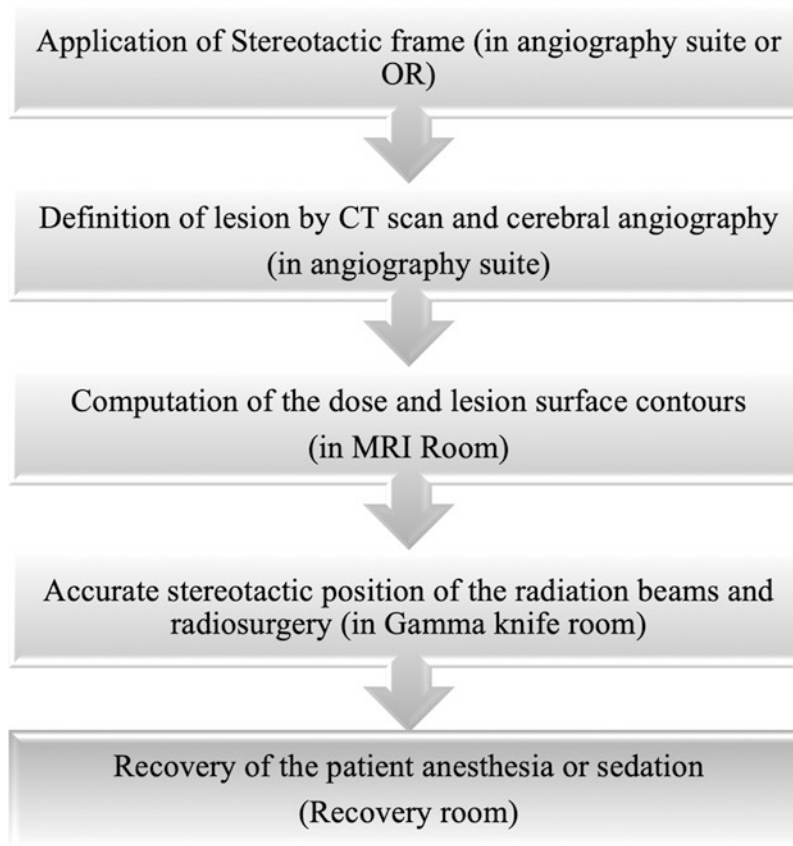

Fig. 21.7 The technical steps of stereotactic radiosurgery. Each step forward depicts the movement of the patient. *OR* operating room; *CT* computed tomography; *MRI* magnetic resonance imaging

[104, 107, 108]. There is almost complete occlusion of AVM in 80% of patients within 2–3 years [110]. The features of the anesthetic management and technique of SR are mentioned in Table 21.6.

- **Specific Concerns During Stereotactic Frame Placement**

  Application of the stereotactic frame usually requires general anesthesia with endotracheal intubation or laryngeal mask airway [111–113]. General anesthesia is usually indicated for reasons such as better control of hemodynamics and airway [61]. As pediatric patients are uncooperative for proper placement of frame, they usually require a deeper sedation depth if sedation is planned. Excessive sedation can compromise both the airway and hemodynamics and increase the ICP due to hypoxia and hypercapnia. The stereotactic

Table 21.6 Unique features of anesthetic management for stereotactic radiosurgery

• Anesthesia is required at multiple different locations, including transport
• Patients should be calm and cooperative for long hours
• Decreased access to the patient's airway and the patient for resuscitation
• Transport must be quick and safe at a different location
• Underlying pathophysiology and neurological deterioration can occur while transport
• Remote location, radiation hazards, contrast-induced reactions, and hemorrhage during catheterization of femoral artery
• Movements during stereotactic position and delivery of the radiation beams might result in treatment failure, skull fracture, and pin displacement leading to epidural or subdural hematoma
• Procedures might extend up to 10–12 h with continuous anesthesia in a single setting

frame overlies the nose and mouth, rendering the airway difficult to secure in case of an emergency. To overcome such problems, the lower arch of the frame can be placed so that the mouth is free (Fig. 21.8). Also, a mask with a shorter height and lesser dead space should be used to negotiate the smaller available space (Fig. 21.9). Besides this, the essential precaution is to carry the frame's wrench along with the patient to quickly remove the frame if there is an inadvertent airway compromise.

- **Concerns During Patient Transport**

  These patients need multiple means of transport. The first stereotactic frame is applied under sedation or GA, and then MRI is done, followed by transfer to the gamma knife center (Fig. 21.6). Appropriate precautions should be adopted during the transport of these children.

  The transport itinerary must be mapped in advance with knowledge of emergency exits. The availability of a sufficient transport workforce should be ensured. Transport routes must be checked prior to the barriers to ensure smooth transport. All portable transport monitors, including pulse oximetry, blood pressure and ECG, and infusion systems, must be charged and confirmed for battery backup. Emergency reintubation and ventilation equipment supplies must be available. Adequate depth of anesthesia should be maintained during the transport. Inhalational agents are not favored as the agent delivery as it is not possible during the transport. Usually, anesthesia is maintained with propofol infusions.

- **Concerns During Radiation Exposure**

  The patients are monitored through closed-circuit cameras in the console rooms. The room temperature of the gamma knife center is usually very low, and it becomes necessary to monitor and maintain the temperature of these patients for early awakening [111, 114]. To avoid bladder distention, catheterization should be considered. All pressure points should be adequately padded to avoid compression injuries [114]. Most of the patients with good preprocedural neurological status can be extubated after accessing the patient's neurological status. Delayed awakening is very common as most of these patients are extubated in the postoperative period [82]. AVM is associated with an increased risk of

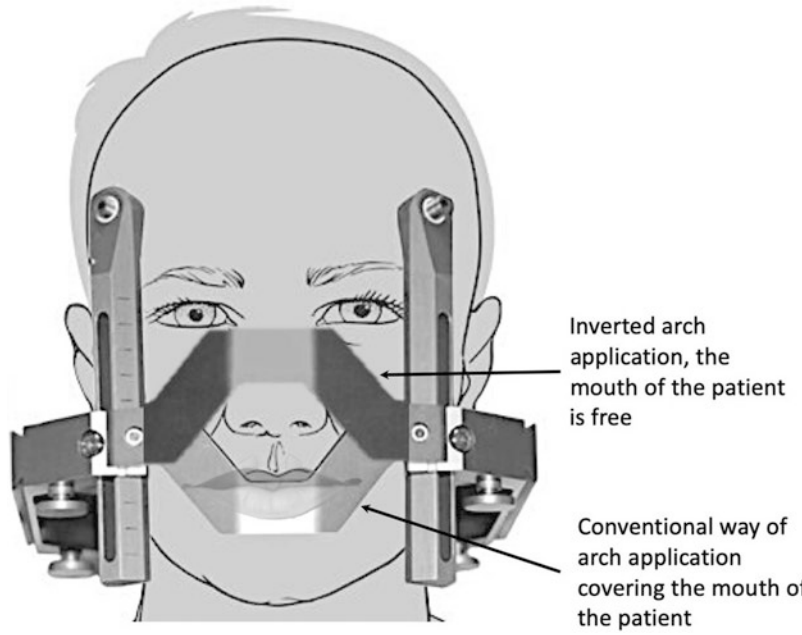

Fig. 21.8 Sketch of stereotactic radiosurgery frame applied on patient's face. Usual placement (with convexity of arch facing downward) covers the mouth and nose and makes it difficult to secure the airway if need arises. Rotating this bar by 180° (indicated by pink-colored and dotted image) uncovers the face and part of the nose making mask holding and intubation easier

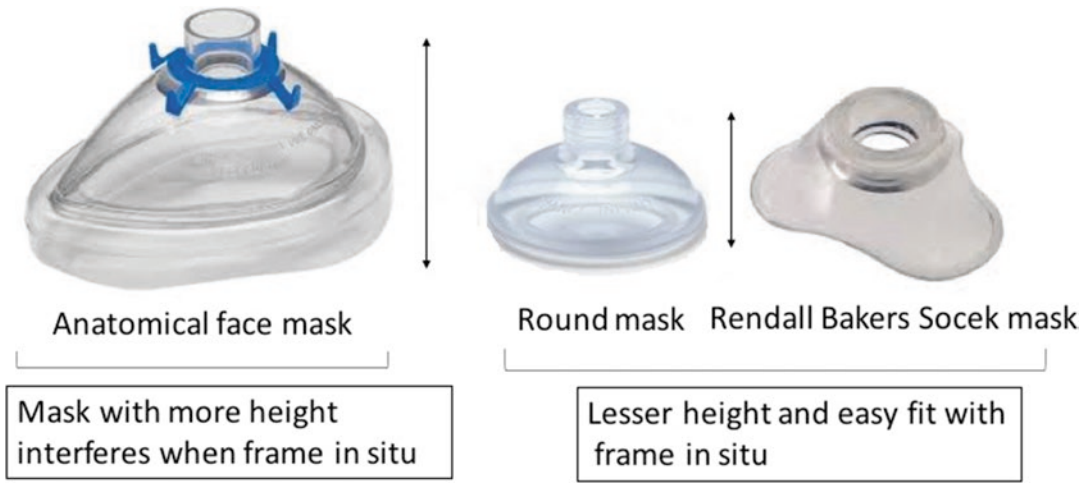

Fig. 21.9 Shows anatomical face mask (extreme left) having more height and larger dead space and is difficult to negotiate underneath the stereotactic frame. Other two masks (round, middle, and Rendell-Baker-Soucek mask, extreme right) carry shorter height and can be easily fitted underneath the frame

spontaneous deep vein thrombosis in children, and this risk is further increased due to prolonged immobility during anesthesia in stereotactic radiosurgery. Hence, the use of sequential compression devices is advised in these children [115, 116]. Immediate complications occurring after radiosurgery are rare. Most of the complications are delayed and matching the time frame of AVM occlusion secondary to inflammation. Intracerebral hemorrhage and inadequate occlusion persist up to 3 years in 14–19% of cases [82].

21.9 Conclusion

AVM is a rare congenital tangle of abnormal blood vessels associated with an increased risk of bleeding, seizures, and/or CHF, especially in neonates. The complex pathophysiology of AVM might pose a great challenge for anesthesiologists. The anesthetic management of AVM includes thorough preoperative assessment and optimization, meticulous planning of anesthesia, and appropriate monitoring. One has to be prepared for intraoperative and postoperative complications, including massive hemorrhage, venous air embolism, and sudden severe cerebral edema after AVM resection. Postoperative management should be planned as per preoperative status, intraoperative hemodynamic disturbances, and immediate postoperative complications in these groups of children.

Conflict of Interest None.

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22 Anesthetic Management of Cerebral Aneurysm Surgery in Children

Ritesh Lamsal and Charu Mahajan

Key Points

- Subarachnoid hemorrhage is the most common presentation in children with cerebral aneurysms.
- Although both surgical clipping and endovascular techniques are popular, endovascular techniques are increasingly preferred in recent times.
- During the conduct of anesthesia, it is crucial to maintain stable hemodynamic parameters, perform smooth induction of anesthesia, adequate depth of anesthesia, control intracranial pressure, maintain normothermia, and ensure adequate cerebral oxygenation.
- Rebleeding, delayed cerebral ischemia, hydrocephalus, seizure, fluid imbalance, and dyselectrolytemia are commonly encountered complications in children with cerebral aneurysms.
- Timely management of complications is important to prevent secondary neurological injury.

22.1 Introduction

Cerebral aneurysms are abnormal, focal dilatations of cerebral arteries that are usually found at points where vessels branch. In children less than 20 years of age, over 10% of cases of hemorrhagic strokes are caused by spontaneous rupture of cerebral aneurysms [1].

Less than 5% of total intracranial aneurysms are seen in patients who are younger than 18 years [2]. Although rare, ruptured intracranial aneurysms have been reported even in neonates [3, 4]. More than 70% of pediatric cerebral aneurysms are found in the anterior circulation with a slight male preponderance [2, 5, 6]. Adult cerebral aneurysms have been studied in-depth and discussed in several clinical studies. Still, much less is known about the pathogenesis, risk factors, classification schemes, and optimal treatment modalities of pediatric aneurysms. Even though pediatric aneurysms differ from adult aneurysms in many ways, a lot of the existing information has been extrapolated from adult literature.

22.2 Etiopathogenesis

The pathogenesis of pediatric intracranial aneurysm is not fully understood. Two main hypotheses have been proposed. The first hypothesis proposes luminal factors such as high blood flow velocity, shear stress, and blood turbulence in the

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etiogenesis of aneurysms based on the observation that aneurysms are common at sites of arterial bifurcation and arterial-anatomic variants. The second hypothesis suggests abluminal factors such as a morphological abnormality of the vessel wall, functional dysfunction of vessel wall, exogenous risk factors, and systemic diseases as the cause of the development of aneurysms.

It must be noted that many of the established risk factors in adults such as advanced age, chronic hypertension, smoking, drug abuse, and chronic kidney disease are not found in children, underscoring the differences in the formation and natural course of this condition from adults. The underlying cause of aneurysms in children with no systemic diseases remains perplexing; however, several genetic mutations have been implicated, such as the TSC2 and the PKD1 genes (weak vascular wall in tuberous sclerosis and polycystic kidney disease, respectively), the COL3A1 gene (abnormal procollagen in Ehlers-Danlos syndrome), and sickle cell genes (abnormal red cells that cause endothelial injury) [7–10]. The presence of coarctation of the aorta is a well-established risk factor for the development and rupture of aneurysms in children [11]. Some comorbidities associated with the development of cerebral aneurysms in children are listed in Table 22.1.

Table 22.1 Some associated comorbidities in children with aneurysms

Renal Polycystic kidney disease Alport syndrome Fibromuscular renal artery hyperplasia	**Connective tissue, genetic** Ehlers-Danlos syndrome Marfan's syndrome Angelman syndrome Cystic fibrosis
Cardiovascular Coarctation of aorta Hypoplastic left heart Aortic valve stenosis Double outlet right ventricle Moyamoya disease	**Others** Meningocele Autism Arachnoid cyst
Hematological, inflammatory, autoimmune Sickle cell anemia Kawasaki disease Takayasu's disease Thalassemia Lupus erythematosus Idiopathic thrombocytopenic purpura Polyarteritis nodosa Tuberous sclerosis Neurofibromatosis type I Von Hippel-Lindau disease Ataxia telangiectasia	

22.3 Types and Location

The four main types of pediatric intracranial aneurysms are saccular (berry), fusiform, traumatic, and infective. Saccular aneurysms are formed because of the disintegration of the elastic layer of the artery. The aneurysmal sac is composed of hyalinized intima and adventitia, with an abnormal tunica media. The internal elastic lamina terminates at the neck of the aneurysm and is absent in the sac. Saccular aneurysms were earlier thought to be congenital or developmental in origin, while recent evidence points toward hemodynamically induced degenerative vascular injury. Fusiform aneurysms are caused by severe atherosclerosis or degenerative changes in childhood. Traumatic aneurysms constitute 5–40% of pediatric aneurysms and are most commonly seen in the distal anterior cerebral artery (ACA) or in the major vessels along the skull base [12]. In the truest sense, traumatic aneurysms are pseudo-aneurysms because they are caused by endothelial damage and thus have a different pathophysiology. Children with traumatic aneurysms have a history of blunt or penetrating head injury or prior intracranial surgery. Infective aneurysms can be multiple and are more common in the anterior circulation, and many children have associated comorbid conditions like congenital or acquired immunodeficiency, endocarditis, and meningoencephalitis. Bacterial infections are more commonly implicated in aneurysms of infective etiology. Dissecting (nontraumatic) aneurysms have the dissection between the tunica intima and the media. These

are four times more common in children compared with adults [13]. Posterior circulation aneurysms are overrepresented in children and are three to four times more common than in adults. Complex aneurysms such as giant, multiple, mycotic, or those in unusual locations are more common in children than adults [5, 14]. Nearly one-fourth of pediatric aneurysms can be giant [5].

22.4 Clinical Presentation

The most common presentation of intracranial aneurysms in symptomatic children is subarachnoid hemorrhage (SAH). Patients may present with headache, features of direct compressive effects, focal neurologic deficits, and seizures. Fusiform aneurysms tend to bleed less. Giant aneurysms commonly present with mass effects. In children, they can sometimes be confused for intracranial tumors on neuroimaging [15]. Seizures or acute hydrocephalus at presentation are twice as common in children compared with adults. Clinical examination and laboratory investigations may reveal a decreased level of consciousness, features of intracranial hypertension, fever, meningism, photophobia, retinal hemorrhage, dyselectrolytemia, and electrocardiographic changes. In young children with elevated ICP and mass effect, additional findings like tense fontanelle, splayed sutures, and opisthotonic posturing may be seen. For unclear reasons, children generally present with better clinical grades than adults and also seem to be less susceptible to developing delayed cerebral ischemia [14].

22.5 Diagnosis

A non-contrast computed tomography (NCCT) of the head is the first investigation in a child with suspected intracranial bleeding. If the NCCT or clinical findings suggest SAH, additional imaging in the form of CT angiogram (CTA) or magnetic resonance angiogram (MRA) of the circle of Willis can be done (Fig. 22.1). The sensitivity of both CTA and MRA to pick aneurysms more than 5 mm in size approaches 100%. With recent advances, the sensitivity to pick even small aneurysms approximates 98–100% [16]. The potential advantage of MRA over CTA is that it does not require iodinated contrast use and limits the exposure of harmful ionizing radiation in young children. Digital subtraction angiography (DSA), while invasive, is the gold standard for the diagnosis of cerebral aneurysms and gives detailed information about the exact site, size, configuration, and neck of the aneurysm, which is important for making treatment decisions (Fig. 22.2).

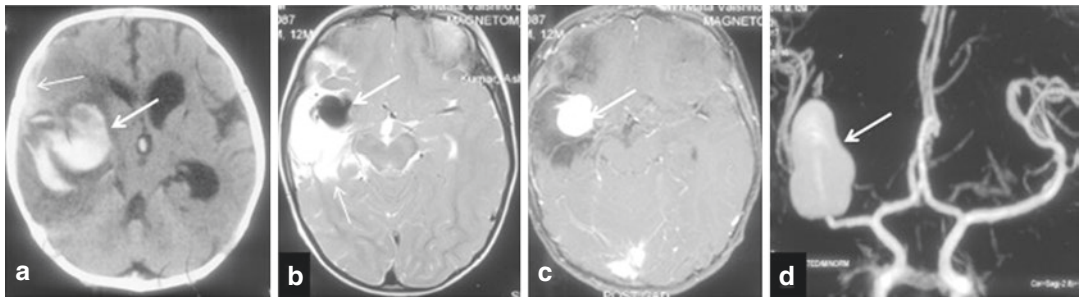

Fig. 22.1 In a 4-year-old child, axial NCCT head showed (**a**) well-defined hyperdense lesion (thick white arrow), s/o bleed with perilesional hypodensity (edema) in right temporal lobe with thin SDH in right temporal lobe convexity (thin white arrow). Axial T2 MRI showed (**b**) well-defined flow void in right distal M1 MCA (thick white arrow) with gliotic changes in the right temporal lobe (thin white arrow). Phase contrast MRI showed (**c**) intense enhancement within the aneurysm (thick white arrow). Time of flight MRA showed (**d**) a well-defined aneurysm in right distal M1 MCA (thick white arrow)

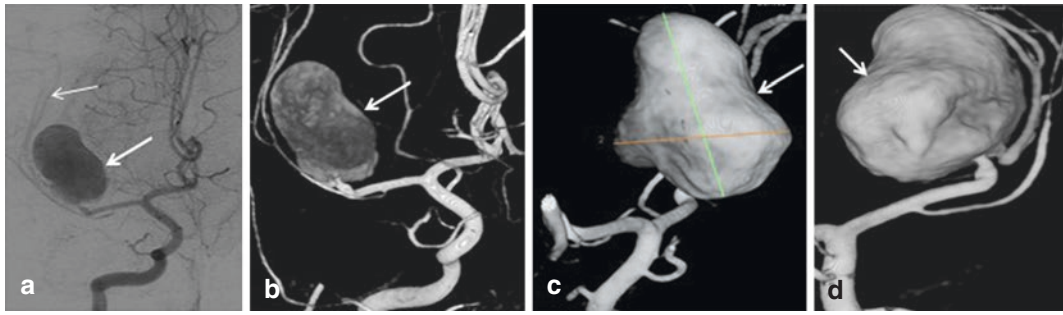

Fig. 22.2 Digital subtraction angiography right ICA AP run showed (**a**) a well-defined lobulated aneurysm in right distal M1 MCA (thick arrow) with paucity of cortical vessels in right MCA territory (thin arrow). DSA 3D images (**b**–**d**) showed lobulated aneurysm in right distal M1 MCA, directed antero-supero-laterally (thick white arrow)

22.6 Clinical Grading

The first popular grading of SAH based on the severity of clinical findings was done by Botterell et al. (into five grades) and was later modified by Hunt and Hess [17, 18]. A further modification added "Grade 0" for unruptured aneurysms (Table 22.2) [19]. The modified Hunt and Hess (H&H) scale is most commonly used to grade the aneurysm at presentation, prognosticate, and guide neurosurgical or interventional therapy. However, it has been criticized for interobserver variation owing to the ambiguity in the terms used while grading, with poor operational definitions. Terms like lethargy, confusion, and stupor may be interpreted differently by different observers. Similarly, some patients may have clinical features that overlap in two different grades (e.g., severe headache in an unruptured aneurysm). No separate clinical grading scale exists in children. Predicted mortality rates based on H&H grades have been calculated in adults and are probably not applicable to children.

The World Federation of Neurological Surgeons (WFNS) scale was introduced in 1988 to improve upon the H&H scale and increase objectivity while assigning grades. The WFNS scale compresses the Glasgow Coma Scale (GCS) into five categories and also incorporates neurological motor deficits [20] (Table 22.2).

Recently, a modified WFNS (mWFNS) scale has been proposed in which adult patients with SAH and a GCS score of 14 are assigned to grade II, and those with a total score of 13 are assigned to grade III, irrespective of the presence of neurological deficit [21]. Although untested in children, the mWFNS score may be better at accurately prognosticating SAH patients than the original score, but further validation is required.

The Fisher grading is based on computed tomography (CT) findings in SAH (Table 22.2). The original Fisher grading was modified by Frontera et al. to account for concomitant intraventricular hemorrhage (IVH) in admission CT scans. It was found to predict symptomatic vasospasm after SAH more accurately than the original Fisher grade (Table 22.2) [22, 23].

Although the Fisher grading is widely used to grade SAH in adults, its applicability in children (using adult CT scan measurement values) is unclear. No separate grading system based on CT findings is available in children.

22.7 Complications of Aneurysmal SAH

22.7.1 Rebleeding

Rebleeding of the aneurysm occurs in nearly half of the children with intracranial aneurysm, and for reasons that are not clear, it is consistently more frequent than in adults [24–26]. The classic presentation of rebleeding is a child with a dete-

Table 22.2 Different grading systems for aneurysmal subarachnoid hemorrhage

Grading	Grade 1	Grade II	Grade III	Grade IV	Grade V
Modified Hunt and Hess [19] [a]	Asymptomatic or mild headache and normal neurological examination	Moderate-severe headache, nuchal rigidity, no neurologic deficits other than cranial nerve palsy	Lethargy, confusion, or mild focal deficits	Stupor, moderate to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbances	Deep coma, decerebrate rigidity, moribund appearance
World federation of neurological surgeons [20]	GCS-15, no motor deficit	GCS 13–14, no motor deficit	GCS 13–14, motor deficit present	GCS 7–12, motor deficit present or absent	GCS 3–6, motor deficit present or absent
Fisher [22]	No blood detected	Diffuse or thin layer of SAH (<1 mm thick)	Localized clot or thick layer of SAH (≥1 mm thick)	Intracerebral or intraventricular blood with diffuse or no SAH	
Modified Fisher [23] [b]	Focal or diffuse thin SAH, no IVH	Focal or diffuse thin SAH with IVH	Thick SAH, no IVH	Thick SAH with IVH	

[a]Grade 0—unruptured aneurysm
[b]Grade 0—no SAH/IVH
GCS Glasgow Coma Scale, *SAH* Subarachnoid Hemorrhage, *IVH* Intraventricular Hemorrhage

rioration of consciousness, new-onset neurological signs, and abnormal vital signs. Some factors that predispose to rebleeding include poor-grade aneurysm, presence of an intracerebral or an intraventricular hematoma, posterior circulation aneurysm, deranged coagulation parameters, and delayed surgery. Rebleeding has also been described during induction of anesthesia, laryngoscopy, intubation, and during other intraoperative events such as brain retraction and sudden evacuation of the hematoma. The incidence of rebleeding is highest in the first 24–48 h of the first bleed. Studies carried out in adults have found that antifibrinolytic drugs like tranexamic acid protect against rebleeding, especially when administered early in the course of treatment [27]. However, there are conflicting results of ischemic complications with their use [27, 28]. A recently published meta-analysis of ten trials concluded that there is no conclusive evidence to support the use of antifibrinolytics in treating patients with aneurysmal SAH, and further trials are required to evaluate its effectiveness [29]. The same results may also be corroborated to children.

22.7.2 Vasospasm and Delayed Cerebral Ischemia

Vasospasm is the reactive narrowing of the conducting vessels around the area of the subarachnoid bleeding caused by the irritant effect of blood and its breakdown products. Vasospasm is an important cause of morbidity and mortality in patients before and after the therapeutic procedure. Vasospasm is generally not seen before 3 days of the initial bleed, peaks at the end of 7 days, and wanes by 3 weeks. In adults with aneurysmal SAH, angiographically evident vasospasm is estimated to be present in 40–60% of patients, and clinically significant vasospasm is seen in 20–30% of patients. However, the incidence of delayed cerebral ischemia (DCI) is lower in children (~10%) compared with adults, and children tolerate SAH better [3, 30–33]. Reasons for better outcomes in children may be related to higher cerebral blood flow, better collateral circulation, and less sensitivity to post-hemorrhagic spasm [30, 34]. Nevertheless, vasospasm causing cerebral ischemia or infarction is an important cause of significant morbidity in children.

22.7.2.1 Diagnosis of Vasospasm

(a) *Clinical:* The sudden or gradual appearance of neurological deficits after 3 days of the onset of hemorrhage unexplained by concurrent structural or metabolic abnormalities suggests vasospasm.

Transcranial Doppler (TCD) is the most common noninvasive modality to diagnose vasospastic arteries. Vasospasm narrows the caliber of cerebral vessels and increases the flow velocity through these vessels. A rise of TCD-determined flow velocity more than 50 cm/s in 24 h or a flow velocity >120 cm/s are taken as indicators of vasospasm in adults. However, the cerebral blood flow velocity is lower in children and has a wide variation across age groups compared with adults. TCD studies show that the cerebral blood flow velocity is approximately 24 cm/s in neonates, which increases and peaks at around 7–9 years of age (approximately 100 cm/s) [34]. In older children, the cerebral blood flow velocity gradually decreases to parallel adult values (approximately 50 cm/s) [35]. Thus, it is difficult to establish flow velocity cut-off values in children to diagnose vasospasm. Serial TCD monitoring to establish trends may be more useful than absolute numbers.

(b) *Cerebral angiography* is the most sensitive tool to diagnose cerebral vasospasm; however, the invasive nature of this modality precludes its frequent use in children. Around one-third of adults with angiographically detected vasospasm develop clinical features. This number is lower in children.

(c) *Jugular bulb oximetry:* By detecting changes in cerebral oxygen extraction, jugular bulb oximetry is useful in predicting impending vasospasm. Patients who develop clinically significant vasospasm have an elevated cerebral oxygen extraction a day earlier than it can be recognised by the onset of symptoms of cerebral ischemia.

(d) Xenon-enhanced CT scans, single photon emission computed tomography, and several other cerebral blood flow measuring tools, although not common in routine clinical practice, can be used for the diagnosis of vasospasm.

22.7.2.2 Treatment of Vasospasm and Delayed Cerebral Ischemia

Early endovascular or neurosurgical treatment of the aneurysm is the most important strategy to prevent vasospasm. *"Triple H" therapy*, including hypertension, hypervolemia, and hemodilution, has long been the mainstay for the management of cerebral vasospasm. This strategy, believed to increase cerebral blood flow (CBF) by expanding intravascular volume and reducing blood viscosity is no longer favored. Hemodynamic augmentation is now considered to be the first-line therapy to treat DCI. This can be achieved by increasing intravascular volume alone or by the use of vasopressors like norepinephrine and phenylephrine. There are practical problems of defining the target threshold for augmentation of blood pressure in children, as normal blood pressure has a wide range in children across different age groups. Hypervolemia increases cardiac output and may result in improved perfusion to the hypo-perfused regions, even though its use has been challenged in studies [36]. Even though in adults with DCI, there is emerging evidence to support euvolemia instead of hypervolemia, this is not clear in children. The risks of hypervolemia include congestive cardiac failure, pulmonary edema, coagulopathy, dilutional hyponatremia, and rebleeding. The benefit of hemodilution is not clear either and is the most controversial element of Triple H. A target hematocrit of 30–35% has been suggested in adults to provide an optimal balance between oxygen-carrying capacity and blood viscosity. The target hemoglobin value to achieve adequate cerebral oxygenation with optimal CBF is not known in children. Blood pressure augmentation should not be done before the aneurysm is secured. Even though there is a paucity of studies in children, no controlled trial has shown improved mortality with Triple H therapy [37, 38].

Nimodipine, which is a calcium channel blocker, is used for the prevention and treatment of vasospastic arteries and is the only proven pharmacological therapy to improve outcome

after aneurysmal SAH in adults. The typical pediatric dose of oral nimodipine is 1 mg/kg every 4 h. However, some studies in children with SAH suggest that oral nimodipine use does not eliminate risk of vasospasm and cannot improve prognosis in cases having rebleeding and infarction [39]. In some children, significant hypotension has been seen after oral nimodipine use [39]. Owing to the risk of significant hypotension, the use of intravenous nimodipine in children is uncommon. Large prospective studies examining different dosing regimens and clinical benefits of nimodipine are warranted in children.

Magnesium sulfate has several physiological effects such as cerebral vasodilation, calcium antagonism, inhibition of excitatory postsynaptic potentials, and inhibition of the formation of free radicals after tissue injury. It has shown some promise in reducing vasospasm and improving outcomes with minimal side effects. However, two large randomized trials have found conflicting results on the benefits of magnesium in SAH [40, 41]. A follow-up meta-analysis also failed to demonstrate a favorable neurological outcome of magnesium after SAH [42]. Studies in children are not available. *Endothelin receptor antagonists* such as clazosentan were found to improve vasospasm in animal models, but the benefits did not translate in human trials [43–46]. *Statins* were earlier believed to be of benefit in SAH because of their anti-inflammatory and immunomodulatory effects, but large studies have not shown a significant benefit with their use [47]. Several *other drugs* that showed early promises, such as tirilazad, which a lipid peroxidation inhibitor, and nicaraven, a hydroxyl radical scavenger, are not useful either. *Interventional strategies* such as balloon angioplasty for focal stenosis and intra-arterial administration of vasodilators are labor intensive, involve significant risks, and are less commonly performed in children compared with adults.

22.7.3 Hydrocephalus

Hydrocephalus can be acute, occurring within 72 h of the initial bleeding, or chronic, occurring weeks or sometimes even months after the initial episode. Patients with poor-grade and large-sized aneurysms, thick SAH or intraventricular bleeding, and posterior circulation aneurysms have an increased risk of developing hydrocephalus. Hydrocephalus occurs in 20–30% of adults with aneurysmal SAH and is more common in children, probably because of the greater incidence of posterior circulation and complex aneurysms. Acute hydrocephalus may require the placement of an external ventricular drain (EVD) for decompression, and many children with chronic hydrocephalus require a CSF shunting procedure like ventriculoperitoneal shunt.

22.7.4 Seizures

Seizures are detrimental and should be promptly terminated because they increase CBF and increase oxygen requirements in an already compromised brain. Up to one-third of children with SAH can have seizures, which is more than in adults [48]. Seizures are more likely in patients with poor-grade SAH, intracerebral bleed, severe vasospasm, cerebral infarct, and rebleeding. There is no high-quality evidence on the benefit of prophylactic anti-seizure medications in adults or children with cerebral aneurysms [49].

22.7.5 Fluid and Electrolyte Disturbances

Intracranial volume contraction, hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia are common findings in children with SAH. Hyponatremia is extremely common and has been found in up to one-third of patients with SAH. The peak incidence of hyponatremia is between the 2nd and 10th days of SAH. Uncorrected hyponatremia lowers the seizure threshold, worsens cerebral edema, and can alter the level of consciousness. Prompt identification of the cause of hyponatremia is important to determine the appropriate treatment. In cerebral salt-wasting syndrome (CSWS), there is hyponatremia with concomitant extracellular volume contraction. Treatment with isotonic

crystalloids to replenish sodium and water is appropriate. If syndrome of inappropriate antidiuretic hormone secretion (SIADH) is present, it is reasonable to restrict fluid intake and administer hypertonic saline. In children with SIADH, the fluid restriction should be done judiciously, as it can lead to rapid intravascular volume depletion and hemodynamic instability, which increases the risk of cerebral ischemia.

22.7.6 Pulmonary and Cardiac Complications

Pulmonary edema and hospital-acquired pneumonia are common problems in children with aneurysmal SAH. Myocardial dysfunction and arrhythmias are also common. Although 50–100% of adult patients with SAH have ECG changes, such as T-wave inversion, ST depression, U waves, and QT prolongation, the true incidence of electrocardiographic changes in children is not known. Arrhythmia most frequently occurs in the first week of SAH. Possible causes include injury to the posterior pituitary with norepinephrine release resulting in subendocardial injury, and concomitant dyselectrolytemia.

22.8 Treatment of Cerebral Aneurysm in Children

The treatment of unruptured cerebral aneurysms in children can be divided into surgical, endovascular, and conservative approaches [50]. The management of pediatric intracranial aneurysms differs from adults because of the complexities and heterogeneity of aneurysms seen in children. Children with SAH are most appropriately cared for in dedicated neuro-centers that have experienced neurovascular surgeons, neuroanesthesiologists, neurointerventionalists, and neurointensivists. In any child with SAH, medical management should be immediately started to stabilize the child and prevent secondary neurologic complications. It is important to be cognizant of the child's intravascular volume status and hemodynamic parameters, which usually require the placement of a urinary catheter and strict charting of fluid balance. In a critically ill child, an indwelling arterial line is useful to optimize blood pressure and titrate vasoactive drugs. The requirement of sedatives and analgesics to treat the child's anxiety and the headache of SAH should be balanced against the need to perform a frequent neurological examination. In some children with hydrocephalus, CSF flow diversion may be required before or after securing the aneurysm.

The best modality of securing pediatric aneurysms remains a matter of debate. Both endovascular procedures and surgical clipping have been widely performed with good results [51, 52]. There are concerns about the durability of endovascular devices as children's life expectancy is longer compared with adults [12, 52]. However, a recent meta-analysis found both endovascular and surgical treatments yielded comparable long-term clinical outcomes in children [53]. The International Subarachnoid Aneurysm Trial (ISAT) in adults with ruptured aneurysms showed that endovascular coiling was more likely to result in independent survival than neurosurgical clipping, albeit with a slightly increased risk of rebleeding [54]. A long-term follow-up of the same cohort suggested that even though rebleeding is slightly increased after endovascular coiling, the probability of disability-free survival is higher in the endovascular group compared with neurosurgical clipping at 10 years [55]. Even though endovascular therapeutic options are increasingly preferred, treatment choice in different hospitals seems to be guided by protocols for adults, the preference and expertise of the neurosurgical units, and patient preference.

22.8.1 Surgical Treatment

Clipping of the aneurysm has been extensively described in the neurosurgical literature. There are reports of several surgical techniques, such as clipping, proximal occlusion with or without bypass, trapping, and wrapping of the aneurysm. The most commonly employed method is to clip the neck of the aneurysm. Aneurysms are increas-

ingly being clipped early, within 24–48 h. The anesthesia goals are tailored for each child primarily based on the preoperative grade of the aneurysm, the proposed surgery, and the need for additional modalities such as intracranial-extracranial bypass procedures. Induced hypotension during the dissection phase of the aneurysm is no longer practiced, and instead many surgeries are carried out using proximal occlusion with temporary clips. Mild hypothermia (32–34 °) and various drugs like mannitol, thiopental, etomidate, propofol, and steroids have been proposed for cerebral protection during temporary clipping with no reliable evidence of their effectiveness [56–58].

22.8.2 Anesthetic Consideration During Surgical Clipping

The goals of neuroanesthesia during surgical clipping are to ensure stable perioperative hemodynamic parameters, perform smooth induction and extubation, provide adequate depth of anesthesia, lower the ICP, and maintain adequate cerebral oxygenation, normothermia, and normocarbia to mild hypocarbia. Unlike in adults, optimal perioperative blood pressure targets are not defined in children. It is reasonable to maintain the intraoperative blood pressure close to the baseline value throughout the conduct of anesthesia. Importantly, the blood pressure should not be allowed to drop below 20% of the baseline value, especially in poor-grade aneurysms, when the brain is already at a critical perfusion threshold. The neuroanesthesiologist should be prepared for a sudden and massive blood loss; it is crucial to have blood and blood products readily available for immediate administration.

22.8.2.1 *Induction of Anesthesia*

Propofol (1–2 mg/kg) or thiopental (4–6 mg/kg) in combination with opioids like fentanyl (2–4 μg/kg) or sufentanil (0.3–0.5 μg/kg) is commonly used for induction of anesthesia. Atracurium (0.5–0.8 mg/kg), vecuronium (0.1–0.12 mg/kg), or rocuronium (0.6–1.2 mg/kg) can be used for muscle paralysis. Laryngoscopy and intubation should be quick and smooth. Adjuncts such as lidocaine (1–2 mg/kg), beta-blockers like esmolol (0.25–1 mg/kg), or labetalol (5–20 mg) and additional boluses of fentanyl or propofol are useful to reduce the hemodynamic surge of laryngoscopy and intubation and before other intensely stimulating procedures like insertion of skull pins. A sudden rise of blood pressure will increase the transmural pressure gradient across the aneurysm wall, potentially leading to aneurysm rupture. The intraoperative rupture of the aneurysm carries a very poor prognosis, and it is important to take appropriate preventive measures. Although quite difficult in children, the placement of an arterial catheter before induction of anesthesia is useful for better controlling blood pressure.

22.8.2.2 *Monitoring*

Besides standard ASA monitoring (ECG, NIBP, $EtCO_2$, SpO_2, and temperature), direct intra-arterial blood pressure monitoring helps in beat-beat monitoring of blood pressure and close titration of vasoactive medications. At least one large-bore intravenous cannula and a central venous catheter are typically inserted. Monitoring the depth of anesthesia (derived electroencephalograph monitor, like bispectral index) and the degree of neuromuscular block (neuromuscular transmission monitor, like train-of-four) may be useful to titrate anesthetics and muscle relaxants. Unlike in adults, the use of intraoperative neuromonitoring like cerebral oximetry, jugular bulb oximetry, transcranial Doppler, and evoked potentials have rarely been described during pediatric aneurysm surgeries.

22.8.2.3 *Maintenance of Anesthesia*

With the increasing trend of early surgery for cerebral aneurysms, the challenges of providing a lax brain in an under-prepared patient while at the same time maintaining intraoperative hemodynamics are increasing. Volatile anesthetics like isoflurane, sevoflurane, and desflurane or total intravenous anesthesia with propofol and fentanyl (0.5–2 μg/kg/h) or remifentanil (0.125–0.25 μg/kg/min) can be used. There is no strong evidence to avoid the use of nitrous oxide, and its

use varies in different institutions. However, it is prudent to avoid nitrous oxide in patients with high-grade SAH or those with intraoperative "tense brain." Mannitol (20%), an osmotic diuretic, is frequently used to provide brain relaxation as a slow infusion in dosages of 0.25 mg/kg. Hypertonic saline is an alternative; no intraoperative study has shown a clear outcome benefit of one over the other in children [59–62]. Experimental models have shown possible benefits of inducing mild hypothermia (33–35 °C) for neuroprotection; however, this has not translated into a clinical benefit in aneurysm surgeries [63]. Normocarbia to mild hypocarbia ($PaCO_2$: 35–40 mmHg) is most commonly employed. Controlled hypotension during the early dissection phase of the surgery is no longer practiced. Instead, occlusion of the feeding vessels using temporary clips may be used to facilitate exposure and prevent aneurysm rupture. The potential problems using temporary clips are focal cerebral infarction and arterial damage because of the clip application. It is important to augment the blood pressure during temporary clipping to maintain regional cerebral perfusion by an increased collateral blood flow.

Sometimes, the surgeon may request the anesthesiologist to administer intravenous indocyanine green (ICG) dye after clipping the aneurysm. ICG is a near-infrared fluorescent dye used to detect major surgical issues like residual filling of the clipped aneurysm and parent or branching artery occlusion, while the surgical field remains exposed intraoperatively so that immediate revision can be done if required [64]. It is available as a lyophilized green-colored powder that is dissolved in sterile water before intravenous administration. The safety and effectiveness of ICG have been established in children, and the maximum permissible dose is 2 mg/kg [65].

22.8.2.4 *Recovery and Extubation*

The decision to extubate the trachea at the end of the surgery is based on preoperative patient status and intraoperative surgical or anesthetic events. Good-grade aneurysm patients with an uneventful intraoperative course may be extubated inside the operating room. Others may require a period of postoperative mechanical ventilation. These patients should be shifted to the intensive care unit for ventilation and further management.

22.8.3 Endovascular Treatment

In the last few years, there has been a tremendous shift in the treatment approach for pediatric aneurysms from open surgery to endovascular techniques and multi-modality therapeutic plans. A growing body of evidence points at the safety of the endovascular approach and its effectiveness in preventing early rebleeding [66, 67]. Several observational and small cohort studies have found the overall clinical outcome of endovascular treatment to be as good or even superior to open surgical methods in children [68–71]. It is particularly useful when a difficult anatomic location of the aneurysm precludes the use of open surgical methods, such as with posterior circulation aneurysms. Similarly, partially clipped aneurysms and patients with poor-grade aneurysms benefit from endovascular methods. The most popular endovascular technique uses the Guglielmi detachable coil (GDC), which is inserted into the aneurysmal sac, setting up secondary thrombosis. Adjuvant techniques like balloon-assisted coiling or stent-assisted coiling can be used to support a wide-necked aneurysm and prevent coil prolapse into the parent artery [72]. Other endovascular options such as placement of flow-diverting stents (like Pipeline Embolization Device), liquid embolization, or endovascular vessel sacrifice may be required to treat complex aneurysms [53, 73].

22.8.3.1 *Anesthetic Considerations During Endovascular Treatment*

The major considerations include providing anesthesia care in a suboptimal anesthetic environment outside the operation rooms, transportation of patients, anticoagulation, management of sudden catastrophic events such as aneurysm rupture and contrast-related anaphylaxis, ensuring early recovery from anesthesia for neurologi-

cal assessment, protection from radiation hazards, and the care of generally sicker and underprepared patients, who may have been considered too risky to undergo urgent neurosurgical procedures.

22.8.3.2 *Choice of Anesthesia*

General anesthesia with endotracheal intubation is preferred in children as it allows immobility for accurate imaging and intervention, control of $PaCO_2$, and prompt management of possible catastrophic complications. Patient accessibility is always a problem in radiological suites; using two large-bore cannulas with extension tubing is important. Standard ASA monitoring is mandatory. An invasive arterial catheter is useful for beat-to-beat BP monitoring as well as for blood sampling.

22.8.3.3 *Maintenance of Anesthesia*

Like in surgical clipping, both total intravenous anesthesia and volatile anesthetics have been used. There is no clear superiority of one anesthetic technique over another. Anticoagulation is achieved using a loading dose of 60–80 units/kg heparin followed by either intermittent boluses or a continuous infusion to maintain activated clotting time (ACT) two to three times the baseline [72].

22.8.3.4 *Recovery and Extubation*

The course of recovery from anesthesia and the decision to extubate the trachea at the end of the procedure follows the same basic principles outlined in open surgical methods.

22.9 Conclusion

Intracranial aneurysms in children are rare. As there are very few studies in pediatric cerebral aneurysms, little is known about their pathogenesis, clinical grading, and treatment modalities. Most of the anesthetic practices have been simply extrapolated from evidences that are derived from adult literature. Even though the basic principles of neuroanesthesia and neurocritical care may remain the same, caution must be exercised when extrapolating such evidences. Large prospective studies in pediatric aneurysm surgeries are clearly warranted.

Conflict of Interest None declared for each author.

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Anesthetic Management of Vein of Galen Malformations

23

Jayanth R Seshan and Girija Prasad Rath

Key Points

- True vein of Galen malformations are fistulous communications in the cerebral midline resulting in high-flow shunts and present as high-output cardiac failure in neonates.
- The advent of modern endovascular embolization techniques has drastically reduced mortality and improved neurological outcomes.
- Medical management of cardiac failure takes priority over definitive treatment, but emergency endovascular embolization may be carried out in a neonate with cardiac failure refractory to medical management.
- Anesthetic challenges in managing this group of children involve age-related considerations, difficult airway primarily due to increased head circumference, possible hemodynamic instability during the course of anesthesia, and requirement of postoperative ventilation.
- In neonates posted for emergency embolization, additional anesthetic considerations include difficulty in securing intravenous and invasive arterial lines, dyselectrolytemia (diuretics, digoxin, acidosis), maintenance of adequate systemic perfusion to prevent volume overload and worsening of heart failure and prevent hypoperfusion and worsening of renal injury (contrast and drug-induced).

23.1 Introduction

Vein of Galen malformations (VOGMs) are rare congenital anomalies that constitute 1% of all intracranial vascular malformations and represent 30% of vascular malformations in the pediatric population [1]. The anomaly was mentioned initially by Steinheil (1895); however, the first clinical description of a vein of Galen aneurysm was given by Jaeger et al. (1937) [2]. Variably referred to as "aneurysms of the vein of Galen," "arteriovenous aneurysms of the vein of Galen," "vein of Galen aneurysmal malformations," and "vein of Galen malformations," true VOGMs are actually persistence of the embryonic median prosencephalic vein and not the vein of Galen. The incidence of this condition in the population is 1:25,000 with a male preponderance (3:1) [3]. Left untreated, the mortality rate is almost 100% and with high morbidity in the form of cardiac failure and long-term neurodevelopmental delay [4].

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23.2 Anatomy and Embryology of VOGM

The normal vein of Galen, or the great cerebral vein, is a part of the deep venous system of the brain. It is a short (1–2 cm) thick vein located behind the splenium of the corpus callosum in the midline. It courses posteriorly where it joins the inferior sagittal sinus to form the straight sinus that ultimately drains into the confluence of sinuses (torcular Herophili) [5].

Vein of Galen arteriovenous malformations are congenital abnormal communications between arterial feeders and draining veins located in the midline in the choroidal fissure. The feeding arteries include the anterior and posterior choroidal arteries and the anterior cerebral artery, supplying the choroid plexus. Venous drainage is through the median prosencephalic vein (MPV) of Markowski, which is the embryonic precursor of the vein of Galen (Fig. 23.1) [2].

The development of cerebral vasculature can be divided into three stages, initial extra embryonal stage, extrinsic vascularization (around the neural tubes), and intrinsic vascularization, where blood vessels develop within the cerebral parenchyma. Between 6 and 11 weeks of gestation, the cortical arterial network develops from the internal carotid artery. The venous drainage of the brain at this stage is through the median prosencephalic vein, which develops in the root of the diencephalon. Except for its most distal part, regression of this vein occurs at around 11 weeks of gestation when the newly formed internal cerebral veins take over the venous drainage. The distal part of the median prosencephalic vein joins the internal cerebral vein, and the paired internal cerebral veins join to form the great vein of Galen [2].

Any abnormality in the development of cerebral vasculature during this phase between 6 and 11 weeks of gestation results in direct arteriovenous communication between the arterial network and median prosencephalic vein. The lack of a fibrous wall and its presence unsupported in the cistern of velum allows the vein to expand and balloon out as the flow increases preventing its regression [6]. The falcine sinus (connecting straight sinus and superior sagittal sinus), which usually disappears beyond the fetal stage, may continue to persist. Straight sinus may be absent.

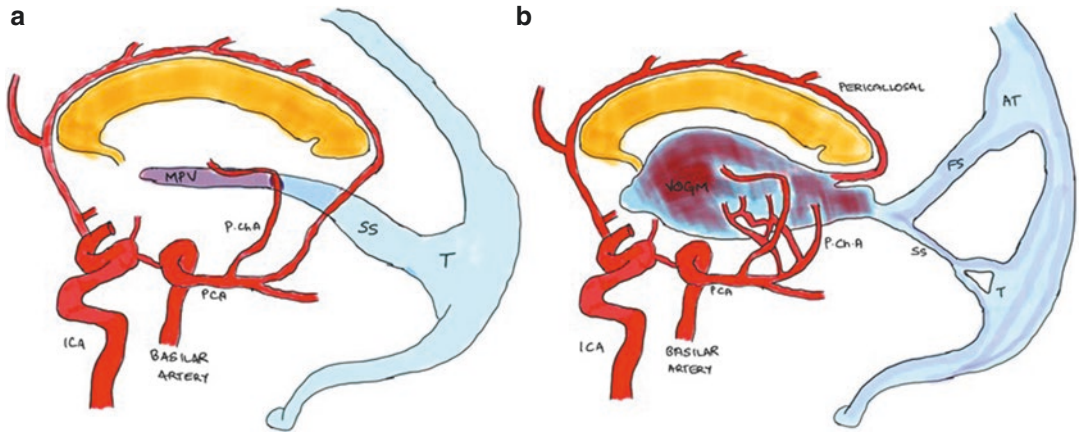

Fig. 23.1 Schematic diagram showing the development of vein of Galen aneurysmal malformation with its feeders. (**a**) The median prosencephalic vein (MPV) drains into the straight sinus (SS) and further into the torcula (T). Normal anastomosis exists between the pericallosal and the distal branches of the posterior cerebral artery (PCA). (**b**) Enlarged and malformed MPV with arterial feeders from pericallosal and posterior choroidal arteries (PChA) draining into an accessory torcula (AT) through a persistent embryonic falcine sinus (FS) and a possible stenotic straight sinus (SS)

23.3 Pathophysiology

Cardiovascular: VOGM is characterized by a low-resistance and high-flow shunt. Changes in cardiovascular physiology and blood flow patterns between fetal circulation and postnatal life determine the pathophysiology of this condition. During fetal life, the low-resistance placental circulation prevents higher shunt fraction across the VOGM. But, changes in vascular resistance in the postnatal period results in a sudden and progressive increase in blood flow through the cranial shunt. It is estimated that around 80% of cardiac output flows through the VOGM, which results in increased venous return and pulmonary overload (pulmonary hypertension), and cardiac failure. Cyanosis may result due to increased right-sided pressures and a right-to-left shunt through the ductus arteriosus and the patent foramen ovale [7].

Secondly, the large arteriovenous shunt causes wide pulse pressure, and the resistance across the shunt may be so low that it can cause a reduced or retrograde flow in the aorta during diastole, which results in reduced coronary perfusion and increases the risk of myocardial ischemia and hence cardiac failure. Thus, cardiac failure may be multifactorial and be refractory to medical management [8]. Aortic flow reversal may also lead to renal hypoperfusion and injury.

Neurological: Immaturity of the cerebral venous system is the major pathophysiological factor in VOGM. Cerebral venous hypertension results from the large amount of blood flowing through it due to the VOGM. Structural defects like an immature deep cerebral venous system, absent sinuses including the straight sinus, and jugular bulb stenosis might result in aggravation of the cerebral venous pressure. Also, cerebrospinal fluid (CSF) reabsorption in the neonate occurs through the ventricular ependyma and brain parenchyma into the medullary veins as the arachnoid granulations do not mature until 16–18 months of age. The increased venous pressure in the brain in VOGM is reflected in the cortical and medullary veins impairing CSF reabsorption and results in hydrocephalus [9].

Together, cerebral venous hypertension and hydrocephalus lead to impaired cerebral oxygenation, edema, and subependymal atrophy. The most severe form of this cerebral atrophy is called *melting brain syndrome* [10, 11].

23.4 Clinical Manifestations

The clinical features are mainly cardiac and neurological. Age and severity of presentation may vary based on the shunt size (Table 23.1). The presentation in neonates varies from asymptom-

Table 23.1 Differences in vein of Galen malformation based on age of presentation [17–19]

	Age at diagnosis			
Parameter	Prenatal	Neonate	Infant	Older child
Clinical presentation	Incidental diagnosis	Heart failure (left-to-right shunt causing volume overload on the heart)	Macrocephaly and hydrocephalus	Headaches, developmental delay, hydrocephalus
Angiographic type		Choroidal	Mural > choroidal	Mural
Severity	Melting brain detected on fetal MRI detects poor prognosis	Most severe forms in this age group. Mortality increases with delay in diagnosis or prompt treatment of heart failure	Less severe. Heart failure controlled with medications and presenting for elective embolization	Usually mild. Developmental delay may persist
Management	Facilitate the delivery of a child at a tertiary care center equipped to manage the condition	Medical management of heart failure. Emergency embolization of feeders to reduce the shunt fraction	Elective embolization	Elective embolization

atic cardiomegaly to refractory cardiac failure. Common initial presentation in a neonate is that of the rapid deterioration of an initially unremarkable postnatal period; there is worsening of cardiac failure presenting with severe respiratory distress and usually requiring mechanical ventilation. Signs include prominent carotid pulsation and weak peripheral pulses, acrocyanosis, coarse breath sounds over both lung fields, ejection systolic murmur heard over the precordium, a continuous carotid bruit, and a soft cranial bruit (heard better over the posterior cranium) based on the shunt fraction and severity of heart failure [12, 13]. Unless promptly detected and managed, multiorgan failure may ensue. Other forms of presentation include mild cardiac failure and failure to thrive. Neurological features include seizures and macrocephaly secondary to hydrocephalus. Older children generally present with milder symptoms, which include those of venous outflow obstruction like increased head size and prominent facial veins. Initial presentation in adulthood is extremely rare but has been reported. Presenting features include headaches (SAH), focal deficits, and even incidental diagnosis [14–16].

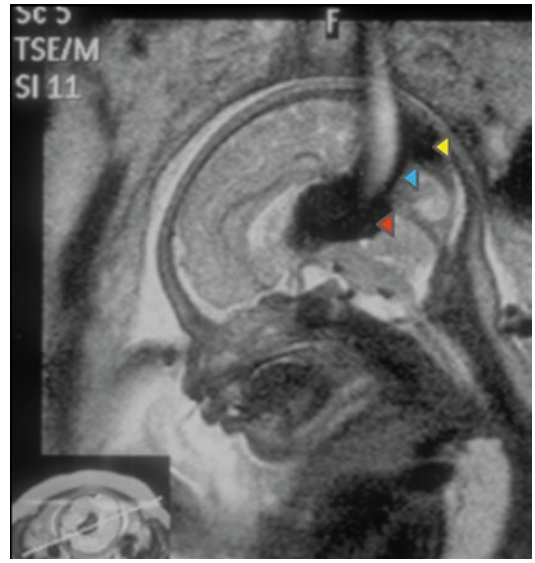

Fig. 23.2 Antenatal T2 MRI sagittal view showing a hypointense enlarged sac near the floor of the third ventricle communicating with the torcula suggestive of the vein of Galen malformation (arrowheads: red, VOGM; blue, falcine sinus; yellow, torcula)

23.5 Diagnosis

The presentation of a high-output cardiac failure in a neonate with normal cardiac anatomy on a transthoracic echocardiogram should prompt the clinician to look for a high-flow extracardiac vascular shunt in the form of a VOGM. Various investigative modalities are available for the diagnosis:

- *Prenatal ultrasound* occasionally detects the VOGM as a midline pulsatile hypoechoic lesion during the third trimester of pregnancy (28–34 weeks of gestation). Confirmation of the diagnosis is obtained with a color flow Doppler. The major significance of prenatal diagnosis is to assess the extent of the cerebral damage, to plan delivery and treatment of the lesion at a center equipped with appropriate specialties [20]. Fetal echocardiogram and antenatal MRI (Fig. 23.2) reveal the extent of cardiomegaly and neurological damage, respectively, which helps decide an appropriate further plan of management, including termination of pregnancy (abortion) [21–23].
- *Trans-fontanelle ultrasound* is done in a neonate with cardiac failure and an unremarkable thoracic echocardiogram.
- *Contrast-enhanced computed tomography (CT)/magnetic resonance imaging (MRI)* is usually the initial mode of evaluation. *MR angiography* (MRA) helps assess the type of lesion, presence of a nidus, venous drainage, and thrombosis, if any, and determine the number and the nature of arterial feeders. Imaging also reveals other features like hydrocephalus, the extent of cerebral atrophy, and calcifications and helps plan treatment appropriately (Fig. 23.3). *Susceptibility-weighted imaging (SWI)* is a recent MRI technique which allows for high-resolution imaging of the cerebrovascular architecture without the requirement of intravenous contrast administration, making it more useful in this group of patients with a higher risk

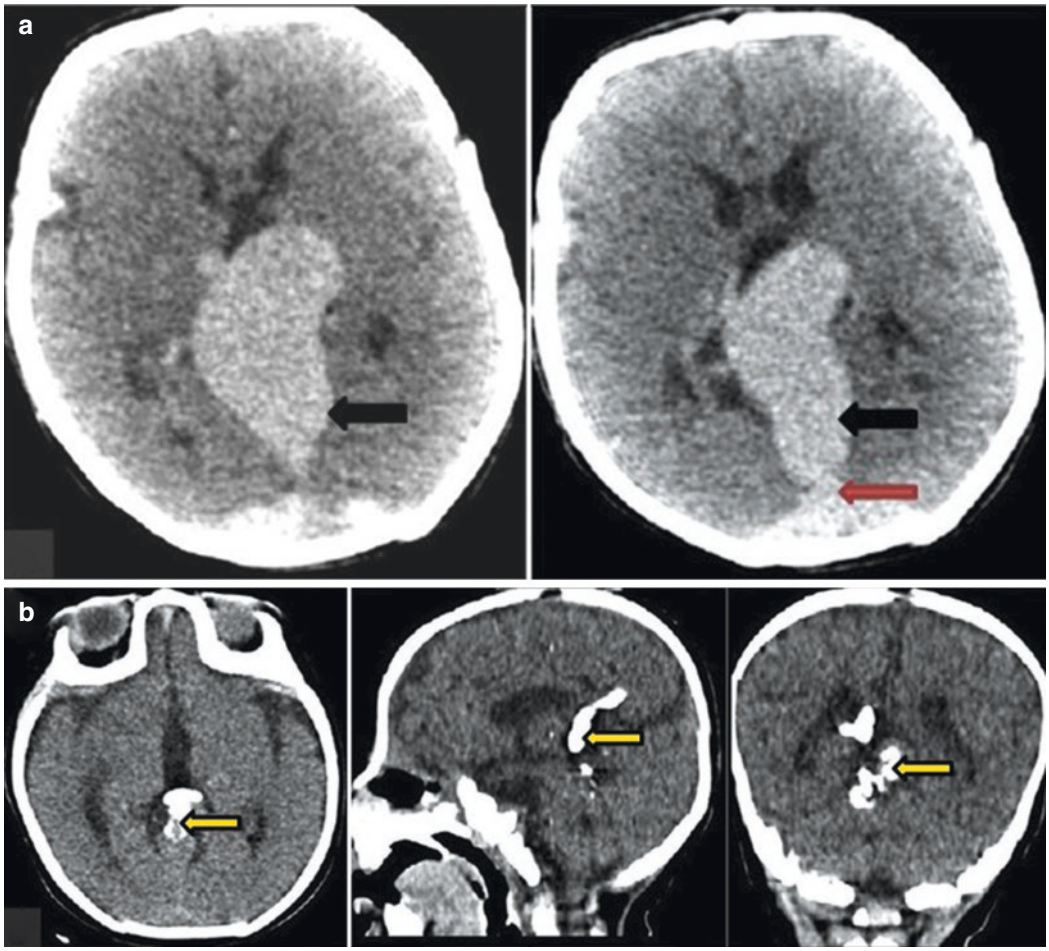

Fig. 23.3 (**a**) Non-contrast axial CT scan of the head pre-embolization showing dilated venous sac (black arrow) near the floor of the third ventricle with communication with the torcula (red arrow) and no significant evidence of brain parenchymal damage or calcifications. (**b**) Axial, sagittal, and coronal non-contrast CT showing obliteration of the venous sac post-embolization with glue cast (hyperdensity indicated by yellow arrows)

of renal injury (prematurity, multiorgan dysfunction, and multiple procedures requiring contrast agents—MRI, DSA). It also assesses the extent of cortical venous congestion, which is an indicator of cerebral parenchymal damage [24].

- *Digital subtraction angiography (DSA)* is the gold standard for the diagnosis of VOGM. It is best done at the time of embolization considering the risk of high doses of contrast dyes required for CT/MRI and DSA and the subsequent risk of renal damage and preventing the need for multiple anesthesia exposures in a neonate (Fig. 23.4).

23.6 Differential Diagnosis

The differential diagnosis of a midline hypoechoic lesion in the brain on ultrasonographic evaluation should include arachnoid cysts, porencephaly, and choroid plexus cysts. They can present with hydrocephalus, seizures, and neurodevelopmental delay, but the presence of cardiac failure effectively rules out their diagnosis. Even in the absence of cardiac manifestations, a simple demonstration of blood flow in the lesion with a color flow Doppler is sufficient [25, 26]. Further, true vein of Galen malformation has to be differentiated from a varix and an ectasia:

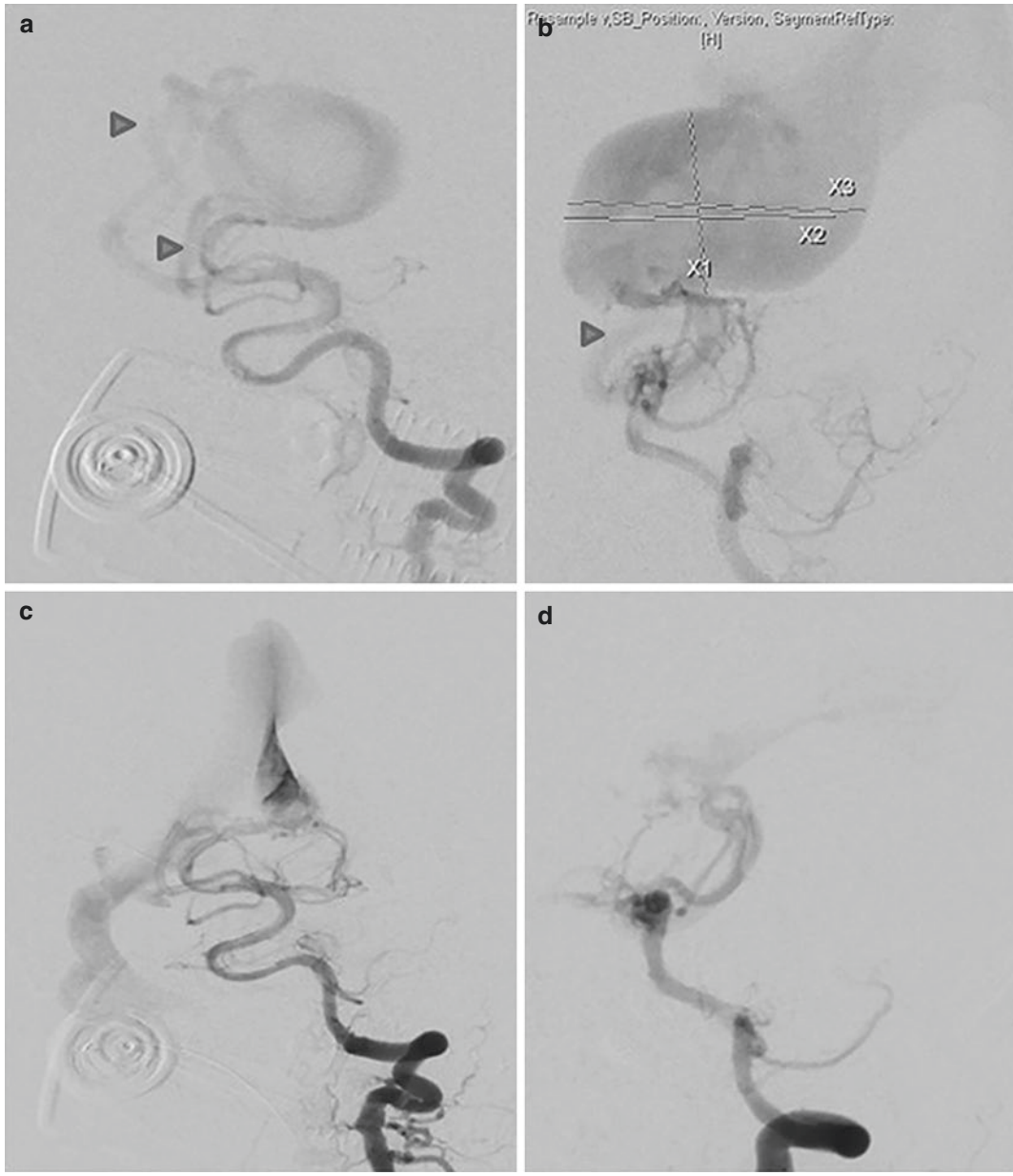

Fig. 23.4 Left vertebral angiogram: frontal (**a**) and lateral (**b**) projections showing mural-type vein of Galen malformation supplied by feeders from posterior choroidal arteries (blue arrowheads). (**c**, **d**) Post-glue embolization showing obliteration of the venous sac

- **Vein of Galen varix** represents a dilated vein of Galen without any arteriovenous shunt [17]. Neonates present with right-sided cardiac failure due to hypoxia and pulmonary hypertension. Treatment of cardiac failure generally results in the resolution of varix without the need for operative intervention [27].
- **Vein of Galen ectasia (dilatation)**: It occurs due to an outflow obstruction. The dilated vein usually drains an aneurysm in the subarachnoid space and the adjacent parenchyma. It

usually presents later in childhood with delayed psychomotor development, intracranial hemorrhages, or focal deficits depending on the degree of stenosis or thrombosis of the vein. Clinical presentation in the neonatal period is rare. Seizures and heart failure are also uncommon [28, 29].

23.7 Classification VOGM

Multiple classification systems have been proposed in the past, based on the angiographic appearance of the vessels. The most commonly used is the system proposed by Lasjaunias, which classifies the malformations into two types: choroidal and mural [30].

Choroidal type is characterized by the location of the fistula at the anterior end of the median prosencephalic vein and mural type by the fistula on the wall of the median prosencephalic vein, mostly on the inferolateral margin. The major difference between the two types is the nature of the feeding vessels. Multiple feeders in choroidal-type VOGM give the appearance of an arterial maze in contrast to the fewer feeders in mural type, which makes embolization relatively less complicated. Mural-type VOGM also presents with lesser degrees of heart failure [31].

23.8 Medical Management

Treatment of VOGM consists of initial medical management and stabilization of heart failure in the neonates before proceeding with endovascular intervention. Optimal heart failure management includes reducing pulmonary hypertension, facilitation of adequate perfusion to vital organs, and prevention of multiorgan dysfunction. Beta-adrenergic agonists (dopamine, dobutamine, adrenaline) commonly used for heart failure results in tachyarrhythmias, which can further reduce diastolic coronary perfusion and potentiate the risk of myocardial ischemia [32]. The improvement in cardiac contractility expected with these drugs may not be significant due to right ventricular dilatation. The addition of arterial vasodilators such as sodium nitroprusside (SNP) 1–5 μg/kg/min, glyceryl trinitrate (GTN) 1–5 μg/kg/min, or milrinone (0.75 μg/kg/min) to low-dose dopamine (<10 μg/kg/min) produces considerable improvement in systemic perfusion and reduces metabolic acidosis. Milrinone, in particular, reduces both systemic and pulmonary vascular resistances. Hence, it favors forward flow into the systemic circulation and reduces the afterload on the failing right ventricle, respectively [33]. It also plays a significant role in preventing neurological damage by stabilizing hemodynamic parameters in the intraoperative period and preventing cerebral hyperemia in the immediate postoperative period. Once acute heart failure is resolved, maintenance therapy with a combination of digoxin and diuretics may be initiated. Although digoxin continues to be a part of the treatment for chronic heart failure, its role in offering mortality benefits has been questioned by recent trials [34, 35]. As a general rule, diuretics and varying doses of inotropic support may be initiated in mild to moderate cardiac failure without cyanosis for initial stabilization.

23.8.1 Management of Pulmonary Hypertension [36–40]

The development of pulmonary hypertension leads to severe hypoxemia, respiratory distress, and cyanosis. An increase of pulmonary artery pressures to supra-systemic levels can occur, leading to the development of a right-to-left shunt through the patent ductus arteriosus (PDA) or an arterial septal defect (ASD). Knowledge of management of such cases posted for emergency embolization is of prime importance to the neuroanesthesiologist:

1. The medications are usually continued in the perioperative period and may result in exaggerated effects of anesthetic agents.
2. Optimization of ventilatory strategies.
3. Perioperative events causing hypoxia, hypercarbia, or acidosis can further aggravate the pulmonary vascular resistance and pose difficulties in management.

Initial management of pulmonary hypertension is oxygen therapy (pulmonary vasodilator), the delivery of which depends on the severity. Usually, these neonates are intubated and mechanically ventilated with high oxygen requirements. General management includes maintenance of normothermia, normoglycemia, correction of dyselectrolytemia (neonates are prone to hypocalcemia) and adequate intravascular volume, and initiation of inotropic support.

Conventional volume-targeted mode of ventilation with low peak inspiratory pressures (PIP) and optimal positive end-expiratory pressure (PEEP) to maintain normocarbia ($PaCO_2$: 40–45 mmHg) or mild permissive hypercarbia ($PaCO_2$ up to 60 mmHg) is preferred. The target is to correct hypoxia, recruit alveoli, and also prevent ventilator-induced lung injury. Ventilator dyssynchrony increases the work of breathing, and hence the neonates should be adequately sedated, preferably with fentanyl (1 μg/kg/h), considering its hemodynamic stability.

Pharmacotherapy includes the use of inhaled nitric oxide (iNO) at a dose of 20 parts per million (ppm). iNO is a selective pulmonary vasodilator with little effect on systemic circulation. Once initiated, the effect is observed as early as 30 min, noted by an increase in PaO_2. Phosphodiesterase (PDE) inhibitors milrinone (PDE-3) and sildenafil (PDE-5) can be used as additional therapy or as alternatives to iNO. SNP and GTN can also be used as both are NO donors and cause systemic as well as pulmonary vasodilatation.

It is recommended to maintain the patency of ductus arteriosus in this condition to allow for systemic circulation (and counter for significant diastolic steal phenomenon) by using prostaglandin infusions (PGE1 or PGE2).

23.9 Definitive Treatment

The major goal of treatment of VOGM is to prevent neurodevelopmental delay that occurs as a consequence of cerebral venous hypertension. The definitive treatment for the obliteration of the VOGM is carried out once heart failure is managed initially on presentation. Treatment options available include endovascular embolization, surgery, and stereotactic radiotherapy (Table 23.2). Surgery is associated with extremely high mortality and morbidity. Radiotherapy is less effective compared to surgery and endovascular therapy.

Table 23.2 Comparison of treatment options for the vein of Galen malformation [41–44]

	Endovascular	Microsurgery	Gamma knife
Preference	Almost all treatable cases undergo embolization	Obsolete (with the advent of modern endovascular methods)	Done only in atypical presentation or secondary to failure of endovascular treatment
Success rates (clinical outcomes)	Up to 75%	10–15%	40–50%
Advantages	1. Immediate relief 2. It can be done as an emergency procedure even in patients with severe heart failure 3. Less invasive and hence less morbidity	1. Complete occlusion and immediate relief albeit in a relatively stable (some amount of neurological/cardiac compromise) patient after the failure of embolization	1. Cure rates similar to or even better than microsurgery
Disadvantages	1. Technical difficulties in the neonate 2. Complications related to embolic materials: dislodgement, hemorrhage, etc.	1. A high rate of complications: massive blood loss, cardiac arrest 2. The requirement of hypotension, deep hypothermia 3. Complications related to positioning—sitting position	1. No immediate relief 2. Done only in the simplest angioarchitecture 3. Theoretical concerns of tumors post-radiation

23.9.1 Endovascular Embolization

Endovascular embolization of the feeder vessels is a safe treatment option with superior results. It is usually performed at around 5 months of life as the procedure may be difficult in the neonatal period, where medical management of heart failure takes precedence [3, 45]. In cases of heart failure refractory to medical therapy, emergency embolization may be performed in the neonatal age group to reduce the shunt fraction and not majorly focus on complete obliteration of the malformation [9].

The decision about emergency embolization may be considered based on the Bicetre score, a 21-point scale that assesses cardiac, respiratory, neurological, hepatic, and renal functions [46, 47]. The system involvement is graded from normal (score 5) to derangements resistant to medical management such as refractory cardiac failure, permanent neurological deficit, hypoxia despite mechanical ventilation, coagulopathy with deranged liver enzymes, and anuria (score 0). A score of more than 12 indicates well-preserved major organ function, and ideal treatment in such cases would be to delay embolization until 5 months of age. A score of 8–12 indicates worsening function and is an indication for emergency embolization. A score of less than 8 indicates a poor prognosis.

23.9.1.1 Route of Embolization

Trans-arterial, transvenous, and transtorcular approaches have been described. The transtorcular route, previously believed to yield better results, has now been replaced by the arterial route, which is safer and yields better results even with embolization of limited feeders rather than complete occlusion [28, 48]. Access is usually established through the femoral artery. In neonates, the umbilical artery can also be cannulated for the procedure (up to the third day of life). It is essential to preserve this artery, especially in cases where the prenatal diagnosis has been established [49]. The transvenous route is associated with complications like hemolysis due to flow through a partially occluded feeder and disseminated intravascular coagulation (DIC) [50, 51].

23.9.1.2 Embolic Agents

Liquid acrylic agents (n-butyl cyanoacrylate) and coils are used for embolization. Liquid agents have the advantage of being able to be injected through the microcatheter into the tortuous circulation of the neonate and the infant. The advantages are a better chance of permanent occlusion and a reduced procedure time, which is crucial in these patients. Coils, used currently, are replacing the liquid agents as they can be better maneuvered to the exact location of the malformation. There is a reduced risk of distal migration with coils. Even if it occurs, coils can be retrieved easily, unlike the liquid agents [28]. Recently, Onyx glue has been used in the endovascular embolization of cerebral AVMs, including VOGM. It is a non-adhesive slow-polymerizing agent composed of a mixture of ethylene-vinyl alcohol (EVOH) in dimethyl sulfoxide (DMSO). When placed, the occlusion of flow is achieved, not by thrombosis but by the mechanical obstruction, further reducing the risk of distal migration [52]. The injection of this agent is also better controlled compared to other agents.

23.9.2 Stereotactic Radiosurgery

Different types of radiation—gamma knife, linear accelerator, and proton beam—have been used to treat cerebral arteriovenous malformations, the main mechanism being radiation-induced intimal injury. The role of stereotactic radiotherapy is currently restricted to cases with atypical presentation and those not amenable to endovascular therapy [41, 53, 54]. The disadvantages include a longer duration of treatment required, typically months or years.

23.10 Anesthetic Considerations in Vein of Galen Malformations

The anesthetic goals in VOGM are similar to other neurosurgical procedures, such as avoidance of increase in intracranial pressure (ICP), maintenance of cerebral perfusion pressure (CPP), and cerebral oxygenation. The induction and maintenance of anesthesia should be done carefully while preventing hypotension or desaturation. The anesthetic concerns for a neonate or child posted for embolization of VOGM and preparedness are mentioned in Table 23.3.

Table 23.3 Anesthetic concerns in children with the vein of Galen malformation

Anesthetic concerns	Preparedness
• Neonatal age: low weight, susceptibility to anesthetic drugs, and hypothermia • Anticipation and management of difficult airway: macrocephaly and hydrocephalus • Managing heart failure perioperatively • Fluid management and electrolyte imbalance • Considerations of anesthesia in a remote location • Considerations in interventional neuroradiology suite • Detection and management of intraoperative complications associated with the procedure	• Strict weight-based fluid calculations and administration, titration of drugs to effect, forced air warmers, warming blankets, warm intravenous fluids • Appropriate head positioning, difficult airway cart • Continue inotropic medications, maintain hemodynamic stability, and adequate depth of anesthesia, opioids, muscle relaxants • Prevention of fluid overload, maintaining adequate perfusion, use of diuretics if required, frequent monitoring of ABG for electrolytes, lactate, and blood sugar levels • Equipment availability—oxygen, suction, resuscitation, defibrillator, and monitoring. Personnel availability: reducing chances of errors [55, 56] • Radiation safety, anti-coagulation and reversal, intravenous contrast agents, and flush [57] • Bradycardia, blood loss, and hemodynamic instability. Close communication with neuroradiologist to detect and manage complications

23.10.1 Preoperative Evaluation

A complete preoperative evaluation should be carried out in a neonate/child being posted electively to embolize VOGM. This includes eliciting an appropriate history of events from the postnatal period, including heart failure and management. Records should be sought for which may reveal evidence of multiorgan dysfunction. The child may continue to be on anti-failure medications and anti-seizure prophylaxis; details of such medications should be noted. The systemic examination should be carried out to evaluate the current status of cardiac function and identify signs of heart failure if any. Neurological examination should focus on documentation of focal deficits. The presence of macrocephaly is an indicator of a potentially difficult airway and requires proper head positioning during the anesthetic induction.

Investigations to be sought include hemoglobin levels to assess for anemia and coagulation profile to rule out possible hepatic dysfunction related to cardiac failure. Failure to thrive and recurrent infections due to malnourishment may be observed in these children, resulting in anemia, altered blood counts, and hypoproteinemia. Dyselectrolytemia may be evident following nausea and vomiting associated with hydrocephalus and raised ICP and diuretic use for cardiac failure management. Digoxin, if used, warrants caution as co-administration with diuretics may cause hypokalemia and precipitate toxicity. It may also occur due to renal failure associated with multiorgan dysfunction or contrast-induced. Though not routinely recommended, a clinical suspicion or anticipation of critical events should warrant estimation of serum digoxin levels (normal therapeutic range: 0.8–2 ng/mL) [34]. Chest roentgenogram findings include cardiomegaly with pulmonary congestion (plethora), increased right

atrial and right ventricular size, widening of the superior mediastinum, and anterior displacement of the upper airway. An electrocardiogram shows right axis deviation, right atrial enlargement, right ventricular hypertrophy, severe/fulminant heart failure, or biventricular hypertrophy [18, 58]. A transthoracic echocardiogram reveals important information for the neuroanesthesiologist, like associated congenital anomalies like septal defects and coarctation of aorta, and evidence of pulmonary hypertension. Both these lesions are hypothesized to be related to the blood flow characteristics and shunt flow related to VOGM. The common findings are dilatation of cardiac chambers suggestive of volume overload, elevated pulmonary artery pressures (pulmonary hypertension), tricuspid regurgitation, PDA, or an intracardiac right-to-left shunt [52]. The presence of a sinus venosus ASD increases the chances of paradoxical embolism, especially in the case of distal migration of liquid embolizing agent; it should be carefully considered [60].

23.10.2 Induction

The major anesthetic concerns of induction are hemodynamic responses associated with the use of pharmacological agents and those of laryngoscopy and intubation. Both inhalational and intravenous agents can be used for induction while attempting to maintain hemodynamic parameters within baseline levels. Opioids like fentanyl (1–2 μg/kg) to prevent hemodynamic responses and non-depolarizing muscle relaxants to facilitate smooth endotracheal intubation are routinely used. Also of equal concern is the relatively short apnea time and possible hypoxia in this age group.

There may be difficulty securing IV lines in neonates posted for the emergency procedure due to the peripheral vasoconstriction secondary to heart failure and its pharmacological management. In such cases, it is prudent to opt for central venous cannulation, preferably under ultrasound guidance.

23.10.3 Monitoring

Apart from the American Society of Anesthesiologists (ASA) standard monitors, namely, peripheral oxygen saturation (SpO_2), non-invasive blood pressure, ECG, capnography ($EtCO_2$), and temperature, all the patients undergoing embolization should have invasive arterial blood pressure monitoring. Central venous cannulation might pose challenges due to a pulsatile venous column due to the high-flow shunt and a bright red appearance of blood due to a higher oxygen content secondary to the lower oxygen extraction in the brain [61]. Temperature monitoring, warm IV fluids, and forced-air warming blankets are essential for preventing hypothermia and its associated complications. Urine output monitoring is an indirect estimator of volume status and should be continued in the post-procedural period as there is a risk of contrast-induced renal injury. Furthermore, the child may be on diuretics, and the possible use of osmotic agents warrants urinary catheterization and monitoring in the periprocedural period.

23.10.4 Concerns During the Procedure

During the procedure, anesthesia is maintained with a balanced technique consisting of inhalational agents, opioids, and a non-depolarizing neuromuscular blocker to maintain immobility.

23.10.4.1 Fluid Management

Fluid management is challenging due to multiple factors. Little evidence is available regarding the optimal fluid therapy during the procedure, especially in neonates with VOGM and heart failure. Various concerns are discussed below:

1. Neonates do not tolerate fluid overload in cardiac failure. The volume of contrast dye and arterial flush used during the procedure are major contributors to fluid overload. Although the literature suggests the use of up to 10 mL/kg

body weight, it is advisable to restrict the usage of contrast to a maximum of 5 mL/kg (preferably iso-osmotic) to reduce the risk of volume overload and contrast-induced nephropathy [62–64]. At the same time, pre-procedural dehydration due to fasting status and diuretics might result in hypotension and possible cardiovascular collapse due to depressant effects of anesthetic agents; blood loss due to any cause may further complicate hypotension.

2. Determining the volume of maintenance fluids using the standard Holliday and Segar method in these children does not account for the fact that the method devised was intended for use in children assuming normal urine output and energy expenditure. Energy expenditure in mechanically ventilated children reduces due to various reasons: sedation, humidification of inspired air resulting in reduced insensible water loss, and increased ADH secretion. Ultimately, the fluid requirement is reduced by approximately one-third [65, 66].
3. Choice of fluid in the perioperative period is also a matter of concern and debate over several years considering the metabolic requirements of glucose in neonatal age group, concerns of sodium handling by the immature renal system, and tonicity of fluid administered influencing cerebral edema in a susceptible population [66, 67].
4. During the procedure, the neonate usually receives fluid and infusions of inotropic medications and anesthetic agents (opioids and muscle relaxants) that add to the total volume of fluids administered.
5. Monitoring intravascular volume status through central venous pressure (CVP) is unreliable in such neonates.
6. Urine output monitoring is hindered by factors like osmotic diuresis induced by contrast media, creating a false impression of adequate volume status, while it may also precipitate renal failure.
7. Other indicators of fluid responsiveness, both static (including CVP) and dynamic, do not apply to the pediatric population, whereas no such study is available for the neonatal age group. The reason cited for this includes a more compliant thoracic wall and arterial tree, unlike adults. Studies indicate that only a few parameters are better indicators of fluid responsiveness in the pediatric population undergoing mechanical ventilation, which include plethysmography variability index (PVI) and pulse pressure variation (PPV). However, these (findings) are small studies, and the values are confounded by vasoactive medications or hypothermia causing peripheral vasoconstriction, both common to neonates with CCF undergoing emergency embolization [68–70].

With the available evidence, it may be reasonable to consider isotonic crystalloid (0.9% normal saline) as the maintenance fluid of choice and restriction of the volume administered to two-thirds of the total calculated requirement. It is essential to monitor the total volume of contrast and flush injected during the entire procedure. At the authors' institute, the maximum volume of contrast agent is restricted to 5 mL/kg and used in a diluted form (with normal saline). It might be prudent to monitor and maintain the hourly urine output at 0.5–1 mL/kg/h. This can be facilitated by a continuous infusion of diuretic (furosemide 0.1–0.4 mg/kg/h) and titrating the dose of inotropic agents to maintain the arterial blood pressure at preoperative levels or that appropriate for age. Arterial blood gas (ABG) analysis may be performed at regular intervals to monitor for electrolyte levels (sodium, base deficit), blood glucose levels (supplement if levels below 70 mg/dL), serum lactate levels (an indicator of peripheral perfusion; fluid bolus if levels are high), PaO_2 (hypoxia may be aggravated by fluid overload), and $PaCO_2$. Available dynamic indices of fluid responsiveness may be used according to institutional practice.

23.10.4.2 Other Concerns

During the procedure, hypotension may be requested before injection of the embolizing agent in order to reduce the high flow across the shunt

that can cause migration of the embolizing agent. The child with heart failure may not tolerate it and, hence, be avoided. Currently, detachable coils are deployed at the distal end of the feeding arteries to reduce the flow at the required. This avoids the need for induced hypotension [71].

The general consensus in emergency embolization is that the goal should be to achieve acceptable levels of improvement in heart failure. This can be achieved with partial embolization, which should be done in an acceptable duration (2 h). By limiting the procedure and the time is taken, certain complications like hypothermia and contrast-induced toxicity can be prevented. Also, the redistribution of cerebral blood flow after embolization can be limited to levels that can be handled by the immature cerebral vasculature [72].

23.10.5 Complications

Intra-procedural complications include bradycardia during or immediately after embolization attributed to a transient increase in ICP. Strict vigilance is required during this step, and pharmacological intervention is rarely required. Communication between the neuroanesthesiologist and the interventional neuroradiologist is essential. Other procedure-related complications include rupture of the thin-walled fistula or the feeding vessels from an iatrogenic perforation or a microcatheter rupture resulting in hemorrhagic complications [71]. Commonly encountered preventable complications include hypothermia in the interventional neuroradiology suite and fluid overload. Repeated femoral artery puncture may lead to occlusion and lower limb ischemia. It can be prevented by imaging-guided cannulation at the beginning of the procedure, and proper care, including compression and hemostasis after the procedure is over [73].

Major procedural complications are expected with larger shunts. The immature cerebral vasculature at neonatal age groups results in poor handling of the increased blood volumes that occur immediately after the procedure. Venous hypertension secondary to embolization may result in intracranial hemorrhage and perfusion pressure breakthrough. It can be prevented by doing a staged embolization and maintaining normotension postoperatively [74]. A less common but dreaded complication is distal migration of the embolizing agent resulting in pulmonary embolism. In the presence of a right-to-left cardiac shunt, a paradoxical embolism can occur too.

23.11 Post-Procedure Management

Mechanical ventilation may be required in the post-procedural period to maintain hemodynamic and respiratory stability until improvement is noted in the clinical condition [75]. Indicators of response to emergency embolization in neonates include improvement in signs of heart failure evidenced by a reduction in the requirement of inotropic support echocardiographic findings of reduced pulmonary artery pressure and closure of the right-to-left shunt (PDA) [59]. These changes may be seen in the first few hours to few days after emergency embolization. Maintaining the lower limb in a neutral position for 6 h (if femoral artery access was obtained), frequent neurological assessment and monitoring of distal pulses at regular intervals all form a part of post-procedural care [73]. In this period, the role of neuroanesthesiologist involves, and not restricted to, maintenance of adequate sedation, monitoring for clinical improvement, and weaning from mechanical ventilation.

Development of new focal neurological deficits, seizures, worsening of hydrocephalus, cerebral hyperperfusion, cerebral edema, venous infarcts, and precipitation of congestive cardiac failure are all possible in the immediate post-procedural phase [61]. Maintenance of hemodynamic stability is essential to prevent possible post-procedure complications, including cerebral venous thrombosis and hemorrhagic complications akin to perfusion pressure breakthrough.

23.12 Brain Melting Phenomenon and Hydrocephalus

The brain melting phenomenon refers to the most severe form of neurological injury in VOGM. It is characterized by progressive and extensive cerebral atrophy, white matter calcifications, hydrocephalus, and severe cognitive dysfunction that occurs secondary to cerebral venous hypertension. It may also occur after CSF diversion procedures for hydrocephalus in VOGM [23, 45]. In utero diagnosis of this condition is one of the indications for termination of pregnancy.

Hydrocephalus in VOGM is described as hydrodynamic (hydrocephalus without raised ICP) with defective CSF absorption due to immature arachnoid granulations and the increased venous sinus pressure [76]. Primary treatment of the lesion usually leads to gradual resolution of hydrocephalus. Rarely, hydrocephalus results due to obstruction of the aqueduct of Sylvius by the lesion as well. In such conditions, the child may require a CSF diversion procedure (ventriculoperitoneal shunt or endoscopic third ventriculostomy). Such procedures are usually done after primary embolization and are associated with a significant risk of hemorrhage due to the venous engorgement [77, 78]. Placement of ventricular shunts before embolization reverses the pressure gradient between the ventricles and brain parenchyma, resulting in aggravation of cerebral atrophy and white matter calcification [45, 46].

23.13 Prognosis

One of the major prognostic factors in VOGM is the age of presentation: earlier onset indicates a higher severity of the disease and probable severe brain damage in utero, decreasing the possibility of good neurological recovery [28, 79]. Near-normal neurodevelopmental outcomes have been described in children with a later age of presentation consistent with lesser degrees of cerebral damage and lower shunt flows. Treatment strategies also influence the outcome. Surgery carries the highest risk of mortality with large amounts of blood loss and poor neurological outcomes in survivors. Although considered safer, mortality rates of nearly 40% have been reported after the endovascular interventions [79, 80]. According to a recent meta-analysis, significant risk factors indicating poor outcomes include prenatal diagnosis, neonatal cardiac failure, and low neonatal Bicetre score [80].

23.14 Conclusion

Management of VOGM poses multiple periprocedural challenges and requires a multidisciplinary approach consisting of neonatologists, neurologists, pediatric cardiologists, interventional neuroradiologists, and neuroanesthesiologists. Adequate pre-procedural planning and vigilant procedural monitoring help prevent and prompt management of complications, thereby preventing neurodevelopmental dysfunctions.

Conflict of Interest None to declare.

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24 Anesthetic Concerns in Children with Brain Abscess and Congenital Heart Disease

Surya Kumar Dube and Girija Prasad Rath

Key Points

- Brain abscess is one of the serious complications encountered in children with congenital cyanotic heart disease (CCHD).
- At the time of presentation, these children may have symptoms related to both cardiac and neurological disorders, which makes anesthetic management more challenging.
- Management of brain abscess depends upon the neurological status of the patient, the location of the abscess, and the number and size of the abscesses.
- Surgical options available are burr-hole craniotomy and stereotactic aspiration, open craniotomy, or neuroendoscopic drainage of the abscess.
- Depending upon the clinical condition of the child as well as the type of surgery, the choice of anesthesia can be a monitored anesthesia care or general anesthesia.
- Multi-systemic involvement as a part of a few syndromic associations along with dehydration, electrolyte abnormality, coagulation disorders, and hemodynamic instability complicates the perioperative management further.
- A clear understanding of the pathophysiological processes involved is highly desirable for a successful outcome.

24.1 Introduction

Brain abscess is a serious complication of congenital cyanotic heart disease (CCHD). The reported prevalence of brain abscess through the hematogenous spread of microorganisms in CCHD is about 6–51% [1, 2]. However, CCHD accounts for about 13–70% of all cases of brain abscesses with identified risk factors [1, 2]. The commonly affected age group is between 4 and 7 years. The introduction of antibiotics and the advent of better diagnostic and therapeutic modalities have improved the outcome in this group of patients.

Any intracranial procedure in a child with CCHD poses a unique challenge to the anesthesiologist, who has to simultaneously manage the demands of the deranged heart and the brain without compromising the functionality of either. With a better understanding of the physiology and advent of newer monitoring modalities, anesthetic management in these children with CCHD undergoing noncardiac surgeries has been improved significantly.

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24.2 Etiopathogenesis of Brain Abscess in Children with Cardiac Disease

Various risk factors, including cardiac and dental conditions, have been described (Table 24.1) for the causation of brain abscess [3], which is relatively more common in children with CCHD (Fig. 24.1). Although any type of CCHD may cause an intracranial abscess, the most common condition associated is Fallot's tetralogy or tetralogy of Fallot (TOF) [3–6]. Other CCHDs predispose to brain abscess including transposition of great vessels, tricuspid atresia, pulmonary stenosis or atresia, and double-outlet right ventricle [1–3, 7, 8]. The common association of TOF with cerebral abscess could be because it is the most common type of CCHD and is amenable to surgical correction with a relatively greater life span in these patients. In contrast, other CCHDs are more complex cardiac abnormalities; hence, less chance of patient survival. Children with CCHD may have diminished arterial oxygen saturation, metabolic acidosis, and increased blood viscosity due to compensatory polycythemia. The altered viscosity of blood may cause focal cerebral ischemia, often in the distribution of the middle cerebral artery (MCA) [1, 7–9]. These children (with CCHD) may also develop minute encephalomalacia, a hypoperfused and hypoxic brain tissue. During dehydration or cardiac dysfunction, the hyperviscosity and decreased microcirculatory blood may exaggerate minute encephalomalacia or induce focal cerebral thrombosis; these areas subsequently serve as a nidus for bacterial infection. The hematogenous infection can spread into the systemic circulation through a right-to-left shunt bypassing the pulmonary capillary bed, which possesses phagocytic filtering action. The shunted blood with infectious organisms reaches the sites of cerebral thrombosis or encephalomalacia, which may initiate focal cerebritis and, ultimately, a cerebral abscess [12]. The hematogenous mode of spread also accounts for the subcortical and multiple numbers of abscesses often encountered in these children [1]. Brain abscess in children with CCHD has a relatively higher predilection for MCA territory. It is more common in the supratentorial compartment, and the most common site is the frontal lobe. The other possible sites for brain abscess can be the temporal lobe, parietal lobe, and occipital lobe, and in a few cases, it can be at multiple locations [1, 7, 10, 11]. The most common organisms isolated from brain abscess in patients with CCHD are *Streptococcus viridans*, microaerophilic streptococci, anaerobic streptococci, and occasionally *Haemophilus* species [12, 13]. However,

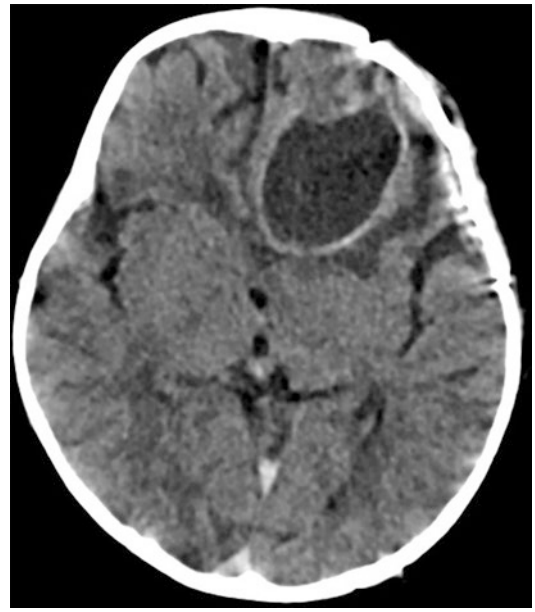

Fig. 24.1 Computed tomographic scan of the brain of a 10-year-old boy shows a large well-defined cystic lesion with thin enhancing walls (ring enhancement) in the left frontal lobe suggestive of cerebral abscess

Table 24.1 Risk factors for the formation of brain abscess [3]

• Congenital heart disease
• Sinus and otogenic infections
• Poor dental hygiene
• Complications from dental procedures
• Immunosuppression
• Neurosurgical interventions
• Penetrating skull injury
• Comminuted fracture of the skull
• Congenital lesions of the head and neck (e.g., dermal sinuses)
• As a complication of meningitis (rare)

anaerobic organisms and polymicrobial infections may also contribute toward the development of brain abscess.

24.3 Clinical Presentation and Management of Brain Abscess

24.3.1 Clinical Presentation

As reported in the literature, the peak incidence of brain abscess in children with CCHD is in between 4 and 7 years [7]. These children may present with signs and symptoms of both CCHD and brain abscess. Besides, they may have clinical presentations of other associated congenital anomalies as well. The classic clinical triad of fever, headache, and the focal neurologic deficit is relatively uncommon and is present in about 16–25% of brain abscess cases [14–16]. Usually, the presentation of brain abscess is because of mass effect, and often the signs and symptoms of systemic infection are not evident. The most common presentations are headache and vomiting secondary to increased intracranial pressure (ICP). Seizures have been reported to be present in 10–50% of cases [1, 17, 18]. Depending upon the size and location of the abscess, children can have focal neurological deficits. Some children may present with altered sensorium with nuchal rigidity because of increased intracranial mass effect or intraventricular rupture of the abscess. The clinical signs are papilledema, lateralizing signs such as hemiparesis or cranial nerve palsies, exaggerated deep tendon reflexes, pupillary signs, and aphasia. Third or sixth cranial nerve palsies, anisocoria, and papilledema may indicate increased ICP [19, 20]. The clinical presentations due to various CCHDs are summarized in Table 24.2.

Tetralogy of Fallot (TOF) is one of the most common CCHD associated with brain abscess. It comprises four cardiac abnormalities: right ventricular outflow obstruction, right ventricular hypertrophy, ventricular septal defect, and dextroposition of the aorta. The clinical presentation of TOF is described in Table 24.2. Plain X-ray chest may show the characteristic boot-shaped heart (coeur en sabot in French) with upturned cardiac apex due to right ventricular hypertrophy, increased concavity of pulmonary artery segment, and enlarged aorta along with decreased pulmonary vascularity causing oligemic lung fields (Fig. 24.2). Uncorrected TOF children may have a high mortality rate, but current medical and surgical advancements enable many patients to survive longer. The different perioperative problems encountered in a patient with TOF are cyanotic spells, coagulation abnormality secondary to polycythemia, cardiac failure, hemodynamic instability, and electrolyte and acid-base abnormality.

24.4 Management Options

Management of brain abscess in children depends on the patient's neurologic status, location, number, and size of the abscess. The children are usually started with intravenous (IV) broad-spectrum antimicrobial agents, which are continued until appropriate antibiotics are initiated based on the pathogens identified after culture and sensitivity established from the intraoperative specimens [17]. Patients with surgically inaccessible lesions, early cerebritis, abscesses with a size of less than 2 cm, multiple small abscesses, or medical comorbidities are treated with nonsurgical means, and serial imaging studies are conducted to assess the effectiveness of antibiotic therapy [3, 17, 23, 24]. The duration of IV antimicrobial therapy is usually 4–6 weeks in immunocompetent patients and longer in immunosuppressed patients. The role of corticosteroids in brain abscess management is controversial since steroids are known to inhibit capsule formation around the abscess, that limits the brain abscess. Steroids are usually considered in patients with considerable mass effect secondary to significant cerebral edema causing neurological deficits and/or impending herniation [25]. The role of prophylactic anticonvulsant medication in these patients is not well defined. Short-term prophylactic use of anticonvulsants in children with brain abscess involving cortical structures is often practiced. However, some cen-

Table 24.2 Signs and symptoms of congenital cyanotic heart diseases [21, 22]

Disease(s)	Clinical presentation(s)
Tetralogy of Fallot (TOF)	• Easy fatigability, dyspnea on exertion, frequent squatting, cyanotic spells • Cyanosis (depends on the degree of right ventricular obstruction), cyanotic spells, ejection systolic murmur, heard at left upper sternal border • Chest X-ray shows boot-shaped heart (Fig. 24.2) with decreased pulmonary vascular markings; ECG characteristics of right axis deviation; right bundle branch block pattern, if tetralogy is repaired
Transposition of the great arteries (TGA)	Easy fatigability, dyspnea, poor feeding, lethargy The degree of cyanosis and auscultatory findings is different depending on the types of cardiac defect. Children may present with heart failure. (a) **TGA with intact ventricular septum**: Central cyanosis. Cyanosis is at birth. Soft murmurs or none at all. S_1 is usually normal in these patients. S_2 is single and accentuated (b) **TGA with large ventricular septal defect (VSD):** Cyanosis may be mild initially, although it is usually more apparent with stress or crying. Increased right ventricular impulse; a loud, single S2; usually no systolic murmurs (c) **TGA with VSD and left ventricular outflow tract obstruction:** Cyanosis is prominent at birth. A single S2 and a systolic ejection murmur may be present (d) **TGA with VSD and pulmonary vascular obstructive disease:** A loud, single S2 is present. Cyanosis is usually present and can be progressive despite palliative therapy. Chest X-ray is non-specific. Sometimes "egg on string" appearance due to anteriorly placed aorta compared to the main pulmonary artery
Tricuspid atresia	• Cyanosis at birth • Easy fatigability, dyspnea, tachypnea, poor growth, and development • Evidence of right heart failure, older children, exhibit digital clubbing • S1 often normal and S2 often single; murmur with variable intensity heard, best heard at the lower left sternal border • Chest X-ray may show moderate to massive right atrial enlargement; pulmonary vascular markings are usually decreased • ECG shows left axis deviation with tall peaked P waves (secondary to right atrial hypertrophy). Left ventricular hypertrophy is seen in almost all cases, and right ventricular influence on ECG is usually little or absent
Pulmonary atresia	• Clinical features depend upon the presence or absence of VSD • Cyanotic at birth if the ventricular septum is intact. May present with cyanosis later in the presence of VSD depending upon the collateral blood flow channels • Systolic murmur may be heard at the pulmonary area; a pansystolic murmur may be heard because of associated tricuspid insufficiency • Chest X-ray shows from small to markedly enlarged heart depending on the degree of tricuspid insufficiency. Right atrial enlargement may be present in case of significant tricuspid insufficiency • ECG shows left axis deviation
Double outlet right ventricle (DORV)	• Always associated with VSD • If VSD is subaortic and without pulmonary stenosis (PS), the clinical picture resembles that of a large VSD • If a subaortic VSD and pulmonic and subpulmonic stenosis are present, the physiology and the clinical features resemble that of TOF • If VSD is subpulmonic, the presentation resembles TGA with VSD

ters reserve the use of anticonvulsant medications only for children who had a seizure at the time of presentation [3].

Operative management is beneficial in terms of diagnostic and therapeutic context. The different surgical options available include burr-hole craniotomy and stereotactic aspiration, open craniotomy, or neuroendoscopic drainage of the abscess. Cerebral hemispheric lesions of <2.5 cm in diameter may be managed with antibiotics and stereotactic aspiration to document causative microorganism(s). However, a lesion of more than 2.5 cm diameter may require stereotactic aspiration or surgical excision, depending upon the location of the abscess (within or near the eloquent brain cortex). For deep-seated abscesses

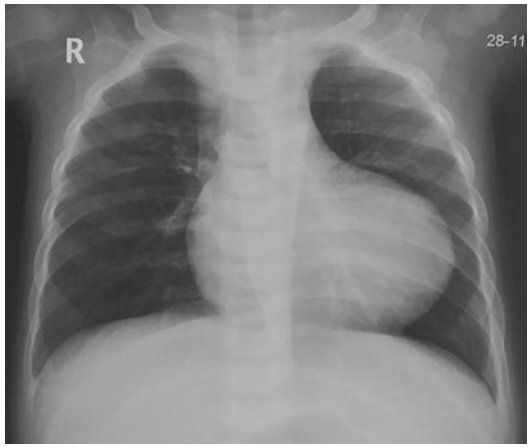

Fig. 24.2 Plain chest X-ray of a child with Fallot's tetralogy shows a typical boot-shaped heart with upturned cardiac apex and hyperlucent lung fields

and/or abscesses nearer the eloquent brain areas, stereotactic aspiration may be more appropriate. Large abscesses with a significant mass effect should undergo decompression as early as possible. Additionally, intraventricular rupture of an abscess usually needs surgical debridement, ventricular drainage, and the use of systemic and intraventricular antimicrobial agents.

- **Stereotactic Aspiration**

  It involves image-guided stereotactic aspiration followed by irrigation of the abscess cavity with antibiotic solution. It can be conducted at any stage of evolution of the abscess, and it can help obtain samples for cultures [26]. The advantage of this technique is that it allows access to multiple and deep-seated abscesses, it has a low complication rate, it permits a minimal craniotomy, and it allows multiple aspirations [27, 28]. The reported complications of this technique are the formation of an intracerebral hematoma or intraventricular rupture of the abscess [17].
- **Craniotomy and Aspiration**

  This approach is beneficial if the abscess is superficial and is located close to the brain surface. A miniature craniotomy or burr hole may be used for abscess drainage. It may be helpful in cases of failure of resolution of the abscess following multiple aspirations [24]. The shortcomings of this approach are the unsuitability of its use for lesions in the early stage or lesions located within or near the eloquent cortex and relatively higher surgical risk in children with comorbidities/heart disease [17]. Regarding the surgical management of brain abscess near the eloquent cortex, the recent reports have highlighted the feasibility for awake craniotomy in patients with CCHD or severely compromised cardiac function [29, 30].
- **Neuroendoscopic Aspiration**

  This is another approach that is gaining popularity among neurosurgeons. Unlike the stereotactic approach, neuroendoscopic aspiration permits the direct visualization of the abscess and aspiration of its contents. This technique is speculated to be useful in the management of multiloculated abscesses [17, 31].

24.5 Anesthetic Considerations

Any intracranial procedure in a child with CCHD poses a unique challenge during anesthesia. An equilibrium must be set up between prerequisite of the heart and brain without further imperiling the functions of either. Children with CCHD and brain abscess have various associated problems concerning the underlying cardiac disease as well as ongoing medications. The problems are mainly related to chronic hypoxemia and its resultant manifestations in the forms of delayed milestones of development and growth retardation, persistent breathlessness, easy fatigability, recurrent pulmonary infections, fever, metabolic abnormalities, and multi-organ failure. There may be a neurological sequelae secondary to cerebral ischemia and cerebral abscess. Also, children of TOF with pulmonary stenosis or pulmonary atresia may have other structural and functional abnormalities due to associated syndromes such as Down's syndrome, DiGeorge syndrome, Velocardiofacial syndrome, and conotruncal anomaly face syndrome.

24.6 Preoperative Evaluation

It involves the evaluation of a neurologic patient with particular attention to its cardiovascular system. Patients with CCHD are invariably cyanotic, and the state of cyanosis does affect the other systems, which require careful consideration. It is desirable to include the data regarding the type of lesion, previous surgery, previous cardiac catheterization, or echocardiography in the history related to the cardiovascular system. Details of previous complications related to heart disease and history of heart failure, arrhythmias, medication changes, and residual shunts should be taken into account. Arrhythmia and heart failure are the two most important cardiac issues in patients with congenital heart diseases (CHDs) [32]. Children who underwent palliative procedures for cyanotic heart diseases may present with pathophysiological abnormalities in the form of the residual shunt, heart block, or arrhythmias. Various arrhythmias described in this context include atrial fibrillation, atrial flutter, supraventricular tachycardia, ventricular arrhythmias, and bundle branch block(s) [32]. The ECG after repair of tetralogy typically shows a right bundle branch block (RBBB) pattern in the majority of the children [33]. There is a possibility of complete heart block among a few, which the anesthesiologist should be aware of. A significant cardiac arrhythmia may lead to life-threatening hemodynamic instabilities and even sudden cardiac death during the perioperative period. Hence, a pediatric cardiologist's opinion should be sought to ascertain the child's current status whenever in doubt. It would also help decide appropriate antimicrobial prophylaxis to prevent endocarditis, optimize cardiac medication(s), help interpret ECG in doubtful situations, or even get a bedside echocardiographic evaluation of cardiac function/abnormality.

It is prudent to enquire about the growth pattern, exercise tolerance, and ability to feed, as these are considered general measures of adequate cardiac compensation. A child with a decreased cardiac reserve may not be able to keep up with peers/siblings. Patients with CCHD may have associated heart failure as a result of volume overload or arrhythmia. In infants, poor feeding and poor weight gain are usual manifestations of heart failure, whereas the older children may present with tachycardia, respiratory difficulty (tachypnea or dyspnea), poor exercise tolerance, cool extremities, cardiac gallops, and rales [32].

Other relevant history like history of cyanosis, fainting spells, adoption of unusual position like squatting, and predisposing factors that cause hypercyanotic spell will be helpful. Apart from the cardiovascular system examination, a focused neurologic examination, which includes assessing the level of consciousness, motor/sensory abnormality, pupillary responses, and equality and cranial nerves function, must be carried out. The preoperative investigations should include routine hemogram, hematocrit, serum electrolytes, liver, renal function tests, coagulation study, ECG, chest X-ray, and recent echocardiography. The preoperative evaluation should also include an inquiry about the dose and duration of ongoing medications as well as any complication related to those medications.

24.7 Preoperative Optimization

The children of CCHD and brain abscess have certain conditions that need to be optimized before surgery.

24.7.1 Dehydration and Electrolyte Abnormality

These children often present with dehydration secondary to vomiting, fever, poor oral intake, use of hyperosmolar agent/diuretics, excessive heat, and diarrhea due to various reasons. Dehydration can exacerbate CCHD-induced blood hyperviscosity. In children, skin turgor, moistness of mucous membrane, and urine output are more reliable indications of volume status than are blood pressure and heart rate. A hypovolemic child with CCHD can have profound hemodynamic alteration during anesthetic induction and surgical positioning. Hypovolemia leads

to hypotension, which might decrease cerebral blood flow, especially when combined with positive pressure ventilation. A lethargic patient will become more alert with fluid therapy, and a more accurate preoperative neurologic assessment can be made. Hence, it is essential to identify and aggressively manage dehydration. Besides, prolonged preoperative fasting should be avoided, and hyperosmolar agents should be administered cautiously.

Efforts should also be made to correct metabolic and electrolyte abnormalities. Children with heart failure and on diuretic medication may have preoperative electrolyte abnormalities; severe hyperchloremic metabolic alkalosis may occur in some children [32]. There may be the presence of hypokalemia and hypocalcemia, which predispose to arrhythmias. Hence, correction of calcium and potassium abnormalities and avoidance of hyperventilation may be emphasized [32]. If the child received digoxin, the decision on its continuation should be consulted.

24.7.2 Coagulation Abnormality

Children with CCHD may have different coagulation abnormalities such as thrombocytopenia, abnormal platelet function, coagulation factor deficiencies due to impaired hepatic function or vitamin K deficiency, primary fibrinolysis, and disseminated intravascular coagulation (DIC) [34, 35]. The exact reason for the coagulation abnormality is still not known. However, polycythemia and associated hyperviscosity are the major contributing factor for the pathogenesis of coagulation abnormalities [35, 36]. Congenital coagulation disorders like von Willebrand factor and factor XII deficiency may present in these children, further complicating the bleeding problems. Every effort should be made to detect and correct hemostatic abnormalities with suitable therapy to minimize perioperative blood loss. The different methods adopted for improving coagulation status in these children include phlebotomy, administration of blood components such as fresh frozen plasma (FFP), platelet concentrate or cryoprecipitate, and pentoxifylline [35]. Severely cyanotic patients with hematocrit ≥60% may develop coagulopathy, and preoperative phlebotomy may benefit them [34, 35]. Vitamin K supplementation helps in the normalization of coagulation abnormalities in the presence of normal hepatic function. However, in cases with hepatic dysfunction, there will be qualitative and quantitative defects in coagulation factors; hence, vitamin K supplementation is unlikely to be beneficial.

24.7.3 Hyperviscosity Syndrome

Children with CCHD have a compensatory increase in red blood cell (RBC) mass due to renal release of erythropoietin as an adaptive response to chronic hypoxemia. Under normal circumstances, the serum erythropoietin level returns back to baseline values once there is a sufficient increase in RBC mass and hemoglobin concentration. However, in cases of CCHD, an exaggerated response is observed due to the continuing release of erythropoietin owing to the failure of tissue oxygen concentration to improve beyond a limit. Hence, there is a further rise in hematocrit without increasing blood volume; it increases the blood viscosity even further [37]. The continued increase in erythrocyte mass leads to decompensated erythrocytosis and produces various harmful effects by compromising tissue oxygen delivery. The resultant hyperviscosity syndrome is characterized by headache, faintness, dizziness, fatigue, depressed mentation, paresthesia of limbs, blurred, or double vision [38].

Iron deficiency anemia is another concern in children with CCHD. In infants and children, the usual causes are nutritional deficiency, repeated phlebotomy, epistaxis, or hemoptysis. Iron deficiency causes a change in RBC shape from normal biconcave to micro-spherical, thereby reducing its deformability. Reduced deformability of RBCs prevents the normal passage of RBCs through the microcirculatory bed [39, 40]. Iron deficiency and polycythemia together can seriously impact the tissue perfusion because of increased viscosity. It also leads to symptoms of hyperviscosity at a level of packed cell volume

much lower than that known to produce these symptoms [35, 41].

Phlebotomy is beneficial for patients with hematocrit levels of >65% with symptomatic hyperviscosity when dehydration is not the cause [34, 37]. Dehydration is detrimental in children with CCHD as it may lead to a rapid rise in the hematocrit level with clinical features of hyperviscosity. The rational approach is volume repletion rather than phlebotomy in those patients. Phlebotomy is generally not required in patients with compensated erythrocytosis and, if not appropriately employed, may result in symptomatic iron deficiency and an increase in whole blood viscosity [35]. Detailed description of phlebotomy is beyond the scope of this chapter. However, in simpler terms, phlebotomy involves gradual extraction of blood from the circulation through a large-bore venous catheter in a small aliquot. The resultant volume depletion is replenished with an equivalent volume of colloid or isotonic saline solutions. It is advisable to check for the coagulation parameters before phlebotomy and 24 h later [35]. Phlebotomy without volume repletion can cause dehydration and may adversely affect tissue oxygenation, which is not advisable [42]. Phlebotomized blood can be appropriately stored for the possible need of an autologous transfusion [32]. If hyperviscosity symptoms persist even after phlebotomy, a possible association of iron deficiency has to be ruled out [35].

24.7.4 Cyanotic Spell

Cyanotic spells are the hallmarks of severe TOF described with varied synonyms such as *hypoxemic*, *anoxic*, *or hypoxic spells*, *hyper-apneic spells*, *tetralogy or tet spells*, *blue spells*, etc. The anesthesiologist may encounter these episodes during the perioperative period. The spells may be manifested as sudden onset of cyanosis or deepening of cyanosis, sudden onset of dyspnea, alterations in consciousness (irritability/syncope), and decreased intensity or even disappearance of the systolic murmur [21]. These episodes may begin in the neonatal period, but most commonly, they start at the age of 4–6 months of life [21]. These spells occur due to increased right-to-left (R-L) cardiac shunt triggered by an increased sympathetic activity resulting from crying, agitation, feeding, defecation, or fright [21, 43]. The exact pathophysiology of these spells is poorly understood. It is usually initiated with paroxysmal hyperpnea that leads to increase work of breathing, causing increased oxygen consumption. The venous return also increases due to decreased intrathoracic pressure by the hyperpnea. Associated hypoxia prompts a fall in systemic vascular resistance (SVR) that increases the R-L shunt. There is also associated infundibular spasm or constriction, which results in increased pressure in the right side of the heart leading to the R-L shunt. During a spell, the infant will appear pale and limp secondary to poor cardiac output [43, 44]. Different management strategies are suggested during a cyanotic spell (Table 24.3). However, β-adrenergic agonists are absolutely contraindicated, as they increase cardiac contractility, which may lead to further infundibular narrowing. Prophylactic use of propranolol 1 mg/kg orally every 4 h is recommended, which may prevent subsequent cyanotic spells [21].

24.7.5 Oxygen Therapy

Erythrocytosis is uncommon in children with CCHD if systemic arterial oxygen saturation is more than 85% [45]. Oxygen supplementation is beneficial in them as it improves saturation and prevents an increase in blood viscosity. Oxygen should be supplemented during severe cyanosis episodes and short intervals of hypoxia, which some children may develop during crying or straining. Facemask oxygenation is effective, but it may not be acceptable to a few children leading to further excitements, which may predispose to a cyanotic spell. Oxygen hood is more acceptable and remains an alternative in such situations.

Table 24.3 Management of cyanotic spells [21, 43]

Medication(s)/maneuver(s)	Rationale(s)
Supplementation of 100% oxygen	It alleviates hypoxemia
Knee-chest position or compression of the femoral artery	Transiently increases SVR and prevents R-L shunt
Morphine sulfate (0.05–0.1 mg/kg)	Some degree of sedation, depressant action on respiration, and hyperpnoea
Sodium bicarbonate (1–2 mEq/kg)	Correction of metabolic acidosis helps normalize SVR and lessen hyperpnoea
Phenylephrine (5–10 μg/kg IV or 2–5 μg/kg/min as an infusion)	Increases SVR and reduce R-L shunting
β-Adrenergic blockers like propranolol (0.1 mg/kg) or esmolol (500 μg/kg followed by an infusion of 50–300 μg/kg/min)	Reduce cardiac contractility, thereby reducing infundibular spasm Reduced heart rate would improve diastolic filling, increase heart size, and increase the diameter of the right ventricular outflow tract
Isotonic crystalloid solution	Enhances preload and increases heart size, which may further increase the diameter of the right ventricular outflow tract

24.7.6 Antibiotic Prophylaxis

As per the American Heart Association (AHA) recommendations, antibiotic prophylaxis to prevent infective endocarditis (IE) is required for patients with different conditions (Table 24.4) [46]. Hence, appropriate IE prophylaxis should be given to the children with brain abscess, if indicated.

24.8 Preoperative Preparation

The general fasting rule of 2 h for clear liquids, 4 h for breast milk, 6 h for formula feeds, and 8 h for solid food is acceptable for children with congenital heart disease. Prolonged preoperative fasting should be avoided as dehydration can rapidly increase the hematocrit level, leading to symptomatic hyperviscosity. There are several benefits of starting IV fluid and oxygen supplementation. Glycopyrrolate causes less tachycardia than atropine and hence is preferred in patients with cardiac disease when the anti-sialogogue effect is desirable. Corticosteroids and anticonvulsants should be continued during the perioperative period. Generally, sedative premedicants are avoided in a child with an altered level of consciousness. For children with heart disease undergoing the neurosurgical procedure, oral midazolam is useful, which may induce sedation with little cardiovascular or respiratory effects compared to opiates [47]. There are several benefits of premedication with morphine in patients with TOF. However, morphine is contraindicated in neurosurgical patients due to its respiratory depressant action, which causes retention of carbon dioxide leading to increased ICP.

Table 24.4 American Heart Association (AHA) recommendations for conditions requiring antibiotic prophylaxis to prevent infective endocarditis [46]

- Patients with prosthetic cardiac valves
- Patients with prior infective endocarditis
- Patients with unrepaired or palliated cyanotic congenital heart disease including shunts and conduits
- Patients with congenital heart disease repair with prosthetic material or device placed by surgery or catheter intervention during the first 6 months after placement
- Patients with congenital heart disease repair with residual defect at the site or adjacent to the site of prosthetic patch or device that inhibits endothelialization
- Cardiac transplantation recipients who develop cardiac valvulopathy

24.9 Anesthetic Techniques

As compared to the healthy patient population, a higher rate of perioperative complication and/or mortality has been observed in children with CCHD undergoing noncardiac surgeries. The factors responsible include age <2 years, emer-

gency surgery, children having severe cyanosis, poorly compensated congestive cardiac failure, and major cardiac anomalies [34, 48, 49]. Different surgical options available for brain abscess management are stereotactic aspiration, craniotomy, and neuroendoscopy. Likewise, the anesthetic techniques can be either general anesthesia (GA) or monitored anesthesia care (MAC). The choice of anesthetic technique depends on the clinical condition of the child as well as the type of surgery. Among the children who undergo aspiration of intracerebral abscess are those with significant midline shift or cerebral edema or those who had cyanotic spells, and these children may have relatively higher perioperative mortality or morbidity [50, 51]. Anxiety, pain, excessive cry, and struggle may trigger a cyanotic spell or further increase ICP. MAC is usually not a preferred option in children as they are uncooperative and psychologically not prepared. However, awake craniotomy can be an option for managing brain abscess in eloquent brain areas among cooperative adolescents [29, 30]. The key to successful management, in this case, is to have a thorough understanding of the physiological derangements and to modify the anesthetic techniques as per the need. In children with prior respiratory abnormalities, altered consciousness, significant midline shift, mass effect, cerebral edema, and deep-seated abscess, the choice is GA with controlled ventilation.

Standard monitors such as noninvasive blood pressure measurements, ECG, pulse oximetry, temperature monitoring, capnography, and arterial blood gas analysis are normally utilized. In addition, invasive monitoring such as arterial blood pressure, central venous pressure (on a case-to-case basis), and transesophageal echocardiography (TEE) may be needed depending upon the type of surgery. The anesthetic goals in such children should be the maintenance of oxygenation (both cerebral and systemic), hemodynamic stability, and cerebral perfusion pressure; prevention of further rise in ICP; prevention and management of cyanotic spells; and management of perioperative arrhythmias. The target also should be to decrease the R-L shunt as much as possible and avoid factors that increase systemic oxygen demand [32, 43]. This can be achieved with the maintenance of intravascular volume, systemic vascular resistance, and adequate hydration, provision of satisfactory sedation and analgesia, and avoidance of additional increase in pulmonary vascular resistance.

Anesthetic management of children with uncorrected CCHD requires a meticulous understanding of the factors that might influence the extent of R-L intracardiac shunt. An increase in R-L shunt may cause a decrease in pulmonary blood flow, thereby causing arterial hypoxemia. Factors responsible for the decrease in SVR, like volatile anesthetic agents, vasodilators, histamine-releasing drugs, β-adrenergic receptor agonists, α-adrenergic receptor antagonists, and hyperthermia, should be avoided. The anesthesiologist should have immediate access to medications that increases SVR, such as phenylephrine. Different neurosurgical positions may produce different effects on the SVR, which should be dealt with appropriately. An increase in PVR causes an increase in the magnitude of the R-L shunt. Hence, the factors that increase PVR, such as hypoxia, hypercarbia, hypothermia, excessive airway pressure, and metabolic acidosis, should be avoided. Increased myocardial contractility is another important factor that has to be avoided. It may increase resistance to right ventricular outflow due to resultant infundibular obstruction, thereby increasing the magnitude of R-L intracardiac shunt [43, 52, 53]. Hence, β-adrenergic receptor agonists are absolutely contraindicated. In fact, it is advisable to continue the β-blockers till the induction of anesthesia in children who received it to prevent cyanotic spells [52]. One should be aware of the possibility of migration of air bubbles into the systemic circulation. Therefore, every effort should be made to prevent the entry of even the slightest of air into the systemic circulation. Due to the presence of an R-L shunt, the onset of action of intravenously administered drugs may be quicker. Hence, IV anesthetics need to be administered in a slow, titrated manner. On the contrary, minimal amounts of the inhaled anesthetic agents reach the systemic circulation, thus delaying anesthesia

Table 24.5 Effects of different anesthetic agents on systemic and pulmonary vasculature [53–59]

Agent	Effect on SVR	Effect on PVR
Propofol	Decrease	No effect/decrease
Ketamine	Increase/no effect	No effect/decrease
Thiopentone	Decrease	Increases
Etomidate	Decrease[a]/minimal effect	Minimal/no effect
Dexmedetomidine	Increase	Decrease/no effect
Midazolam	No/minimal effect	No/minimal effect
Morphine	Decrease	Increase/no effect
Fentanyl	Decrease/no effect	No effect
Nitrous oxide[b]	No effect	No effect
Potent volatile agents	Decrease	Decrease/no effect

[a]Etomidate also causes a decrease in SVR, but as compared to propofol and thiopentone, the magnitude of the decrease is less, and the SVR returns to baseline values faster than thiopentone and propofol
[b]Nitrous oxide has little effect on pulmonary hemodynamics in infants, with or without pulmonary hypertension. However, it increases PVR in adults with pulmonary hypertension

induction. Different anesthetic agents have different effects on systemic and pulmonary circulation (Table 24.5).

The evidence in favor of any particular anesthetic agent in children with CCHD and brain abscess is limited. However, the anesthetic technique should be designed in such a way that it prevents a sudden remarkable change in intracardiac shunt, myocardial contractility, SVR, PVR, ICP, or compromise in CPP. Intravenous induction is favorable owing to delay in the onset of action of inhaled agents and potential cardiovascular depressant effect of potent inhalational anesthetics, which are to be utilized at high concentrations during induction. Hence, it is wiser to obtain IV access before induction of anesthesia, if possible. Based on its favorable effects on the SVR and PVR, ketamine is the ideal agent for induction anesthesia in children with CCHD. It is the induction agent of choice when a decrease of SVR is unwarranted and also in children with pulmonary hypertension [60]. However, ketamine is not a preferred agent in neuroanesthesia practice, especially in cases where the ICP is raised or the intracranial compliance is altered. Nevertheless, in the absence of increased ICP or altered cerebral compliance, ketamine can safely be used. Etomidate is a good alternative with its less deleterious cardiovascular effects (Table 24.5). The concerns of adrenal suppression with etomidate are not significant in clinical practice, and the effect usually lasts up to 24 h [56, 61]. It is worthwhile noting that whatever induction agent is used, it has to be injected slowly with titrated doses in order to avoid sudden hemodynamic changes.

For the maintenance of anesthesia, both isoflurane and sevoflurane can be used; they have a minimal effect on myocardial contractility or shunt fraction [60]. Halothane decreases myocardial contractility and maintains SVR and hence a good agent for these patients [43]. However, it has unfavorable effects on cerebral physiology and ICP, and hence it is not preferred in patients with intracranial pathology. There are limited data regarding the effect of desflurane in children with CCHD. The use of nitrous oxide is controversial in the setting of increased ICP or deranged intracranial compliance. There are chances of paradoxical air embolism in these children; hence, nitrous oxide should not be used, particularly when there is an obvious risk of VAE s (e.g., right-to-left shunt). In cases of TGAs, delivery of high-inspired oxygen concentration is desirable, and hence nitrous oxide is better to be avoided. Opioids or benzodiazepine can be used to maintain anesthesia with precautions to avoid decrement of systemic blood pressure and SVR. Muscle relaxants with histamine-releasing potential are to be avoided as they may decrease SVR. Pancuronium is considered a good muscle relaxant in these children as it minimally affects systemic blood pressure and SVR. However, its prolonged duration of action is undesirable in cases where early recovery is necessary.

Controlled mode mechanical ventilation is preferred, and care should be taken to avoid excessive positive airway pressure, which may increase the resistance to pulmonary blood flow. Hypercarbia has deleterious effects on cerebral physiology and increases PVR; hence, it should be avoided. Normocarbia is desirable, and prolonged hyperventilation is also avoided. Dehydration is detrimental to these children and adequate intravascular volume has to be maintained. Isotonic crystalloid remains the maintenance fluid of choice. Blood and blood products may be required depending upon the magnitude of blood loss. Whenever possible fresh-packed RBCs are to be used. As these children present with erythrocytosis, blood replacement is not considered until 20–25% of intravascular blood volume is lost [34, 52]. Ideally, glucose-containing fluid is avoided in a neurosurgical setting, but hypoglycemia is undesirable. Glucose supplementation is required in sick pediatric patients, and it is better to monitor intraoperative blood glucose levels for guidance. Hyperosmolar agents are often used in neurosurgical settings which can cause dehydration if the intravascular volume is not well maintained. In addition, there are certain hemodynamic effects of mannitol infusion, which may be undesirable. The data on the use of hypertonic saline in this subset of patients lacks any recommendation. It is prudent to keep a watch on hemodynamic parameters during the administration of hyperosmolar agents. Both hypo- and hyperthermia are considered harmful; normothermia should be ensured with appropriate measures. If there are no concerns, early tracheal extubation is preferred to prevent further reduction in pulmonary blood flow due to prolonged mechanical ventilation.

Two serious intraoperative complications need special mention in these cases: VAE and intraoperative cyanotic spells. The management of VAE is beyond the scope of this chapter. Intraoperative cyanotic spells can occur in these patients, which needs to be managed appropriately (Table 24.3) [62]. Major causes of intraoperative cyanotic spells are inadequate depth of anesthesia and hypovolemia. A decrease in saturation during a cyanotic spell is often preceded by a decrease in $EtCO_2$ and an increase in $PaCO_2$ and $EtCO_2$ gradient due to the decrease in pulmonary blood flow. A similar picture may also occur with VAE and severe hypotension. It is sometimes tricky, but it is important to distinguish these conditions as their management strategies are different.

These children should be managed in the neurosurgical ICU during the postoperative period. Invasive monitoring should be continued until the child is hemodynamically stable. Postoperative management should focus on the maintenance of hemodynamics; oxygenation, and ICP; seizure control; and adequate postoperative analgesia.

24.10 Conclusion

Brain abscess is a dreadful complication associated with CCHD in children. Anesthetic management in a case of CCHD with brain abscess can be challenging for the anesthesiologists who have to simultaneously meet the demands of both the heart and brain without jeopardizing either. A clear understanding of cardiovascular and intracerebral pathophysiology is essential for a successful outcome in these children.

Conflict of Interest None to declare.

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Anesthesia for Moyamoya Disease in Children

25

Kenji Yoshitani

Key Points

- Moyamoya disease (MMD) is a chronic, progressive, occlusive cerebrovascular disease of the circle of Willis with unknown etiology, which predominantly occurs in Eastern Asia.
- The pathogenesis of MMD remains unknown and is diagnosed by angiography, computed tomography, and magnetic resonance imaging.
- Clinical presentation of MMD is mainly as transient ischemic attack, headache, seizure, and hemorrhage in pediatric patients.
- Perioperative dehydration, and agitation leading to hypocapnia, should be avoided; premedication is necessary to prevent crying.
- Cerebrovascular reserve is important to prevent perioperative cerebral infarction.
- Perioperative normocapnia, normovolemia, and normotension are recommended.
- Maintenance of normal hematocrit (30%) is essential to prevent the deleterious effects of hemodilution as well as hyperviscosity.
- Total intravenous anesthesia is preferable to prevent the emergence of delirium; dexmedetomidine helps prevent it.

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25.1 Introduction

Moyamoya disease (MMD) is a chronic, occlusive cerebrovascular disease of the circle of Willis with unknown etiology predominantly seen in Eastern Asia. The estimated annual prevalence and incidence of MMD in Japan are 3.16 and 0.35 per 100,000 population, respectively [1]. It has a female predominance, with a female/male ratio of 1.8:1 [2]. On the other hand, the incidence of MMD in the United States is 298 patients in California and Washington (0.086/100,000). The estimated incidence in European countries is approximately one-tenth of that in Japan [3, 4]. Takeuchi and Shimizu from Japan (1957) were the first to describe this condition as "hypogenesis of bilateral internal carotid arteries" [5]. Later on (1969), Suzuki and Takaku described it as moyamoya disease in English literature. MMD is a progressive disorder; bypass surgery (revascularization) remains the treatment of choice [6].

25.1.1 Moyamoya Disease Versus Moyamoya Syndrome

Moyamoya syndrome can be defined as patients who, along with the characteristic moyamoya vasculopathy, also present with recognized associated conditions such as sickle cell disease, neurofibromatosis type 1, previous therapeutic irradiation of skull, Down's syndrome, congeni-

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tal cardiac anomalies, renal artery stenosis, giant cervicofacial hemangiomas, or hyperthyroidism. This may also be considered moyamoya secondary to the primary condition, distinguished from MMD. The pathogenesis of cerebral vasculopathy seen in MMD is usually a part of the underlying disease/syndrome. Moyamoya syndrome differs from MMD in clinical presentations, the natural history and course, and treatment considerations. It is to be kept in mind that the term Moyamoya phenomenon is simply used to describe the characteristic vasculopathy features of the condition on angiography regardless of the cause. Bilaterality and no associated conditions described above are characteristic of MMD, whereas unilateral presentation and any of the abovementioned conditions favor the diagnosis of moyamoya syndrome [7].

25.2 Pathophysiology of Moyamoya Disease

The prevalence of MMD shows an ethnic difference. MMD may be associated with genetic inheritance with multiple chromosomes being involved: 3p24.2-p26, 6q25, 8q23, 12p12, and 17q25 [8–10]. An autosomal dominant mode of inheritance is suggested with low penetrance or polygenic mode [8]. The pathogenesis of the disease remains unknown. The histopathological changes in major intracranial arteries, the carotid artery, and the middle cerebral artery terminations in patients with MMD are eccentric fibrocellular thickening of the vascular intima resulting from the proliferation of smooth muscle cells (SMCs) and fibrosis leading to the vessel occlusion from hyperplasia of smooth muscle cells and thrombosis, suggesting the involvement of various growth factors as well [11].

MMD is characterized by moyamoya vessels, which are basically a network of fragile collateral vessels at the brain's base. These moyamoya collaterals are perforating arteries that, on histopathological examination, show different features like fibrin deposits in their walls, fragmented elastic lamina, and attenuated media. It is believed that arterial stenosis due to regional brain hypoxia induces the production of moyamoya collaterals [12]. In addition to the moyamoya vessels, increased microvascular density and diameter—a finding referred to as cortical microvascularization and responsible for regulating cortical perfusion—is suggested to be specific to MMD [13, 14].

25.3 Clinical Presentation

MMD has two peaks in terms of age distribution, the first in young children around 6 years old and the second in young adults. The two main clinical features of MMD are ischemic attacks and intracranial hemorrhage. Ischemic symptoms are the most common clinical presentation across all age groups, while hemorrhage, though less common overall, is found in the adult population. Ischemic features include transient ischemic attacks (TIAs) and cerebral infarctions [1]. The brain is rapidly developing in children under 6 years of age, resulting in a relatively high cerebral metabolic oxygen ratio and, thus, higher cerebral blood flow (CBF) [15]. Pediatric patients with MMD have lower CBF than healthy children [16], and they, therefore, develop TIAs more frequently. It is important to prevent and adequately treat ischemic attacks in such children. In addition, headache, seizure, and involuntary movement are also common presentations. Others include hemiparesis, dysarthria/aphasia, and cognitive impairments. Intracranial hemorrhage occurs due to the fragility of the collateral vessels and is rarely found in Asian countries [17].

25.4 Diagnosis

The diagnostic criteria of MMD include [1] steno-occlusive changes at the terminal portion of the internal carotid artery (ICA), which may or may not be associated with similar findings at the proximal portion of the anterior cerebral artery (ACA) and/or middle cerebral arteries (MCAs),

and [2] demonstration of a network of abnormal vessels in the vicinity of the occlusive or stenotic lesions in the artery by digital subtraction angiography (DSA). The diagnosis of MMD requires that both these findings be present bilaterally. The steno-occlusive disorder may be associated with compensatory collateral networking of vessels in the base of the brain, angiographically described as a "puff of smoke," from which the term moyamoya (in Japanese) is derived.

Although DSA is the gold standard diagnostic modality for MMD, the steno-occlusive changes of the circle of Willis can also be reliably demonstrated with magnetic resonance angiography (MRA) and three-dimensional computed tomography angiography (3D-CTA). Especially in pediatric cases, MRA would be preferred compared with invasive DSA. Magnetic resonance imaging (MRI) can be used to demonstrate acute or chronic infarcts with diffusion-weighted imaging (DWI) or T1-/T2-weighted imaging, respectively. More significant findings suggestive of MMD include the "ivy sign" and demonstration of flow voids. Ivy sign refers to the linear high-intensity signals that follow a sulcal pattern, as seen in fluid-attenuated inversion recovery (FLAIR) sequences due to the reduced cortical blood flow. Flow voids in MRI are common in the stenotic vessels (ICA, MCA, ACA) and also in the region of basal ganglia and thalamus from the collateral vessels (Fig. 25.1) [18, 19].

25.5 Electroencephalography

The role of electroencephalography (EEG) in MMD is restricted to screening in children and not for specific diagnosis. "Re-build-up" phe-

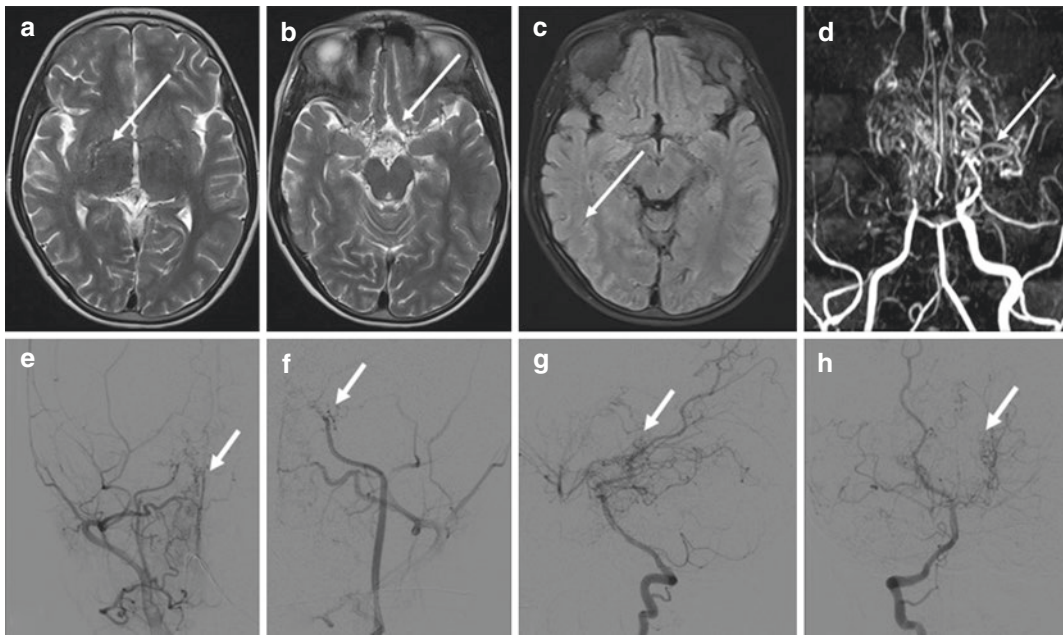

Fig. 25.1 Imaging in moyamoya disease: (**a**, **b**) Axial T2 MRI sections showing multiple basal collaterals with non-visualization of both terminal ICAs (long white arrows). (**c**) Axial FLAIR image showing multiple collaterals in sulcal space suggestive of "ivy sign" (long white arrows). (**d**) Time of flight MR angiography (technique to visualize flow within vessels without the need for contrast) of circle of Willis showing non-visualization of the both terminal ICAs with multiple basal and pial collaterals (long white arrows). (**e**, **f**,) Right and left carotid angiogram (DSA) in AP projection showing non-visualization of the both terminal ICAs with multiple basal collaterals (short thick arrows) (Suzuki grade III). (**g**, **h**) Right vertebral angiogram lateral and AP projections with multiple compensatory pial collaterals, forming the anterior circulation (short thick arrows) (Suzuki grade III)

nomenon is a rare yet, well-recognized EEG phenomenon in a child with MMD. It is characterized by a slowing of frequency and appearance of slow waves that appear after attenuation of the ordinary build-up, which is the appearance of monorhythmic high-voltage generalized slow activities during hyperventilation. It occurs because of the reduced cerebrovascular reserve.

25.6 Other Diagnostics

25.6.1 Cerebrovascular Reserve

To prevent perioperative ischemic stroke, cerebrovascular reserve should be evaluated before surgery. Cerebral angiography and MRA are used for classifying the stage of MMD according to Suzuki's angiographic classification, which is categorized into five stages [6] (Table 25.1). However, since neither modality can evaluate cerebral hemodynamics, these must be assessed with functional neuroimaging techniques such as ^{15}O-positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

Misery perfusion, defined as an increased oxygen extraction fraction according to ^{15}O-PET, indicates that oxygen transport and supply are insufficient to compensate for reduced CBF and oxygen extraction is increased as a result (Fig. 25.2). Misery perfusion is thought to indicate impaired cerebral hemodynamics and is an operative sign of revascularization [20]. Whether it occurs unilaterally or bilaterally is important for preventing ischemic stroke. Anesthesiologists should carefully monitor preoperative functional neuroimaging results.

Table 25.1 Classification of moyamoya disease by angiographic features

Stage	Details
Stage 1	Narrowing of the carotid fork
Stage 2	Initiation of moyamoya vessels
Stage 3	Intensification of moyamoya vessels
Stage 4	Minimization of moyamoya vessels
Stage 5	Reduction of moyamoya vessels
Stage 6	Disappearance of moyamoya vessels

25.7 Medical Management

The goals of treatment in MMD are to prevent the aggravation of cerebral ischemia, prevent the recurrence of ischemic attacks, and ameliorate the symptoms. Neither medical nor surgical modalities reverse the previously existing cerebral ischemia.

Pharmacological management involves the use of antiplatelet, anti-epileptic and calcium channel blocking (CCB) agents. Antiplatelets like aspirin are used to prevent embolism from microthrombi seen at the stenotic regions. Controversies exist regarding its use in MMD as the cause of stroke in this condition is not thromboembolic; rather, it occurs due to hemodynamic phenomena [21, 22]. CCBs are used to reduce symptoms like headaches or migraines. It is essential to use them cautiously as their hypotensive effect can reduce cerebral perfusion in the absence of autoregulation [23]. The medical treatment does not prevent the progression of adult MMD. In a previous study, the 5-year risk of recurrent ipsilateral stroke in MMD patients who were treated surgically was 17%, while in conservatively treated symptomatic patients, the risk was 65% in those with unilateral disease and 85% in those with bilateral disease [24]. Therefore, pediatric MMD patients with recurrent or progressive TIAs are candidates for surgery, mainly superficial temporal artery (STA) to middle cerebral artery (MCA) anastomosis (bypass).

25.8 Surgical Treatment: Direct Versus Indirect Bypass

The basis of surgical management is to use the external carotid artery as a blood flow source to the cerebral cortex (revascularization). There are many different operative techniques, but surgery is basically classified as a direct and indirect revascularization procedure (Table 25.2). Direct procedures result in an immediate increase in CBF, while several weeks are required before a significant change is seen with indirect procedures. Multiple factors decide the choice of procedure like patient's age, anatomical size of the vessels, preoperative hemodynamics (CBF and

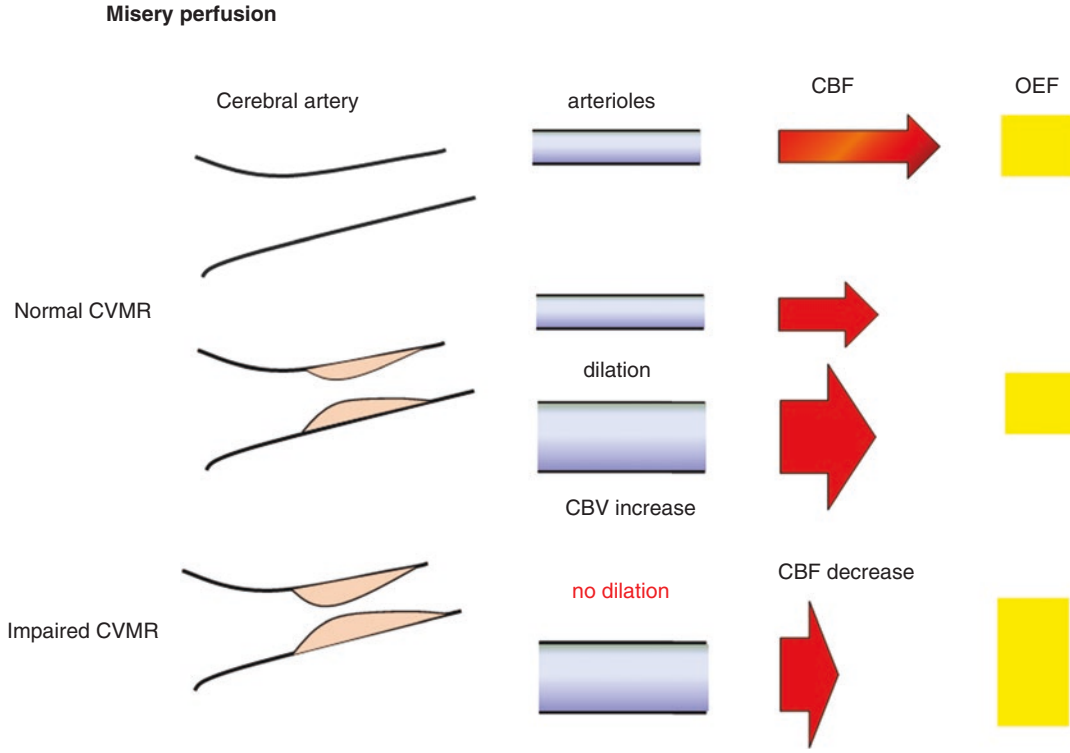

Fig. 25.2 Schematic diagram of misery perfusion. *CBF* cerebral blood flow; *CBV* cerebral blood volume; *CVMR* cerebro-vasomotor reactivity; *OEF* oxygen extraction ratio. As stenosis becomes more severe, cerebral perfusion pressure decreases. To keep cerebral blood flow constant, small arterioles dilate, thus increasing cerebral blood volume. Further stenosis causes CBF reduction and an increase in the oxygen extraction ratio, called misery perfusion

Table 25.2 Surgical procedures for moyamoya disease

Procedure	Details
Direct bypass surgery	Most performed superficial temporal artery (STA) to middle cerebral artery (MCA) bypass surgery
Encephaloduroarteriosynangiosis (EDAS) [25]	A favorable indirect revascularization procedure in which the STA is mobilized and then sutured to the edges of the opened dura, which is often combined with STA-MCA bypass
Pial synangiosis [26]	Pial synangiosis is a procedure rerouting healthy scalp blood vessels to the brain, bypassing the narrowed vessels of moyamoya, which is performed in pediatric cases
Encephalomyosynangiosis (EMS) [27]	A surgical procedure performed most commonly in pediatric moyamoya disease as indirect revascularization to bypass the occlusive terminal internal carotid and/or circle of Willis vessels promotes collateral vessel formation
Encephaloduroarteriomyosynangiosis (EDAMS) [28]	Combination of EDAS and EMS

status of cerebral vasculature), and the degree of preoperative conditions. Historically, direct procedures were reserved for adult patients as the smaller caliber of vessels made the procedure technically difficult in children. Nowadays, with the advent of better diagnostic and surgical techniques, many centers perform direct revascularization in feasible children.

25.9 Preoperative Management

The major goal of perioperative management in MMD is to maintain adequate cerebral perfusion. Any undue increase or decrease in hemodynamic parameters alters cerebral perfusion and results in ischemic or hemorrhagic manifestations. Several factors influence perioperative management and are discussed below.

25.9.1 Dehydration

Higher CBF is required to supply sufficient oxygen to developing brain tissue, but CBF is decreased in children with MMD [15, 16]. Preoperative dehydration due to fasting should be avoided. To help prevent hypovolemia, aggressive preoperative intravenous (IV) hydration beginns on the day before surgery is recommended [29]. This administration route enables rapid induction of anesthesia in patients with MMD, which helps prevent crying.

25.9.2 Review of Medications

It is critical to review the chronic medications taken by patients with MMD. Aspirin, antiseizure medications, and anti-hypertensives like calcium channel blockers, which are used to prevent vasospasm, should be continued until the day of surgery. Because the serum concentrations increase rapidly after oral administration, aspirin can be administered intraoperatively via a gastric tube to treat acute thrombus formation in the bypass graft. Aspirin treatment is normally resumed on the first postoperative day.

25.9.3 Premedication

Premedication has been widely used to prevent crying before the induction of anesthesia. Crying leads to hypocapnia with cerebral vasoconstriction, reduced CBF, and cerebral ischemia. We previously reported that premedication was not associated with postoperative transient neurologic events (TNEs) [30]. Although no clear evidence has supported the use of premedication for MMD, midazolam is frequently used as premedication in these groups of children [31]. Regarding postoperative analgesia, clonidine may be effective in children. A Cochrane Database Systematic Review reported that clonidine could have a beneficial effect on postoperative pain in children [32], and it may therefore be effective as premedication. We believe that premedication is beneficial to prevent crying.

25.9.4 Induction of Anesthesia

Induction of anesthesia must be smooth, ensuring maintenance of hemodynamic parameters within baseline levels to prevent any increase in intracranial pressure (ICP) and at the same time to ensure adequate depth of anesthesia. Both intravenous and inhalational induction techniques can be used in children, but it is important to prevent hyperventilation. After establishing an intravenous line, the use of opioids and lidocaine to prevent hemodynamic responses to laryngoscopy and intubation may be beneficial. Non-depolarizing neuromuscular blocking agents with less histamine release are to be preferred for maintenance of hemodynamic stability [33, 34].

25.10 Intraoperative Anesthetic Management

25.10.1 Monitoring

Apart from the standard American Society of Anesthesiologist (ASA) techniques, other important techniques such as invasive arterial blood pressure measurement, electroencephalography, and cerebral oximetry are employed frequently in patients with MMD. Capnography

is one of the most important assessments because $PaCO_2$ should be titrated to achieve normocapnia. The other intraoperative goals are to maintain normothermia and normotension, prevent hypoxia, and maintain normal hematocrit. The hematocrit of 30–42% is suggested to maintain adequate oxygen supply to the brain [35].

25.10.2 Partial Pressure of Arterial Carbon Dioxide ($PaCO_2$)

The role of carbon dioxide as a potent modulator of the tone of cerebral vessels is well-known. It influences CBF in the setting of ventilator use and is a major determinant of neurologic complications in MMD [36]. By increasing cerebral blood volume, vasodilation compensates for reduced CBF in the context of reduced cerebral perfusion pressure (Fig. 25.2). Generally, hypercapnia increases CBF by vasodilating healthy vessels. However, already dilated diseased vessels to compensate for reduced CBF could not dilate. Furthermore, the blood flow moves to dilate healthy vessels from the already dilated vessels, known as the *steal phenomenon*. Hypercapnia-induced reductions in blood flow have been observed with intraoperative regional CBF monitoring [37]. As the collateral vessels which are responsible for perfusion of these regions are already maximally dilated, they are unable to dilate with hypercapnia [38]. We need to take care to maintain normocapnia to prevent intraoperative ischemia.

25.10.3 Blood Pressure

Invasive arterial pressure monitoring is mandatory to maintain blood pressure within age-appropriate target ranges. The habitual blood pressure level in patients with MMD is lower target range of intraoperative blood pressure, and CBF is completely pressure-dependent due to loss of autoregulation in ischemic regions [39].

25.10.4 Cerebral Oximetry (Near-Infrared Spectroscopy)

There have been few reports of intraoperative monitoring of regional cerebral oxygen saturation (rSO_2), but Lin et al. reported reduced rSO_2 during the *re-build-up phenomenon* typically due to hyperventilation-induced hypocapnia in patients with MMD [40]. In this phenomenon, EEG shows slow polymorphous high voltage in the frontal lobes, whether unilaterally or bilaterally.

Cerebral oximetry devices have been developed that can be used in STA-MCA bypass [41]. The usefulness of rSO_2 in STA-MCA bypass has not been reported but should be demonstrated soon.

Furthermore, rSO_2 has been used to evaluate cerebrovascular autoregulation in pediatric MMD [42]. Impaired autoregulation was observed when rSO_2 increased as a result of elevated blood pressure. This technique has been applied in cardiac surgery and may be effective in neuroanesthesia.

25.10.5 Anesthetic Agents

During the anesthetic management for revascularization surgery, it is crucial to prevent cerebral infarction perioperatively in children presented with TIAs. Anesthesia is normally maintained intravenously using propofol or with volatile agents, sevoflurane or desflurane. There is no definitive recommendation regarding which approach is better for patients with MMD. However, volatile anesthetic agents increase intracranial pressure (ICP) more than propofol (Tables 25.3 and 25.4); in one craniotomy study, the subdural pressure was 5.8 ± 4.6 mmHg with propofol and 9.4 ± 6.6 mmHg with sevoflurane ($p < 0.05$) [43]. The effect of inhalational anesthesia on regional CBF was also examined in patients with MMD [44]. Isoflurane may reduce the regional cortical blood flow levels, provoking the intracranial steal phenomenon (Table 25.2). Based on the above findings, propofol is recommended during revascularization in pediatric

Table 25.3 Intracranial pressure and cerebral hemodynamics in patients with cerebral tumors: difference among anesthetic agents

	Propofol	Isoflurane	Sevoflurane
MAP (mmHg)	87 ± 13	71 ± 12	74 ± 11
Subdural pressure (mmHg)	5.8 ± 4.6	9.8 ± 6.3*	9.4 ± 6.6*
CPP (mmHg)	82 ± 14	61 ± 11*	64 ± 10*
$PaCO_2$ (mmHg)	28.5 ± 3.0	29.3 ± 2.3	30.8 ± 3.0*
SjO_2 (%)	52 ± 11	57 ± 12*	56 ± 12*

Data are expressed as mean ± SD. *MAP* mean arterial pressure; *CPP* cerebral perfusion pressure; SjO_2 jugular bulb oxygen saturation. *$p < 0.05$
This table has been modified from Anesthesiology 2003; 98:329–36

Table 25.4 Effect of inhalational anesthesia on cerebral circulation in moyamoya disease

	Propofol	Isoflurane	*p*-Value
Parietal middle (mL/100 g/min)	14.3 ± 8.3	10.1 ± 7.0 ↓	0.006
Parietal inferior (mL/100 g/min)	15.8 ± 5.2	12.4 ± 7.0 ↓	0.004
SjO_2 (%)	57 ± 9.8	67 ± 8.5 ↑	0.0006

SjO_2 jugular bulb oxygen saturation. ↑↓: $p < 0.05$
This table has been modified from J Neurosurg Anesthesiol. 1999;11(1):25–30

patients with MMD. Another benefit of propofol is that it causes less agitation than inhalational anesthetic agents. This topic is discussed in the next section.

25.10.6 Emergence Delirium

Crying after surgery is associated with transient neurological deficits in children with MMD [30]. To prevent crying, it is imperative to avoid emergence delirium (ED). It has been observed that the incidence of crying or restlessness in the recovery room in children (10 months to 6 years of age) was up to 30% upon arrival and in the first 10 min of awakening [45].

Risk factors for ED were found to be the age of the patient, mental state, postoperative pain, anesthesia technique, and surgical procedure [46]. Generally, children less than 6 years of age belonging to either gender, those with active, impulsive, emotional, or unsociable personalities who use volatile anesthetic agents (sevoflurane or desflurane) are associated with increased risk of ED [47]. Regional anesthesia, combined with general anesthesia, reduced the incidence of ED. In a study on surgery for inguinal hernia in children, the combination of caudal block and sevoflurane anesthesia significantly reduced the incidence of ED [48–50]. Propofol is a preferable anesthetic in pediatric patients with MMD. Pain control is also crucial for preventing ED.

Pharmacological therapy, for instance, with sedatives, effectively reduces the incidence of ED. In children with MMD, sedation administration after extubation has significantly lowered the incidence of transient neurological events [30]. Generally, to confirm whether intraoperative motor deficits have occurred, neurosurgeons require anesthesiologists to extubate immediately after the surgery is over. To avoid ED, a sedative agent is started just before the end of the procedure. Dexmedetomidine, a highly selective alpha-2 agonist with both analgesic and hypnotic properties and a weak respiratory depressant effect, is suitable for postoperative sedation. Intravenous administration of dexmedetomidine during the intraoperative period has been observed to reduce the incidence of ED in children [51]. Analgesic effects of alpha-2 agonists have been proposed to contribute to the lower incidence of ED in pediatric patients [52].

25.11 Postoperative Management

25.11.1 Postoperative Ischemic Complications

Postoperative ischemic complications occurred in 10.3% of pediatric patients with MMD. Risk factors for ischemic complications were preoperative infarct on CT, younger age, higher Suzuki grade, and posterior cerebral artery stenosis or occlusion [53].

25.11.2 Cerebral Hyperperfusion

Cerebral hyperperfusion was seen in 4.5% of patients who underwent surgical revascularization for MMD [54]. As stated in the previous section, post-extubation sedation was associated with a reduced incidence of transient neurological events [30]. Sedative agents for extubation would reduce the likelihood of ED and transient neurological events. Hyperperfusion may cause delayed intracranial hemorrhage postoperatively, which should be avoided. Kemayama and colleagues reported that 3.0% of revascularization patients with 270% increases in CBF had delayed intracranial hemorrhage compared with patients without cerebral hyperperfusion syndrome [54]. In addition to postoperative sedation, additional strategies should be explored for preventing postoperative hyperperfusion.

25.11.3 Pain Control

Pain can cause postoperative agitation and can also cause crying. Crying should be avoided as it causes hyperventilation and decreases cerebral blood flow. Multiple options are available to reduce postoperative pain. They include perioperative sedation, painless wound dressing techniques, or absorbable wound suture closures, which help reduce the incidence of strokes, TIAs, and length of stay [55].

25.12 Conclusion

Despite the higher prevalence of MMD, particularly in Asian countries, only a few reports are available on pediatric patients with MMD. Consequently, the evidence is limited concerning the anesthetic management for preventing perioperative ischemic events. Hence, the current practice of anesthetic management of MMD depends mostly on the opinions of experts. Under such circumstances, a continued focus on the upcoming literature may help optimize the anesthetic management of MMD in pediatric patients.

Conflict of Interest No conflict of interest to declare.

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Anesthesia for Pediatric Deep Brain Stimulation Surgery

26

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Key Points

- Dystonia is the most common indication for deep brain stimulation in the pediatric population.
- Anesthetic implications are to provide optimal surgical conditions and patient comfort, with ideally no or minimal anesthetic interference to intraoperative microelectrode recording, including neuromonitoring for target localization with stable, controlled intraoperative hemodynamics.
- The choice of the anesthetic technique is individualized for safe and effective anesthesia.
- Good patient outcomes depend on team work, well-designed multidisciplinary consensus protocols, and systems.
- Several refinements and evolution of the surgical and the anesthetic techniques have been documented; future multicentric, collaborative trials will help formulate recommendations.

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26.1 Introduction

There is a broad spectrum of neurological illnesses in pediatric patients leading to movement disorders and finally affecting the developmental and functional capacities. Historically, functional neurological disorders like Parkinson's disease were treated with surgeries like thalamotomy, pallidotomy, and cingulotomy, which involved mainly the lesioning of deep brain structures. These procedures were irreversible and frequently associated with various permanent side effects [1]. Wertheimer, a psychologist, compiled a book on movement disorders for the first time, while Otfrid Foerster, a German neurologist and neurosurgeon, has been recognized as the pioneer of surgery for movement disorder. In 1960, advances in stimulator technology and Melzack and Wall's gate theory initiated a paradigm shift tiled the way for deep brain stimulation (DBS) [2]. In 1987, DBS was finally recognized as an alternative to the ablation procedures for reducing symptoms of Parkinson's disease [3]. Advantages like reversibility, the possibility of bilateral stimulation, ability to titrate the stimulation dose and safety, and long-term benefits have made DBS a favorable option for not only Parkinson's disease but also many functional neurosurgery procedures [4]. Various indications of DBS are tabulated in Table 26.1. The other indications are juvenile parkinsonism, Tourette's syndrome, pediatric obesity, epilepsy, and

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Table 26.1 Indications for DBS

Common indications	
1.	Parkinson's disease
2.	Dystonia: generalized, focal, tardive
3.	Obsessive-compulsive disorder, Tourettes
4.	Epilepsy
5.	Pain: neuropathic, nociceptive, cluster headaches
6.	Depression: major depressive disorder, bipolar disorder
7.	Tremors: essential, post-traumatic, multiple sclerosis, post-stroke, rubral
Uncommon indications	
1.	Post-traumatic stress disorder
2.	Progressive supranuclear palsy
3.	Obesity/anorexia
4.	Addiction
5.	Autism
6.	Aggression
7.	Persistent vegetative state, minimally conscious state
Potential future indications	
1.	Alzheimer's disease
2.	Tinnitus
3.	Urinary incontinence
4.	Anti-social behavior/morality
5.	Hypertension

obsessive-compulsive disorder (OCD) [5]. In the entire spectrum of childhood movement disorders, dystonia is the most common, most severe, and most challenging movement disorder. Dystonia is described here in detail, and other pathologies, where DBS is indicated in pediatric patients, are elaborated in Table 26.2. The management of movement disorder needs a multidisciplinary approach that includes a neurologist, neurosurgeon, neuroanesthesiologist, neuropsychologist, nursing staff, and physiotherapist to help in rehabilitation.

26.2 Dystonias

Dystonia is a group of movement disorders characterized by intermittent or sustained, abnormal muscle contractions and twisting movements resulting in painful and debilitating postures. These are classified as primary (idiopathic) or secondary (due to other pathologies, including stroke, cerebral palsy, and neurodegenerative diseases) [6]. Depending upon the clinical manifestations, primary dystonias can be generalized (involving muscles of the entire body), segmental (involving adjoining parts of the body), or focal (involving a single muscle or one group of muscles) [7].

To understand the pathophysiological changes in dystonia, one must understand the normal motor circuitry. Figure 26.1 provides the schematic diagram to understand the control of movements by basal ganglion [8]. This data is derived from neurophysiological and anatomical studies. The basal ganglia are a group of nuclei that include caudate nucleus and putamen (known as striatum), globus pallidus internal segment (GPi) and external segment (GPe), subthalamic nucleus (STN), and the pigmented substantia nigra (SNr), also known as the pars compacta (Fig. 26.2). The major function of the basal ganglion is planning and modulation of movements. Major inputs to basal ganglion originate in the cerebral cortex (motor and sensorimotor) and thalamic nuclei (centromedian and parafascicular nuclei). The nigrostriatal pathway (SNr to the striatum) synapses via dopaminergic type 1 (D1) receptors in direct (facilitatory) pathway neurons and via D2 receptors in indirect (inhibitory) pathway neurons. The outflow pathways from the basal ganglion are of two types, direct and indirect pathways. The direct pathway is output via GPi and SNr to the thalamus and brain stem. It is a monosynaptic inhibitory pathway, which acts through gamma-aminobutyric acid [GABA] neurotransmitter. The indirect (polysynaptic, excitatory) pathway is output via GPe and STN, where glutamate is a neurotransmitter. The GPi and SNr neurons tonically inhibit thalamocortical projection neurons of the thalamus (ventral anterior, ventrolateral, and intralaminar nuclei), and brain stem. Hence, increased basal ganglia output may decrease the movements, whereas reduced basal ganglia output may lead to the increased movement because of the disinhibition of these neurons.

In dystonia, the direct pathway appears to be overactive, resulting in less GPi activity and enhanced thalamocortical activation. It most probably leads to the changes in patterning and

Table 26.2 Indications of deep brain stimulation (DBS) in pediatric patients

Disease	Clinical features	DBS target
Dystonia	• Syndrome of sustained muscle contractions, frequently causing – Twisting – Repetitive movements – Painful, abnormal postures	Bilateral pallidal DBS
Tourette's syndrome	• Chronic motor and vocal tics • In combination with concomitant behavioral disorders including obsessive-compulsive disorder (OCD) and attention-deficit/hyperactivity disorder	• DBS: thalamus is the most common target (Cm-PoF and Voa) • STN • VC/VS • NAc
Juvenile parkinsonism	• Juvenile parkinsonism is defined as the development of: – Parkinsonian symptoms or signs before the age of 21 – Tremor – Bradykinesia – Focal dystonia	DBS of the STN and GPi has been highly successful
Pediatric psychiatric disorders OCD	• Obsessional symptoms compulsive acts that cause distress and interfere with daily activities	• Anterior capsule • NAc • STN • Inferior thalamic peduncle • VC/VS-DBS
Pediatric obesity	• BMI >35 with a serious comorbidity • BMI >40 with only mild comorbidities	• Lateral and ventromedial hypothalamus • NAc • Rationale is based on hypothalamic involvement in homeostasis, feeding behavior, and energy expenditure • For NAc is based on the reinforcing properties of high-calorie food
Epilepsy	Refractory to pharmacotherapy	Anterior nucleus of the thalamus

DBS deep brain stimulation; *Cm-PoF* centromedian–parafascicular nuclear complex of the thalamus; *Voa* ventralis-oralis complex; *STN* subthalamic nucleus; *VC/VS* ventral capsule/ventral striatum; *NAc* nucleus accumbens; *GPi* globus pallidus interna; *BMI* body mass index

synchrony of discharge, resulting in manifestations of the disease. There is a complex interplay of cholinergic internuncial neurons (excitatory) and dopamine (inhibitory) on the projection neurons.

This makes the basis of surgical treatment and DBS in dystonia. Surgical treatments involve lesioning of thalamic nuclei or the pallidum. These procedures are associated with a risk of severe complications, including hemiparesis and dysarthria [9, 10]. DBS is a more promising treatment modality in patients who are refractory to medical therapy.

The medical management includes anti-Parkinsonian, anticholinergic drugs, baclofen, or botulinum toxin injections, but these are only marginally effective [5, 11].

26.3 Deep Brain Stimulation (DBS)

DBS is approved for pediatric and adult patients with dystonia and should be considered only when conservative management has failed to control the symptoms optimally. Unlike pallidotomy, DBS is less damaging, reversible, and adjustable and has a lesser effect on cognitive and motor functions. Based on the pathophysiology of dystonia, the GPi is the common target of DBS

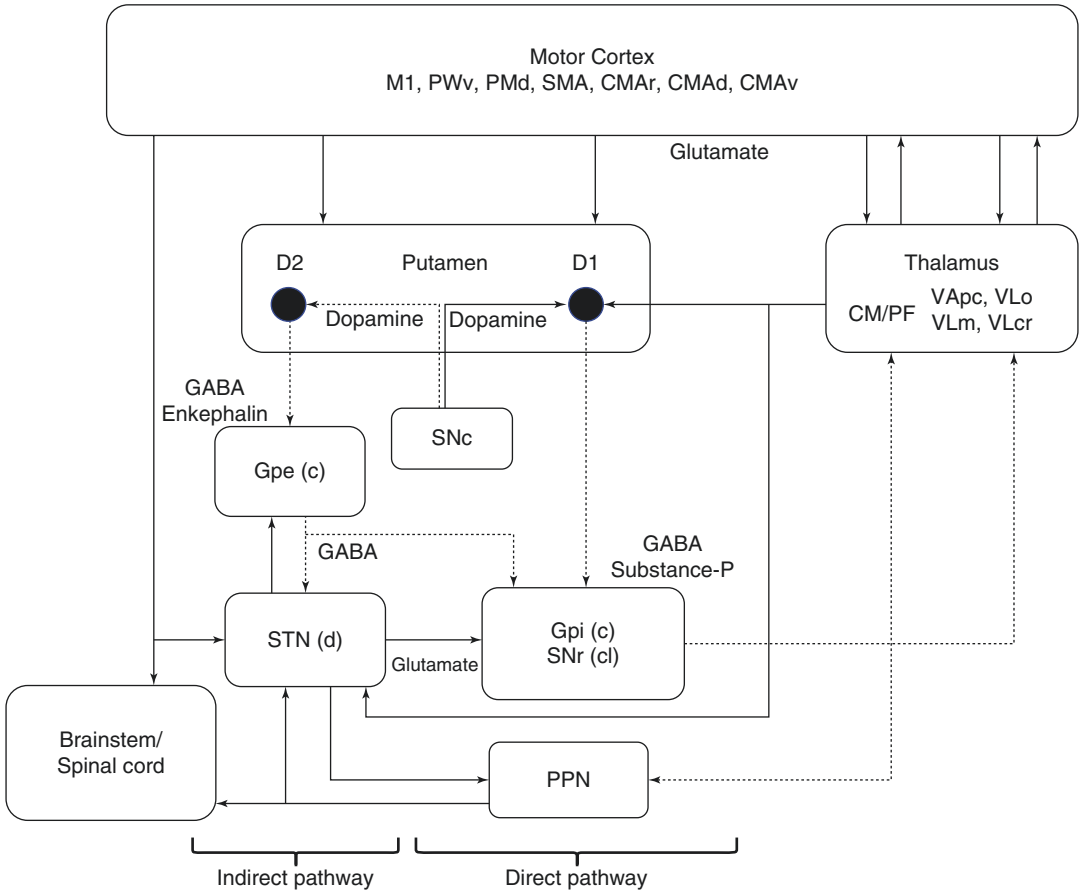

Fig. 26.1 Anatomy of basal ganglion. *GPe* globus pallidus externa; *GPi* globus pallidus interna; *STN* substantia nigra; *A* anterior; *MD* medial dorsal; *LD* lateral dorsal nuclei of thalamus

for dystonia [12–14]. It has been demonstrated that primary generalized dystonia (PGD) and segmental dystonia have a good response to bilateral pallidal DBS [15]. The outcomes of GPi-DBS are more favorable in pediatric patients with DYT1 mutation and focal cervical dystonia [16, 17]. In secondary dystonia, DBS is not very effective due to underlying neurodegenerative pathology.

Accurate electrode placement is important in determining the success of DBS. It is highly effective in controlling the rigidity, bradykinesias, dyskinesias, and tremors. The bilateral implants improve the gait quality and gait freezing effectively. It is more successful in younger patients with lesser disabilities. Currently, it is mostly performed stereotactically. DBS involves three surgical procedures and two magnetic resonance imaging (MRI) sessions. Various steps of the DBS procedure are depicted in Table 26.3 [18].

The entire procedure can be done on the same day or in two stages, where the internalization of the generator can be done on another day, generally within 3 days to 2 weeks of the intracranial insertion of the electrode. The overall result is the same, whether staged or same-day surgery is performed [19]. Frameless stereotaxy has also been used for DBS. Trajectories are planned preoperatively on a contrast-enhanced volumetric MRI. On the day of surgery, six skull fiducials are placed circumferentially around the skull and a thin cut computed tomographic (CT) scan obtained, which is merged with the preoperative MRI. The trajectory is manually aligned by a

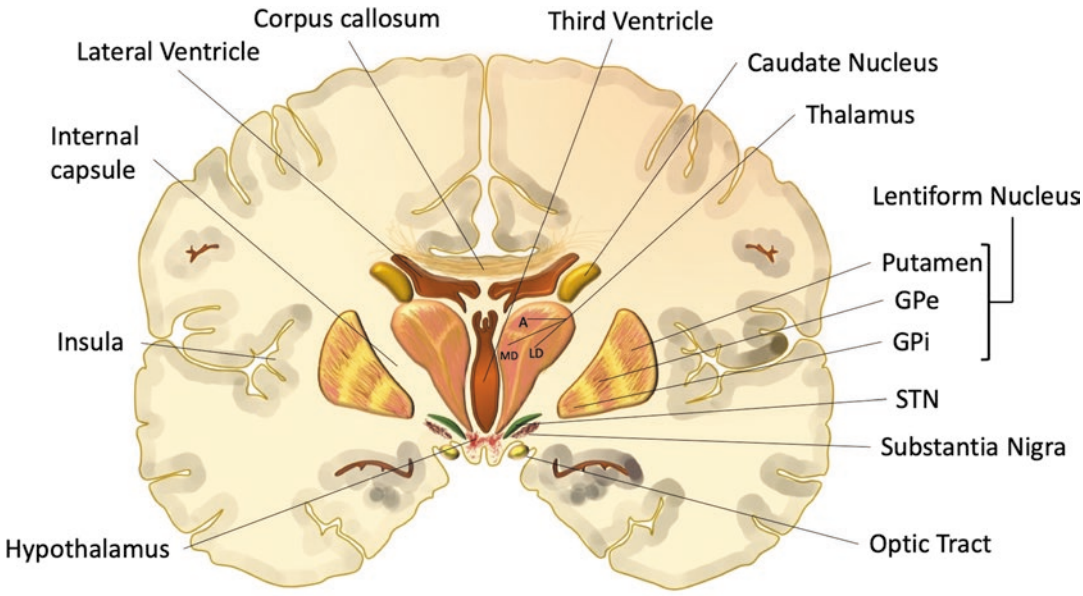

Fig. 26.2 Circuits for the control of motor system. Dotted arrows indicate inhibitory (γ-aminobutyric acid [GABA]-ergic) connections; solid arrows, excitatory (glutamatergic) connections. *CM* centromedian nucleus of thalamus; *CMAr* rostral portion of cingulate motor area; *CMAd* dorsal portion of cingulate motor area; *CMAv* ventral portion of cingulate motor area; *GPe* external segment of the globus pallidus; *GPi* globus pallidus interna; *M1* primary motor cortex; *Pf* parafascicular nucleus of the thalamus; *PMd* dorsal premotor cortex; *PMv* ventral premotor cortex; *PPN* pedunculopontine nucleus; *SMA* supplementary motor area; *SNc* substantia nigra pars compacta; *SNr* substantia nigra pars reticulata; *STN* subthalamic nucleus; *VApc* ventral anterior nucleus of thalamus pars parvocellularis; *VLm* ventrolateral nucleus of thalamus pars medialis; *VLo* ventrolateral nucleus of thalamus pars oralis; *VLcr* ventrolateral nucleus of thalamus rostral pars caudalis; *c* caudal; *cl* caudolateral; *d* dorsal

neuronavigation system and guide cannula placed above the target [20]. Microelectrode recording (MER) and intraoperative MRI confirm the lead placement. Robot-assisted frameless DBS has also been performed in a similar fashion. It has been shown to increase operational efficiency while improving accuracy and safety [21].

26.4 Anesthetic Challenges

DBS is usually opted in patients with severe dystonia. Such patients may be receiving multiple medications and are prone to drug interactions. Generally, the goal of anesthesia for the DBS procedure is to have immobile and awake patients. In awake patients, the MER is preserved, intraoperative testing can be done to improve symptoms with a stimulus, and unwanted neurologic or psychological side effects can be detected early. Dystonia surgeries are an exception and are usually performed under general anesthesia. Due to abnormal postures and muscle contractions, patients may not be able to lie down for a prolonged period on the operating table. There may be an increased risk of movement or even fracture of the stereotactic fixation system. Pediatric dystonia is even more problematic as small children may not cooperate for the awake procedure, and heavy sedation may be needed that can prove fatal. GA is also not without problems. It interferes with clinical testing and assessment of adverse effects such as paresthesia or abnormal motor activity due to the damage of adjacent structures (internal capsule and medial lemniscus). If DBS is planned under GA, intraoperative MRI is essential for the electrodes' accurate placement [22]. The older children (adolescents) with preserved cognition may be the candidate for the awake procedure [23]. Thus, a suitable anesthetic plan should be discussed with the surgeon and the patient before the procedure.

Table 26.3 Surgical steps during deep brain stimulation (DBS) procedure

Step 1	Frame fixation/ventricular implantation: a stereotaxic base ring together with a localizer is fixed to the patient's head (Fig. 26.3a)
Step 2	Targeting MRI: High-resolution images of the target area are obtained and transferred via Ethernet to the computer workstation, which is used to derive the target coordinates and pathway or trajectory for the recording and stimulating electrodes and DBS electrode (Fig. 26.3b)
Step 3	Implantation of electrodes in target: Right and left frontal bur holes are made. The aiming arc is then placed on the base ring, and the microelectrode guide is attached to it (Fig. 26.3c). An array of four microelectrodes is advanced to the right (and subsequently the left) targets with continuous recording of electrical activity known as microelectrode recording (MER). A microelectrode is passed along its trajectory toward the target nuclei (STN or GPi) as neuronal activities are simultaneously recorded. Specific brain structures can be identified based on their unique patterns of spontaneous neuronal firing [18] Macrostimulation testing is done if the procedure is performed under sedation. It helps confirm whether stimulation at the confirmed location improves patient symptoms and causes no side effects Proper positioning is confirmed with intraoperative fluoroscopy The DBS electrode is then locked in place with a silastic ring, and fluoroscopy is repeated to assure proper electrode position; the other side is implanted similarly (Fig. 26.3d)
Step 4	Post-implant control MRI (Fig. 26.4b)/CT (Fig. 26.4b): to confirm the position of the electrodes
Step 5	Implantation of programmable stimulator: After the test stimulation has been found to be satisfactory, the permanent stimulator is inserted in the sub-clavicular region in a subcutaneous pouch

MRI magnetic resonance imaging; *DBS* deep brain stimulation; *STN* subthalamic nuclei; *GPi* globus pallidus interna

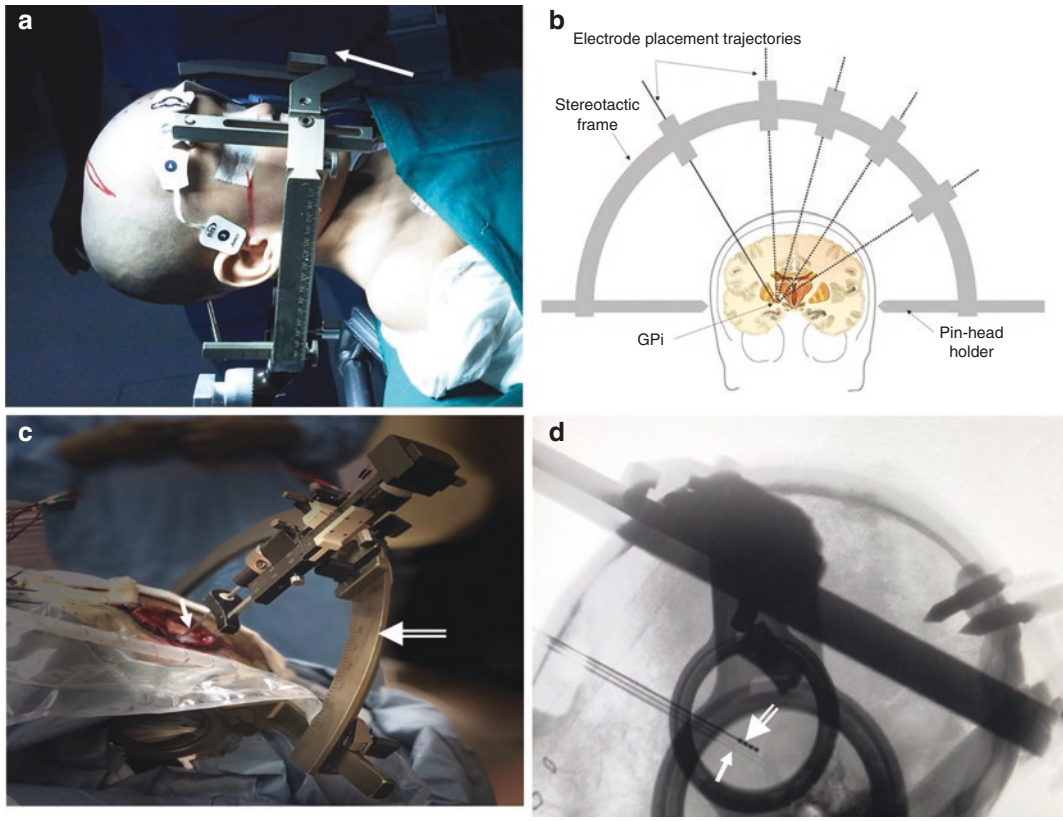

Fig. 26.3 Steps of DBS procedure. (**a**) Fixation of head frame (shown by arrow). (**b**) Planning for trajectory. (**c**) Implantation of electrodes: aiming arc (Leksell stereotactic frame, double arrow) and DBS guide tube (single arrow). (**d**) Fluoroscopic image during the procedure with DBS electrode (double arrow) and guide tubes (single arrow)

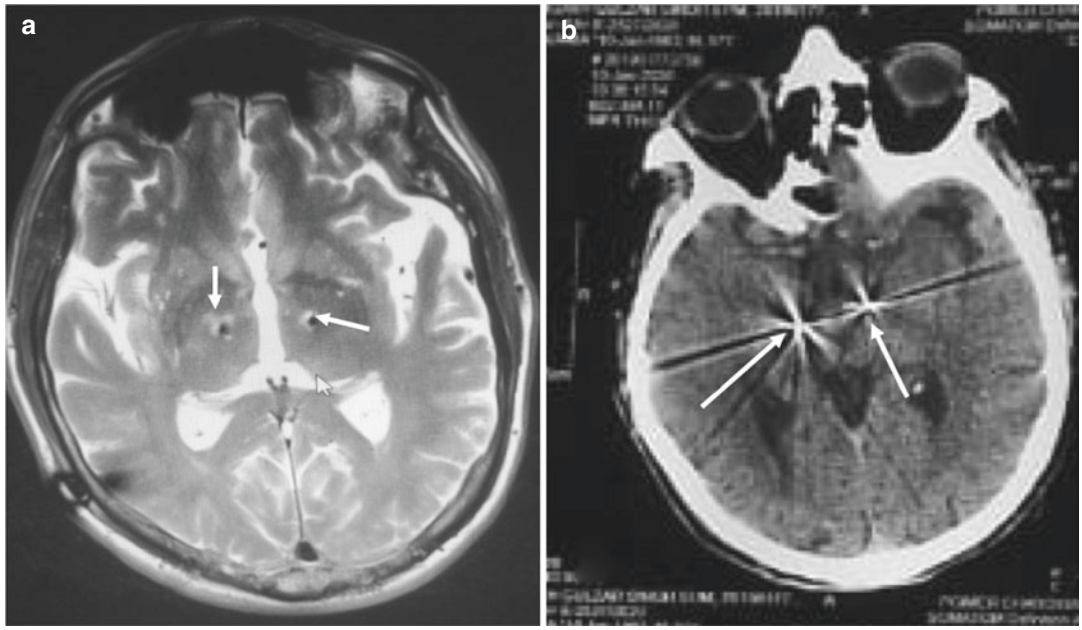

Fig. 26.4 Magnetic resonance imaging (**a**) and computed tomography (**b**) showing confirmation of placement of DBS electrodes (indicated by arrows) at the target site

The effect of various anesthetic agents on MER is mentioned in Table 26.4 [24–30].

26.5 Preanesthetic Preparation

A detailed preanesthetic checkup is needed before the procedure, emphasizing the primary pathology and pharmacotherapy therapy, explaining the perioperative risks, establishing a rapport with the patient, ruling out contraindications to MRI, and formulating the anesthetic plan. Adequate preoperative fasting should be followed as per guidelines. Among the routine blood investigations, the coagulation profile is most important as a deranged coagulogram is a risk of intraoperative intracranial bleed. The procedure should be delayed if the INR >1.5 until optimized. The concerns for the patient undergoing DBS are summarized in Table 26.5 [31].

26.6 Monitoring

Intraoperative monitoring includes an electrocardiogram (ECG), noninvasive blood pressure (NIBP), pulse oximetry (SPO_2), end-tidal carbon dioxide ($EtCO_2$), and bispectral index (BIS). As the total duration of anesthesia is prolonged, the patients are vulnerable to hypothermia. Hence, temperature monitoring and prevention of hypothermia is essential. The vital monitoring (ECG, NIBP, SPO_2, and $EtCO_2$) should be continued during transport to the MRI suite and then back to the operating room (OR). The monitoring poses a great challenge in the MRI suite as all the equipment should be MR safe or compatible. MR-safe devices are those which do not pose any additional risk to the patient while being used in an MRI suite. MR-compatible devices are MR safe and, besides, do not affect the image quality. Besides monitors in MRI suite, a slave monitor

Table 26.4 Effect of anesthetic agents on microelectrode recording

Anesthetics such as benzodiazepines, barbiturates, propofol, etomidate, and volatile agents [24]	• The effect of anesthetic drugs is non-homogeneous at different brain regions and varies with the target nuclei and specific disease • Potentiate the inhibitory actions of gamma-aminobutyric acid (GABA) within the basal ganglia. Hence, the effect will depend upon the amount of GABA input to the various nuclei • GPi neurons are known to have higher GABA input than STN. Hence, GPi neurons are more suppressed [25] • The effect on Vim nuclei is unclear • As subcortical areas are susceptible to GABA receptor-mediated medications, these can abolish the MER and stimulation testing [26] • Less than 1 MAC of desflurane has been successfully used in DBS surgeries [27]
Propofol [28, 29]	• Though it attenuates MER, it has been successfully used for MER from GPi, STN, and Vim • Reduces the firing rates of the GPi nucleus also in patients with dystonia and PD, more pronounced in PD • Should be stopped at least 15 min before the simulation testing
Dexmedetomidine	• Considered an ideal sedative agent for DBS surgeries • At doses of 0.3–0.6 μg/kg/h does not interfere with MER and assessment of motor functions in PD
Ketamine	• Has little effect on MER and has been used successfully in pediatric patients undergoing DBS [30]

GPi globus pallidus interna; *MER* microelectrode recording; *STN* subthalamic nucleus; *MAC* minimum alveolar concentration; *Vim* ventral intermediate nucleus; *PD* Parkinson's disease; *DBS* deep brain stimulation

Table 26.5 Anesthetic considerations and drug interactions for patients undergoing deep brain stimulation (DBS)

Parameters	Concerns
A. Disease-related	
Dystonia	• Risk of hemodynamic instability and laryngospasm • Spasmodic dysphonia and associated neurodegenerative disorder • Cerebral palsy—poor communication • Growth retardation
Epilepsy	• Recurrent seizures • Developmental delay • Multiple seizure medications: altered drug interactions
B. Drug related	
Drug interactions	**Levodopa** • Drugs decrease the efficacy of levodopa – Anticholinergic – Antispasmodics (dicyclomine and hyoscyamine) – Anti-histamines – Antiepileptic (phenytoin) – Tricyclic antidepressants (amitriptyline) – Metoclopramide • Drugs increase the effects of levodopa – Acetaminophen – Antacids containing aluminum – Calcium and magnesium • Severe nausea and vomiting • Levodopa potentiates the effects of antihypertensives resulting in a precipitous fall in blood pressure • Halothane increases the potential for arrhythmias in patients taking levodopa

may be placed in the console room. A closed-circuit television monitoring focused on the patient, and the monitor should be used to zoom in on the patient in the gantry. The anesthesiologist must be familiar with the fringe fields and the place where various resuscitation equipment can be used safely. MRI being a noisy procedure, earplugs, or other auditory protection during MRI may reduce the patient stimulation and may permit lesser doses of sedatives or hypnotic agents.

26.7 Anesthetic Techniques

Studies show that the accuracy of lead placement, outcome/success of DBS, cost of surgery, and the risk of complications are statistically the same when performed under GA with/without MER due to advances like neuronavigation and intraoperative MRI suite [22, 32–34].

Varied anesthesia techniques have been used, such as propofol infusion alone or in combination with fentanyl or remifentanil [35, 36]. These sedation techniques may be associated with airway and respiratory complications such as airway obstruction, respiratory depression, and aspiration [37, 38]. GA is usually administered in the pediatric population and patients with severe dyskinesias. In contrast, scalp nerves blocked with conscious sedation may be used in cooperative children [39–41].

26.7.1 Local Anesthesia/Awake Craniotomy

This technique is not very popular in pediatric patients and patients with dystonia. Local infiltration at the pin site for frame fixation and burr-hole incision site must be preferred with longer-acting drugs like bupivacaine and ropivacaine. Scalp block can also be given along or as a sole technique and has better hemodynamics than local infiltration [37]. The following nerves are blocked for DBS procedure: supratrochlear, supraorbital, zygomaticotemporal, and auriculotemporal. At each nerve, 1–2 mL of 0.25% bupivacaine with adrenaline (1 in 200,000) is given. The maximum dose of local anesthetic should be calculated before the infiltration. If the volume is insufficient, the strength can be diluted by adding normal saline to achieve the desired volume. As the scalp block is extremely painful, it should be given after adequate sedation-analgesia or under inhalational anesthetic agents, in pediatric patients. Re-infiltration at closure can be done if the patient complains of discomfort. The pulse generator procedure is obviously done under general anesthesia.

26.7.2 Monitored Anesthesia Care

Monitored anesthesia care (MAC) with sedation is a frequently used technique for electrode placement for DBS. The most commonly used drugs are midazolam, fentanyl, propofol infusions, and dexmedetomidine infusions. As benzodiazepines are known to cause interference with the MER, it should be given well before the procedure. All infusions are continued till the burr-hole part and then stopped 20–30 mins before the MER stage, except dexmedetomidine. Some authors have continued dexmedetomidine in low dose 0.2–0.3 μg/kg/h throughout the procedure without any significant effect on MER [42]. Supplemental oxygen is provided via nasal prongs or Hudson mask. BIS monitoring helps titrate sedation and arousal state for MER. Studies show that when BIS value >80, MER signals were equivalent to an awake state [31]. There is a limitation of using BIS to titrate sedation; it is not affected by non-GABA receptor sedative agents such as dexmedetomidine. Hence, it may underestimate the depth of anesthesia. Difficult airway equipment like fiberoptic bronchoscope and various sizes and types of laryngeal mask airway (LMA) need to be kept handy, as the rigid frame may hinder airway manipulation.

26.7.3 General Anesthesia (GA): Induction and Maintenance

GA provides a higher level of acceptance in some patients with anxiety, severe movement disorders,

pediatric age groups, and a preferred technique in children. The child is pre-oxygenated before induction, and GA is induced with intravenous fentanyl citrate (1 μg/kg), in the absence of the availability of shorter-acting remifentanil, followed by propofol (1–1.5 mg/kg) and atracurium besylate (0.5 mg/kg). The appropriately sized cuffed endotracheal tube should be used and taped securely after confirming the accurate placement. Both volatile anesthetic agents such as sevoflurane, isoflurane, desflurane, and total intravenous anesthesia (TIVA) using propofol and dexmedetomidine can be used. Antiemetics, such as ondansetron, a serotonin antagonist, should be used to prevent or treat emesis. After the fixation of the head frame, the child is transported for the targeting MRI.

Following the MRI, the child is transported back to the OR, the head prepared and fixed, to insert the electrodes into the target areas. During the MER phase, BIS is kept between 70 and 90. After the implant is placed, the patients are shifted for control MRI or CT scan. The patient is again transferred to the OR for implantation of the programmable stimulator. The neuromuscular blockade is reversed using neostigmine (0.05 mg/kg) and glycopyrrolate (0.08 mg/kg).

26.8 Complications

A larger series have described various surgical complications, including hematoma formation (supraventricular, micro-hematoma with minor symptoms, asymptomatic micro-hematoma, or subdural hematoma) and intraventricular bleed (trans-ventricular approach). Late complications include local site infection, hematoma in subcutaneous pocket, and rupture of external extension requiring re-implantation. To avoid hemorrhagic surgical complications, preoperative optimization coagulation profile is a must. Other complications reported are thromboembolism, venous air embolism, postoperative confusion, apraxia of the eyelid, and transient psychological complications such as mania, paranoia, and depression [43]. However, no mortality has been reported. Rarely, intraoperative ischemic events have been reported due to the deviation in entry point on the cortex or along the path causing vascular injury [44]. If intra-extracranial pressure gradient is preserved, it can avoid pneumocephalus and consequent brain parenchymal shift resulting in accurate electrode placement and better long-term outcome [45]. A case of tension pneumocephalus has been reported after pulse generator implantation. It was observed that the patient developed mild pneumocephalus after DBS electrode placement, and this air expanded due to the use of nitrous oxide during pulse generator placement under GA [46]. The common complications and their management are tabulated in Table 26.6.

26.9 Postoperative Care

Postoperatively, patients are shifted to an intensive care unit (ICU) or a high dependency unit (HDU) for overnight care and are discharged home on the postoperative day 3. Later on, the programming of the stimulators is done. When the procedure is performed under sedation and has proceeded uneventfully, some centers recently follow fast track (FT) protocol and shift patients to a neurosurgical ward after a CT scan in 6 h [47]. Thus, safe perioperative care needs a teamwork and well-designed protocols and infrastructure.

26.10 Patient with DBS Implant for Non-DBS Surgery

Preoperatively assess the patient for the indication for DBS insertion and optimize medical issues. The severity of symptoms should be assessed when the DBS stimulator is deactivated. When the device is turned off, and symptoms are severe, oral medications may be needed. Get information about the DBS device and check the battery status and last check by neuro physician. A chest x-ray should be done to identify the course of DBS wires not to be damaged during surgery.

Consult a neuro physician and make sure the programmer is aware and present during surgery

Table 26.6 Common complications in deep brain stimulation (DBS) surgery

Complications	Sign and symptoms	Prevention and management
Airway complications (during awake technique)	• Coughing • Sneezing • Laryngospasm or bronchospasm	• Judicious use of sedation • Administration of aspiration prophylaxis • Secure airway, if needed • Clear the airway < use nasal cannula/ nasopharyngeal/oropharyngeal airway < LMA < intubate
Respiratory depression (during awake technique)	• Desaturation • Tachycardia and hypertension • Bradycardia • Arrhythmias	• Check patency of airway, breathing, and circulation • Check level of sedation • Supplement oxygen or increase the flow and concentration • If still persists secure the airway
Intracranial hemorrhage	• Features of raised ICP • Loss of consciousness • Bradycardia, hypertension, irregular respiration • Seizures	• Optimize coagulation preoperatively • Manage airway/breathing/circulation • Measures to decrease ICP (decongestants/ give anesthetic agent to reduce $CMRO_2$/ control blood pressure)
Seizures	Due to cortical irritation and damage/ICH	• Check patency of airway, breathing, and circulation • Give Propofol boluses if MER is still planned • If not controlled, benzodiazepines and antiepileptics should be used
Venous air embolism	• Fall in end-tidal carbon dioxide • Hypotension • Tachycardia • Arrhythmias	• Immediately lower the head end and resuscitate as per hemodynamics • Supplement high oxygen concentration • Symptomatic treatment: manage vitals
Pneumocephalus	• If patient is awake: deterioration of consciousness, confusion, with or without lateralizing signs, severe restlessness • Seizures • If patient is under G-delayed awakening	• Urgent CT head • Small amount of air may get clear on its own, but tension pneumocephalus may need a burr hole and drainage
Neurological deficit	Injury/stimulation of internal capsule	• Neurological status should be examined periodically during electrode placement during MAC and LA • And immediately after awakening if the patient is under GA
Hypothermia	• Shivering • Acidosis	• Cover the patient as much as possible • Use warming blankets • Warm intravenous fluids
Deep vein thrombosis	Painful swelling in the legs	• Use compression stockings/graduated compression stockings

LMA laryngeal mask airway; *ICP* intracranial pressure; *$CMRO_2$* cerebral metabolic rate of oxygen; *ICH* intracranial hemorrhage; *CT* computed tomography; *MAC* monitored anesthesia care; *LA* local anesthesia; *GA* general anesthesia

[48]. ECG artifacts are seen due to DBS and, more so, in the unipolar stimulation type. If ECG interpretation is very difficult, one may have to put off the DBS and increase the medicine dose to tide over the off period [18].

Intraoperatively, turn the device off to decrease electromagnetic interference. During regional anesthesia, a higher level of sedation may be needed in patients with severe symptoms. The use of electrocautery can lead to thermal damage in the brain, reprogramming, or damage of the DBS [49, 50]. The use of bipolar diathermy may reduce these risks. If monopolar diathermy is used, place the grounding pad as far as possible

from the pulse generator, and diathermy should be delivered in the lowest energy with short pulses. When reprogramming is not possible during emergency surgery, proceed with precautions, such as use bipolar cautery, minimum power settings, and short bursts. Remember to turn on the device before reversal and extubation. Postoperatively assess the device function by doing a neurological examination, and the relevant representative should check the device.

Pacemakers may have cross-interference with DBS devices. Therefore, the pacemaker pulse generator and DBS stimulator should be implanted far from each other [51]. The use of both external and intracardiac defibrillators may cause thermal injury around the DBS device, resulting in malfunctioning or damage. The external defibrillator's paddles should be placed perpendicular to the DBS lead system and as far as possible from the pulse generator [18]. Electroconvulsive therapy (ECT) does not cause interference with the DBS system, but ECT electrodes must be applied away from the DBS system [52, 53]. A peripheral nerve stimulator also does not interfere with the DBS system. MRI can cause heating of the DBS system resulting in brain damage and reprogramming or damage of DBS devices, and these devices may cause image artifacts.

26.11 Conclusion

Deep brain stimulation in pediatrics is a well-established procedure for various neurological disorders. The anesthesia optimum technique is the one, which provides maximum patient comfort without interfering with electrophysiology. The choice of the anesthetic technique is individualized for safe and effective anesthesia. Several refinements and evolution of the surgical and the anesthetic techniques have been documented. However, larger multicentric collaborative studies are needed to provide evidence-based recommendations in the future. Good patient outcomes depend on teamwork and well-designed multidisciplinary consensus protocols and infrastructure.

Conflict of Interest Nil.

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Awake Craniotomy in Children

27

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Key Points

- Awake craniotomy is a commonly performed neurosurgical procedure that helps intraoperative electrocorticography (ECoG) or brain mapping to prevent injuries of the eloquent cortex when the surgery is carried out in its vicinity.
- In children, it is mainly indicated for epilepsy surgery and excision of supratentorial tumors on or near the eloquent cortex.
- The success of the procedure depends on the child's psychological preparedness to undergo the brain surgery in an awake state, hence, the importance of preoperative counseling.
- Uncooperative children, those with mental retardation, dysphasia, language problems, and diminished consciousness level, should not undergo awake craniotomy.
- The procedure is usually carried out with anesthetic techniques such as an asleep-awake-asleep (AAA) maneuver and monitored anesthesia care (MAC).
- Awake craniotomy is a safe and feasible pediatric practice option, which should be performed based on appropriate surgical and patient selection criteria.

27.1 Introduction

Awake craniotomy is a well-accepted neurosurgical procedure in adult patients that helps resection of lesions on or close to the eloquent cortex when surgery is carried out in its vicinity (Fig. 27.1). In the pediatric population, extraoperative mapping with strip or grid electrodes or intraoperative neurophysiologic monitoring (IONM) under general anesthesia (GA) is commonly preferred for brain mapping. As the GA is known to suppress the cortical responses, the brain mapping requires the patient to remain awake. The noninvasive functional mapping may also guide the resection of lesions around the eloquent cortex. Diagnostic modalities such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and magnetoencephalography are utilized, preoperatively, to localize sensory, motor, and language func-

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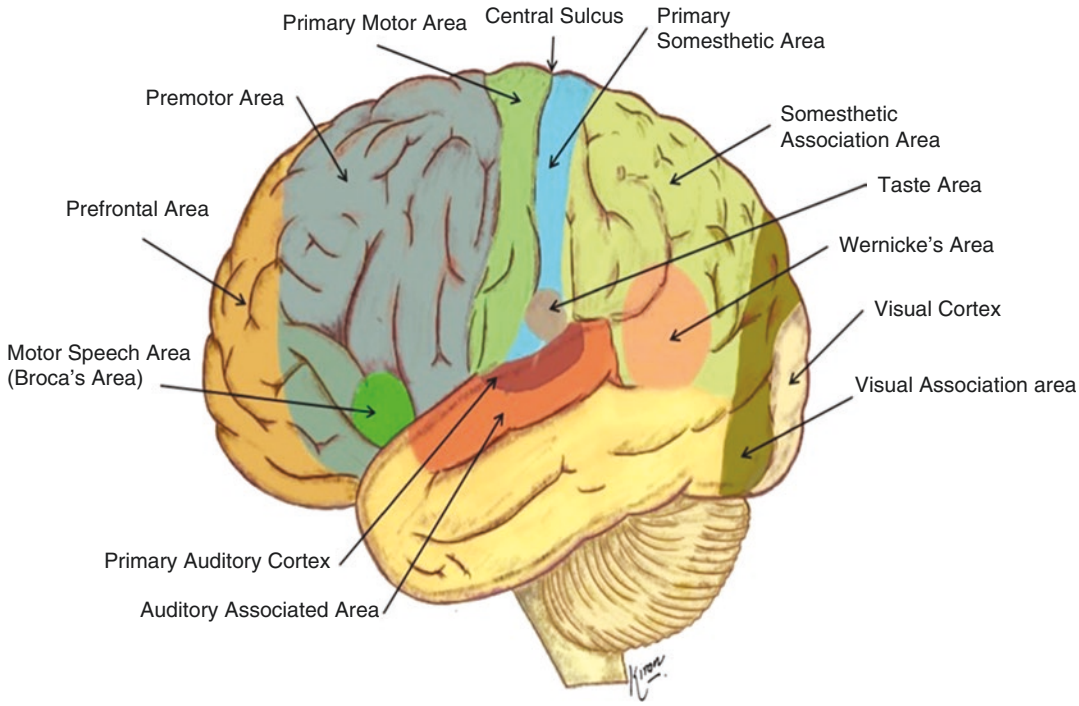

Fig. 27.1 Eloquent areas of the brain

tions [1, 2]. However, in children, these techniques have limitations in identifying the ictal foci; hence, they may have limited utility when the surgery is carried out near the critical cortex. Moreover, the fMRI identifies a specific cortical area during a definite task rather than the area critical to these functions. Hence, there is a possibility of overestimation of a functional cortex amounting to inaccuracies during resections of the lesions [1, 3]. Therefore, the procedure of awake craniotomy may be preferred in children, as in adults with similar indications, to overcome these inadequacies.

An eloquent cortex may be defined as a functional area of the brain, damage of which might lead to permanent neurologic deficits (Table 27.1; Fig. 27.1); the main areas of interest during awake craniotomy are Broca's motor speech area, Wernicke's sensory speech areas, and the motor cortex. The main goal of awake craniotomy is to preserve brain function with the performance of maximal possible resection of the lesion (e.g., tumor or epileptic foci) [4]. It may be associated with better operative outcomes as it avoids perioperative morbidity and complications of GA [5–7].

27.2 History of Awake Craniotomy

In ancient times, patients were treated for seizure disorder by trephination of the skull [8, 9]. Awake craniotomy was introduced for seizure disorders; its use was extended to different surgeries around near-critical regions of the brain. The modern methods of awake craniotomy took shape in the 1950s when Dr. Wilder Penfield, the first director of the Montreal Neurological Institute, performed craniotomies under local anesthesia (LA) in patients with epilepsy [10]. The realm of awake craniotomies further progressed with the advent of neuroleptic anesthesia techniques. However, the side effects of dopaminergic drugs such as dystonia and extrapyramidal symptoms led to less usage of this technique. During the 1960s, opioids combined with neuroleptics provided sedation and pain control; it was the preferred

Table 27.1 Eloquent cortex of the brain and its functions

Eloquent cortex	Brain area	Clinical implication
Primary motor cortex (Brodmann area 4)	Precentral gyrus, situated in the posterior portion of the frontal lobe. Located immediately anterior and parallel to the central sulcus (central fissure or Rolandic fissure)	Involved in executing voluntary motor (skilled) movements Stimulation causes focal movements of muscle groups in the opposite side of the body, based on area stimulated
Primary somatosensory cortex (Brodmann areas 3, 1, 2)	Postcentral gyrus lies in the parietal lobe, posterior to the central sulcus	Somatosensory homunculus represents the distribution of the contralateral body parts on the gyrus Process afferent somatosensory input and contributes to the integration of sensory and motor signals necessary for skilled movement
Primary visual cortex Striate cortex (Brodmann area 17)	Posterior pole of the occipital lobe; in the gyrus superior and inferior to the calcarine sulcus	Receives, integrates, and processes visual information relayed from the retinas
Primary auditory cortex (Brodmann area 41, 42)	Superior temporal gyrus in the temporal lobe	Responsible for the conscious perception of sound (pure tones and pitch)
Broca's motor speech area (Brodmann area 44)	Lateral frontal lobe in the dominant hemisphere, usually the left	Associated with speech production and articulation
Wernicke's sensory speech area (Brodmann area 22)	Posterior superior temporal lobe in the dominant hemisphere	Responsible for the comprehension of speech; associated with language processing (written/spoken) and understanding

method during awake craniotomies. The resurgence practice of awake craniotomy occurred in the early 2000s with the use of shorter-acting hypnotic agents like propofol, fentanyl, remifentanil, and dexmedetomidine. The use of propofol-remifentanil combination has revolutionized the concept of awake craniotomy, allowing advanced neurosurgical techniques and expanding the indications in various surgeries for supratentorial tumors, arteriovenous malformations (AVMs), and aneurysms near critical regions of the brain as well as in deep brain stimulation (DBS). With the advent of modern neuroaesthetic techniques and better perioperative care, the procedure of awake craniotomy became feasible and promising in pediatric patients where the use of noninvasive functional mapping methods such as fMRI and magnetoencephalography has not been proven effective to identify the eloquent cortex. Despite extensive literature in the adult population, only a few case series have been published to date regarding awake craniotomy in children [1, 11–15]. The most challenging aspects on which the success of these procedures depends are appropriate criteria for patient selection and psychological readiness of the child toward a surgical procedure to be carried out in an awake state.

27.3 Age and Awake Craniotomy

With decreasing age, a child's ability to understand, cooperate, and cope with the stressful surgical environment becomes more difficult. The minimal age for neurosurgery in awake state has not been well-established despite the fact that the youngest patient operated is 8 years old [16]. There is, however, no defined role for awake craniotomy in children less than 10 years because of non-cooperation and poor sensitivity of brain

mapping due to axon myelinization. The scarcity of literature regarding the procedure may also be attributed to the perception that the eloquent functions may recover and re-organize after an injury in very young children. Nevertheless, awake brain surgery (ABS) is considered feasible in the age group of 10 and 18 years (adolescents). Screening and preparation are essential during the preoperative period to identify a cooperative child who can safely undergo the procedure.

27.4 Indications and Contraindications for Awake Craniotomy in Children

Awake craniotomies were initially performed for epilepsy surgery and the excision of the tumors near the eloquent cortex; they have been expanded to involve managing other lesions such as intracranial hematomas, abscesses, and aneurysms and AVM bleeds. A stereotactic brain biopsy, burr-hole craniotomy for subdural hygroma, and deep brain stimulation (DBS) surgery may be the other indications for awake craniotomy in children. Refusal to consent and uncooperative children are common contraindications. Table 27.2 provides a comprehensive list of the indications and contraindications for awake craniotomy in children.

Table 27.2 Indications and contraindications for pediatric awake craniotomy

Indications and benefits	Contraindications
Tumors • Identification of eloquent areas • Better resection and preservation of neurological function	**Absolute** • Patient/parental refusal to consent • Uncooperative child • Mental retardation • Agitative child • Profound dysphasia and language problem • Learning/cognitive disabilities
Epilepsy • Identification of seizure foci • Preservation of eloquent cortex • Permits intraoperative ECoG monitoring without undue suppression by anesthetic agents	**Relative** • Anticipated difficult intubation • Obstructive sleep apnea • Chronic cough/ wheezing • Uncontrolled seizures • Highly vascular tumors • Down's syndrome • Medical conditions preventing the child from lying down for long hours
Vascular lesions • Arteriovenous malformations • Intracranial aneurysms • Cavernomas	
Dystonia • Deep brain stimulation (DBS) surgery	

27.5 Preoperative Preparation of the Child

27.5.1 Preoperative Team Visit

A multidisciplinary team involving neurologists, neurosurgeons, neuroanesthesiologists, neuropsychologists, and neurophysiologists together should assess the suitability for the procedure and risk-benefit ratio; it helps achieve maximal postoperative neurosurgical and cognitive outcome. Children who are uncooperative, those with mental retardation, dysphasia, language problems, and diminished level of consciousness should not undergo awake craniotomy. Children with comorbid conditions like obstructive sleep apnea, difficult airway, cognitive disorders (e.g., Down's syndrome), pre-existing neurological deficits, and features of significant brain swelling should also not be considered for the procedure (Table 27.2).

The team members (Fig. 27.2) should take part in the preoperative counseling of the patient. The counseling normally includes a thorough psychological assessment to build trust and allay anxiety at both the child and parental levels. Poor communication and inappropriate preparations may lead to a lack of intraoperative cooperation; these are the most common causes of failure of performing awake craniotomy in children [17, 18]. Suppose the native language of the child differs from the operative team. In that case, a language translator should be part of the team who should build rapport during the preoperative visit for better intraoperative communications. Adequate patient preparation appears to have a

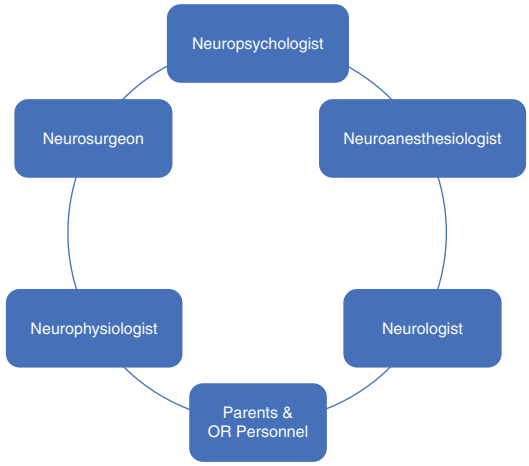

Fig. 27.2 Team management for pediatric awake craniotomy

protective effect on the psychological sequel of an awake craniotomy [19]. Despite adequate psychological preparation, at least 10–15% of adults reportedly develop intraoperative anxiety issues [20]. Therefore, the risk of psychological and anxiety problems is expected to be even more, in the pediatric population. Hence, an evaluation by a child psychiatrist and speech therapist is essential. Many clinicians proposed their institutional protocols to deal with such issues. Labuschagne et al. [21], in an 11-year-old, planned for awake brain surgery (ABS) and arranged a simulated theater experience before the actual surgery being carried out, with a close replication of the operating room (OR) attire, lighting, monitors, and positioning. This exercise enabled the OR team to assess the child's coping skills and helped the anesthesiologists decide appropriate anesthetic techniques. Riquin et al. [22] described a very comprehensive preparation phase, including having the child examined by a child psychiatrist and exposing to hypnotic conditioning. The child was offered an opportunity to meet another child who underwent surgery in an awake state by showing the patient pictures and a video describing the atmosphere of the OR, a visit to the OR, and a chance to meet the surgical and anesthetic team. The technique of hypnotic conditioning was utilized at the time of anesthesia induction. None of the patients reported any long-term psychiatric or psychological issues when evaluated at 3 months, thus concluding that ABS is an equally safe and feasible option for pediatric patients. McDowell and colleagues [23] developed and implemented a novel protocol in collaboration with certified child life specialists (CCLS) to enhance the patient experience and compliance surrounding awake craniotomy, thereby strengthening the ability to tolerate the procedure in pediatric patients. The protocol was found to be feasible, although it requires prospective validation. Huguet et al. [24] proposed a protocol for institutional practice and derived a set of selection criteria based on medical, psychological, and institutional factors. It was highlighted that the age of the child should not be the main criterion for selection. Instead, developmental and psychological maturity should be given priority while selecting a pediatric patient for ABS. Nevertheless, the age cut-off of 10 years seems appropriate mainly due to methodological reasons. There is limited child collaboration at age less than 10 years, the higher current intensity requirement, and reduced mapping sensitivity of both motor and language functions apart from the anesthetic reasons.

27.5.2 Preoperative Workup

It should include fMRI to locate the dominant hemisphere precisely apart from conventional MRI. The fMRI has been advocated in adults as well as children not only for its diagnostic superiority but also for its use during neuronavigation.

From an anesthesiologist's perspective, a thorough evaluation of the airway and the risk of airway obstruction under sedation should be assessed, and the anesthesia technique should be chosen accordingly. The extent of the lesion, degree of brain edema, intracranial pressure (ICP), surgery duration, and the expected intraoperative blood loss should be discussed by the operative team and planned as desired. Patient drug charts need to be reviewed for the antiepileptic medications if any and should be continued till the morning of surgery.

27.5.3 Premedication

Antibiotic and antiemetic prophylaxis should be given at the start of surgery. Parenteral presence before induction of anesthesia (PPIA) in children to reduce anxiety is controversial but is expected to reduce psychological impact. PPIA has been suggested to be an effective means of anxiety management in neurosurgical procedures for both parents and children [25]. But whether PPIA could be extended to the practice of pediatric awake craniotomy or not is debatable. Premedication with short-acting benzodiazepines has been opted by few clinicians [11], but many still reject it as it interferes with the cortical mapping and ECoG recordings [26]. However, some physicians prefer short-acting benzodiazepines such as midazolam for anxiolysis. Intravenous (IV) cannulation may be carried out by a painless method with prior (30 min to 2 h) application of a eutectic mixture of LA (EMLA) cream. The dorsum of the hand on the side not to be used for intraoperative evaluation, i.e., ipsilateral to the side of the lesion, is preferred for this purpose. It is better to secure another IV access under sedation for further requirements during the perioperative period.

27.5.4 Operating Room Setup

On the day of surgery, all necessary anesthetic equipment for GA should be prepared. An airway trolley that includes appropriate sizes of face masks, laryngeal mask airways (LMAs), nasopharyngeal airways, and endotracheal tubes (ETTs) should be available. It is better to keep the video laryngoscope and fiberoptic bronchoscope of appropriate sizes ready for possible airway loss during the intraoperative period. The OR temperature should be set as per the comfort of the child, and unnecessary noise should be strictly avoided. Warming mattresses or blankets should be kept ready along the prewarmed fluids to prevent hypothermia and shivering during the surgical course. Possible locations of different OR personnel and equipment are depicted in Fig. 27.3. It is essential to place a board at the OR's entrance informing others that an awake procedure is going on. The OR staff should also be restricted from speaking appropriately and not utter anything that may upset the child.

27.5.5 Positioning of the Child

The location of the lesion always decides the position of the patient. Usually, a supine or lateral position is preferred for awake craniotomy. A sitting or semi-sitting position may be utilized for lesions located in the occipital cortex; however, the comfort of the child is of utmost importance. The OR temperature must be appropriate; the surgical table should be covered with a soft, thick mattress. The surgical team must be instructed to speak softly inside the OR. It is important to remember the instruments' position (Fig. 27.3) to minimize unnecessary movements of objects and OR personnel. The face must be in a position that allows the child to look at the anesthesiologist, interact whenever required, and participate in various brain mapping tasks (Fig. 27.4). The face should also be adequately accessible to secure the airway during intraprocedural emergencies. An L-shaped bar attached to the operating table's left side is used to hang the surgical drape; it prevents the patient's face from being covered. Tenting of the drapes over the face helps achieve these objectives. A rigid pin fixation is used for the head holding; immobility is beneficial during the stimulation mapping. An audio-video recorder system may be used so that the operating surgeon can see and hear the patient's responses during cortical mapping [27].

27.5.6 Anesthesia Techniques

The goals for anesthesia are to optimize the child's conditions for cortical mapping and keep the child awake yet cooperative during intraoperative neurological testing while minimizing the surgical pain and anxiety (Table 27.3). The choice of anesthetic regimens depends on an interplay of multiple factors, which include age and psychological maturity of the child; psychological pre-

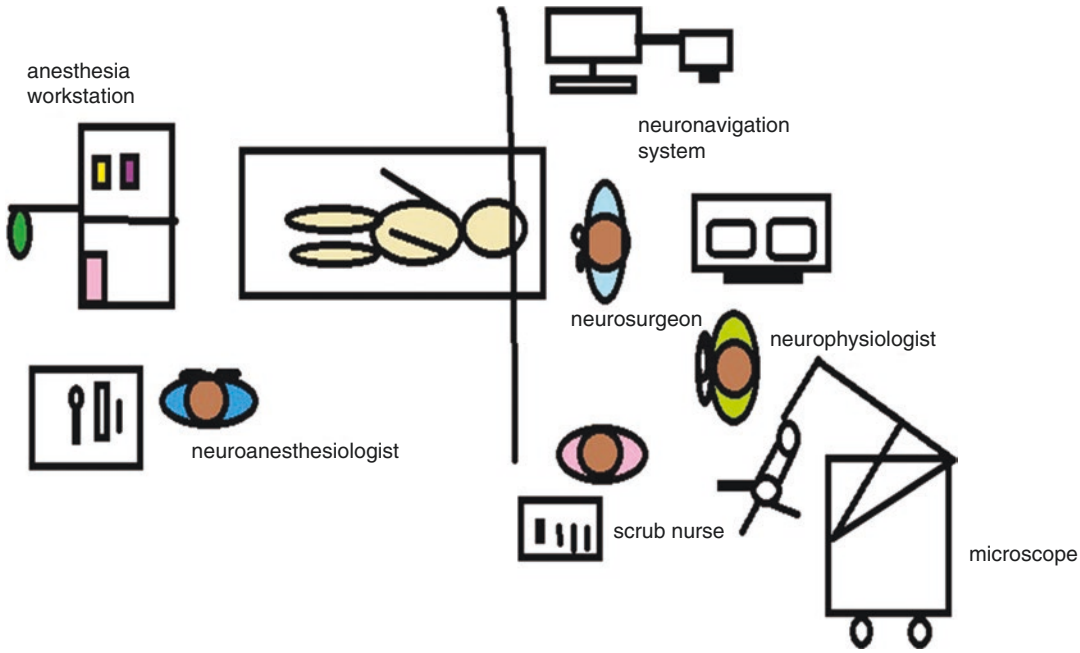

Fig. 27.3 Proposed operating room set up for pediatric awake craniotomy

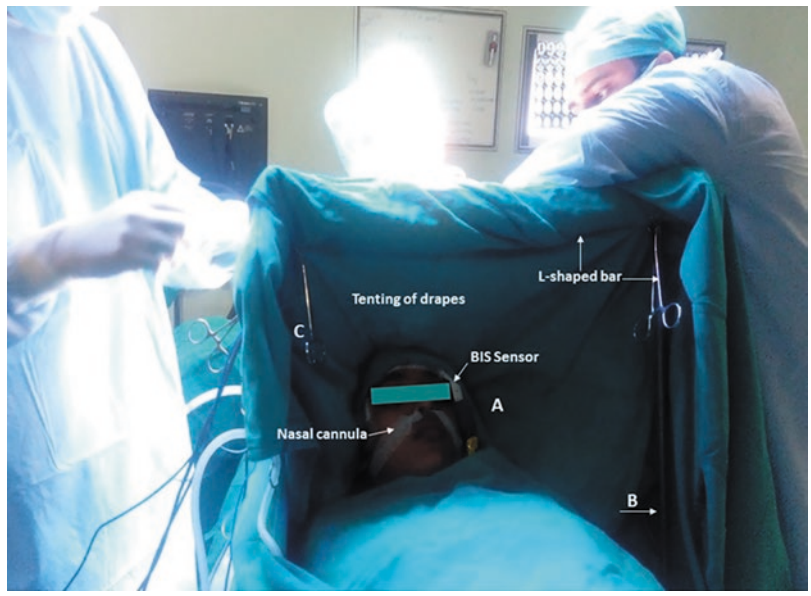

Fig. 27.4 Shows patient positioning in a 14-year-old female child undergoing awake craniotomy. (A) Child head fixed with Mayfield clamp, not visible, and the tenting of surgical drapes helps the child's face visible and accessible to the anesthesiologist. (B) L-shaped bar attached to one side of the Table. (C) Surgical clamp utilized to secure the drapes on the L-shaped bar

paredness; comfort in patient positioning; duration of surgery; extent of the lesion; adequacy of analgesia, including the scalp nerve block; and appropriate communication among the team members. The anesthetic regimens commonly used in pediatric ACs are (a) sleep-awake-sleep (SAS) or asleep-awake-asleep (AAA) technique and (b) conscious sedation (CS) or monitored anesthesia care (MAC). In the AAA technique, the child is anesthetized (GA) with or without airway devices until dural opening and is allowed to wake up with airway

Table 27.3 Anesthetic goals for pediatric awake craniotomy

• **Maintain cooperation of the child**
Provision of optimal analgesia, sedation, and anxiolysis
Comfortable positioning of the child
Prevention of nausea, vomiting, and seizures
• **Achieve homeostasis**
Provision of safe airway/adequate ventilation
Ensure hemodynamic stability
• **Minimal interference with ECoG recording**
During epilepsy surgery

removal; GA is again induced after excision of the lesion. In MAC, the patient is kept comfortable for surgery, targeting different sedation levels at various points of surgery and maintaining spontaneous breathing. MAC techniques [28, 29] and AAA or SAS [1, 14] methods have been utilized quite often, with none recommended superior to the other. However, the most extensive study on pediatric awake craniotomies favored the AAA technique over MAC [26]. Agitation and non-cooperation due to pain are significantly higher in children as compared to adults. Hence, the utmost goal of a regimen in children should be to provide balanced anesthesia or sedation to prevent anxiety and agitation and simultaneously achieve intraoperative neurophysiologic and cognitive benefits.

27.5.6.1 Asleep-Awake-Asleep (AAA) Technique

Here, the first part of the surgery is conducted under the asleep phase after the induction of GA using hypnotics such as propofol and short-acting opioids such as remifentanil and fentanyl. The airway may be secured with LMA as it causes less coughing and gagging as compared to the ETT. The child can be kept under either spontaneous or mechanical ventilation. Procedures such as an arterial cannula, a central venous catheter (CVC), and Foley's catheter placements should be carried out after induction of anesthesia. Utmost care should be taken while positioning the child; adequate padding, warmth, and comfort should be ensured as the surgical procedure with multiple tasks may get prolonged and tiresome for the child. Surgical drapes are kept in a tented position away from the face for easy communication; it helps prevent claustrophobia in the awake phase (Fig. 27.4). Before applying Mayfield clamps, the scalp block is given using LA agents like bupivacaine and ropivacaine. Additionally, the skin may be infiltrated at pin insertion as well as the skin incision sites.

The asleep phase can proceed until the dura is open, after which the patient needs to be awakened for resection of the lesions under various neurophysiological monitoring methods. During the awake phase, LMA may be removed using a "no-touch technique" [26], following which supplemental oxygen can be given via nasal prongs or an oxygen mask.

During the third phase (asleep phase), after the resection of the lesion, the child may be allowed to remain asleep again, using light sedation or GA. This phase is crucial as the child might be tired of a persistent posture for a prolonged time and may not cooperate until skin closure. However, some clinicians prefer not to anesthetize the patient at this stage, which is known as the *asleep-awake (AA) technique* [27].

The AAA technique is more comforting to the child and the operative team as the asleep phase causes lesser anxiety and agitation in the intraoperative period, the ability to provide adequate analgesia, and the ability to control brain swelling by controlled ventilation advantages of this technique. However, the choice of anesthetics should be done judiciously and be appropriately timed off so that they do not affect the neurophysiologic monitoring.

27.5.6.2 Monitored Anesthesia Care (MAC) or Conscious Sedation (CS)

With this technique, the child remains awake or moderately sedated and maintains a spontaneous airway throughout the surgery [30]. This approach needs a completely relaxed, matured, and cooperative child as several painful procedures are performed such as IV catheter placement, screw fixation, craniotomy, dural incision, and scalp closure though adequate analgesia is assured by using scalp block and short-acting analgesics. This procedure is performed in such a

way that the child remains sedated but is arousable with the use of short-acting agents to avoid respiratory depression and airway compromise. The child is made fully awake just after dural opening till dural closure for cortical mapping and tumor (lesion) excision. A frequently used sedative regimen includes low-dose propofol 20–50μg/kg/min and remifentanil 0.01–0.06μg/kg/min infusions titrated to make the child drowsy yet arousable without any airway obstruction. Awake craniotomy under MAC may also be carried out with an infusion of dexmedetomidine 0.2–0.7μg/kg/h [31].

27.5.6.3 Regional Scalp Block

Regional scalp block is a well-described procedure in adult neurosurgical patients undergoing awake craniotomy [32]. The scalp is locally anesthetized in children by blocking of both the anterior scalp (supraorbital and supratrochlear nerves) and posterior scalp (greater occipital nerves) using 0.25% bupivacaine with 1:200,000 epinephrine along with frequent aspirations to prevent intravascular injection (Fig. 27.5). The "scalp block" in children has been extended to block six nerves on either side, such as the supraorbital, supratrochlear, zygomaticotemporal, auriculotemporal, lesser occipital, and greater occipital nerves for awake craniotomy [33]. The regional scalp block remains an adjunct to the anesthetic techniques followed. As the procedure is painful, it should be carried out once the child is sedated or anesthetized. Apart from scalp block, LA infiltration of the Mayfield head clamp's pin site and along the incision lines, preferred. Scalp block also offers advantages of intraoperative hemodynamic stability, decreased side effects of high-dose opioids (nausea, itching), respiratory depression, and postoperative pain relief. As an alternative to the bilateral nerve blocks of the scalp, some clinicians prefer performing a ring block of the scalp where LA is infiltrated circumferentially around the scalp 2 inches apart to complete a ring to prevent nerve impulses to that area. As the scalp block requires a large volume of LAs infiltrated, it is desirable not to exceed the upper limit for the individual agents suggested (Table 27.4) [34]. The use of vasoconstrictors such as adrenaline at dilution of 1:200000 (5μg/ml) helps minimize LA toxicity by reducing absorption and maximizing the blockade duration.

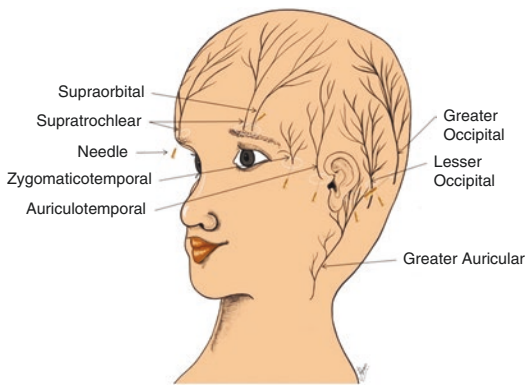

Fig. 27.5 Schematic diagram of regional scalp block in a child

27.5.7 Choice of Sedatives and Anesthetics

Various sedatives and anesthetic drugs have been used during pediatric awake craniotomy with the AAA technique. They include propofol, remifentanil/fentanyl combinations, and dexmedetomidine either alone or in combination with propofol infusions. Propofol is preferred over volatile anesthetic agents for easy titrability, the effect on ICP, and the ability to maintain cerebral perfusion pressure (CPP). It is used in dose ranges of 90 to 150μg/kg/min for anesthesia maintenance in the AAA technique and 50–100μg/kg/min for sedation [26]. However, at higher doses, especially in patients under MAC, complications such as hypoventilation, respiratory depression, and hemodynamic instability may be encountered. Propofol does not have an analgesic effect; and hence, it has to be given in combination with opioid-based regimens, which may further aggravate respiratory depression. It has antiepileptic properties that may interfere with ECoG responses, and hence, the infusion is preferably stopped 20 min before the recording.

Dexmedetomidine is a highly selective α-2 agonist added to the armamentarium of awake

Table 27.4 Commonly used local anesthetic drugs for scalp block in children

Drug(s)	Dose (mg/kg)		Onset of action	Duration of action[a] (h)
	Without adrenaline	With adrenaline		
Lidocaine	4.5	6–7	Fast (1–3 min)	1–3
Bupivacaine	2–2.5	2.5–3	Slow (2–10 min)	2–8
Levobupivacaine	2	3	Slow (2–10 min)	4–12
Ropivacaine	2–3	3–4	Slow (3–15 min)	5–8

[a]Maximum duration of action mentioned includes the addition of adrenaline

craniotomy. It provides sedation, analgesia, and anxiolysis without any significant respiratory depression. When added to propofol and opioid regimens, dexmedetomidine decreases the requirements of opioids, the incidence of respiratory depression, and interference with intraoperative neurophysiological monitoring (IONM) [35]. The data available on dexmedetomidine use in pediatric awake neurosurgery is limited. Ard et al. [12] were the first to report its use in the SAS technique for the smooth conduct of awake neurosurgery and neurophysiologic testing in children. It was used in doses of 0.15–0.3μg/kg/h without causing any interference with ECoG recordings. Since then, it has been used in many pediatric awake neurosurgeries safely. Dexmedetomidine infusion (0.2–0.7μg/kg/h) is normally started after a loading dose of 0.5–1μg/kg given over 10–15 min. Due to its central sympatholytic action, dexmedetomidine may cause hypotension and bradycardia. When given too rapidly, it may cause intense hypertension due to peripheral vasoconstriction.

Standard analgesia for awake craniotomy can be achieved with scalp block. Despite the reliability and efficacy of scalp block, some patients may complain of pain; moderate pain incidence is approximately 20% [26]. The use of short-acting opioids like fentanyl boluses or remifentanil infusion is indispensable in such scenarios.

27.5.8 Routine Monitoring

Standard monitors such as electrocardiography, pulse oximetry, respiratory rate, and noninvasive and invasive blood pressure are applied (Fig. 27.6). In sedated and spontaneously breathed children, the end-tidal CO_2 can be monitored along with a nasal cannula, which helps simultaneous supplementation of oxygen (2–3 l/min). Foley's catheterization should be done after the child is sedated or anesthetized during the initial asleep phase; it helps monitor the urine output. Various depth of anesthesia monitoring modalities using processed electroencephalogram such as bispectral index (BIS) and spectral entropy [36] may help titration of sedatives and anesthetics as well as help well-timed emergence. Clinical sedation assessment scores such as Ramsay sedation score (RSS) [37, 38] and Mackenzie and Grant score [39] are commonly utilized to keep track of the sedation level, with RSS targeted between 2 and 3 during the procedure.

27.5.9 Neurophysiologic Monitoring

Historically, preoperative functional brain mapping has been used to identify the eloquent areas of the cortex. However, recent advances recommend the use of intraoperative neurophysiological mapping. An experienced neurophysiology team is essential for evaluating the functional testing and monitoring during the stimulation mapping. Constant communication among the team members, particularly during the procedure, is an important aspect. This procedure has the added benefit of keeping a patient awake and, hence, considered as the standard care during excision of supratentorial lesions. Other benefits of intraoperative stimulation and mapping include its ability to provide direct, quick feedback to the neurosurgeon, its reliability on brain shifts, and the advantage of identifying and continuously monitoring all functionally important

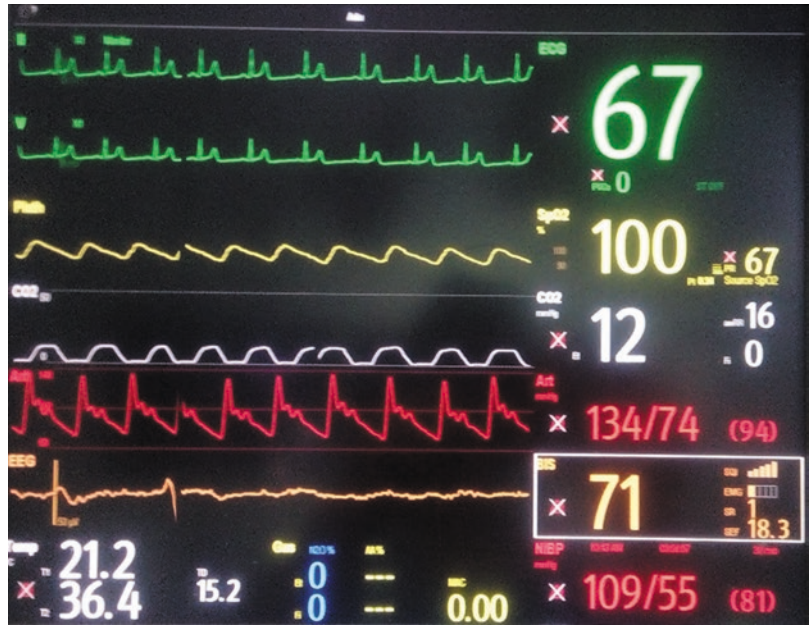

Fig. 27.6 Standard monitoring in a child undergoing awake craniotomy under monitored anesthesia care (MAC)

structures during the resection. Penfield method is the most common technique which utilizes bipolar stimulation at 50–60 Hz for this purpose.

Functional mapping for the sensorimotor areas is safe and effective in children belonging to different age groups, including infants (motor only) [40].

27.5.9.1 Motor Mapping

Motor cortical mapping is done primarily in lesions close to the precentral gyrus (frontal lobe) and corticospinal tracts. It is performed by direct electrical stimulation of the brain using a hand-held stimulator and performed by placing a bipolar or monopolar electrode on the cortical surface with typical initial use of current at a frequency of 60 Hz and amplitude 1 mA. The stimulation parameters may vary based on various studies: between 0.14 and 200 ms for pulse width, 20 and 50 Hz for frequency, 0.5 and 200 mA for current intensity, and 3–25 s for the train [40].

The motor strip location is estimated, and this area is stimulated at increasing amplitudes until movements are visually demonstrated on the contralateral side of the body. As the stimulation mapping requires repetitive electrical stimulation of the cortex with higher currents, there is a possibility of focal or even generalized seizures. Iced cold saline is kept ready for irrigation; its use aborts the focal seizures and prevents secondary generalization. Simultaneous motor-evoked potential (MEP) recordings may also be done to corroborate the findings. Identification of the central sulcus can easily be made using the phase reversal technique on somatosensory-evoked potential (SSEP), alternatively [41]. However, it should be borne in mind that cortical mapping in children less than 10 years of age requires higher charges (amperage threshold) than adults due to the presence of a higher percentage of unmyelinated fibers resulting in lesser excitability of the motor cortex.

27.5.9.2 Language Mapping

Language (speech) mapping is normally performed in the left hemisphere of the brain, where most of the language areas are present. It includes a battery of tasks to be completed by patients while the cortical regions are stimulated. The language functions tested depend on the site of the lesion. They include verbal fluency (e.g., enumeration of the months of the years, days of the week, engaging conversation about hobbies, about families), repetition (of word or sentences), comprehension (pyramids and palm test or sentence completion), visual object naming, word

generation, reading, and writing. For language mapping, the technique involves using bipolar current at a frequency of 50–60 Hz. Two types of responses are obtained after electrical stimulation, namely, "positive response" when the speech is facilitated by stimulation, and "negative response," where the speech is suppressed or arrested. Continuous ECoG should also be monitored to detect subclinical seizures, which could be a source of naming errors.

27.5.9.3 Mapping of Visual Function

Few neurosurgeons prefer visual mapping for tumors located near the occipital cortex; it is carried out more in younger patients with anticipated partial or complete loss of vision that may significantly compromise the quality of life. The simple responses include the visualization of dark spots and shapes that correlate with the calcarine fissure and peristriate cortex stimulation, respectively. The complex responses include the visualization of formed hallucinations corresponding to stimulation of basal temporo-occipital cortex [42, 43]. The drawbacks of visual mapping are the possibility of seizures induced by the direct stimulation of the cortex, and the technique does not ensure the functional integrity of motor tracts. Moreover, the injuries of nerve tracts due to vascular injuries or pressure of retractors are gradual in onset and may not be directly evident on mapping techniques.

27.5.9.4 Electrocorticography (ECoG)

ECoG provides recordings directly from the surface of the cerebral cortex employing grid and/or strip electrodes. It is frequently applied during surgery for tumors accompanied by secondary epilepsy or medically refractory seizure disorders to identify the seizure foci and the irritative zone and to predict the surgical outcome in epilepsy surgeries. The major advantages of using ECoG readings are that it provides pre- and post-resection seizure foci and helps in better delineating the eloquent cortex by direct electrical stimulation. Cortical stimulation mapping is normally carried out along with ECoG for functional mapping of the cortex and identifying critical areas with the patient in an awake state. The simultaneous ECoG recording is used to determine spontaneous or stimulation-induced epileptic discharges known as after discharges (ADs). The ADs occur after the current stimulation of the cortex to detect non-convulsive seizures. Ideally, the current strength used for cortical stimulation should not exceed the threshold for the occurrence of ADs [44]. However, the concept is limited by the variations shown in the threshold of ADs across the cortex [45].

27.5.10 Management of Complications

Various complications known to adult awake craniotomies such as seizures, intraoperative hypertension, airway obstruction, agitation, and brain bulge may also occur during pediatric awake surgeries (Table 27.5). Serious complications may occur in 20% of the children [26]. Seizure incidence may vary from 3% to 16%, with a higher incidence occurring in children with epilepsy on presentation. Continuous and successive stimulation of cortical areas during mapping amounts to higher risk. Local anesthetics, if used at higher than the maximum allowable doses, may lead to seizures. The prevention of seizure is important during awake craniotomy as a generalized tonic-clonic seizure (GTCS) may lead to Todd's palsy. Later on, it may be difficult to get motor responses

Table 27.5 Possible complications during pediatric awake craniotomy

System(s)	Complications
Respiratory complications	• Airway obstruction • Respiratory depression
Cardiovascular complications	• Hypotension or hypertension • Tachycardia or bradycardia
Neurological complications	• Seizures • Neurological deficit • Brain swelling
Other complications	• Pain • Agitation • Nausea/vomiting • Non-cooperation and conversion to general anesthesia (GA) • Venous air embolism (VAE)

on the affected side. Therefore, the LA doses must be kept within the maximum safe limit to prevent toxicity [46]. Preoperative antiepileptic medication is necessary except during excision of epileptic foci. Low-voltage stimulation used for cortical mapping is expected to reduce the incidence of seizures. In case of intraoperative seizures, ice-cold saline (3–4 °C) should be irrigated using an aseptic syringe, and the patient's head must be supported. The cold saline irrigation remains the first line of management, followed by small propofol or midazolam boluses to abort the continuous seizures. Additionally, antiepileptic drugs (AEDs) such as phenytoin, benzodiazepines, barbiturates, and valproate may be given. However, AEDs might not be a good choice as they interfere with cortical mapping and ECoG recordings. Conversion to GA should be the final option if nothing helps control seizures that may lead to bodily harm or excessive sedation and respiratory depression leading to loss of airway. Seizures are reported in 3.3% of cases [26] and are usually self-limiting and stopped with ice-cold saline irrigation.

To avoid local anesthetic systemic toxicity (LAST), calculated doses of LA with intermittent aspiration should be used. Adrenaline may be added to reduce systemic absorption; however, it is essential to watch for probable seizures and the cardiovascular toxicity of LAs. Management should include rescue measures, thiopentone sodium, or propofol boluses to control seizures; even conversion to GA may be required. IV intralipid may also help counter LAST.

Agitation (incidence 6.7%) has been suggested to be the most common complication; it is an expected effect of the young age and may also due to fear of pain. Hypertension may occur secondary to agitation, anxiety, and pain.

Pain is a frequent complaint during awake craniotomies; it leads to more severe agitation and non-cooperation in children. Special care should be taken at the time of application of Mayfield pins, skin incision, dural incision, and surgical handling around perivascular structures. Scalp block is efficacious but may not be sufficient always. Hence, there is a need to perform additional skin infiltration at pin sites, pledgets soaked with LA solutions to be placed on the dura, and boluses of short-acting opioids or administration of IV paracetamol. Care should be taken to avoid excess opioid administration, which may cause respiratory depression and somnolence interfering with the mapping tasks. Excessive opioid administration may lead to nausea and vomiting sensations, which might be quite disturbing both for the patient and the operating neurosurgeon, mainly when the head is pin-fixed. Pre-emptive antiemetics and dexamethasone may preferably be given at the start of surgery to prevent nausea and vomiting.

Respiratory depression may occur due to various reasons, most commonly, as the sedative agents' side effects. It may lead to loss of airway, and may require different maneuvers for treatment, ranging from awakening the child, jaw thrust, and insertion of a nasopharyngeal cannula to the placement of an appropriately sized supraglottic device. A high-flow nasal cannula (HFNC) may be considered [47] in children where airway obstruction is a concern (e.g., obese child).

Brain swelling (tight brain or brain bulge) is another serious problem that requires careful attention. The patient may be encouraged for self-hyperventilation (hypocapnia). An extra bolus of the hyperosmolar solution may be given, particularly during tumor surgeries. Generally, large tumors with significant peritumoral edema are not advisable to undergo awake surgery as they are prone to intraoperative brain bulge.

VAE is a rare but catastrophic complication; sitting awake craniotomy increases the risk further. In an awake child, continuous coughing with a fall in oxygen saturation and tachypnea should raise suspicion toward VAE. It is well reported among adults undergoing awake craniotomy [48–50]. VAE is also reported to children undergoing awake craniotomy [51], although pertinent data concerning the pediatric patients is scarce.

27.6 Postoperative Care

In the postoperative period, the child should be nursed in a head-up position. Vitals should be monitored with special attention toward tempera-

ture, urine output, and pain assessment. Children younger than 6 years can be evaluated by the Faces, Legs, Activity, Cry and Consolability Scale (FLACC, 0–10 scores) [52] and the Wong-Baker Faces Pain Rating Scale (WBFS) [53]. For children older than 6 years, both the numeric rating scale (NRS) [54] and WBFS scale may be considered. The WBFS is composed of sequences of facial images suggesting the "worst pain imaginable" to the happiest face, depicting "no pain." NRS is a line of pain intensity, marked with numbers 0–10, where "0" indicated "no pain" and "10" suggests "worst pain imaginable." The patient might complain of nausea and vomiting and needs to be managed as per the protocol. Early and "on-demand" oral feeding should be started in the postoperative period in these children. Although fluids can be started as early as possible, yet caution should be exercised for solids as opioids are administered during the intraoperative period. Continued assessment for the new-onset neurological deficits and seizures should be done in the postoperative period.

27.7 Conclusion

Awake craniotomy is a safe and feasible pediatric practice option that should be performed based on appropriate surgical and patient selection. Cooperation and psychological preparedness are more important than the child's age, which should be stressed during the preoperative evaluation, preferably by a multidisciplinary team involving pediatric neurologists, neurosurgeons, neuroanesthesiologists, and neuropsychologists. Preoperative psychological preparation has been suggested to improve both surgical and cognitive outcomes. The choice of the anesthetic technique should depend upon the overall psychological maturity of the child. It should be targeted toward a balanced approach complementing both the child and OR personnel. Constant communication throughout the procedure is necessary for the success of awake brain surgery.

Conflict of Interest None declared for each author.

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Anesthesia for Epilepsy Surgery in Children

28

Ashish Bindra and Manjari Tripathi

Key Points

- The global prevalence of surgical epilepsy among pediatric patients is reasonably high.
- The type of surgery required varies from lesionectomy to complex disconnective surgeries.
- Anesthesiologists are involved in the provision of anesthesia during preoperative imaging, surgical excision of the epileptic focus, and management of perioperative complications.
- Preoperative evaluation of a child with chronic epilepsy should consist of assessing the neurological status, screening for syndromic associations, and adverse effect/interactions of antiepileptic drugs (AEDs).
- Intraoperative goals include maintenance of cerebral and systemic hemodynamics, facilitation of surgical dissection, intraoperative neuromonitoring, and early emergence.
- Most epilepsy surgeries are conducted under general anesthesia; awake craniotomy is done in cases with lesions near the eloquent cortex.
- The ideal anesthetic technique causes minimal interference with electrocorticography (ECoG) and other neurophysiological recordings.

28.1 Introduction

Epilepsy is one of the most common neurological disorders and results in significant disability in individuals of all ages worldwide [1]. According to recent literature, 11.2% of the world's children and adolescent suffer from one of the disabilities, including childhood epilepsy, intellectual disability, and sensory impairments [2, 3]. The prevalence of pediatric epilepsy is high across the globe, and the treatment gap is wide [1]. The incidence and prevalence of epilepsy in developing countries are not well documented due to irregular reporting, diagnostic difficulties, and lack of standardization. The prevalence of pediatric epilepsy in India is around 5.5 per 1000 population [4]. A considerable stigma is associated with epileptic disorders. Illiteracy, poverty, and lack of a trained workforce make the treatment further difficult [5].

Long-standing epilepsy results in adverse effects on brain development, learning, language,

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and life quality besides posing a major financial burden. The burden of disability, thus arising, is substantial, hampers the quality of life, and keeps increasing with age [2]. Surgery is offered to patients with surgically remedial epilepsy. There is enough evidence suggesting the advantages of surgery over medical management alone for seizure control and mitigating the effects of recurrent seizures on the developing brain [6].

This chapter emphasizes the perioperative management of children for epilepsy surgery, including perioperative drug review, preoperative workup, anesthetic considerations, and perioperative complications.

28.2 Epileptic Seizure

International league against epilepsy has given a set of definitions for better understanding and diagnosis of the disease [7, 8]. An **epileptic seizure** is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. The term transient is used to demarcate time, with a clear start and finish. Neonatal seizures, acute symptomatic seizures, neurocysticercosis, and febrile seizures are commonly encountered seizures in childhood [9]. **Epilepsy** is a tendency to have recurrent unprovoked seizures. According to **the conceptual definition**, epilepsy is a brain disorder characterized by an enduring predisposition to generate epileptic seizures and the neurobiological, cognitive, psychological, and social consequences of this condition [9]. The definition of epilepsy requires the occurrence of at least one epileptic seizure. According to the **practical definition**, epilepsy is characterized by at least two unprovoked (or reflex) seizures occurring >24 h apart or one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years or diagnosis of an epilepsy syndrome [7].

Some epileptic episodes are idiopathic in nature, probably with the genetic background. In contrast, others are secondary to brain tumors, stroke, or other congenital disorders. An acute symptomatic seizure can be due to acute systemic and cerebral causes. Perinatal injuries are a major causative factor in the pediatric group [10].

28.3 Drug Refractory Epilepsy

Drug refractory epilepsy (DRE), also known as intractable epilepsy, is a continuation of seizures despite maximally tolerated doses of more than two antiepileptic drugs (AEDs) with an occurrence of an average of one seizure per month for approximately 18 months with no more than a 3-month seizure-free period in these 18 months [11]. Longer duration of seizure disrupts developmental progress and normal childhood activity and causes cognitive decline. About 30–40% of children are non-responders to medical treatment, out of which 50% can be cured with surgery [12]. With recent advances in diagnosis and surgical and anesthetic methodology, epilepsy surgery is increasingly possible even in very small children without age-related contraindications.

28.4 Resolution of Epilepsy

Epilepsy is resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years [9].

28.5 Seizure Semiology

The seizure semiology is the study of signs of epilepsy and depends upon the brain's area from which seizure originates and its spread pattern. Clinical symptoms are transient and vary from loss of awareness and consciousness or a disturbance of movement, mood, sensation, or mental function. Seizure semiology in children more than 6 years of age is similar to that in adults and may include auras, staring or behavioral arrest, automatisms, and versive and dystonic posturing. However, children less than 6 years of age may present with symmetric motor signs of the limbs. Language and cognitive development are required to describe seizure semiology reliably. Younger

children with long-standing epilepsy and children with cognitive impairment and generalized epilepsy are usually unable to describe their symptoms [13]. The frequency of complex automatisms increases with age. Video electroencephalography (vEEG) is an important tool to study seizures. An anesthesiologist should note seizure semiology correctly to diagnose it during the perioperative period and differentiate it from another perioperative behavioral dysfunction.

28.6 Medical Management of Epilepsy

Most of epilepsies respond to drug management. The most common reason for medical management failure is incorrect diagnosis or drug and suboptimal drug dosing. The initial AED is usually started as monotherapy, if it results in adverse effects, an alternative AED is selected. Lamotrigine and carbamazepine are considered drugs of choice in focal epilepsies, while valproate is probably the most effective drug for primary generalized seizures [14, 15]. In cases of no response, combination therapy is often required. The mechanism of action of commonly used AEDs is summarized in Table 28.1. AEDs are divided into two categories: **older AEDs** like phenytoin, carbamazepine, valproate, phenobarbitone, and primidone have potent enzyme-inducing properties; as a result, there are complex interactions with commonly used drugs in the perioperative period resulting in altered plasma concentration of these medications as well as AEDs. The commonly affected drugs are antibiotics, immunosuppressants, cardiovascular drugs, other AEDs, and muscle relaxants. Macrolide antibiotics, particularly erythromycin, are potent inhibitors of CYP3A4, which is involved in carbamazepine metabolism and can lead to carbamazepine toxicity. Concomitant use of carbapenem antibiotics can lead to a significant decrease in serum valproate concentrations. Despite this, these drugs are cheaper, effective, and hence commonly used to manage epileptic disorders in children. **Newer AEDs** like levetiracetam, lamotrigine, gabapentin, and tiagabine have simple pharmacokinetics and limited hepatic metabolism. They have lesser side effects; no need for serum drug monitoring, once or twice daily dosing; and fewer drug-to-drug interactions. However, there are little data to suggest the efficacy of newer over older AEDs.

Anesthetic agents can have drug interactions with AEDs and may result in suboptimal or overdosing of the latter. Calculation and maintenance dosing of AEDs during periods of starvation are thus of great importance. AEDs are central nervous system depressants and may potentiate the sedative effect of anesthetic drugs.

28.7 Evaluation of Patients with Refractory Seizures

The ideal selection of surgical candidates requires a thorough preoperative workup. The clinical presentation and disease profile decide the type of investigations required. Surgical procedure depends on clinical, electrophysiological, neuroimaging, and neuropsychological evaluations and establishment of an electro-clinical-radiological [electroencephalography (EEG), semiology, and radiological investigations] concordance. Preoperative workup greatly improves the ability to localize the seizure focus and characterize its relationship to the brain's functional areas [16]. Neuroanesthesiologists play a crucial role by facilitating various investigations that may require monitored anesthesia care (MAC), management of status epilepticus, or general anesthetic administration. A battery of tests has been described for preoperative workup, but all the tests may not be required and/or available for each case at all centers. ILAE has made recommendations which help choose between various preoperative investigations depending upon the requirement and feasibility [17].

28.8 Electroencephalography (EEG)

Interictal EEG and magnetic resonance imaging (MRI) are the most commonly used tests to diagnose surgical epilepsy patients. In EEG, *the amplitude* is the height of the wave; *frequency* is the number of cycles per second the wave crosses

Table 28.1 Common antiepileptic drugs (AEDs)

Mechanism of action	Drugs	Properties	Major side effects
Modulation of voltage-dependent sodium channel	Phenytoin	Inducer of hepatic cytochrome P450 and glucuronyl transferase Antiepileptic Antiarrhythmic Therapeutic plasma level 10–20 μg/ml	Hypotension with a rapid infusion rate. Steven-Jhonson's syndrome, rash, diplopia, ataxia, nystagmus, gingival hyperplasia, hirsutism, neuropathy, cerebellar degeneration, decreased bone density
	Fosphenytoin	Pro-drug of phenytoin. IV and IM use	Same as phenytoin except for causes less hypotension and more paresthesia, hyperphosphatemia in patients with end stage renal disease
	Carbamazepine	Undergoes hepatic metabolism Mixed enzyme inducer and inhibitor of hepatic cytochrome P450 and glucuronyl transferase Safe for use during pregnancy The need for serum drug-level monitoring	Gastrointestinal discomfort, rash, ataxia, dizziness, diplopia, hyponatremia, benign leucopenia (no need of intervention unless count falls <1000/mm3), cardiac conduction abnormalities It can increase the metabolism of concomitantly administered anti-seizure drugs like phenytoin, ethosuximide, valproic acid, and clonazepam
	Oxcarbazepine	Less potent than carbamazepine Less potent inducer of hepatic enzymes than carbamazepine	Similar to carbamazepine. Hyponatremia more common
	Eslicarbazepine	Inducer of hepatic cytochrome P450 and glucuronyl transferase	Sedation, headache, dizziness, hyponatraemia, leucopenia
	Lacosamide	Minimal drug interactions	Approved for use in patients greater than 17 years of age. Mild side effects. Dizziness, ataxia, vertigo
	Zonisamide	CYP2C19 inhibitor Drug-level monitoring is not required	Dizziness, nausea, PR prolongation
	Lamotrigine	Minor inducer of own metabolism	Rash, nausea, rarely drug reaction with eosinophilia and systemic symptoms (DRESS), aseptic meningitis
Enhancement of fast GABA-mediated synaptic inhibition	Clobazam	Moderate inhibitor of hepatic enzymes	Sedation, ataxia, dysarthria, behavioral changes
	Phenobarbitone	Oldest and cheapest. Multiple drug interactions. Mostly used for neonatal seizures. Mean steady-state level 14–21 μg/ml	Sedation, restlessness, confusion, skin rash, bone marrow depression, liver failure
	Gabapentinoids (gabapentin and pregabalin)	Used as adjunctive. No hepatic enzyme induction	Generally well-tolerated, somnolence, dizziness, ataxia, headache, tremor, weight gain, and peripheral edema
	Vigabatrin	Weak inducer of hepatic enzymes	Dizziness, ataxia, fatigue
	Tiagabine	Used as adjunctive treatment for seizures	Dizziness, tremor, depression, ataxia

(continued)

Table 28.1 (continued)

Mechanism of action	Drugs	Properties	Major side effects
Calcium channel inhibitor	Ethosuximide	Therapeutic range 40–100 μg/ml Interaction with other anti-seizure medications	Gastrointestinal symptoms, nausea, vomiting, headache, dizziness
Synaptic release machinery	Levetiracetam	Broad therapeutic window. One of the most commonly prescribed AEDs. No drug interactions	Somnolence, ataxia, dizziness, depression
	Brivaracetam	Analog of levetiracetam Minimal drug interactions	Somnolence, ataxia, dizziness, depression
Glutamate receptors	Perampanel	Significant drug interactions with other anti-seizure medications	Behavioral adverse reactions including aggression, hostility, irritability, and anger; dizziness, somnolence
Pleotropic/mixed	Valproate	First-line, broad-spectrum AED, potent enzyme inhibitor. Therapeutic level ranges from 50 to 100μg/ml; but concentrations up to 150μg/ml are well tolerated	Nausea, vomiting, and gastrointestinal upset, weight gain, hepatotoxic, thrombocytopenia (though bleeding is rare), increased blood ammonia concentrations leading to lethargy, hyperammonic encephalopathy in patients with genetic defect in urea metabolism, neural tube defects, orofacial and digital anomalies in fetus
	Felbamate	Minimal drug interactions	Cognitive impairment, acute myopia, angle-closure glaucoma, inhibition of carbonic anhydrase resulting in reduced serum bicarbonate (hyperchloremic non-anion gap metabolic acidosis, oligohydrosis (elevated body temperature), renal stones, weight loss, oral cleft in fetus
	Topiramate	Minimal drug interactions	Drowsiness, cognitive impairment, renal stones, inhibition of carbonic anhydrase, weight loss (similar to topiramate)
	Zonisamide	Minimal drug interactions	Somnolence, pyrexia, diarrhea

the zero-voltage line, and *time* is the duration of epileptic activity. The usual base frequency in a normal conscious patient is in the beta wave range (>13 Hz), and this comes to the alpha range (8–13 Hz) with the closure of eyes or mild sedation. Activation of EEG is a term that refers to the production of higher-frequency waves. EEG depression is predominant in slower frequencies like theta or delta (<4–7 Hz). Epilepsy results in the generation of high-voltage spike waves of certain recognizable patterns in specific epileptic focus in the brain. Ictal EEG is the EEG recording during a seizure, whereas interictal EEG is the waveform between the seizures and is characteristic of epilepsy disorder. The interictal EEG is often utilized for diagnosing epilepsy (Fig. 28.1). However, EEG activity is easily affected by agents causing cortical suppression, common examples being anesthetic agents, and AEDs. Localization of epileptic focus may become difficult under the influence of such drugs.

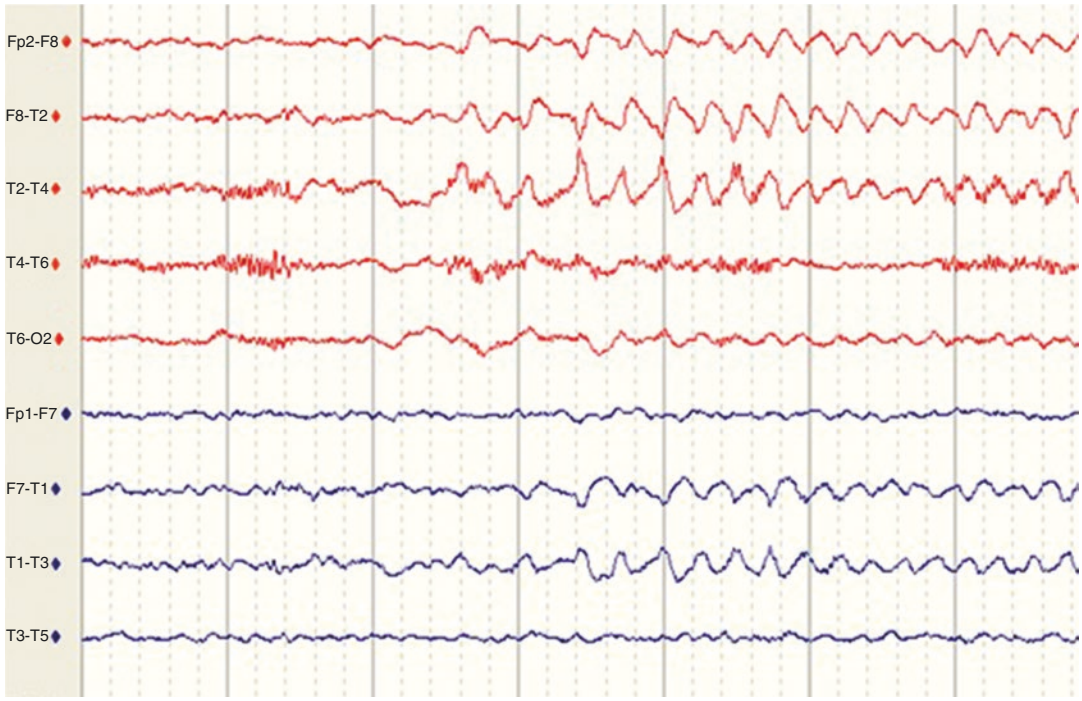

Fig. 28.1 Electroencephalography (EEG) the interictal waveform pattern

28.9 Ictal EEG with Video

The video EEG (vEEG) monitoring refers to EEG with a video recording of patients to see the correlation between the clinical manifestation of seizure and EEG. vEEG may be done for short or long term. It provides information on seizure focus localization, semiology, and differentiation of seizure from non-epileptic events (Fig. 28.2).

28.10 Extra-Operative Invasive EEG Monitoring

It is the procedure of placement of intracranial electrodes under anesthesia and monitoring postoperatively for seizure. It is performed in patients who have had inconclusive noninvasive investigations, dual pathology, or discordant noninvasive data. Subdural, strip, depth, or a combination of electrodes is placed through a craniotomy or a burr hole, and the recordings obtained are thereafter monitored for a few days. It helps in localization of the seizure focus and its spread. It is important for extratemporal seizure localization, which is more common in pediatric patients. Intraoperative MRI and stereotaxy are being increasingly used to guide accurate positioning of these electrodes. The complications include the risk of meningitis, subdural or intracranial hematoma, and herniation. The procedure is done under general anesthesia and is typically followed by repeat surgery after 4–5 days to remove the grid and strip electrodes once the seizure area is demarcated. The use of nitrous oxide may be curtailed during redo surgery, as it may result in the expansion of residual intracranial air [18].

28.11 Magnetic Resonance Imaging (MRI)

High-resolution MRI with a defined acquisition protocol is required for localizing seizure focus; however, the extent of resection may not be

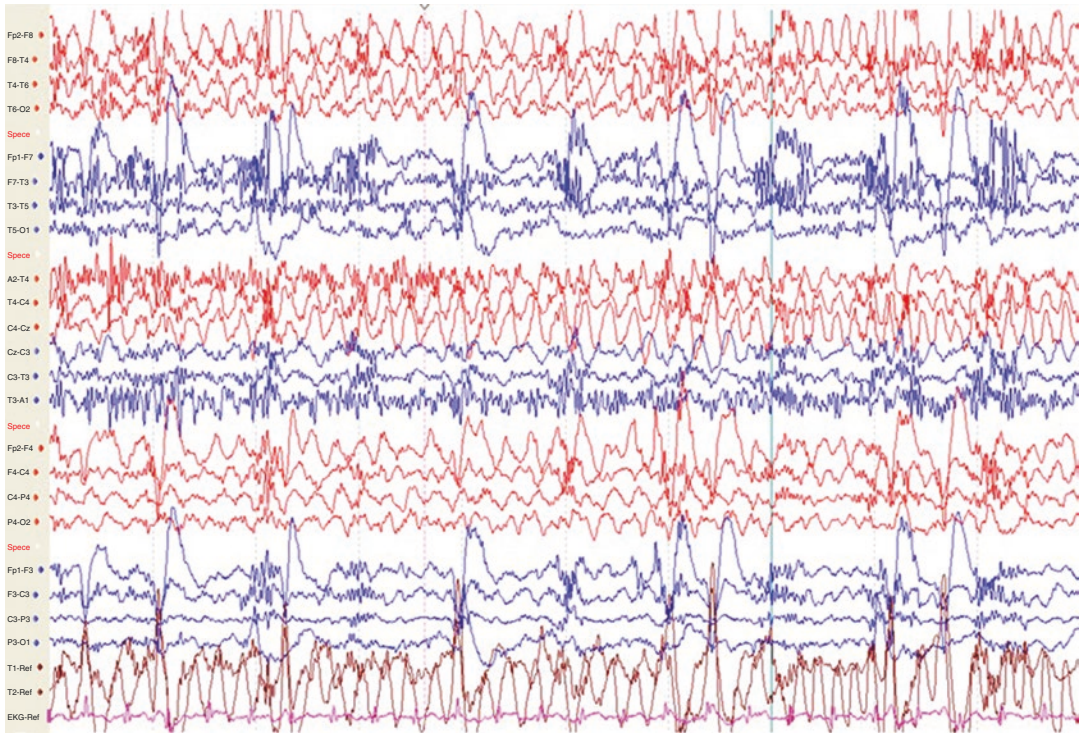

Fig. 28.2 Video EEG recorded four events which show left complex partial seizures with secondary generalization. Ictal rhythmic delta activity seen at F8-T4 (red and blue colors depict right- and left-sided leads, respectively)

defined (Fig. 28.3a–f). There can be multiple areas of pathology visible on MRI, but the exact lesion producing seizure will not be identified. Interpretation of MRI images may be difficult in the pediatric population due to variable development and myelination changes. MRI in children often requires general anesthesia.

28.12 Functional MRI (fMRI)

fMRI is a noninvasive technique to know seizure focus and its relation with eloquent cortex. It is a noninvasive test that helps lateralize language function and motor function but has limited memory localization. It is preferred over other invasive tests like *Wada or cortical stimulation*. It is less accurate in post-ictal states, vascular malformations, and large mass lesions with edema. Interpreting MRI in small children may be challenging due to different central nervous system maturation and evolution.

28.13 Magnetoencephalography (MEG)

MEG is a functional neuroimaging modality used for brain mapping. It records tiny magnetic fields produced by electrical currents in the brain, using magnetometers. It can do three-dimensional localization of the source of interictal spikes. MEG can define smaller foci (4–8 cm^2) compared to EEG (10–15 cm^2). MEG is usually done along with EEG in patients without abnormality on MRI or patients with multifocal lesions [19]. Anesthetic agents greatly affect MEG.

28.14 Single-Photon Emission Computed Tomography (SPECT)

SPECT scan shows hyperperfusion in seizure focus during the ictal period and hypoperfusion during interictal period. The investigation

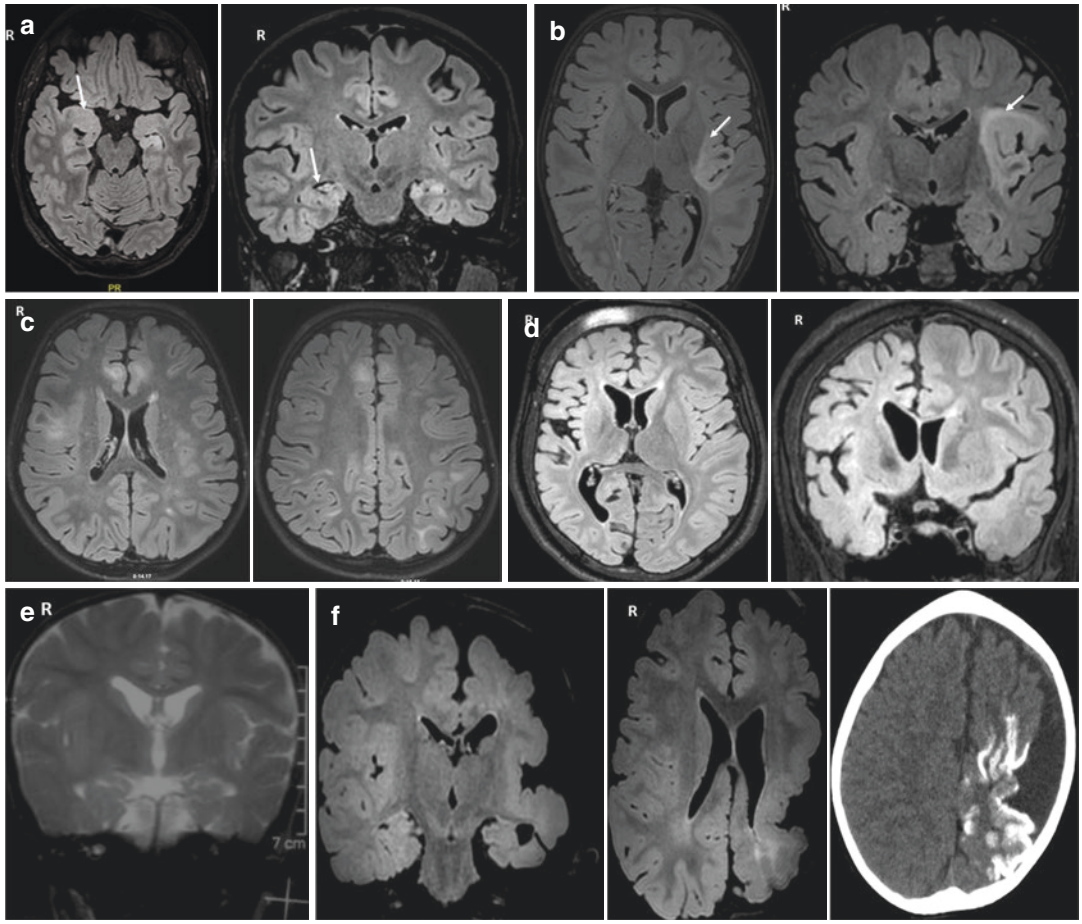

Fig. 28.3 MRI shows different pathologies of surgical epilepsy. (**a**) Right-sided mesial temporal sclerosis, hippocampal atrophy, dilatation of ipsilateral horn, and increased T2 signal. (**b**) Left insular focal cortical dysplasia. (**c**) Tuberous sclerosis. (**d**) Rasmussen encephalitis: MRI showing right cortical atrophy with ex-vacuo ventricular dilation. (**e**) Right-hemispheric hypertrophy (megalencephaly). (**f**) Sturge-Weber syndrome: MRI showing volume loss and prominent leptomeningeal enhancement in the left cerebral cortex

requires the injection of radionuclide at the time of seizure, followed by scanning in the SPECT suite. The timing of radionuclide injection is critical, and late injections may not provide reliable information (Fig. 28.3c).

28.15 Positron Emission Tomography (PET)

PET scan is usually done during the interictal period. The PET scan can further clarify the seizure location by showing an area of decreased metabolism at the seizure focus during the inter-ictal period.

28.16 Wada Test

Wada test is the gold standard test for preoperative language and memory mapping. Most of the data is available from adults. Its applicability in predicting long-term neurocognitive functioning in pediatric patients is limited due to different neurodevelopment seen in the pediatric brain. Wada test and superselective Wada test are used to lateralize language and memory functions in each hemisphere. Wada test is conducted by selectively injecting a short-acting anesthetic agent (amobarbital, methohexital, propofol, etomidate) into one of the internal carotid arteries

directly or through an intra-arterial catheter placed in the femoral artery [20]. Injection of short-acting anesthetic agents results in deactivation of the corresponding half of the brain. If the right carotid is injected, the brain's right side is inhibited and cannot communicate with the left side and vice versa. This inhibits any language and memory function in that hemisphere, and evaluation of the other hemisphere is done by engaging patients in language and memory-related tests. A simultaneous EEG recording confirms that the injected side of the brain is inactive. The superselective Wada test is done by injecting the anesthetic drug directly into the artery supplying the lesion. Wada/superselective Wada simulates the functional outcome following resective or disconnective surgery. Lesion producing epilepsy can be safely removed if inhibiting that half of the brain/selective area produces no major functional deficit. The memory function results are not as reliable as the mesial temporal structures that deal with memory function that are mainly perfused by posterior circulation. Wada test is not practiced widely in children across the globe due to difficulty in its execution in younger children, especially mentally retarded, noncooperative, and apprehensive [21]. Children may be offered short-acting anesthetic at the time of vessel puncture but have to be kept awake and cooperative at the time of intracarotid injection and subsequent testing.

28.17 Role of Anesthesiologist during Preoperative Workup

The anesthesiologist is often involved in the facilitation of preoperative workup of children posted for epilepsy surgery [19]. Most of the imaging procedures require a still and cooperative patient. Young children and patients with cognitive impairment pose special challenges to the anesthesiologist. The required level of sedation can range from anxiolysis to deep sedation. Deep sedation is more commonly required for prolonged procedures such as MRIs and SPECT scans and can be achieved using volatile or inhalational agents. Imaging techniques like MEG are highly sensitive to anesthetic agents. There should be clear communication with the neurologists discussing the influence of drugs on the investigation results. Hypnotic agents like propofol and thiopental may produce myoclonic movements without EEG activity, whereas etomidate and methohexital produce myoclonic activity along with epileptiform activity in EEG [22]. The drug-induced activity should be differentiated from an epileptic seizure. The drug-induced EEG changes are nonspecific and do not have any localization value [17]. Similarly, volatile agents can also produce changes in EEG. Dexmedetomidine, an alpha-2 agonist, is a promising agent for providing sedation in epileptic patients without much effect on electrophysiologic recordings.

28.18 Choice and Types of Epilepsy Surgery

The type of surgery is determined by the nature of the abnormality and results of preoperative testing. Surgical procedures commonly performed are described in Table 28.2. The procedure may vary from simple lesionectomy to complex disconnection surgeries. Thorough knowledge of pathology, seizure semiology, drug history, type of surgical procedure, and possible complications is required for successful perioperative management [23–27].

Vagus nerve stimulator consists of two main parts, a programmable pulse generator implant and a helical electrode wrapped around the left vagus nerve in the neck. The device delivers open-loop stimulation. The current output, pulse, frequency, and signal can be adjusted as per predetermined protocols. The device can be controlled externally by a handheld magnet. Vagus nerve stimulator is usually implanted under general anesthesia. No specialized neuromonitoring is required [28].

Deep brain stimulation for control of seizures is becoming increasingly popular. However, neurostimulation techniques are more defined in patients above 18 years of age. Its role in pediatric patients is still under study. Complex disconnective surgeries are increasingly being

Table 28.2 Disease characteristics and intraoperative concerns during epilepsy surgery

Pathology (Fig. 28.3a–f)	Disease characteristics	Surgical procedure	Anesthetic plan and concerns
Focal lesions • Mesial temporal sclerosis (Fig. 28.3a) • Dysembryoplastic neuroepithelial tumor (DNET) • Focal cortical dysplasia (Fig. 28.3b) • Hippocampal sclerosis • Sturge-weber syndrome (focal) • Hypothalamic hamartoma • Gliosis (traumatic) • Ganglioglioma • Vascular lesions/cavernoma	These lesions are usually without the involvement of functional motor, visual, and language cortex	• Lesionectomy • Decision to operate and results depend upon good presurgical evaluation and concordance of evidence • Good result with minimal morbidity	Up to 20% pediatric patients have temporal lobe epilepsy Extra temporal lobe epilepsy requires neurophysiological monitoring to demarcate lesion Lesions near the eloquent cortex may require an awake craniotomy Fairly stable perioperative course
Multifocal lesions • Lennox-Gastaut syndrome • West syndrome • Bi-hemispheric sequelae of traumatic/ vascular/infectious pathology	Drop attacks characteristic of Lennox-Gastaut syndrome Variable mental retardation	Generally palliative • Corpus callosotomy • Vagal nerve stimulation	Corpus callosotomy: Done under general anesthesia, standard anesthetic technique for craniotomy, no EEG recordings required, surgery near sagittal sinus, risk of bleeding, and venous air embolism. Vagus nerve stimulation: Done mostly on left-side, day-care procedure, under general anesthesia Intraoperative complications: Bradycardia, cardiac arrest, vocal cord, and laryngeal muscle dysfunction
Sub-hemispheric lesions Bi-hemispheric sequelae of traumatic/ vascular/infectious pathology Incidence: Around 5%	Epileptogenic zone extends to large areas of temporal, parietal, and occipital lobes. Central and frontal areas are generally spared	• Multilobar resective surgery • Disconnective surgery • Depends upon concordance between imaging and functional evaluations	Require intraoperative demarcation of epileptogenic zones using ECoG

Pathology (Fig. 28.3a–f)	Disease characteristics	Surgical procedure	Anesthetic plan and concerns
Hemispheric lesions • Tuberous sclerosis • Infantile hemiplegic syndrome • Rasmussen's encephalitis • Disorders of neuronal migration • Hemimegalencephaly • Sturge-weber syndrome (encephalotrigeminal angiomatosis) • Cerebrovascular accidents • Thromboembolic episodes	Tuberous sclerosis: Intracranial, cutaneous, cardiac, renal, pulmonary tubers. Needs detailed cardiac and renal workup Infantile hemiplegic spasm: Pathology affecting the entire hemisphere, resulting in early-onset unilateral paralysis Imaging: Hemispheric atrophy with dilated ventricular system Rasmussen's encephalitis: Typically, unilateral, chronic childhood encephalitis, viral or autoimmune in origin Presents as hemiplegia, cognitive dysfunction, and focal motor seizures Hemimegancephaly: Neuroblast migratory defect. Hamartomatous malformation of brain resulting in extreme asymmetry. May be isolated or associated with other neurocutaneous syndromes Symptoms: Seizure, mental retardation, hemiparesis, hemianopia MRI: Abnormal gyration, ventriculomegaly, colpocephaly, occipital sign, overall increased size of hemisphere, giant neurons, neuronal heterotopias These may occur in children with heart disease, undergoing cardiac surgery, use of extra-corporeal membrane oxygenation Struge Weber Syndrome: Characterized by pial angiomatosis and intracranial calcifications. May be localized or diffuse, unilateral or bilateral. Presents as port-wine stains, glaucoma, seizures, and variable degrees of mental retardation depend on the extent of lesion. Look for airway hemangiomas	Disconnective surgery • Hemispherotomy Peri-insular Trans-opercular Trans-sylvian Vertical	Based on the interruption of the epileptic network Anesthetic concerns: General anesthesia, highest morbidity epilepsy surgery Long duration, blood loss, electrolyte and metabolic disturbances, coagulopathy, delayed extubation • Complications are Less with functional hemispherotomy practice now a days as compared to hemispherectomy, which was earlier practiced

done using minimally invasive endoscopic techniques [29]. Robot-assisted stereotaxis allows for more precise placement of intracranial depth electrodes [30]. Intraoperative MRI ensures completeness of resection of the epileptogenic area in the peri-eloquent cortex.

28.19 Preoperative Anesthetic Evaluation and Preparation

The preoperative examination should be thorough and includes physical examination, history of perinatal neurological insult, febrile seizures, perinatal hypoxia, preterm/premature birth, CNS infection, head injury, chronic medical illness, prior anesthetic history, and drug allergies. Any recent acute illness should also be noted. Systematic screening for airway anomalies, congenital cardiac defects, associated syndromes like tuberous sclerosis, hemimegalencephaly, Sturge-Weber syndrome, and mental retardation should be done. Table 28.2 enlists the causes of surgically remediable epilepsy, disease characteristics, common surgical procedures, and anesthetic concerns.

In children planned for awake craniotomy, the ability to cooperate during awake procedures should be tested. The onset, duration, type, and frequency of seizure disorder should be noted. Understanding seizure semiology helps identify seizure in the perioperative period and differentiate it from delirious movements, inadequate reversal, myoclonic jerks, or a new-onset seizure. A note of AEDs, adequacy of seizure control with ongoing medication, should be known to the anesthesiologist. Continuation or discontinuation of AEDs and anxiolytic premedication on the morning of surgery depends upon intraoperative requirements and should be guided by institutional protocol.

Age-dependent alterations in physiology should be kept in mind while planning the anesthetic technique. Children under 2 years have lower mean arterial blood pressure and a low cerebral autoregulatory reserve; hence, the perioperative blood loss is poorly tolerated. Massive blood loss, fluctuations in blood pressure, and electrolyte disturbances are critical in neonates with limited cardiac reserve. Immaturity of the renal and hepatic systems should be considered while planning intraoperative fluid and drug dosages of anesthetics/AEDs. Sudden cardiac death and respiratory events are not uncommon in small children. Baseline hemogram, coagulation studies, and arrangement of blood are essential for all craniotomies.

Ketogenic diet is a popular treatment modality for controlling seizures. It is a diet high in fat and low in protein and carbohydrates to produce a ketotic and acidotic state. Hypoalbuminemia is common with this diet. Ketogenic diet is not a contraindication to anesthesia administration [31]. Monitoring for preoperative and intraoperative acidosis, serum glucose, and ketones is recommended, especially during long surgeries [32].

The surgical technique and intraoperative neurophysiological monitoring should be discussed preoperatively with the neurological and neurosurgical team. Commonly carried out intraoperative neurophysiology monitoring includes ECoG and cortical stimulation. Drugs interfering with physiological recordings, especially benzodiazepines, should be avoided as premedicants. AEDs may be omitted where seizure elicitation is planned during the intraoperative period. Many centers prefer to continue the routine AEDs in the morning of surgery, as most of the resections are based on interictal recordings.

Anesthetic agents and AEDs interact with each other and affect each other's efficacy resulting in suboptimal or overdosing or risk of intraoperative seizures. General anesthetics and AEDs interact with Na+ channels and $GABA_A$ receptors at therapeutic concentrations resulting in overlapping of clinical spectrum. Hence, general anesthetics also possess anticonvulsant activity, while many AEDs have sedative effects [33]. AEDs and anesthetic agents also share common metabolic pathways, which results in an alteration in the distribution and clearance during their simultaneous use. It results in a change in the duration and degree of sedation achieved. AEDs that are enzyme inducers decrease the duration of sedatives and muscle relaxants' duration, result-

ing in the need for frequent dose repetitions. Prolonged use of phenytoin and carbamazepine is known to cause resistance to the action of non-depolarizing muscle relaxants. Conversely, AEDs with enzyme inhibitory properties may prolong sedation and recovery time in the postoperative period. Such situations result in frustration and displeasure among the anesthesiologists, children, and their parents.

Preoperative investigations should include a hemogram (significant blood loss with craniotomy in small children), coagulation profile (coagulability changes following neurosurgery, the effect of AEDs), hepatic and renal profile to look for side effects of AEDs (Table 28.1), and other system screenings according to syndromic association.

Planning the preoperative period is important in preschool children who have separation anxiety. Children with mental disabilities pose special challenges. Short-acting drugs in low doses are recommended in these children. Oral, intravenous, or nasal midazolam is commonly used as premedicant. These drugs may interact with ECoG. Thus, the role of the anesthesiologist is to design an appropriate timing and dosage of premedication which does not interfere with waveform recording [34].

28.20 Intraoperative Anesthetic Technique

The intraoperative anesthetic goal is to maintain cerebral and systemic hemodynamics, facilitate surgical dissection, enable intraoperative neuromonitoring, early emergence, and manage perioperative complications. Anesthetic regimen depends on the patient profile, type of surgery, and the anesthetist's experience with each agent. The inherent challenges of pediatric anesthesia, surgery complexity, intraoperative blood loss, hemodynamics, and temperature variability cannot be neglected. Although awake craniotomy is better for intraoperative neurological testing, general anesthesia offers the advantage of comfort, for both patient and physician, in cases with well-demarcated seizure focus on preoperative structural and functional mapping. The children are usually apprehensive and less cooperative; moreover, the availability of advanced perioperative neuroimaging technologies does not make awake craniotomy a commonly utilized procedure for pediatric epilepsy surgery. Anesthesia can be induced using an inhalational or intravenous (IV) technique depending upon the degree of cooperation and IV access availability. Sevoflurane is a commonly used inhalation agent; however, it has an epileptogenic potential. Propofol and thiopentone can be used alternatively in patients with IV access. Hypnotic agents can depress the ECoG potentials. Sevoflurane has been commonly used for induction.

28.21 Intraoperative Monitoring

28.21.1 Anesthesia Monitoring

The type of procedure being performed determines the choice of monitoring [16]. Standard noninvasive monitors would suffice for diagnostic imaging procedures performed under sedation. Under general anesthesia, surgical resections with no intraoperative neuromonitoring testing pose concerns similar to usual craniotomy. Standard ASA monitors including ECG, pulse oximetry, arterial line for blood gases and accurate blood pressure monitoring, and end-tidal carbon dioxide ($EtCO_2$) should be used. Management of smaller children with complex pathology undergoing disconnective surgeries is challenging. Such patients are prone to high blood loss, hemodynamic instability, coagulation abnormalities, and electrolyte disorders. Monitors to diagnose and manage volume loss are paramount. Monitoring invasive arterial pressure, central venous pressure, serial hematocrit, urine output, arterial blood gases, electrolytes, and coagulation are crucial for a successful outcome in such cases. Two large-bore cannulas are required for volume replacement; normovolemia should be the target. Calculation of allowable blood loss and early transfusion avoids hemodynamic instability.

In patients planned for intraoperative brain mapping for seizure localization, additional anesthetic goals include considering anesthetic agents' effect on EEG. Maintenance of normothermia, normocarbia, and depth of anesthesia is especially important (Table 28.3). Titrating anesthesia depth, end-tidal concentration, or minimum alveolar anesthetic concentration (MAC) of anesthetic agents can help optimal ECoG monitoring.

Table 28.3 Anesthetic concerns for intraoperative electrocorticography (ECoG)

Time period	Anesthetic concerns
Preoperative period	• Avoid benzodiazepine and barbiturate premedication as they suppress ECoG • Explain to patient and relatives about the risk of intraoperative awareness • Routine AEDs may be continued
Intraoperative period	• Induction agent: Preferable opioids, short-acting barbiturates. Barbiturates and propofol may suppress the seizure recordings for some time • Maintenance: Either inhalational or intravenous technique may be used along with muscle relaxation, and opioid, and N_2O can be used • **ECoG recordings** • Propofol should be tapered down 20–30 minutes before the recordings • Low concentration volatile agent along with opioid or dexmedetomidine can be continued during ECoG recordings • Muscle relaxant should be continued • Pharmacoactivation in cases where adequate ECoG recordings are not obtained • After ECoG recordings: Regular maintenance anesthetics should be continued

AED antiepileptic drugs, *ECoG* electrocorticography

28.21.2 Neuromonitoring

Intraoperative neuromonitoring aims to localize the epileptogenic zone and guide its complete resection. Anesthetic agents have a variable effect on central neural transmission, thereby producing excitatory or suppressive patterns on EEG. The overall effect depends upon the ratio of suppression of inhibitory or excitatory neurons in cortical and subcortical brain structures with changing anesthetic depth. Broadly at lower doses, anesthetic agents have an excitatory effect, and increasing depth results in neuronal depression. Anesthetic agents like propofol, thiopentone, etomidate, and methohexitone cause myoclonic activity mimicking seizure. Etomidate and methohexitone may produce epileptiform EEG changes [35].

28.21.2.1 Electrocorticography (ECoG)

ECoG is the electrical recording obtained by placing electrodes directly on the exposed cortex [36]. ECoG is similar to scalp EEG, without the dispersion and attenuation of potentials by the scalp and skull. It has a larger amplitude, which ranges between 30 and 50μV/mm. The frequency band-pass filter range is between 0.5 and 70 Hz, which ensures adequate capture of epileptiform discharges. The ECoG electrodes are embedded in flexible plastic sheets of variable size in a grid or strip fashion (Fig. 28.4a, b). The grid/strip electrodes are placed at the cortical surface, whereas depth electrodes are used for recordings from deep structures like the hippocampus and amygdala (Fig. 28.4c). Electrodes are positioned on the seizure focus area already defined by preoperative testing. The signals obtained are graphically displayed on the monitor (Fig. 28.5). ECoG usually interprets the inter-ictal data. The signals obtained are used to demarcate and adequately resect the epileptogenic zone. Co-registration techniques are widely used to delineate discrete epileptic focus; however, ECoG is still a commonly used technique to define epileptogenic zones intraoperatively.

Recording ECoG under anesthesia is a challenge as anesthetic agents can enhance or depress the epileptiform activity or can themselves be epileptogenic. With increasing anesthetic depth, the waveform changes from predominant

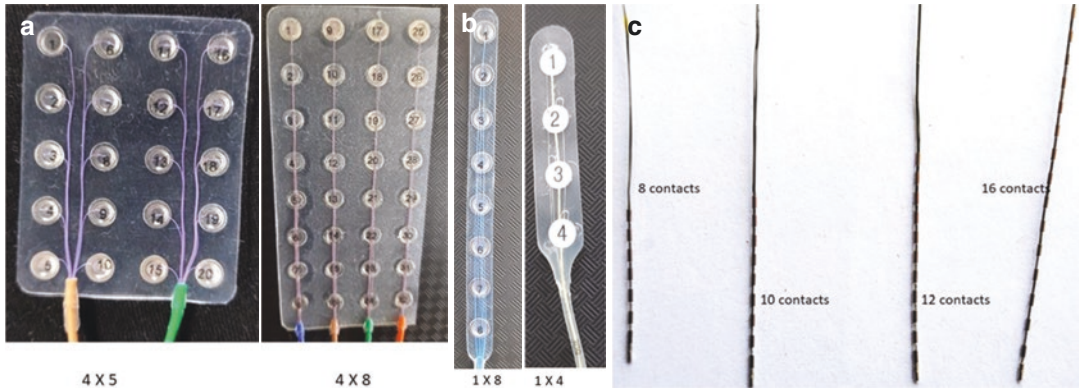

Fig. 28.4 Shows different size grid electrodes (**a**), different size strip electrodes (**b**), and and depth electrodes (**c**)

α-waves (8–12 Hz) to higher frequency β-activity (13–30 Hz), which progresses to high-amplitude low-frequency θ (5–7 Hz) and δ-waves (1–4 Hz) followed by burst suppression. β-Waves can imitate and mask epileptiform activity, and burst suppression pattern quashes interictal discharges. Epileptiform activity is a sharp and transient electrical activity. As ictal activity is difficult to record under anesthesia, ECoG relies on interictal activity manifesting as spikes, poly-spikes, sharp waves, or a combination of all. Maintenance of constant and low anesthetic depth is required for acquisition and interpretation intraoperative ECoG. After the demarcation of the irritative zone by ECoG, surgical resection is performed to ensure its complete removal.

Role of Anesthetic Agents on ECoG

Volatile anesthetics have a dose-dependent effect on neuronal excitability. This effect is minimal at low doses, background interictal spikes are suppressed at 1 MAC, and the effect becomes most noticeable at near-burst suppression doses, i.e., 1.5 times MAC [37]. Thus, lower concentrations of inhaled drugs are required for intraoperative ECoG recordings, though there is a risk of awareness in such situations. Sevoflurane and enflurane have been shown to enhance nonspecific spike activities. Sevoflurane at 1.5–2 MAC has been associated with the generation of a widespread irritative response, especially with hypocapnia [38, 39]. Low-dose sevoflurane may have a proconvulsant effect. These agents are not recommended for ECoG recordings. The neuroexcitatory properties and epileptogenic potential of isoflurane, desflurane, and halothane are low despite a few seizure like movement with isoflurane have been described [40]. Low concentration of isoflurane or desflurane for maintenance is advised for ECoG recordings. Bispectral index (BIS) monitoring may be helpful to titrate the anesthetic depth.

Nitrous oxide (N_2O) is largely considered inactive for both the development and the treatment of seizure activity. However, its complex interactions with other anesthetic agents are known [41]. Alone, the agent can produce fast frontal dominant high-frequency (>30 Hz) activity. The effect N_2O, in combination with volatile anesthetics, has been variably reported. Both decreases in ECoG activity and no change in spike frequency with N_2O (50–70%) use have been observed [42, 43]. Many of the centers use 50–70% of N_2O without any effect on interictal spikes [44]. However, other studies comparing volatile versus IV anesthesia suggested the addition of N_2O as a carrier gas reduced ECoG score [45, 46]. **Propofol** is a common anesthetic used for sedation during diagnostic procedures as well as intraoperatively during surgery. The anticonvulsant properties of propofol are well established, but its proconvulsant potential has also been reported. Propofol generates beta EEG activity, concealing underlying spike-wave activity for up to 20 min after discontinuation of the infusion. A sedative dose of propofol has been

reported not to affect epileptiform activity in patients with complex partial epilepsy [46]. Propofol has been successfully used during electrocorticography in patients with intractable epilepsy and documented no seizure activity or a decrease in the number of spikes or burst suppression patterns. Few authors have reported an increase in spike activity with propofol [47]. A study analyzed the effect of sedative dose of propofol on EEG in 25 pediatric epilepsy patients during sedation for MRI. The use of propofol was not associated with any epileptiform activity. The

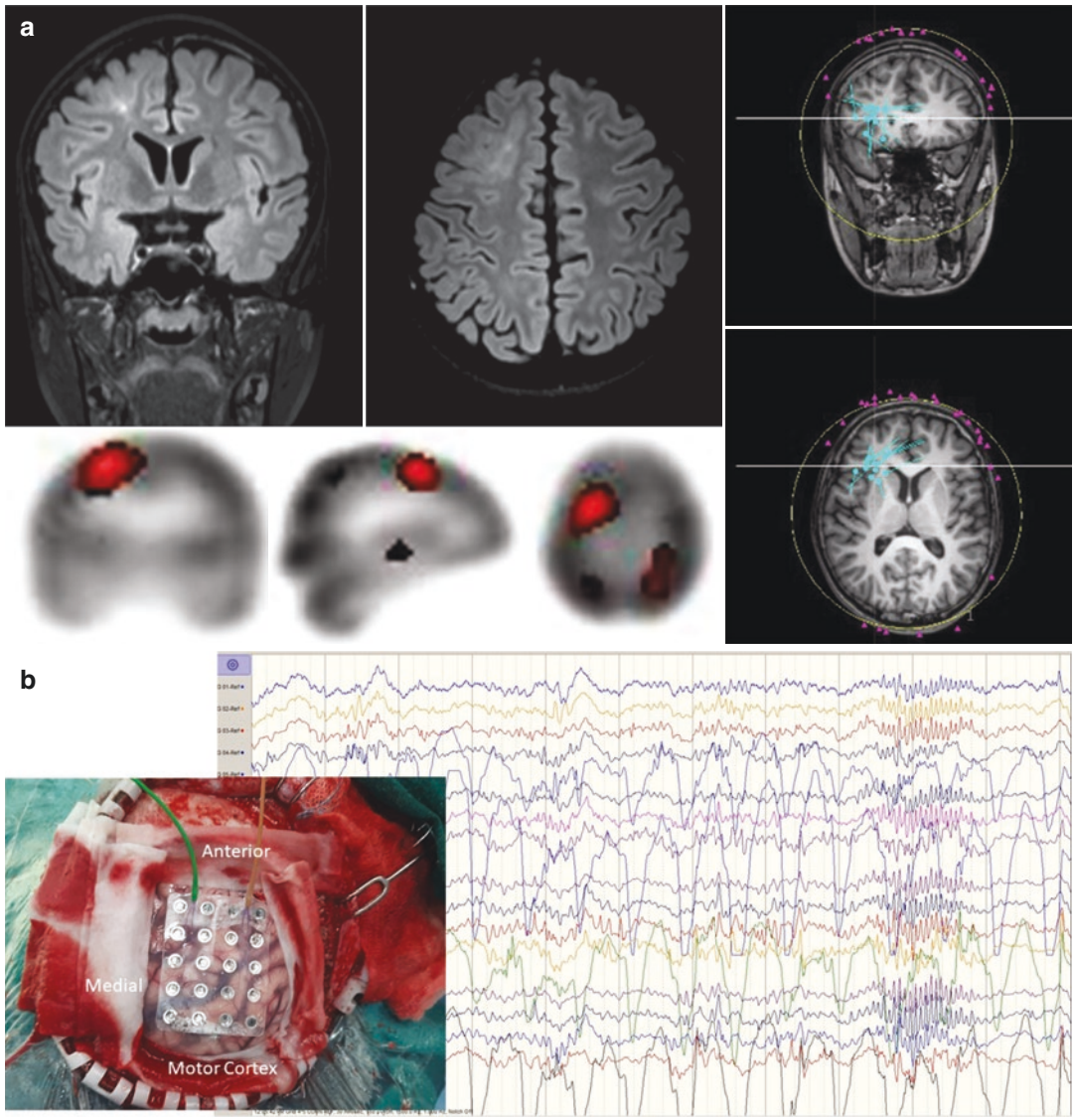

Fig. 28.5 Illustrative case of a 12-year-old, right-handed male, age of seizure onset 2 years, duration of seizure 10 years, seizure frequency four times per week. Seizure semiology included no aura, eyes, and head deviation to left, followed by tonic-clonic movements of all limbs, duration of seizure 30 s–1 min. No neurological deficits. Video EEG localized seizure to the right frontal lobe. The child was posted for resection of the lesion under general anesthesia with isoflurane 0.5 MAC at the time of recording. (**a**) Preoperative imaging shows right premotor cortex focal cortical dysplasia. (**b**) ECoG before resection of the lesion shows high spikes in area localized. (**c**) Post-resection ECoG shows marked improvement in spike activity

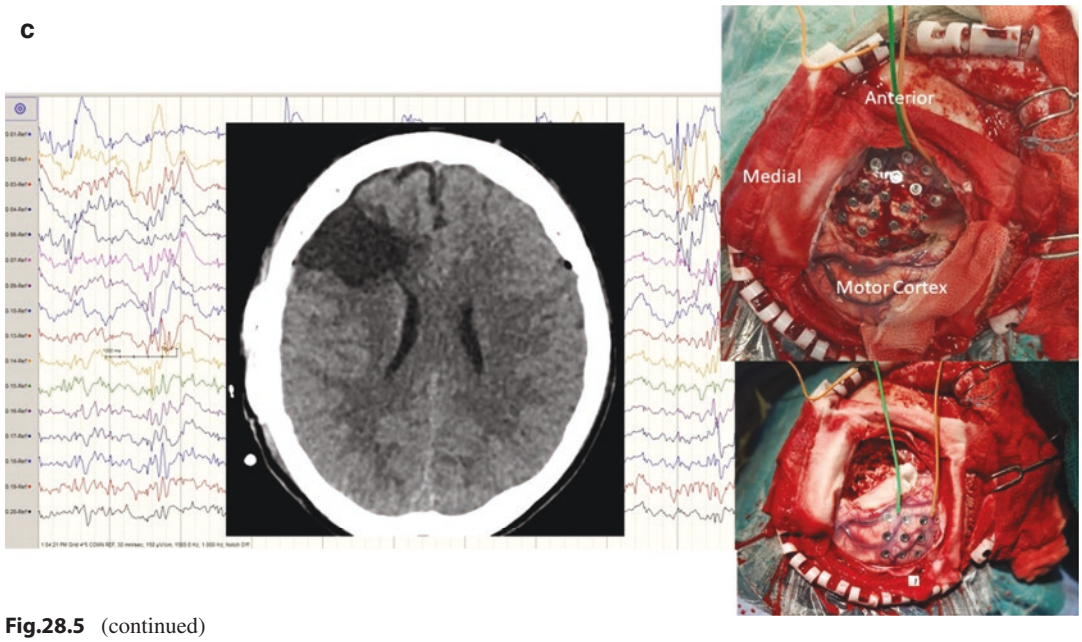

Fig.28.5 (continued)

EEG changes consisted of an increase in beta activity with suppression of theta activity. Propofol induced beta activity and suppression of spike-wave patterns disappeared after 4 h. The data supported the concept of propofol being a sedative-hypnotic agent with anticonvulsant properties [48, 49].

Dexmedetomidine is an α_2-agonist which has gained enormous popularity in neuroanesthesia practice. Though many studies demonstrate the effect of the drug on ECoG in adult patients, the pediatric implications are extrapolated from adult data, stating that dexmedetomidine is a near-ideal agent for obtaining intraoperative ECoG recordings. It does not interfere with interictal epileptiform activity. Dexmedetomidine does not possess any motor-stimulatory effect. It has recently been utilized as an adjuvant for awake craniotomy in children, but the doses used by different authors varied with no standard dosing schedule defined yet [50, 51]. Dexmedetomidine can be used as an adjuvant for intraoperative ECoG recordings. Dexmedetomidine infusion at 1μg/kg has been shown to increase spike activity [52].

Opioids are widely used as adjuvant analgesics and sedatives intraoperatively. Synthetic opioids such as alfentanil, fentanyl, sufentanil, and remifentanil don't increase the risk of perioperative seizures and produce minimal changes in ECoG. However, higher bolus doses result in an increase in interictal spike activity in the abnormal brain and can be used for pharmacoactivation of ECoG [53, 54].

Pharmacoactivation: Activation of cortical electrical activity during ECoG is practiced by some centers when there is no spontaneous interictal discharge (IID) activity on ECoG. Drugs are used to increase the excitability of epileptogenic focus, help demarcate, and identify resectable zone(s). The use of drugs should increase the frequency of spiking or increase in the spike distribution and/or both; however, the induced electroclinical seizure should have the same characteristics, onset, and propagation as the patient's typical spontaneous seizure. Short-acting opioids like alfentanil (20–100μg/kg), etomidate (0.2 mg/kg), and methohexital (25–100 mg) are most widely used for pharmacoactivation [53]. Alternately, isoflurane, sevoflurane N_2O, fentanyl, and remifentanil can be used in high doses to activate ECoG. Ketamine causes global cerebral stimulation rather than specific activation. Hyperventilation is known to cause ECoG activation. Nonspecific activation of ECoG, overesti-

mation of seizure zone, and frank seizure development are few of the important concerns during pharmacoactivation. Hence, many centers refrain from using pharmacoactivation.

The most popular general anesthetic technique utilizes low levels of volatile anesthetic agents along with opioid administration during ECoG monitoring (Table 28.3). Dexmedetomidine infusion at the time of ECoG is another useful technique. Neuromuscular blockers should be continued during this time to prevent movement and interference with EcoG. A low level of anesthetics used at the time of recordings may lead to awareness; depth-of-anesthesia monitoring may be useful at this stage [17, 45, 53, 54].

28.21.2.2 Cortical Stimulation under General Anesthesia

Intraoperative cortical mapping is used for the localization of the eloquent cortex (sensory/motor strip). It can be done using sensory-evoked potential and/or direct cortical stimulation. In direct cortical stimulation, through the ECoG grid, the short-duration electric current is used to stimulate a particular area of the cortex. High-frequency stimulation consists of 50 Hz, 1 ms, 0.5–2.5 mA, and < 5 s stimulus threshold. Low-frequency protocol uses a stimulation threshold of 1 Hz, 20–40 s, and 0.5–5 mA [55]. The cortical stimulation results in activation or inhibition of a particular function controlled by it, such as limb movement, memory function, etc. The subdural and/or stereo encephalography (depth) electrodes allow cortical stimulation to be done in small children during the perioperative period (bedside) [56, 57]. Seizures can be induced by cortical stimulation, which helps in the delineation of the epileptogenic zone. Stimulation protocols are defined for children. Incomplete myelination and a greater proportion of small fibers render this modality of monitoring unpredictable [58]. Electrocortical stimulation mapping is considered the "gold standard" for functional localization. It can be used in either the intraoperative or extra-operative setting. The monitoring can be done using subdural or stereotactic depth electrodes. It is specially used for language mapping in the younger patients [59]. Intraoperative mapping helps delineate subcortical white matter tracts during surgical resection. TIVA is a popular regimen for intraoperative cortical mapping. The use of intraoperative MRI demarcates resectable zone and decrease the postoperative neurological deficit [21, 60].

28.21.3 Awake Craniotomy and Excision for Epilepsy

Awake craniotomy is done to resect lesions near the eloquent areas of the cortex and was first described for epilepsy surgery. The patient remains awake for neurophysiological testing during lesion resection. Awake craniotomy is particularly challenging in pediatric patients since the success of the procedure lies in patient cooperation. However, it has been successfully described in children [61, 62]. Generally, it is done in patients above 10 years of age. A thorough preoperative workup for localization of seizure focus is required in smaller children. Two anesthetic techniques are described for awake craniotomy, asleep-awake-asleep (S-A-S or AAA), and awake-awake-awake or conscious sedation supplemented with scalp block and pin site infiltration of local anesthetic agents [63]. In the former, the patient receives general anesthesia and secured airway for most of the time when patient cooperation is not required. The patient is made awake at the time of neurophysiological testing. In the latter technique, the patient remains under sedation throughout the procedure [64]. S-A-S technique is preferred in children. Depending upon the lesion location, a patient must perform a set of tests related to motor, language, and memory testing. Direct electrical cortical stimulation is done to localize motor and speech areas. The stimulation may result in seizures. It can be treated by irrigation of the surgical field by ice-cold saline, or with intravenous midazolam, propofol, or thiopental bolus.

28.21.4 Emergence and Awakening

The children should be reversed, and rapid awakening should be facilitated at the end of surgery. Patients going extensive surgery, massive fluid,

or intraoperative hemodynamic disturbances resulting in brain edema may require short-term postoperative ventilation. Children on multiple AEDs, disconnective procedures may have delayed awakening.

28.21.5 Complications in the Perioperative Period

The perioperative complications of epilepsy surgery are dependent upon the type of surgery being performed. Resection of lesions is less challenging for anesthesiologists than disconnective surgeries in pediatric patients, which may pose hemodynamic challenges due to complexity and longer duration of the procedure. Commonly encountered perioperative complications are enlisted below.

An intraoperative seizure may occur during awake craniotomy, pharmacoactivation, or cortical stimulation. It generally stops with the removal of the stimulus. If it does not stop, the irrigation of cold saline over the cortex is the best treatment since it will not interfere with subsequent electrical recordings [65]. If the seizure does not stop with cold saline irrigation, then propofol bolus (10–30 mg), subsequently followed by midazolam (2–5 mg), or thiopentone (25–50 mg), can be given. Long-acting antiepileptic drugs like phenytoin can be given. However, all these drugs can have a substantial effect on ECoG monitoring. Patients with **continued seizure** may have problems with awakening and require prolonged ventilation in the postoperative period. Titration of AEDs and EEG monitoring to localize the cause of seizures is required in these cases [66]. Treatment protocol to manage seizure should be in place. The management of airway, breathing, and circulation is of paramount importance.

Intraoperative brain swelling is not a common finding during epilepsy surgery. It may be seen during the implantation of electrodes for invasive recordings or pathology with mass effect. It can be managed by head-up position, hyperventilation, and a repeat dose of hyperosmotic agent [9]. Brain shift: brain swelling has been reported with hemispherectomy.

Intraoperative hemodynamic changes: The risk of blood loss may be higher in infants because they tend to require extensive surgery in the face of a small blood volume. Complex disconnective surgeries and large resective surgeries can result in hemodynamic disturbances due to greater blood loss associated with them. Hemispherectomies are particularly prone to excessive blood loss, hypothermia, and electrolyte disturbances [67–69]. Coagulation issues secondary to excessive blood loss and thromboplastin release during disconnection surgeries can be detrimental in pediatric patients. with the advent of functional, minimally invasive procedures, blood loss and surgery duration are decreased. Intraoperative bradycardia and transient asystole have been reported during the electrodes' initial stimulation and positioning during vagus nerve implant.

Delayed emergence and postoperative drowsiness may be attributed to post-ictal confusion, the effect of AEDs, and the anesthetic agents' residual effect. Many patients with complex disconnective surgery need elective ventilation postoperatively due to drowsiness [67–69]. Such patients are at risk of airway obstruction and aspiration; hence, they need to be continued with mechanical ventilation for some time.

Postoperative neurological deficits: Surgery can result in anticipated neurologic deficits related to the region of brain resection [6]. Most of the neurological complications are minor and transient. Minor neurologic complications up to 11.2% have been reported in the pediatric population. The most common complications are minor visual field defects, especially superior quadrantanopia, stroke, hemiparesis, monoparesis, third and fourth nerve palsy, and dysphasia [70]. Another complication is postoperative hydrocephalus, especially in patients undergoing hemispherotomy. Perioperative mortality is uncommon following epilepsy surgery and has been reported in 0.4% of temporal lobe epilepsy and 1.2% extratemporal epilepsy [71]. Brain swelling, hypovolemia secondary to excessive blood loss in pediatric patients, hypoxia, and infection are reported causes of mortality.

Recurrent/residual seizures: Engel's classification is commonly used to describe the out-

come of epilepsy surgery [72]. The score ranges from I to IV, with I being seizure-free and IV being no worthwhile improvement. Seizure outcome depends upon the type of pathology and completeness of resection. Seizure-free outcomes are reported in 40–70% of cases. Simultaneously, palliative procedures aim to reduce the disabling seizures, and resective surgeries target cessation of seizure. Resection of cortical dysplasia, mesial temporal sclerosis, and hemispherectomy is associated with seizure control of up to 80–85%. Neocortical resections have a marginally less good outcome. Seizure control is less effective in patients with multifocal or poorly defined lesions on preoperative testing. Improper localization of seizure focus and incomplete reaction are the most common reasons for surgical failure [73]. Reoperations are common in cases of surgical failure. A perioperative seizure should be recorded and treated immediately. Acute control of seizure can be achieved with benzodiazepines. Most commonly used agent is midazolam 0.15 mg/kg (5 mg in children 15–30 kg) or lorazepam 0.1 mg/kg IV (repeated after 10 minutes if necessary) for immediate control, followed by long-acting agents like fosphenytoin 20 mg/kg, phenobarbital 20 mg/kg, or levetiracetam 10 mg/kg. The choice and dosing of AEDs should be individualized as per treating neurologist.

Infections: There is a risk of septic and aseptic meningitis following epilepsy surgery, especially with invasive EEG monitoring. Infections of vagus nerve implants have been reported and generally require removal of the hardware.

28.22 Conclusion

Anesthesia for epilepsy surgery in the pediatric patient is challenging. Planning a safe anesthetic regimen requires an understanding of the disease characteristics, pediatric physiology, drug interactions in the perioperative period, and requirement of intraoperative hemodynamic and neuromonitoring. Most pediatric epilepsy surgery requires general anesthesia with special attention to titrate anesthetic drugs to facilitate intraoperative monitoring. Awake craniotomy is done in few cases with lesions around the eloquent cortex and with inadequate preoperative localization of the seizure focus. With recent advances in surgery and anesthesia, epilepsy surgery in children carries low mortality and results in seizure reduction and improved quality of life.

Conflict of Interest None.

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29 Anesthetic Considerations for Supratentorial Space-Occupying Lesions in Children

Nidhi Bidyut Panda, Ankur Luthra, Summit Dev Bloria, Sonia Kapil, and Ashish Aggarwal

Key Points

- The supratentorial space-occupying lesions (SOLs) in children are mostly intracranial tumors but may also be due to the occurrence of abscesses, cysts, hematomas, or other lesions.
- Pediatric brain tumors constitute the second most common malignancy amounting to 20% of all malignancies in childhood.
- Astrocytoma, low-grade glioma, craniopharyngioma, and choroid plexus papilloma are the most common subtypes of supratentorial tumors in children.
- The anesthetic goals remain similar to the adults; however, pediatric patients are more frequently amenable to certain complications such as increased blood loss, hypothermia, venous air embolism, electrolyte imbalances, etc.
- The anticipation of the complications and adequate preparations should be made well in advance to prevent catastrophic consequences.
- Special procedures like stereotactic procedures, gamma knife radiosurgery, and awake craniotomy for excision of the eloquent cortex lesions pose great challenges for the anesthesiologist; they require meticulous planning and preparation along with psychological counseling of the child.

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29.1 Introduction

The supratentorial space-occupying lesions (SOLs) in children are mostly composed of intracranial tumors but may also be due to the presence of abscesses, cysts, hematomas, or other lesions. Primary brain tumors are the most common solid tumors in childhood. The brain tumors are considered the second most common malignancy in children after leukemia; they account for approximately 20% of all malignancies in the pediatric age group [1].

The incidence of primary cerebral tumors among the pediatric population is 2.4–3.5/100,000 children, with around 3000 new cases diagnosed every year in the United States. Astrocytic tumors are the most common pediatric intracranial tumors in India, followed by medulloblastomas and supratentorial primitive neuroectodermal

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tumors (PNETs) [2]. Nearly 60–65% of the lesions are located in the infratentorial region; metastasis is rare during childhood. These tumors can be benign or malignant and may have a varied presentation at different age groups.

29.2 Classification of Pediatric Supratentorial Tumors

The WHO classification (2016) of pediatric brain tumors (Table 29.1) includes genetic and epigenetic profiling, which impacts its diagnosis. Thus, it allows for subgrouping of the heterogeneous tumor groups leading to complete renaming of some tumor types. Hence, risk stratification, staging, and treatment planning become easier. Generally, WHO grade I and II tumors are amenable to surgery, and chemo-radiation is provided to WHO grade III and IV tumors.

There are primary brain tumors present during infancy and even during the first week of life (Table 29.2). Most of these tumors grow over the congenital seedlings of the tumors present during the intrauterine life of the fetus.

29.3 Common Pediatric Supratentorial Tumors

29.3.1 Low- or High-Grade Glioma

Pediatric gliomas may be astrocytomas, oligodendrogliomas, and oligoastrocytomas; 30% of these tumors are hemispheric astrocytomas. They constitute around 8–15% of all childhood brain tumors. Typically found deep within the hemispheres, these are slow-growing; they can occur in the white matter or the cortex. They commonly present with seizures (>80%), especially when the lesion is located in the frontal or temporal lobes. The solid part of the tumor is iso- to hypodense (Fig. 29.1a) on non-contrast computed tomographic (CT) scan, and it may enhance partially or completely (Fig. 29.1b) [3]. Low-grade astrocytoma of other histology are homogeneous, well-circumscribed, non-enhancing masses associated with mild or no edema and are free from hemorrhage. High-grade gliomas (e.g., anaplastic astrocytoma or glioblastoma multiforme) are rare in children but grow rapidly when

Table 29.1 WHO classification of pediatric supratentorial brain tumors

Tumor types	WHO grade
1. **Diffuse astrocytic and oligodendroglial tumors**	
• Diffuse astrocytoma	WHO grade II
• Anaplastic astrocytoma	WHO grade III
• Glioblastoma	WHO grade IV
• Diffuse midline glioma	WHO grade IV
• Oligodendroglioma	WHO grade II
2. **Other astrocytic tumors**	
• Pilocytic astrocytoma	WHO grade I
• Subependymal giant cell astrocytoma	WHO grade I
• Pleomorphic xanthoastrocytoma	WHO grade II
3. **Ependymal tumors**	
• Ependymoma	WHO grade II or III
4. **Choroid plexus tumors**	
• Choroid plexus papilloma	WHO grade I
• Atypical choroid plexus papilloma	WHO grade II
• Choroid plexus carcinoma	WHO grade III
5. **Neuronal and mixed neuronal-glial tumors**	
• Dysembryoplastic neuroepithelial tumor	WHO grade I
• Gangliоglioma	WHO grade I
• Desmoplastic infantile astrocytoma and ganglioglioma	WHO grade I
6. **Tumors of the pineal region**	
• Pinealoblastoma	WHO grade IV
7. **Embryonal tumors**	
• Medulloblastoma	WHO grade IV
8. **Tumors of the sellar region**	
• Craniopharyngioma	WHO grade I

WHO World Health Organization

Table 29.2 Tumors of the newborns and infants

Tumors during the first week of life	Tumors during infancy
• Teratoma • Astrocytoma • Primitive neuroectodermal tumor • Ependymoma • Choroid plexus papilloma	• Glioma • Atypical teratoma • Primitive neuroectodermal tumor • Craniopharyngioma • Ependymoma • Choroid plexus papilloma/carcinoma • Teratoma

present, with a poor prognosis. They show heterogeneity from necrosis or hemorrhage and present with more extensive edema on imaging. These tumors require extensive surgery for a prolonged period of time and may be associated with increased intraoperative bleeding.

29.3.1.1 Subependymal Giant Cell Astrocytoma (SEGA)

Subependymal giant cell astrocytoma (SEGA) is a subgroup of supratentorial gliomas, which occurs in 5–15% of patients with tuberous sclerosis. The prognosis in children with SEGA is considered better than that in patients with giant cell components of other astrocytomas. They appear as round to ovoid in the region of foramen of Monro and often extend into the lateral ventricle (Fig. 29.1c). Despite being a low-grade tumor, its location may lead to obstruction of lateral ventricles and hydrocephalus. These children may present with features of raised ICP, seizures, and focal neurologic signs; they require shunt surgery before total excision of the tumor.

29.3.1.2 Supratentorial Ependymomas

Ependymomas are the third most common intracranial tumors (overall incidence 6–12%) in the pediatric population, after astrocytomas and medulloblastomas [4]. One third of the ependymomas are located in the supratentorial compartment. Most of these children present with non-specific symptoms of increased ICP. These are intraparenchymal, well-circumscribed masses and usually present as a large vascular cyst (Fig. 29.1d) with possible areas of hemorrhage and calcification. They usually have limited infiltrations into the surrounding structures. After surgery and radiotherapy, the 5-year survival rate is 50–80%; the role of chemotherapy is not well-established.

29.3.1.3 Primitive Neuroectodermal Tumor (PNET)

These are rare embryonal but highly malignant tumors; they present early in childhood, grow rapidly, and have a poor prognosis. The highly cellular tumors are composed mostly of undifferentiated cells. PNET of the pineal gland is known as pineoblastoma. On imaging (CT scan), the tumor may present with a large, hyperdense solid portion with cystic areas and calcification [3] (Fig. 29.2a); hemorrhage may be found in 10% of cases. MRI may show isointense solid portions in the grey matter on T2 and FLAIR and restricted diffusion on DWI with an increased blood volume [3]. PNETs are often observed in older children and present with features of increased ICP such as early morning headache, vomiting, lethargy, and seizures.

Gangliogliomas and Gangliocytomas are uncommon (<3%) pediatric brain tumors where both nerve and glial cells participate in the neoplastic process. Half of the children present with seizures, mostly complex partial seizure types. The tumors could be described as low-density, well-circumscribed lesions with minimal mass effect or edema on CT scan. Tumors may be solid, cystic, and cystic with a mural nodule or may appear as many small cysts with variable enhancement in the solid portion.

29.3.1.4 Dysembryoplastic Neuroepithelial Tumor (DNET)

DNETs are most commonly diagnosed in children experiencing seizures and are the second leading cause of epilepsy in children. These are slow-growing tumors that contain both glial and neuronal elements. The children present with intractable partial epilepsy due to associated focal cortical dysplasia that may need intraoperative cortical mapping to resect epileptic

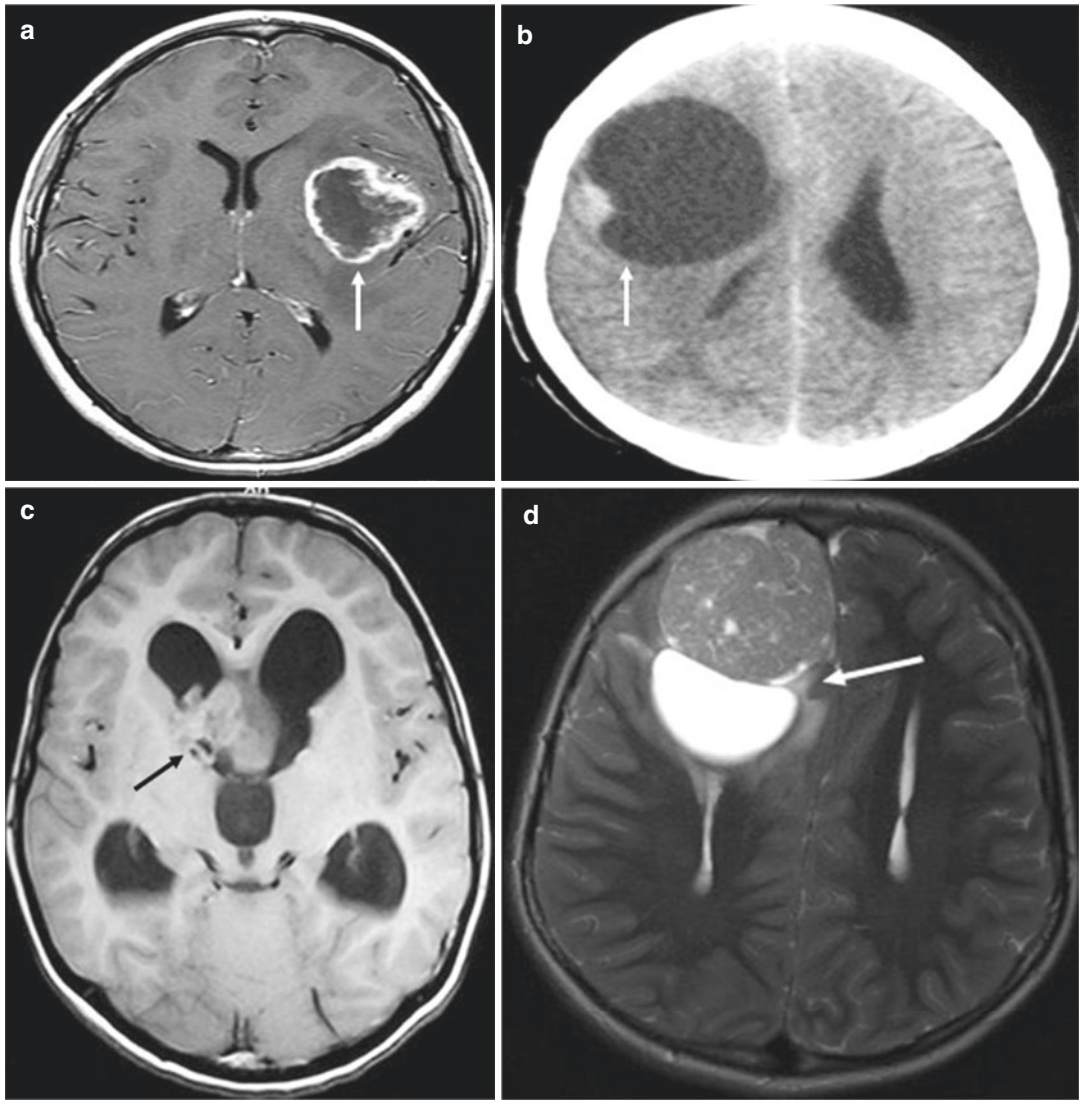

Fig. 29.1 Images of different pediatric supratentorial tumors. (**a**) Axial T1-weighted magnetic resonance imaging (MRI) of the brain shows (arrow) heterogeneous enhancing hypointense lesion with hyperintense borders suggestive of high-grade glioma in left insula. (**b**) Axial non-contrast computed tomographic (CT) scan of the head shows (arrow) hypodense lesion (solid portion) in the right hemisphere with small hyperdensity in the periphery of the lesion, suggestive of large cystic and small solid components of the tumor, respectively. (**c**) Axial T1-weighted MRI shows heterogeneous (arrow) intensity iso-to-hyper-intense irregular lesion near the foramen of Monro extending to right lateral ventricle suggestive of subependymal giant cell astrocytoma. (**d**) Axial T2-weighted MRI shows a large cystic component of the tumor along with a heterogeneously enhancing solid portion (arrow) in the right frontal region suggestive of ependymoma

foci. Most commonly (60%), these tumors are located in the temporal lobe, followed by frontal and parietal lobes. The median age of presentation is 5 months, and they typically present as a hemispheric lesion with a large cystic component (Fig. 29.2b), commonly involving multiple lobes. The peripheral solid component often involves the leptomeninges. The tumor is curable after surgery without recurrence and has an excellent prognosis.

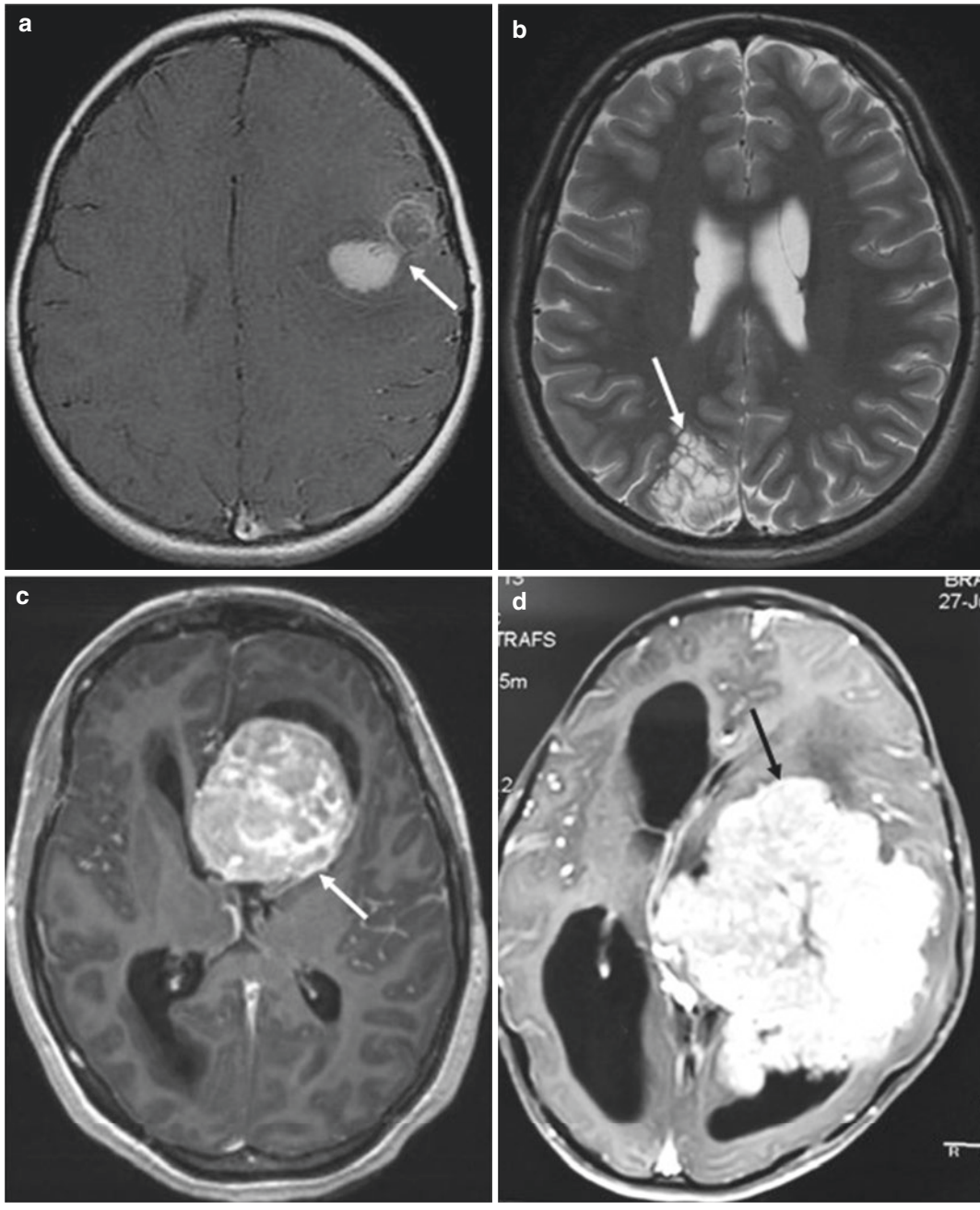

Fig. 29.2 (**a**) Axial T1-weighted MRI shows an isointense lesion with surrounding edema (arrow) in the left parietal region suggestive of the supratentorial central primitive neuroectodermal tumor (PNET). (**b**) T2-weighted MRI shows hyperintense lesion (arrow) suggestive of dysembryoplastic neuroepithelial tumor (DNET) in the right occipital region. (**c**) T1-weighted MRI shows a hyperintense and heterogeneously enhancing lesion in the left frontal horn of lateral ventricle (arrow) suggestive of intraventricular ependymoma. (**d**) Axial section T1-weighted contrast magnetic resonance imaging showing a frond-like enhancing lesion in lateral ventricle suggestive of choroid plexus papilloma

29.3.1.5 Intraventricular Tumors

These are benign tumors projecting into the ventricles or deeply located in the lateral or third ventricles (Fig. 29.2c). Most of these tumors grow slowly and remain clinically silent until they reach a significant size. The most common lateral ventricular tumor in children is choroid plexus papilloma, which presents as obstructive hydrocephalus and intracranial hypertension. These are highly vascular tumors that may remain silent for a long period and, hence, attain an extreme size before the diagnosis. These tumors have particular postoperative problems resulting from the disturbance of CSF circulation.

29.3.1.6 Choroid Plexus Tumors

Choroid plexus papillomas constitute approximately 2–5% of all intracranial neoplasms in children [5]. Nearly 10–20% of choroid plexus tumors occur in infancy [5]. These are the most common lateral ventricular tumors in children, with around 70–90% presenting in less than 2 years. They have a predilection for the fourth ventricle in adults and are common in males. Choroid plexus papillomas are histologically benign lesions; however, focal brain invasion may at times be present. Children usually present with hydrocephalus and marked ventricular dilation. CSF overproduction is the cause of hydrocephalus in most of these children. These lesions are iso-to-hyperdense on CT scans, hypointense on T1-weighted, and iso-to-hyperintense on T2-weighted MR images [3]. They are highly vascular and hence strongly enhanced with contrast administration (Fig. 29.2d). Enlarged choroidal arteries are often present, and the lateral posterior choroidal arteries frequently represent the major blood supply. Both anterior and posterior choroidal arteries may contribute to blood supply depending on the site of the tumor. An anastomosis of both vessels may supply a choroid plexus carcinoma. These tumors calcify in 25% of cases.

Children with choroid plexus papilloma may present with macrocrania, hydrocephalus, and increased ICP. Blood loss during intraoperative resection of the tumor is a major concern in small children. For highly vascular tumors, preoperative embolization may be carried out. Embolization may not be feasible all the time because tiny feeder arteries supply the tumors and the approach is difficult. Complete resection of well-differentiated papilloma is essentially curative, and no adjunctive treatments are needed.

29.3.1.7 Craniopharyngiomas

These benign neuroepithelial tumors constitute around 5–10% of all brain tumors in childhood and are more commonly seen in the age group of 5–14 years [3]. Histologically, craniopharyngiomas are of two types: adamantinomatous type characterized by the frequent presence of cysts and calcification and papillary squamous histology without calcification or cyst formation. Adamantinomatous type is common in children, whereas the papillary type is more common in adults. These tumors are nearly always suprasellar in a location with intrasellar extension present in half of the cases. They hence are considered as the most common childhood tumor in the sellar region. Cystic content tends to be unenhanced on T1-MRI due to high protein content, whereas solid component and cyst walls enhance with contrast [3]. Children with craniopharyngioma often present with visual disturbances and endocrine abnormalities apart from the features of raised ICP (Fig. 29.3a).

29.3.1.8 Pineal Tumors

The pineal neuroendocrine gland is located in the posterior aspect of the third ventricle (Fig. 29.3b, c). Pineal tumors constitute about 3–8% of tumors in children. Increased ICP due to obstruction in CSF flow and diplopia is the most common presenting complaint [6]. Most of the children are clinically present when the tumor is still small, and many are curable with radiation and chemotherapy. At least 17 histologically distinct tumor types may occur in the pineal region, although germinoma and astrocytoma are the most common ones. Literature suggests a strong bias for treatment with ventricular shunting followed by radiation therapy, owing to a history of poor outcomes after surgical excision [6].

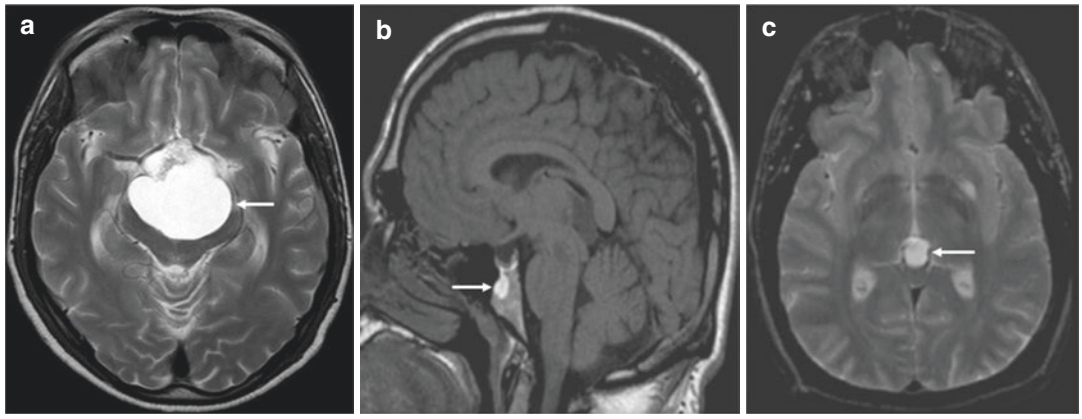

Fig. 29.3 (**a**) T2-weighted MRI shows a large solid cystic lesion (cystic content tends to be unenhanced on T1-MRI due to high protein content, whereas solid component and cyst walls enhance with contrast) in the sellar region. (**b**, **c**) A well-defined homogeneous (non-enhancing) T1-hypointense and T2-hyperintense cyst-like mass in the pineal region suggests a pineal cyst

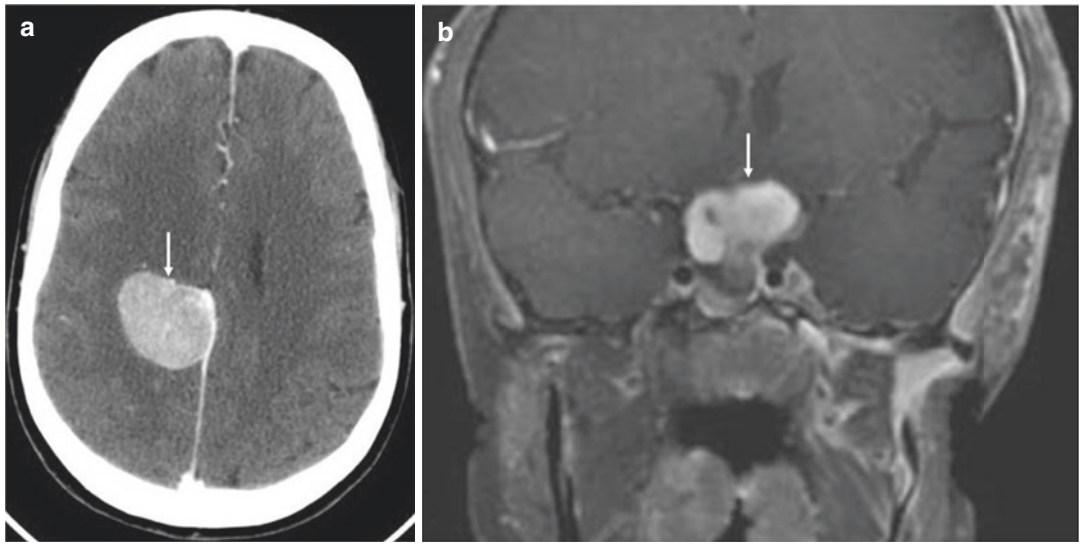

Fig. 29.4 (**a**) CT scan shows a homogeneously enhancing hyperdense extra-axial lesion with a broad base and a dural cleft present around it in the right parietal region, suggestive of supratentorial meningioma. (**b**) The coronal section of T1-weighted MRI shows a hyperintense lesion in the sellar region and extends to para-sellar areas suggestive of optic pathway glioma

29.3.1.9 Supratentorial Meningioma

These are rare (<5%) supratentorial tumors in children. They are highly vascular, more aggressive than adult meningiomas (Fig. 29.4a) and are often excised surgically. The most common locations for meningiomas in children are the cerebral convexity (40%), followed by ventricles (15%), infratentorial space (8%), intraparenchymal (5%), parasagittal (4%), and the sellar and cavernous sinus region (8%) [7]. Complete tumor resection is the best option to prevent recurrence and improve prognosis. Surgical resection of pediatric meningiomas is a neurosurgical challenge due to difficulty in early

diagnosis, large size at presentation, relatively less blood volume in children, occurrence in unusual locations, tight adherence to vital vessels and nerves, and the associated risks of prolonged surgery such as hypothermia, massive blood transfusion, etc. Intraoperative control of bleeding is one of the most important considerations with these tumors.

29.3.1.10 Hypothalamic Astrocytomas or Optic Pathway Glioma

These lesions may be pre-chiasmatic, chiasmatic, and postchiasmatic gliomas based on the location. Up to 20% of children with type 1 neurofibromatosis (NF) will develop optic pathway glioma (OPG), usually at a younger age [3], and rarely occur after 6 years of age. OPG associated with NF1 may have a more indolent course than non-NF1 children. Gliomas of the hypothalamus can grow inferiorly to involve the optic chiasma and, hence, the site of origin of the large tumor. Hypothalamic hamartomas are isointense to cortex on T1 and isointense to slightly hyperintense on T2, and they do not enhance contrast administration (Fig. 29.4b). Hamartomas present with drug-resistant epilepsy; gelastic seizure is the hallmark of the lesion.

29.4 Pathophysiology of Supratentorial Tumors

The narrow autoregulation range (20–60 mmHg) in children makes them susceptible to both cerebral ischemia and intraventricular hemorrhage beyond the lower and upper limits, respectively [8, 9]. Normal ICP is between 2 and 6 mmHg compared to 5 and 15 mmHg in older children. The cerebral blood flow velocities also vary with age, rising to a peak by 6 years.

As governed by the Monro-Kellie doctrine, the sum of volumes of the brain, CSF, and intracerebral blood is constant. A proportionate increase in one compartment causes a reciprocal reduction in one or both of the remaining two. Unlike adults and older children, who have a closed compartment, the presence of open fontanel compensates for any rise in the intracranial volume and masks the effects of any space-occupying lesions in infants and younger children [10, 11].

The symptoms of raised ICP in supratentorial lesions are either due to the mass itself, the surrounding vasogenic edema, or hydrocephalus (overproduction of CSF as in choroid plexus papilloma, obstruction to CSF outflow, or reduced reabsorption). The important consequences of the rise in ICP are cerebral ischemia due to reduced CPP, midline shift, and herniation of the brain. Fast-growing tumors have marked peritumoral edema. It occurs due to disruption of the blood-brain barrier due to "leaky vessels," which responds well to corticosteroid therapy [12]. Cerebral autoregulation plays an important role in preserving cerebral blood flow under normal conditions by causing "myogenic response" at the level of cerebral arterioles.

Rhondali et al. have found that a minimum mean blood pressure of 35 mmHg or within 20% of baseline blood pressure is needed to ensure cerebral perfusion in healthy full-term neonates younger than 6 months of age [13]. The mechanisms of cerebral autoregulation may be disrupted in patients with brain tumors, making them perfusion pressure dependent and, thus, susceptible to ischemia or hyperperfusion even at the normal range of blood pressures [14].

29.5 Clinical Presentation

The patients may present with signs and symptoms of raised ICP or with focal neurological deficits. Headache, nausea, vomiting, blurring of vision, or papilledema may be present in older children (Table 29.3); on the other hand, neonates and infants present with a large head, excessive crying, failure to thrive, and respiratory distress. Irregular respiration (Cheyne-Stokes breathing) along with Cushing's triad (bradycardia, high blood pressure, and irregular respiratory pattern) may occur in the presence of uncal herniation. Seizures and neurological deficits are common in supratentorial pathologies [15]. Children with suprasellar pathologies may also present with

Table 29.3 Clinical presentation of children with supratentorial tumors

Neonates and infants	Children
Irritability and excessive crying	Headache
Decreased level of consciousness	Vomiting
Seizures	Diplopia
Enlarged head	Seizures
Dilated scalp veins, open fontanels	Papilledema
Sunset sign	Decreased level of consciousness
Cranial nerve palsies	Cranial nerve palsies (III, VI)
Cushing's triad	Cushing's triad

slowly progressive vision loss and endocrine dysfunction (growth retardation, delayed puberty). The hypothalamic-pituitary dysfunction is a common presentation and may require steroid therapy and thyroid supplementation in the perioperative period [16].

29.6 Anesthetic Management

29.6.1 Preoperative Evaluation, Optimization, and Premedication

Preoperative evaluation (Table 29.4) aims to assess the signs of the mass effect of the tumor, status of cerebral autoregulation, and comorbidities in the child so that a perioperative anesthetic strategy can be planned to preserve homeostasis and prevent irreversible neuronal injuries. A thorough evaluation includes a detailed history; physical examination; hematological, biochemical, and radiological assessment; and discussion with the neurosurgeon regarding intraoperative concerns for a holistic approach to manage pediatric patients. The presence of signs and symptoms of raised ICP is of particular concern. The presence of vomiting and poor intake may cause dehydration, hypovolemia, and electrolyte abnormality. A decreased level of consciousness may increase the risk of aspiration.

Diabetes insipidus (DI) may occur with an incidence of 8–35% during the preoperative period in the patients with peri-sellar tumors,

Table 29.4 Preoperative concerns in pediatric patients

- Prematurity: Postoperative apnea
- Difficult intravenous cannulation
- Presence of congenital heart disease
- Hypothalamic pituitary disease: Diabetes insipidus (DI), adrenal insufficiency
- Hepatic and hematologic disorders with anticonvulsants
- Electrolyte abnormalities
- Hypovolemia
- Anxiety and premedication
- Gastroesophageal reflux: Aspiration risk

raising concern regarding the volume and sodium status in the patients. The diagnosis depends on the lesion site, serum hypernatremia (>145 mEq/L), urinary sodium levels <20 mEq/L, and the presence of dehydration [17]. An invasive hemodynamic monitoring is rarely needed in the preoperative period itself to replace hourly fluid losses**.** Apart from the neurological examination, a thorough cardiovascular evaluation may be needed in premature neonates and infants to look for intra-cardiac shunts, which may increase the risk of venous air embolism (VAE) [18].

Radiological assessment should include the site and size of the tumor, any significant mass effect, midline shift, herniation, hydrocephalus, and vascularity of the mass. A preoperative discussion with the surgeon regarding the positioning during surgery predicted blood loss and risk of injury to eloquent and vital areas that help in proper perioperative anesthetic care of the child [18]. Preoperative investigations are tailored as per the surgical procedure. Hematocrit, coagulogram, serum electrolytes, renal function tests, and other investigations are ordered if deemed necessary. Blood and blood products are arranged as per the requirement. Patients with suprasellar tumors may need a complete endocrinological evaluation and therapeutic correction [16, 18].

Premedication should be individualized depending on the presence of raised ICP, level of consciousness, anxiety, and age of the child. Neonates and infants up to 7 months do not need any sedative premedication as stranger anxiety has not developed. In older children,

premedication may be needed. Preoperative anxiety and excessive crying can cause a rise in ICP, while excessive sedation may cause hypoventilation, hypercapnia, and apnea, further increasing the ICP. If planned in pediatric patients with intracranial space-occupying lesions, sedative drugs are given in titrated doses under the monitoring and supervision of anesthesiologists. Midazolam is a preferred anxiolytic sedative drug in children and can be administered through oral or intravenous routes. Newer drugs like dexmedetomidine are also showing promising results as non-sedative premedication in pediatric patients. In children with altered consciousness and symptoms of increased ICP, sedative premedication should be avoided [18–21].

Anticonvulsants and steroids are continued till the day of the surgery. Children with a history of seizures should have a preoperative assessment to confirm therapeutic blood levels of anti-seizure medications. Parental presence during the induction of anesthesia may be an alternative to allay anxiety in children.

29.7 Intraoperative Management

29.7.1 Vascular Access

Central venous access is required when there is an anticipation of massive intraoperative blood loss such as large meningiomas, surgeries near the venous sinuses, increased risk of VAE, cardiovascular morbidity such as major congenital heart diseases, decreased myocardial function, prolonged hospital stay, and difficult peripheral IV access. Cannulation of an artery such as radial, femoral, dorsalis pedis, or posterior tibial artery is preferred in children undergoing craniotomy for supratentorial tumors. Continuous monitoring of invasive blood pressure helps guide the hemodynamic management in children with exhausted intracranial compliance. The arterial line also helps in frequent blood sampling for hematocrit, electrolytes, blood sugar, and blood gas analysis [19, 21].

29.7.2 Induction of Anesthesia

The goals of induction of anesthesia are maintenance of adequate cerebral perfusion and avoiding a further rise in ICP. Hypoxia, hypertension, hypotension, hypercapnia, hypocapnia, and venous outflow obstruction should be avoided in children with supratentorial space-occupying lesions. The preoperative status of the child dictates the appropriate technique used for anesthetic induction.

An IV induction with thiopentone (5–8 mg/kg) or propofol (1.5–3 mg/kg) is preferred in children with features of raised ICP. In the absence of IV access, inhalational induction is indicated as crying and struggling may further increase the ICP. Sevoflurane is the agent of choice for inhalational induction in the pediatric population as it is non-irritant with less incidence of laryngospasm and bronchospasm. The cerebral vasodilatory effects of the inhalational agents should always be borne in mind; mild hyperventilation may be instituted to counter this action. Once an IV line has been secured, an opioid and neuromuscular blocking agent is administered. Children at a high risk of aspiration should undergo rapid sequence intubation (RSI). Succinylcholine has been attributed to increasing ICP; however, prior hyperventilation and bolus of IV anesthetic with cerebral vasoconstricting effects may mitigate its effect on ICP. Rocuronium (1.2 mg/kg) may be used as an alternative muscle relaxant in children for RSI when succinylcholine is contraindicated (e.g., long-standing paresis, hyperkalemia, etc.). The possible association of an undiagnosed myopathy in children may dissuade anesthesiologists from administering succinylcholine.

29.7.3 Airway Management

Pediatric airway differs from adults in many ways. Apart from congenital abnormalities, associated hydrocephalus may pose difficulty in securing the airway. Previously, uncuffed endotracheal tubes (ETTs) were recommended for pediatric patients up to 6 years. However,

with the advent of low-pressure and high-volume micro-cuffs, these ETTs are better suited. Nonetheless, minimal air leak should be allowed during ventilation to avoid compromises in perfusion of tracheal mucosa. Reinforced ETTs are preferred during surgeries performed in prone and sitting positions. The ETTs should be properly secured with adhesive tapes after ensuring bilateral equal air entry. Tight bandages around the neck should be avoided to prevent venous outflow obstruction.

29.8 Pharmacology of Anesthetic Agents in Children

The sensitivity of infants to sedatives, hypnotics, inhalational agents, and narcotics is significantly higher due to the immaturity of the CNS, incomplete myelination, immature blood-brain barrier, and increased permeability of the brain. The minimum alveolar concentration (MAC) of inhalational anesthetics is much lower for neonates (0–31 days of age) than for older infants. Although infants have increased anesthetic requirements, the margin of safety, i.e., the difference between adequate anesthesia and profound cardiovascular depression, is relatively lower. Apart from the effect of the anesthetic agents on CBF and cerebral metabolism, their effects on the evoked potentials (EPs) should also be considered.

The inhalational anesthetic agents usually increase CBF due to direct vasodilation and can preserve flow-metabolism coupling up to MAC 1.5–1.8. Beyond this, there may be decoupling of flow-metabolism, which results in a direct rise in CBF and the subsequent rise of CBV and ICP. Unlike inhalational anesthetics, the IV agents preserve flow-metabolism coupling and are cerebral vasoconstrictors. They may cause a reduction of CBF and ICP and, hence, better suited for use in intracranial pathologies. Similarly, their interference with EPs is minimal and is favored during intraoperative neuromonitoring (IONM).

29.9 Maintenance of Anesthesia

The goal of anesthetic maintenance in a child undergoing surgical excision of the supratentorial lesion is to ensure adequate control of ICP, provide "a slack brain" during surgery, maintain hemodynamic stability and bloodless operative field, prompt detection and management of complications, and finally smooth and early emergence from anesthesia at the end of the surgery. The choice of anesthetics during pediatric supratentorial tumor excision is a topic of debate. It depends on the presence of an intracranial mass effect, hemodynamic stability, need for IONM, and plan for elective postoperative mechanical ventilation. IV anesthetic agents are preferred when the child presents with features of increased ICP and decreased intracranial compliance. The proponents of IV anesthetic agents advocate the vasoconstriction and "neuroprotective effects," while those favoring inhalational anesthetics argue over these agents' more predictable recovery profile. Inhalational agents decrease $CMRO_2$, but the direct cerebrovasodilatory effect may further cause a rise in the ICP and "brain bulge" at the time of the bone flap elevation. The IV agents, on the other hand, have both cerebral metabolic suppression and vasoconstrictive effects. Nevertheless, the choice of anesthetic agents has not been shown to have any difference in the outcome of the neurosurgical procedures [20–22].

A comparison of propofol, isoflurane, and the combination of two agents in patients undergoing craniotomy for supratentorial intracranial surgery found no difference in the intraoperative hemodynamics and recovery time with the three regimens [23]. Another similar comparison in patients undergoing supratentorial craniotomy concluded that propofol-maintained and volatile-maintained anesthesia were associated with similar brain relaxation scores. The mean ICP values were lower, and CPP values higher with propofol-maintained anesthesia; however, the neurological outcome was not different [24].

The commonly used technique for maintaining anesthesia during excision of supratentorial

SOL in a child is the combination of an inhalational agent, like sevoflurane or isoflurane, with an opioid (e.g., fentanyl). The inhalational agents may be used safely in patients with small, superficially located tumors with minimum mass effect and midline shift. Anesthesiologists prefer to use propofol infusion in older children to excise large tumors with significant mass effect and signs of raised ICP. The US FDA has approved the use of propofol in the maintenance of anesthesia in children more than 2 months and for induction of anesthesia more than 3 years of age [25].

Fentanyl is the most commonly used opioid in children for intraoperative analgesia. The half-lives of fentanyl and other related synthetic opioids, including sufentanil, may be prolonged with repeated dosing and prolonged infusions. They undergo hepatic metabolism, which is immature in infants, thus increasing the risk of respiratory depression and sedation in the immediate postoperative period. Remifentanil, on the other hand, undergoes rapid clearance by plasma esterases. When administered at a rate of 0.2–1.0 μg/kg/min, it is considered an ideal opioid for rapid emergence from anesthesia. However, delirium and inadequate analgesia (shorter duration of action) may occur during the recovery phase.

Application of skull pin produces a noxious effect resulting in significant hemodynamic stimulation. A bolus of IV anesthetic agent (propofol 0.5–1 mg/kg), a short-acting opioid (fentanyl 1–2 μg/kg or remifentanil 0.25–1 μg/kg), or β-blockers (esmolol or labetalol) is generally administered to obtund the pin response. Pin-site infiltration with local anesthetics or scalp block prevents excessive hemodynamic stimulation without producing any side effects.

Neuromuscular drugs per se do not have any effect on CBF. The children on chronic anticonvulsant therapy may exhibit the early metabolism of the non-depolarizing muscle relaxants (NMDR), thus increasing the frequency and dose of the NDMRs. Atracurium is preferred over vecuronium or rocuronium in neonates and infants because of its rapid metabolism independent of the liver and renal functions, which are immature in infants.

29.10 Intraoperative Monitoring

Monitoring in neurosurgical patients is decided by parameters such as age, neurological status, intracranial compliance, hemodynamic status, site of the surgery, vascularity of the lesion, the position of the patient during surgery, and localization and identification of eloquent areas. Standard monitoring in pediatric patients includes electrocardiogram, invasive arterial blood pressure, pulse oximetry, capnography, neuromuscular monitoring (TOF count), temperature, blood loss, and urine output monitoring. Central venous pressure (CVP) monitoring is preferred in children at risk of massive blood loss, major fluid shift, and high risk for VAE. Intraoperative arterial blood pressure monitoring provides beat-to-beat variability. It is useful in cases with possible massive blood loss (e.g., resection of meningioma, choroid plexus papilloma, etc.), major fluid shifts, electrolyte imbalances (craniopharyngioma surgery and risk of DI), and repeated measures of ABGs.

Pulse oximetry is important in pediatric patients as it not only provides continuous oxygen saturation monitoring but also gives a rough idea of intraoperative fluid status using plethysmographic variability (PPV). However, it is subject to motion artifacts, and its measurement becomes difficult in hypothermic children. $EtCO_2$ monitoring is of vital significance; it provides an estimation of continuous CO_2 levels in the blood and hence an overall idea of other ventilatory parameters and indirectly monitors for VAE and blood loss. VAE is always a risk even in children undergoing craniotomy in the supine position. The head is commonly kept above the heart level during the excision of supratentorial SOLs. The incidence of VAE in children depends upon the intraoperative monitoring technique. An incidence of 9.3% has been reported in the sitting position; VAE-associated hypotension occurs in 2% of children without any direct link between VAE and outcome [26].

Jugular venous saturation monitoring helps guide adequacy of cerebral oxygen supply and demand but is less commonly used in pediatric patients. NIRS and TCD are not commonly used

in children, and the data regarding their intraoperative use is limited. IONM may be required for the identification of eloquent areas during the excision of lesions. Motor mapping with the child under general anesthesia or conscious sedation is increasingly used to localize the motor cortex and optimize tumor excision. Anesthetic requirement and technique should be discussed with the neurosurgeon and the neurophysiologist preoperatively. The IONM modalities used for pediatric supratentorial tumors are somatosensory-evoked potentials (SSEPs), transcranial motor-evoked potentials (MEPs), free-running and triggered electromyography (EMG), direct cortical and subcortical stimulation (DCS, DsCS), and electroencephalography (EEG). Volatile agents have the greatest impact, while the IV agents have less suppressive effects or may even enhance certain evoked potentials (EPs), as in the case of ketamine and etomidate. MEPs are the most susceptible to anesthetic effects, and SSEPs are intermediate, while the auditory brainstem responses (ABRs) and EMGs are fairly resistant to anesthetic effects. Neuromuscular blocking agents will ablate the MEPs and EMGs but improve the quality of SSEPs and ABRs by eliminating the EMG artifact. The application of IONM to pediatric neurosurgical cases poses special problems. Infants and toddlers are neurologically immature and have incomplete myelination, reduced conduction velocities, and fewer monosynaptic connections between the corticospinal tract and alpha-motor neurons. The presence of genetic disorders can also dramatically impact the ability to acquire IONM data and the sensitivity to anesthetic agents.

Advances in intraoperative magnetic resonance imaging (MRI) have enabled neurosurgeons to define tumor margins during the surgical excision. This provides the opportunity for excision of the lesion without causing iatrogenic damage to normal brain tissue or leaving residual tumor in a single operative session. However, this combined surgical and imaging procedure is associated with prolonged anesthesia time and the requirement of proper care of anesthetic equipment in a magnetic environment [27].

29.11 Positioning

Positioning children undergoing neurosurgery is done to provide optimal surgical access to the target area of the brain. The six basic positions are performed during supratentorial tumor resection: supine, lateral, semi-lateral (Janetta), prone, three-quarter prone (park bench), and sitting position. Mayfield pins are usually recommended for children over 5 years of age. Lateral and sitting positions are rarely used in pediatric supratentorial surgeries. The sitting position is most commonly utilized for the excision of pineal tumors. The risks involved in various positioning include hemodynamic instability, upper airway edema, peripheral neuropathies, VAE, postoperative vision loss, etc. All operating room personnel associated with patient care should be involved in taking appropriate precautions to avoid and manage these complications. Excessive extension and flexion of the neck may lead to inadvertent extubation, endobronchial migration of ETT, kinking, and tongue and upper airway edema and may impede the venous outflow from the brain. Access to vascular lines, airway, and breathing circuit should be ensured prior to the commencement of the surgery.

29.12 Fluid Management

Isotonic, non-glycemic, warm fluids are used to target normovolemia and normotension. Isotonic solutions (0.9% normal saline) are preferred over hypotonic solutions (like Ringer's lactate) to maintain target serum osmolality of 290–300 mOsm/L as hypo-osmolality may increase the brain edema. A recent study supported the use of balanced crystalloid solutions in children undergoing brain tumor resection in place of normal saline [28].

CBF constitutes 55% of the total cardiac output making pediatric patients vulnerable to cardiovascular collapse after sudden blood loss during intracranial surgery. Thus, the aim to maintain the intravascular volume status should begin in the preoperative period itself with care-

ful administration of maintenance and replacement fluids. Maximum allowable blood loss should be calculated in all pediatric patients undergoing craniotomy; a minimum hematocrit value of 25% should be targeted. Volume resuscitation in the ratio of 3:1 for crystalloid to blood loss or 1:1 ratio with colloid to blood loss may be carried out. The intraoperative use of colloids in children is still debatable and sparsely studied. A meta-analysis opined that intravascular volume expansion with low molecular weight 6% hydroxyethyl starch (HES) did not modify renal function, blood loss, or transfusion requirements when administered to children during the perioperative period [29]. Rather, large volume resuscitation with rapid infusion of saline (>60 ml/kg) may be associated with hyperchloremic acidosis. Glucose-containing solutions (5% dextrose, DNS, etc.) are no longer used in intracranial surgeries to avoid hyperglycemia, which may further aggravate cerebral injury. However, the risk of hypoglycemia in pre-term and sick full-term neonates (<50 mg/dl) should always be borne in mind. With limited reserves of glycogen and limited gluconeogenesis, small premature infants may require dextrose-containing fluids to maintain a desired blood sugar level. Tight glycemic control (70–100 mg/dL) in the pediatric population is not practiced because of the risk of hypoglycemic episodes; the blood sugar value of less than 180 mg/dl is usually targeted. Goal-directed fluid therapy depends on individual intravascular volume optimization to get a maximum cardiac stroke volume. Both static and dynamic parameters are used to guide fluid administration during the perioperative period. Dynamic parameters include stroke volume variation, pulse pressure variation, systolic pressure variation, aortic blood flow variation, plethysmographic variability index, and 2D echocardiography involving velocity time integral (VTI). These parameters are more reliable and better suited for assessing changes during perioperative fluid requirements. However, the data on the pediatric population is scarce. Gan et al. reviewed the reliability of dynamic variables based on the heart-lung interaction. They observed that respiratory variation in aortic blood flow peak velocity was the only reliable variable predicting fluid responsiveness in children [30]. Literature in adult patients suggests that patients with low SVV had a shorter ICU stay, fewer postoperative neurological events, and lower intraoperative serum lactate [31]. It is pertinent to remember that during surgeries, such as excision of craniopharyngioma or other sellar tumors, frequent monitoring of sodium is warranted. Dextrose-insulin infusions or ½ NS may have to be titrated according to the ongoing hypernatremia and DI.

29.13 Hyperosmolar Therapy and Optimization of Surgical Field

Both mannitol and hypertonic saline at equiosmolar concentrations may be used in children; they provide similar intraoperative brain conditions. A prospective open-label randomized study on 30 children under 16 years of age with severe traumatic brain injury (TBI) found mannitol and hypertonic saline equally beneficial [32]. Adult data demonstrates the maintenance of better hemodynamics with the use of hypertonic saline and may be considered when choosing hyperosmolar therapy in pediatric patients. The other advantage of using 3% hypertonic saline is a more rapid volume expansion compared with mannitol. Therefore, hypertonic saline may have a theoretical benefit in treating refractory raised ICP; however, the outcome remains unchanged.

29.14 Intraoperative Crisis Management

29.14.1 Intraoperative "Brain Bulge" or "Tight Brain"

This is an important and frequently encountered complication, especially in older children. The management becomes important from an anesthesiologist's point of view. The primary goals are to control brain tension via control of CBF and metabolism and provide a relaxed

"slack" brain. The major factors to be considered are proper ventilatory strategies such as avoidance of hypercapnia and hypoxemia and early institution of mild hyperventilation. Similarly, sympathetic and arterial pressure control by ensuring an adequate depth of anesthesia and analgesia and uninterrupted cerebral venous drainage with proper head positioning should be done. Careful attention to these factors improves the status of the intracranial pressure-volume curve and ensures the adequacy of cerebral perfusion while preventing untoward increases in ICP. Important steps to prevent and treat "intraoperative brain bulge" are enumerated in Table 29.5 and Table 29.6, respectively.

29.14.2 Severe Blood Loss

Blood loss can be difficult to assess during craniotomies because of constant oozing onto the surgical drapes and irrigation with saline fluid. Certain tumor types such as choroid plexus papillomas, high-grade gliomas and glioblastomas, pineoblastomas, and suprasellar meningiomas are prone to bleed more than other subtypes. Hence, a greater word of caution needs to be taken in the presence of such pathologies. The maximum allowable blood loss (MABL) should be carefully estimated and replaced with 3 mL of isotonic fluid per ml of blood loss. If blood loss is less than or equal to the MABL and no further

Table 29.5 Steps to prevent intraoperative brain bulge

Parameter	Intervention	Rationale
Smooth anesthetic induction	• Ensure smooth induction by the use of titrated doses of induction agent and preventing hemodynamic responses to laryngoscopy and intubation using boluses of opioids, esmolol, or lidocaine before laryngoscopy • Prevent response to skull pin fixation using local anesthetic infiltration, scalp block, or opioid or propofol/thiopentone bolus	Prevent undue hemodynamic responses and changes in cerebral perfusion pressure (CPP) and intracranial pressure (ICP)
Head and neck positioning	• Give a slight head-up position (10–15°) • Prevent extreme neck flexion (at least two-finger breadth distance between chin and sternum) • Ensure no extreme neck rotation	Appropriate positioning ensures adequate venous drainage Preventing a head-down position is essential to prevent an increase in CPP and, hence, ICP
Ventilatory strategies	• Adjust ventilatory settings to achieve normal peripheral and arterial oxygen saturation, normocapnia, and normal airway pressures • Baseline arterial blood gas to ensure normal $PaCO_2$ and rule out discrepancies between $EtCO_2$ and $PaCO_2$	Both hypoxia and hypercapnia can cause cerebral vasodilatation, increased cerebral blood volume, and a rise in ICP. High airway pressures can impede venous return from the head and neck region
Anesthetic technique	Choose between the use of total intravenous anesthesia (TIVA), a balanced anesthetic technique, and the use of nitrous oxide to control the ICP	Baseline clinical neurological assessment, review of imaging, and communication with neurosurgeon can help identify anticipated intraoperative events to plan an anesthetic technique that prevents worsening of neurological injury
Osmotherapy	Mannitol (0.25–1 gm/kg) or hypertonic saline (3–5 ml/kg) are given over 15–20 mins during craniotomy	Osmotherapy intends to reduce the overall cerebral water content and, thereby, cerebral volume
CSF drainage	Ventriculostomy/external ventricular drainage (EVD)	When severe edema or mass effect is present on imaging, an EVD can be inserted in the contralateral lateral ventricle. CSF aspiration, if required, can be used as a rescue measure to treat "tight brain"

$PaCO_2$ partial pressure of arterial oxygenation, *$EtCO_2$* end-tidal carbon dioxide, *CSF* cerebrospinal fluid

Table 29.6 Interventions to manage intraoperative brain bulge

Intervention	Rationale
Hyperventilation	Institution of moderate hyperventilation ($PaCO_2$ 28–30 mmHg) results in cerebral vasoconstriction and CBF reduction. It is considered one of the most effective as it has an immediate onset of action
Osmotherapy	Mannitol can be repeated and further doses considered if necessary. Alternatively, hypertonic saline can also be used. Additionally, furosemide (0.3–0.4 mg/kg) boluses can be given and redoes, if needed
Reverse Trendelenburg	Ensuring the head-up position (if not given previously) can effectively facilitate venous drainage and reduce ICP
Anesthetic agents	Switch off nitrous oxide. Boluses of propofol/thiopentone may be given. Converting to TIVA helps achieve better cerebral vasoconstriction and should be considered
Stable vital parameters	• Prevent and treat hypotension. Hypovolemia, blood loss, diuretics, and deep anesthesia can all cause hypotension and have to be treated with fluids, blood, and/or vasopressors as required • Prevent and treat hypoxia • Ensure normal airway pressures. High airway pressures in children may be due to bronchospasm, high airway resistance due to small caliber (internal diameter) of the endotracheal tube, rotation or flexion of the neck causing kinking. Inhaled bronchodilators, ET suctioning, and neutral neck positioning can be done • Treat anemia. Low hematocrit can also cause increased cerebral blood flow and contribute to a tight brain
Others	• Steroids. Dexamethasone (4 mg) bolus can be given but ineffective as onset takes a longer time • CSF drainage. If a ventriculostomy or lumbar CSF drain has been inserted, CSF aspiration (maximum of 20 ml and a slow rate of aspiration of less than 2 ml/min) can be a good rescue measure to treat the tight brain

$PaCO_2$ partial pressure of arterial oxygenation, *CSF* cerebrospinal fluid

significant blood loss occurs or is anticipated during the postoperative period, packed red blood cell (PRBC) transfusion is generally avoided. If the child has reached the MABL and significantly more blood loss is expected during surgery, the child should receive PRBCs in sufficient quantity to maintain the hematocrit more than 25%. Fresh frozen plasma (FFP) may be administered to replenish clotting factors lost during a massive blood transfusion.

Infants undergoing complex cranial vault reconstructive procedures such as craniosynostosis repair are at increased risk of intraoperative hemorrhage and need for blood transfusion. Apart from PRBC and FFP, cell salvage techniques, fibrinogen concentrates, off-label recombinant factor VII, and tranexamic acid (10 mg/kg bolus followed by 1 mg/kg/h infusion) have also been used in these children [33]. Similarly, the use of tranexamic acid has also been suggested to reduce intraoperative blood loss during excision of highly vascular tumors such as choroid plexus papilloma [34].

Additionally, thromboelastography carries an important role in the perioperative assessment and monitoring of the coagulation system in pediatric patients undergoing craniotomy for primary brain tumors. Thromboelastography data may help recognize children at increased risk of bleeding or thromboembolic events, thereby closely monitoring and early intervention that may reduce morbidity and mortality. The principle of thromboelastography operation is that it provides a visual representation of viscoelastic changes occurring in a coagulating sample of blood [35].

29.14.3 Intraoperative Hypothermia

Infants and children are especially prone to develop hypothermia due to their large surface-area-to-volume ratio; other causes may include awake non-anesthetized children, large exposed areas, long-duration surgery vasodilation, and low temperature of administered fluid and blood

products. The low muscle mass may cause the inability to shiver, and an absence of thermal insulation, e.g., subcutaneous fat, especially in premature children, makes them prone to developing hypothermia [36–40]. Hypothermia may be prevented by ensuring warm operation theaters, use of prewarmed IV fluids, use of fluid and blood warmer, forced air-warming devices, as well as intraoperative temperature monitoring.

29.14.4 Electrolyte Imbalance

Several conditions are associated with electrolyte imbalance in children including the consequences of osmotherapy, blood transfusion, use of frusemide, and metabolic acidosis. Diabetes insipidus (DI) is a complication of pediatric surgical procedures, commonly seen in association with craniopharyngioma. The occurrence of DI is diagnosed from an increasing serum sodium value (>150 mg/dL) accompanied by a high (>4 mL/kg/h) output of dilute urine. Preoperative central DI is associated with 8–35% of craniopharyngioma patients, and the incidence is 70–90% after excisional surgery [41].

29.14.5 Intraoperative Seizure Prophylaxis

Children on preoperative anti-seizure medications need to be supplemented during the perioperative period. Phenytoin (15 mg/kg) and levetiracetam (10–15 mg/kg) are the most commonly used anti-seizure drugs [42]. Both these drugs, when given, should be diluted and administered over 15–20 min. Because of its propensity to cause hypotension and the risk of extravasation, phenytoin should be diluted to a concentration of less than 10 mg/mL and infused at the rate of 1–3 mg/kg/min (maximum of 50 mg/min) [43, 44].

29.14.6 Emergence from Anesthesia

Emergence from general anesthesia and extubation is a time of immense physiological stress. Sympathetic stimulation during emergence can cause hemodynamic and metabolic reactions. The phase is associated with increased oxygen consumption and catecholamine release leading to tachycardia, hypertension, and hyperglycemia. The events may lead to increased CBF and cerebral oxygen consumption, potentially causing a rise in ICP [45–48]. A prospective randomized study compared the awakening properties of inhalational anesthetics such as isoflurane, sevoflurane, and desflurane in 60 pediatric patients who underwent craniotomy for excision of supratentorial tumors [49]. The mean emergence and extubation times and the time interval to reach Aldrete score 9 were observed to be significantly shorter in the desflurane and sevoflurane groups than the isoflurane group. No significant changes were observed concerning intraoperative brain swelling, hemodynamic fluctuations, and postoperative shivering or vomiting.

29.15 Early Vs. Delayed Emergence and Extubation

The rationale of rapid emergence in the children undergoing neurosurgery is necessary to permit an early neurological evaluation and manage complications. Major complications after intracranial surgery are seen in 13–27% of patients [50]. Majority of the children benefit from early extubation, which outweighs the potential risks. However, conditions such as a preoperative altered level of consciousness, surgeries lasting for a long duration (>6 h), intraoperative complications, massive blood loss, prolonged period of ischemia with the use of retractors, and associated severe cardiac and respiratory diseases may warrant continuation of mechanical ventilation and, hence, delayed tracheal extubation. The advantages of delayed emergence/extubation are lesser chances of hypoxemia, hypercarbia, and proper hemodynamic stabilization of the child.

The recovery and extubation should be planned before the surgery is over after discussing the pros and cons of early vs. delayed emergence with the neurosurgeon (Table 29.7).

Table 29.7 Advantages and disadvantages of early emergence

Advantages of early emergence and extubation	Disadvantages of early emergence and extubation
• Early evaluation of the neurologic status and re-intervention, if needed • Early assessment of the baseline clinical status • Less hemodynamic changes and catecholamine surge • Done in the operation theater by the anesthesiologist familiar with the child • Avoid ICU costs	• The residual effect of opioids and muscle relaxants may increase the risk of post-extubation apnea and hypoxia • The patient may have residual hypothermia • It is difficult to monitor the respiratory parameters during the transfer of the child to postoperative ICU or HDU

ICU intensive care unit, *HDU* high dependency unit

29.16 Postoperative Management

29.16.1 Post-Craniotomy Pain Management in Children

Postoperative analgesia presents a unique problem in the management of pediatric patients. Pain is usually underestimated despite the reported incidence of moderate to severe pain in 60% of the patients during the first postoperative day [51]. Paracetamol and opioids are the most common drugs used for acute post-craniotomy pain. Acetaminophen and paracetamol (10–15 mg/kg; max 60 mg/kg in 24 h) have weak analgesic action and may not suffice as sole analgesic agents. However, they have been used through IV, oral, and rectal routes. NSAIDs such as ibuprofen, diclofenac, naproxen, and ketorolac and selective COX-2 inhibitors have varying degree of analgesic, antipyretic, anti-inflammatory, and antiplatelet effects. The antiplatelet action, risk of bleeding, and possible postoperative hematoma preclude their use in high-risk patients [52, 53].

Morphine, codeine, tramadol, and fentanyl are the most commonly prescribed opioids for post-craniotomy pain. Concerns of vomiting, sedation, respiratory depression, interference with the neurological examination, and delayed weaning exist with the use of opioids [52, 53].

Local anesthetics used in scalp block or wound infiltration also form a part of the multimodality management of post-craniotomy pain [54, 55]. Alpha-2 agonists such as dexmedetomidine have sedative and analgesic effects, with recent evidence supporting its use in supratentorial tumors [56, 57].

29.16.2 Postoperative Nausea and Vomiting (PONV)

PONV is a prevalent problem in children with a demonstrated incidence of around 30–40% [58, 59]. Few case studies have been published in this regard, and literature regarding nausea and vomiting in children mainly focuses on surgeries in the infratentorial region. Routine administration of anti-emetic drugs like ondansetron (0.1 mg/kg) is useful but is currently only recommended for use in children older than 2 years [60]. Dexamethasone may be given to pediatric patients before emergence in recommended doses [61].

29.16.3 Stereotactic Radiosurgery in Children

Stereotactic radiosurgery employs the gamma knife, cyberknife, or linear accelerator. Both neoplastic and non-neoplastic intracranial lesions in children are managed using stereotactic radiosurgery. In children with recurrent astrocytoma, metastatic germ cell tumors, and medulloblastoma, these procedures are used; they make use of imaging techniques such as angiography, MRI, and CT localization along with the actual therapy. These procedures require shifting of an anesthetized child to different locations of interest with added concerns. Stereotactic radiosurgery is indicated for treating highly vascular, nonmalignant intracranial tumors and several inoperable malignant neoplasms. Due to the stereotactic frame and localization of the treated area within 1.2–1.3 mm of spatial error, absolute akinesia and immobilization of the head are needed throughout the length of the procedure. Careful preparation and plan-

ning are required before the actual treatment. The radiosurgery site must have all facilities for administering general anesthesia to a child.

On the day of treatment, GA is induced before placing the cranial pins to secure the stereotactic frame. Children usually do not tolerate this painful and uncomfortable procedure with only the infiltration of local anesthesia. Hence, GA needs to be administered from the beginning of the procedure. The anesthesia goals remain the same with the provisions of hemodynamic stability, absolute immobility, and the use of routine monitoring modalities. Since anesthesia administration may be difficult and challenging in the peripheral environment outside the operation theater with limited human resources and technical skills, special considerations must be carefully looked into.

29.16.4 Awake Craniotomy in Children

Awake craniotomy with direct cortical stimulation and mapping is employed to resect pathological lesions located near the eloquent brain. However, only a small series of awake craniotomies have been conducted in children. The feasibility, safety, and anesthetic management of awake craniotomy in the pediatric population are still being questioned. Mostly, the procedure is carried out in asleep-awake-asleep technique for children over 7 years [62]. Short-acting drugs like remifentanil, propofol, and sevoflurane are used for inducing GA. The child, who has been counseled well in the preoperative period, is awakened during surgery for a neurological examination when the surgeon is handling the eloquent cortex. The main intraoperative complications include agitation, excessive respiratory depression, seizures, increased ICP, and bradycardia. Despite the challenges and complications, this procedure's success depends highly on the preoperative counseling, the child's mentation and psychology, the adequacy of a calm OT environment, and preparation to convert the procedure into GA on a case-to-case basis.

29.17 Conclusion

Pediatric supratentorial SOLs are a diverse group of lesions associated with specific concerns. The combined age-specific patient concerns and tumor-related issues make anesthetic management a highly skilled task with little room for complacency. The major complications like blood loss, hypothermia, air embolism, etc. may be life-threatening in children but can be avoided with meticulous planning. A good team effort with effective coordination among neurosurgeons, anesthesiologists, and operating room personnel helps achieve the desired goal.Conflict of InterestNil.

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30 Anesthetic Management of Posterior Fossa Surgery in Children

Gyaninder Pal Singh and Gaurav Singh Tomar

Key Points

- The posterior fossa is a tight and rigid compartment with poor compliance having important and vital brain structures, including the brainstem and cerebellum.
- The most common pathology affecting the posterior fossa is brain tumor, which accounts for almost 54–70% of all brain tumors.
- The approach to a pediatric neurosurgical patient is different from adults because of age-related changes in neurophysiology and cranial development.
- The signs and symptoms of raised intracranial pressure in pediatric neurosurgical cases are age-specific.
- Sitting craniotomy offers advantages of better surgical access and a clear operative field but poses a significant challenge for anesthesiologists; venous air embolism is an important and potentially life-threatening complication of posterior fossa surgery.
- In children, blood loss due to surgery or tumor bleed into the cavity constitutes a major fraction of total blood volume; adequate replacement of losses by fluids and blood is important to maintain hemodynamic stability and organ perfusion.

30.1 Introduction

Posterior fossa tumors are more common in children as compared to adults. The majority of brain tumors (54–70%) in the pediatric age group occur in the posterior fossa (15–20% in adults) [1, 2]. The reason behind the propensity of these tumors to occur in the posterior fossa has not been elucidated to date. Posterior fossa lesions may be neoplastic, developmental, or vascular lesions amenable to surgical intervention. Chiari malformations occur as congenital defects when a portion of the skull base fails to grow large enough to accommodate the cerebellum that would result in brain tissue extending into the spinal canal. By far, the most common posterior fossa tumors of childhood are astrocytomas, medulloblastomas, ependymomas, and brainstem gliomas. Cerebellar astrocytomas, usually slow-growing and benign, are the most common (40–50%), followed by medulloblastomas (malignant) comprising (20–25%) of all pediatric brain tumors [3]. Other less frequent tumors include atypical teratoid rhabdoid tumor, hemangioblastoma, dermoid, schwannoma, cerebellar gangliocytoma, meningioma, and metastatic tumors [4] (Fig. 30.1). The median age at diagnosis of posterior fossa tumors in children is approximately 6–9 years, with a peak inci-

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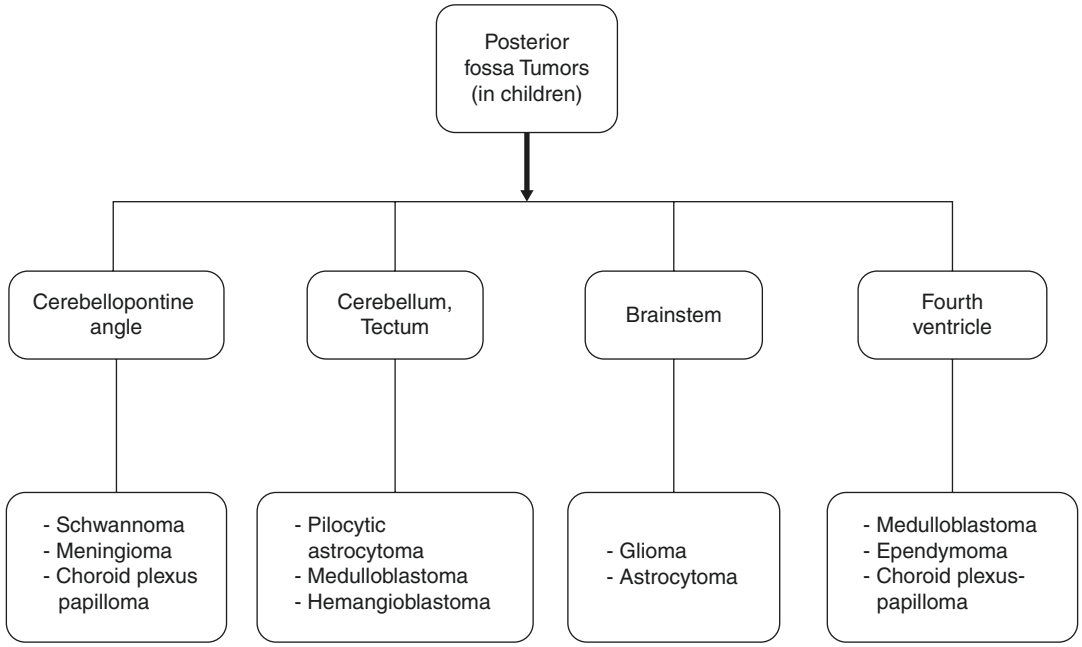

Fig. 30.1 Distribution of posterior fossa tumors in children

dence in the first decade of life. Most of the tumors occur in the midline and are frequently found associated with hydrocephalus (Fig. 30.2). Success with surgical intervention has become possible because of improved understanding of physiology, advances in imaging and microsurgical techniques, excellent anesthetic techniques available, and advances in the child's perioperative care. These, in turn, have improved the survival and quality of life in children.

30.2 Anatomy of Posterior Fossa

Boundaries: Posterior fossa is bounded anteriorly by petrous part of temporal bone and clivus, posteriorly by occipital bone, laterally by the mastoid and squamous part of the temporal bone, superiorly by tentorium cerebelli, and inferiorly by foramen magnum.

Contents: Posterior fossa lodges a large portion of the brainstem, such as the lower midbrain, pons, and medulla, as well as the cerebellum. The

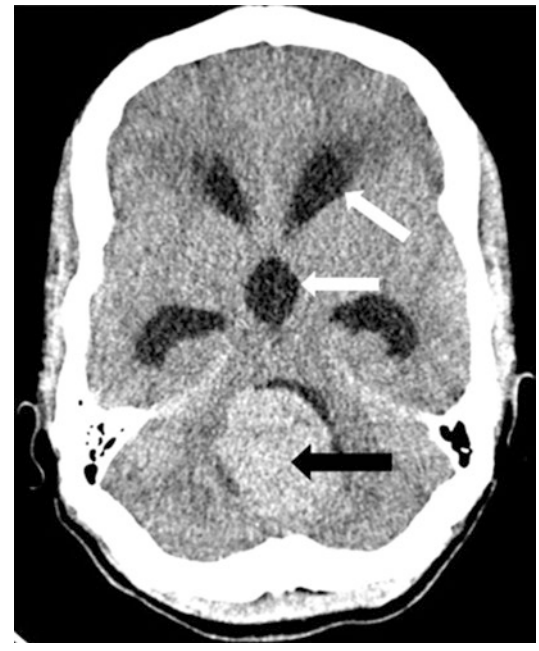

Fig. 30.2 Computed tomographic (CT) scan of the brain, showing a posterior fossa tumor (black arrow) with hydrocephalus. The lateral and third ventricles (white arrow) are dilated due to obstruction to CSF flow

brainstem contains 3rd to 12th cranial nerve nuclei and vital centers such as cardiac, respiratory, etc. The efferent and afferent fiber tracts connect the brain to the spinal cord.

Blood supply: Structures located in the posterior fossa receive their blood supply through the vertebrobasilar system, located on the ventral aspect of the brainstem. The blood is drained by the adjacent venous sinuses, including the petroclival sinus, straight sinus, occipital sinus, transverse sinus, and sigmoid sinus that ultimately drain into internal jugular veins.

Various pathological lesions, both benign and malignant, may occur in the posterior fossa. These lesions can arise from the brain parenchyma, cranial nerves, meninges, vessels, or skull bone. There may be inflammation, infection, neoplasms, traumatic space-occupying lesion (SOL), vascular lesions leading to hemorrhage or infarction, and metastasis from other regions. The lesions in this area present with a variety of clinical manifestations. The presence of hydrocephalus secondary to obstruction of cerebrospinal fluid (CSF) flow through the aqueduct of Sylvius may lead to intracranial hypertension [5]. Moreover, the mass effects of the lesion may lead to a rise in intracranial pressure (ICP).

30.3 Clinical Manifestations

Initially, the child may present with nonspecific symptoms such as listlessness, headache, fatigue, nausea, vomiting, anorexia, and personality changes. Later, cerebellar or brainstem signs like ataxia, dysmetria, hemiparesis, and lower cranial nerve deficits may develop. More specific clinical syndromes may occur with tumors that rapidly involve in neural structures such as acoustic neuromas, other cerebellopontine (CP) angle tumors, and brainstem glioma. Signs and symptoms due to posterior fossa tumors, particularly astrocytoma, are a result of elevated ICP due to CSF outflow obstruction. In infants, an enlarged head or bulging fontanelle, widely spaced cranial sutures, and irritability may indicate hydrocephalus. Malnutrition because of poor feeding in infants and dehydration is also noted among chronically ill children. In older children, signs of raised ICP will include headache, vomiting, papilledema, and a reduced level of consciousness.

Herniation of the cerebellar tonsils through the foramen magnum (especially in children) present with meningismus, head tilt, muscle spasm, opisthotonus, vomiting, skew deviation of the eyes, downbeat nystagmus (vertical nystagmus), and typical "posturing" from tonsillar herniation. The paroxysmal spells that are characterized by drop attacks with or without loss of consciousness, abnormal extensor posturing, and varying degrees of respiratory compromise (known as "cerebellar fits") [6] may occur in conditions causing cerebellar herniation [7]. Bulbar palsies with vocal cord paralysis, swallowing and gag dysfunction, occipital headache, and neck pain may also occur. Further herniation may compress the medulla, subsequently causing irregular respiration and death.

30.4 Preoperative Evaluation of Lesions

Imaging: Computed tomography (CT) and magnetic resonance imaging (MRI) remains the two important imaging modalities for posterior fossa lesion. CT scan is a useful tool to assess the severity of hydrocephalus in an emergency. However, due to bony artifacts, the CT scan is inferior to MRI for posterior fossa imaging. MRI has greatly improved the diagnosis of posterior fossa soft tissue pathological lesions (Fig. 30.3). MRI allows differentiation of intra-axial and extra-axial lesions and visualization of the surrounding anatomical structures. It provides detailed information for the pathological diagnosis of lesions. In extra-axial lesions, there is the displacement of parenchymal structures, bone erosion, well-delineated margins, and contiguity with surrounding dura or bony structures. In contrast, intra-axial lesions do not erode bone and have indistinct margins. A full craniospinal pre- and post-contrast MRI scan should be done before surgery to ensure complete tumor staging.

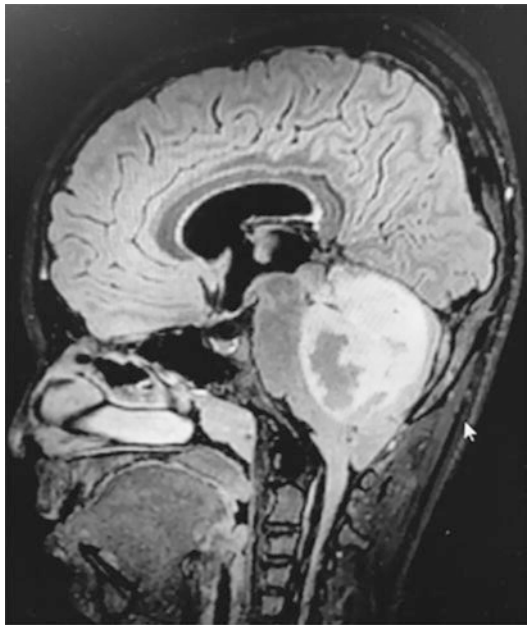

Fig. 30.3 Magnetic resonance imaging (MRI) of a 10-year-old child showing a large lesion in the posterior fossa

Neurophysiologic Studies: Brainstem auditory-evoked responses (BAER) and electronystagmography are occasionally required for diagnosis. However, these can provide useful information for the diagnosis of acoustic neurilemmomas. Intraoperative neurophysiological monitoring (IONM) has an important role in preserving important structures and functions during the surgical procedure.

Preoperative Audiometry: It can be useful in older children for assessing hearing preservation before acoustic schwannoma surgery.

30.5 Management of Posterior Fossa Lesions

30.5.1 Medical Management

Posterior fossa tumors mostly present with cerebral/cerebellar edema and hydrocephalus. There is no primary medical therapy for such lesions. However, to reduce the compression or mass effect of lesions on the surrounding structures, medications like diuretics, corticosteroids, antiemetics, and intravenous (IV) fluid hydration is generally administered. This helps mitigate the secondary effects of the tumor and intracranial hypertension, such as headaches, vomiting, and dehydration. Obstructive hydrocephalus is a common finding, occurring in 71–90% of children with posterior fossa tumors [8]. Managing symptomatic obstructive hydrocephalus (CSF diversion procedure) before surgical removal of the tumor may give relief of symptoms to such children. Moreover, it may allow some delay in resection surgery for pre-resection adjuvant therapy in certain circumstances and avoid resection under emergent conditions [9, 10]. Some children with acute symptoms of brainstem involvement or herniation should undergo an emergency operation [4].

30.5.2 Surgical Management

Symptomatic obstructive hydrocephalus management before tumor excision has two different schools of thought on this aspect as CSF shunting (internal or external) may expose the patient to the additional inherent shunt risks including infection/meningitis, shunt malfunctioning, over/under drainage, or any other surgical complications. Nevertheless, young age ≤ 2 years, medulloblastoma, and brainstem compression are considered as independent predictors for hydrocephalus in the pediatric patient population. Therefore, preoperative intervention is generally advised before surgical excision of posterior fossa tumors at many centers [11].

Perioperative external ventricular drainage (EVD) of CSF, using an Ommaya reservoir, enables the safe removal of tumors. Restoration of CSF circulation provides an effective means to control and prevent hydrocephalus secondary to posterior fossa tumors in children [12].

Craniectomy is generally performed according to the site and size of the tumor. For posterior fossa tumors, the most common operative approaches are midline, paramedian, or retromastoid. The aim of surgery is to obtain gross total resection of the tumor; however, it may not always be possible depending on the type and

location of tumor and involvement of the surrounding structures. The use of advanced intraoperative techniques like neuro-navigation, ultrasonography, and MRI may aid in maximal safe resection of tumors. Radiation therapy may be useful in case of subtotal removal to eradicate the residual tumor on follow-up. In interstitial brachytherapy, radioactive material is implanted into the tumor bed intraoperatively to deliver a continuous, localized dose of irradiation to tumor cells. Chemotherapy with new therapeutic medications may have a role in the treatment of residual tumors after surgery.

Immunotherapy, though under the investigational phase, aims at the activation of cell-mediated cytotoxic responses and humoral-mediated cytotoxic response against the tumor cells. In the near future, advancements in neurosurgical management perspectives include stereotactic radiosurgery that utilizes only the distinct physical properties of the irradiation to deliver radiation doses to the tumor cells only by virtue of the differences in radiobiological properties normal and pathological malignant tissues [13, 14].

30.5.3 Anesthetic Management

The posterior fossa is the home ground for the brainstem, which houses cardiovascular and respiratory centers, reticular activating system (RAS), major motor and sensory pathways, and lower cranial nerve nuclei. It thus poses a challenge for the anesthesiologists, as the intraoperative goals are to maintain cardiovascular and respiratory stability, facilitate surgical access, and minimize nervous tissue trauma.

30.5.3.1 Pre-Anesthesia Checkup

- Complete medical history, including perinatal history, should be sought with respect to intraventricular hemorrhage (IVH) or disability associated with prematurity at birth, respiratory tract infections, vaccination status, and syndromic association since birth. Seizure disorder-related history needs to be assessed for type and adequacy of therapy. Any residual speech, sensory, or motor dysfunction/deficit should be recorded.
- The list of medications patients receive before surgery, such as mannitol, diuretics, benzodiazepines, and steroids, which may alter electrolyte balance or hemodynamics during surgery, needs to be reviewed.
- Physical status of the children, dehydration, body weight (at birth and current), and assessment of syndromic features, particularly about cardiac, respiratory, and airway, are important. These factors also determine the patient's position during posterior fossa surgery.
- The level of consciousness, i.e., Glasgow coma scale (GCS) score at the time of admission and before surgery, should be sought. Any focal motor or sensory deficit should be documented along with examination for signs and symptoms of increased ICP.
- Routine investigations should include complete blood count (CBC) to rule out anemia and sepsis, blood chemistry to rule out dehydration and dyselectrolytemia, baseline coagulation profile to rule out coagulopathy and hemostatic disorder, electrocardiogram (ECG) to rule out cardiac arrhythmia and ischemia, chest radiograph to rule out secondary chest infection, and echocardiography may be done to rule out patent foramen ovale and cardiac septal defects.

30.5.3.2 Preoperative Preparation of the Child

Administration of steroids (dexamethasone) is usually commenced on the child's presentation to mitigate the effect of edema and decrease ICP. This often leads to improvement in symptoms. Besides, diuretics can also be given to reduce the mass effect to some extent. In clinical practice, mannitol or 3% hypertonic saline is not substantially useful in posterior fossa lesions as anti-edema measures. Acute hydrocephalus may require urgent surgical intervention in the form of placement of EVD, ventriculoperitoneal (VP) shunt, or an endoscopic third ventriculostomy (ETV). This intervention significantly reduces the overall morbidity and mortality rates by normalizing raised ICP, improving the patient's gen-

eral condition, and preventing postoperative ICP elevation. However, there is a possibility of upward herniation in posterior fossa tumors undergoing preliminary shunting and the risk of spreading medulloblastomas through VP shunts [15, 16].

Premedication should be individualized after assessing the patient in terms of physical status, evidence of increased ICP, level of anxiety, and corticosteroids intake. Oral benzodiazepines or anti-sialagogues may be given 60 min before surgery under supervision. They are effective in reducing anxiety and oral secretions without a significant effect on ICP. However, in children with evidence of increased ICP, sedatives and narcotic premedication should be avoided as these medications decrease respiratory drive. Thus, resultant hypoventilation and retention of CO_2 may further increase ICP.

30.5.3.3 Induction of Anesthesia

Induction of general anesthesia aims to maintain cerebral oxygenation and to avoid any increase in ICP. It can be performed by either IV or inhalational agent (sevoflurane). Propofol or barbiturates has the advantage of a profound reduction in cerebral metabolic rate of oxygen ($CMRO_2$), cerebral blood flow (CBF), and ICP. Induction is achieved by administering a judicious dose of an induction agent, an opiate, and a muscle relaxant. Following anesthesia induction, endotracheal intubation is performed with an appropriately sized reinforced micro-cuffed endotracheal tube (ETT). The tube position should be checked with the head in a flexed position, as the ETT may migrate few millimeters inside due to head flexion during surgery. The ETT should be properly secured using water-resistant tape (e.g., Tegaderm) to avoid loosening due to blood and/or secretions. It is essential to re-confirm the position of ETT after final positioning the child for surgery. Hypertensive responses and coughing on ETT during laryngoscopy should be avoided by administering additional doses of a short-acting opiate such as remifentanil/fentanyl and/or hypnotic agent. Smooth and gentle induction of general anesthesia is the prime goal. An acceptable induction sequence combines four steps:

1. Pre-oxygenation with or without sevoflurane.
2. Fentanyl 1–2 μg/kg or remifentanil 1 μg/kg IV over 30–60 s; thiopentone 3–4 mg/kg or propofol 1.5–2 mg/kg IV followed by mask ventilation to ensure airway patency and adequate ventilation.
3. Rocuronium 0.8–1.0 mg/kg IV and mask hyperventilation with oxygen until the neuromuscular blockade is achieved.
4. Lidocaine 1.5 mg/kg IV and/or additional propofol 0.5–1 mg/kg or thiopentone 1–2 mg/kg IV just before tracheal intubation may be given, if required.

In emergent situations (patients with a full stomach), modified rapid sequence induction (RSI) can be performed using the same combination of drugs as routine induction. Here, a higher dose of rocuronium 1.0–1.2 mg/kg is used for intubation, and cricoid pressure may be applied, but mask ventilation is avoided. Fentanyl, remifentanil, or sufentanil make induction and tracheal intubation smooth.

30.5.3.4 Intraoperative Monitoring

Monitoring aims to maintain cardiovascular stability, ensure adequate central nervous system (CNS) perfusion, and detect and treat venous air embolism (VAE). For pediatric posterior fossa procedures, the risk of VAE, as well as its monitoring and treatment, are similar to the adults. Precordial Doppler is essential, and central venous access (right heart catheters) is generally required when the procedure is planned in a sitting position. Apart from standard 5-lead ECG, pulse oximetry and non-invasive blood pressure (NIBP), invasive blood pressure (IBP), capnography ($EtCO_2$), end-tidal and minimal alveolar concentration (MAC) of inhalational agents, neuromuscular monitoring, core body temperature, central venous catheter, esophageal stethoscope, and precordial stethoscope along with transesophageal echocardiography (TEE) monitoring are also desirable in such cases if found feasible and available [17]. However, the use of TEE in children for intraoperative neurosurgery remains controversial, with the reported risk of glottic and esophageal trauma.

TEE Monitoring: The pediatric TEE probe, because of its small size and greater flexibility, makes them well suited for use in children and infants and provides high-quality imaging. TEE probe selection for infants and children primarily depends on the weight of the patient and the probe size [18]. Pediatric bi-plane, as well as mini-multiplane probes, is available for use in neonates, infants, and small children. More recently, a pediatric micro-multiplane probe has been introduced for use in the tiniest babies, representing the smallest multiplane device available today. Commercially available pediatric bi-plane and mini-multiplane TEE probe (7–10 mm in diameter) can be used in infants or children weighing more than 3.0 kg, while pediatric micro-multiplane TEE probe can be used for infants over 2.5 kg. Adult TEE probes can be used in children weighing more than 25–30 kg [18].

Neuromonitoring: The brainstem auditory-evoked potentials (BAEPs) is the best option available for direct monitoring of brainstem function. Median nerve SSEPs can also be used simultaneously. BAEPs are resistant to most anesthetic agents. Somatosensory-evoked potentials (SSEPs) are affected by the inhalation anesthetics, and the addition of nitrous oxide potentiates the depressant effects of inhalational agents on SSEPs [19] (Table 30.1). The desired safe level of MAC to obtain the recordings is considered to be less than 0.5. A 50% reduction in amplitude, greater than 10% increase in latency, loss of waveform, or any alterations in vital signs should be considered as warning signs to stop tumor manipulation and/or relax retractor pressure on the brain and to allow vital signs to normalize. Intraoperative electromyography (EMG) can be recorded from direct stimulation of cranial nerves fifth, sixth, seventh, ninth, tenth, eleventh, and twelfth.

Table 30.1 Effect of various anesthetic agents on evoked responses

	SSEP		
Anesthetic agent	Amplitude	Latency	MEP
Halothane (0.5–1 MAC)	↓	↑	++
Isoflurane (0.5–1 MAC)	↓	↑	++
Sevoflurane (0.5–1 MAC)	↓	↑	++
Desflurane (0.5–1 MAC)	↓	↑	++
Nitrous oxide (0.5–1 MAC)	↓	–	++
Thiopentone	↓	↑	++
Propofol	↓	–	++
Etomidate	↑		+
Ketamine	↑		+
Opioids	↓	↑	–
Benzodiazepines	–	–	+++
Dexmedetomidine	–	–	+
Muscle relaxants	–	–	+++

MAC minimum alveolar concentration, *SSEP* somatosensory-evoked potential, *MEP* motor-evoked potential, (–) negligible/no effect, (+) minimal effect, (++) significant effect, (+++) profound effect

30.5.3.5 Positioning the Child during Posterior Fossa Surgery

Posterior fossa surgeries may be performed in various positions depending on the location of the lesion, patient's condition, surgeon's experience, and preference. Different positions used are supine with head rotation to the opposite side, prone, Concorde (modified prone position), lateral decubitus, park bench, and sitting position. Pediatric patients are commonly operated on in prone position for posterior fossa surgeries.

Though it remains controversial, the sitting position remains preferred by a small percentage of neurosurgeons for posterior fossa surgery. In this position, the head of the patient (older children) is secured in a three-pin head holder. Infiltration of the scalp and periosteum with local anesthetic at pin-site reduces hypertensive responses. Bony prominences such as ischial tuberosity, heal, knee, elbow, vertebral column are properly padded. Intermittent pneumatic compression devices or elastic compression stockings are applied on bilateral legs to limit blood pooling. Elbows and the legs are supported and kept padded to avoid stretching of brachial plexuses and common peroneal nerves. The distance of at least 2–2.5 cm is maintained between the chin and chest to avoid stretching of the cervical spinal cord and obstruction of venous drainage from the head, face, and tongue. Also, the placement of a large airway or bite block and

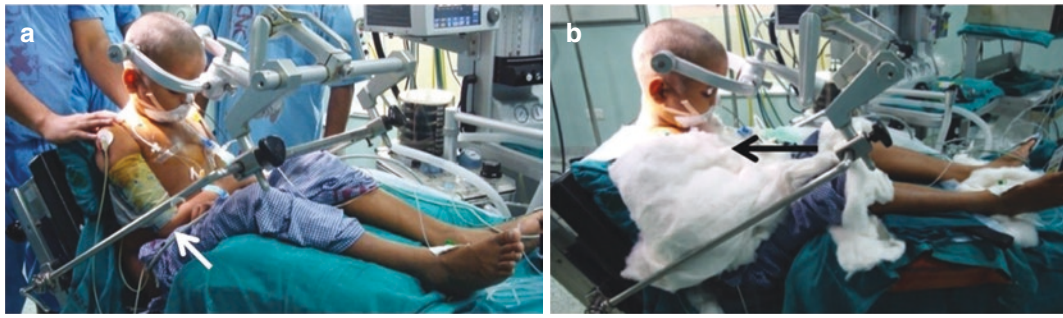

Fig. 30.4 Sitting position for posterior fossa surgery in a child. (**a**) The elbow is supported over the thigh (white arrow) to prevent drooping of shoulders and injury to brachial plexus. (**b**) All pressure points are adequately padded with cotton. The knees and legs are at the heart level (black arrow) to prevent pooling of blood in the lower limbs and improve venous return to the heart

Table 30.2 Advantages, disadvantages, and contraindications of surgery in the sitting position

Advantages	Disadvantages	Contraindications
– Lower airway pressure – Easy diaphragmatic excursion – Better access to ETT and thorax for monitoring – Improved erebral venous drainage and less blood loss – Visualization of the face for motor responses during neural stimulation – Better surgical exposure, less tissue retraction, less cranial nerve damage, and complete resection of tumor possible	– Increased risk of VAE – Tension pneumocephalus – Cardiovascular instability/ hypotension – Airway/tongue edema – Peripheral nerve injuries – Deep vein thrombosis – Subdural hematoma – Rapid escape of CSF from ventricular system	– Intracardiac defects – Severe hypovolemia – Cachexia – Severe hydrocephalus – Open ventriculoatrial shunt – Extremes of age – Impaired cardiac function – Degenerative cervical spine disease – Significant cerebrovascular disease and signs of cerebral ischemia when upright and awake

ETT endotracheal tube, *VAE* venous air embolism, *CSF* cerebrospinal fluid

excessive neck rotation is avoided. Excessive flexion at the hip joint is avoided to prevent sciatic nerve injury and abdominal compression. Knees and legs are usually kept at the heart level to prevent pooling of blood to the lower limbs and prevent hypotension (Fig. 30.4). Advantages, disadvantages, and contraindications of neurosurgery in the sitting position are summarized in Table 30.2 [17, 20, 21].

The prone position is advantageous as it lowers the incidence of VAE as well as provides optimal surgical access to the posterior fossa, craniocervical junction, and upper spinal cord. The patient's head is elevated to decrease venous bleeding and is rested over the horseshoe headrest or fixed using a three-pin head holder or Mayfield clamps, particularly in older children. Compression over the face in a prone position may be prevented by using a horseshoe with gel padding or keeping cotton paddings over the face. Care should be taken to prevent compression of the eyeballs. Despite precautions, there may be pressure sores on malar prominences, transient or long-term blindness from retinal artery thrombosis due to compression on the eyeball, and edema of conjunctiva; the access to the surgical field may be adequate, unlike sitting position [21–23].

The lateral position is suitable for the unilateral procedures of the posterior fossa, such as excision of cerebellopontine angle lesions. It improves surgical access by draining CSF and blood from the operating field and helps autoretract the cerebellum by gravity. The VAE is reported in 10–15% of cases operated in lateral or prone (horizontal) position [24]. The major

problems associated with the lateral position are ventilation-perfusion mismatch in the dependent lung and peripheral nerve injuries such as stretching of brachial plexus and pressure injuries to the nerves.

The supine position with the head rotated to the contralateral side is utilized to gain access to the lateral structures of the posterior fossa. Reverse Trendelenburg positioning to improve venous drainage from the brain is usually given. However, it should be kept in mind that each 2.5 cm increase in the vertical height of the head above the level of the heart leads to a 2-mmHg reduction in cerebral perfusion pressure (CPP).

30.5.3.6 Maintenance of Anesthesia

The goal for maintenance of anesthesia is to decrease the ICP and to maintain hemodynamic stability. It can be achieved with either a balanced technique or TIVA. Each technique has some benefits, and there is no evidence that one technique is superior to the other. The choice for the anesthetic agent is based on the child's condition, the requirement for surgery and monitoring, and the anesthesiologist's preference. Propofol has the theoretical advantage that it reduces cerebral blood volume (CBV) and ICP and preserves autoregulation and vascular reactivity. During TIVA, propofol is generally used in doses of 100–300 μg/kg/min infusion along with opioid either fentanyl 1 μg/kg or remifentanil at 0.1–0.2 μg/kg/h combined with or without N_2O in O_2. Mannitol may be administered in doses of 0.25–1 gm/kg to attenuate an acute increase in ICP, but its role in posterior fossa surgery has not been well-defined. Moreover, it may potentiate hemodynamic instability in the sitting position. Development of pneumocephalus resulting from sudden decompression of the ventricles following the drainage of CSF has been reported, with the risk being higher in sitting position [25].

Tachycardia or hypertension at the time of skin closure should be treated with either β-blocker (esmolol) or both (α + β) blocker (labetalol). Nitrous oxide is better avoided if the patient is anticipated to develop the intraoperative tight brain, VAE, or pneumocephalus (recent intracranial surgery or trauma); it may aggravate both the air embolus and pneumocephalus.

30.5.3.7 Fluid Management

Isotonic 0.9% normal saline (NS) or balanced salt solution is considered as the fluid of choice for neurosurgical patients; it holds good for children, as well. Avoid dextrose-containing solution in children older than 1 month. Hypoglycemia during surgery is rare in most children except premature infants, neonates less than 48 h old, and children below the third centile in weight [26]. Children with a duration of surgery of more than 3 h may also be at risk of hypoglycemia, and thus, in them, the blood sugar should be monitored intraoperatively. Routine administration of dextrose-containing fluids should be reserved for those at risk of hypoglycemia [27]. The volume of fluid to be administered should be calculated according to weight, hours of fasting, and ongoing losses. An adequate amount of fluid should be given and kept in accordance with blood loss, hemodynamic stability, and urine output. Excessive fluid administration may cause brain edema at the sites where the blood-brain barrier is disrupted.

30.5.3.8 Blood Loss and Transfusion Trigger

Bleeding from scalp wounds and bone makes it difficult to quantify the blood loss accurately. Moreover, blood loss due to surgery or tumor bleed into the cavity constitutes a major fraction of total blood volume in the pediatric population. Blood products are invariably required, perioperatively, in vascular lesions, other large tumors, and head trauma patients. Blood loss of more than 10% of a child's body weight is considered significant. It should be timely replaced with blood and/or blood products to maintain hemodynamic stability and systemic organ perfusion. Target hematocrit is to be maintained in the range of 30–35%.

30.5.3.9 Temperature Regulation

The goal is to maintain normothermia throughout the perioperative period. Fluid warmers, forced-air warming devices, and blankets are generally

needed to maintain the child's body temperature. However, mild permissive hypothermia (34–35 °C) decreases $CMRO_2$ and may act as a neuroprotectant in conditions with raised ICP. However, the complications due to hypothermia (e.g., coagulopathy, dyselectrolytemia, metabolic acidosis) should also be acknowledged and, hence, better avoided.

30.5.3.10 Emergence from Anesthesia

Early and smooth emergence from anesthesia is the primary goal. Coughing and straining over the ETT should be avoided. It is generally assumed safe to extubate the trachea if surgery is accomplished uneventfully without much traction on the brainstem or hemodynamic instability. However, the patient may be electively ventilated and be allowed to awaken slowly in the ICU after continued ventilation and a period of monitoring. Such cases include patients with large and deep-seated tumors with frequent traction on the brainstem and hemodynamic changes during the surgery, large intraoperative blood loss and fluid shifts requiring inotropes and vasopressors, etc. These patients may have apnea or decrease sensorium with diminished airway reflexes after tracheal extubation. Failure to recover from anesthesia should prompt further investigations such as a CT scan of the brain to exclude any complications.

30.5.3.11 Postoperative Care

Post-craniotomy/craniectomy children are generally managed in an intensive care unit or high dependency unit. Postoperative mechanical ventilation for 24 h is generally required among children after large-sized posterior fossa tumor surgery posing difficulty in tumor dissection with more incidence of brainstem handling intraoperatively. Extubation trial is only attempted after ascertaining the integrity of bulbar and lower cranial nerve function by the anesthesiologist, along with adequate recovery from the anesthesia.

Pain in postoperative patients should not be ignored. It is prudent to adopt a multimodal strategy to provide adequate analgesia. Acetaminophen in the form of suppository given per-rectally is usually commenced during the intraoperative period and continued after surgery. Debate still exists around non-steroidal anti-inflammatory drugs' potential contribution to postoperative bleeding, but recent evidence does not support this hypothesis [28].

30.5.4 Complications of Posterior Fossa Surgery

30.5.4.1 Brainstem and Cranial Nerve Stimulation (Trigemino-Cardiac Reflex, Glossopharyngeal-Vagal Reflex)

Direct stimulation of the trigeminal nerve or its nucleus may elicit trigemino-cardiac reflex (TCR), leading to bradycardia/asystole and hypotension. Vagus nerve stimulation can cause bradycardia and escape rhythms [29, 30]. Hypotension can result from pontine or medullary compression. Ventricular and supraventricular arrhythmias can also occur due to brainstem stimulation during the procedure. Brainstem encroachment and handling by the surgeon is considered a critical period of surgery and warrants close monitoring of hemodynamic parameters.

30.5.4.2 Endotracheal Tube Kinking and Accidental Extubation

Kinking or dislodgement of ETT may be encountered during the perioperative period. It causes a rise in airway pressure and the inability to ventilate the patient adequately. It may further lead to intraoperative brain swelling. Intraoperative manipulation of head positions such as extreme flexion or head rotation may cause the ETT to kink. The use of reinforced ETT may prevent this complication. During brain surgery, dislodgement of ETT is a dreaded complication requiring immediate intervention and placement of ETT back into the trachea. This is particularly important in infants and small children as the margin of safety is less (small length of tube). Accidental extubation is more frequent with uncuffed ETT in the prone position as the tapes loosened due to secretions or pull of gravity.

30.5.4.3 Venous Air Embolism (VAE)

VAE is considered to be the most feared complication associated with the sitting position.

Etiopathological factors include negative intravascular pressure relative to the atmosphere, gravitational effects of low CVP, open veins and non-collapsible venous channels, and poor surgical dissection/technique. End-tidal nitrogen monitoring is most specific for the diagnosis of VAE and can detect its occurrence 30–90 sec earlier than end-tidal carbon dioxide ($EtCO_2$) [29]. The sensitive monitor for the detection of VAE includes precordial Doppler and TEE. The use of precordial Doppler is limited by electrocautery interference while TEE being most sensitive. TEE has reported a risk of glottic and esophageal trauma with restrictions imposed by patient size and position. The reported incidence of VAE in children is 9.3–33% [20, 31–33], while the incidence of VAE associated with hypotension among children ranges from 20.9% to 33% [20, 34]. This is significantly less than the adults where the reported incidence is 25–50% [35] and even up to 85–100% in some studies [36]. This discrepancy in the incidence of VAE could be because of many factors like different methods of monitoring [31, 32], the variation in age groups among studied cohort, the variation in cerebral sinus pressure according to the age group, the effect of fluid preloading of the patients before final sitting position, the use of compression stockings in lower limbs, hemodynamic fluctuations in the sitting (or lounging) positions, and also the study design [20, 31, 32, 34]. The lower incidence of VAE detected in children may be attributed to the presence of relatively higher (positive) dural sinus pressure or the confluence sinus pressure in children as compared to the adults [20, 37].

30.5.4.4 Hydrocephalus

Almost 80% of children with posterior fossa tumors present with hydrocephalus. It persists among 30% during the postoperative period, possibly due to scarring at the aqueduct or distortion of the fourth ventricle or fourth ventricular outlet foramina [30, 31]. They may require a postoperative VP shunt surgery if not inserted during the preoperative period.

30.5.4.5 Pneumocephalus

The incidence of pneumocephalus varies with position and is seen in 100% of cases operated in a sitting position [32]. However, the progression of pneumocephalus into tension pneumocephalus requiring intervention is reported among 3–6% cases [34]. Etiopathogenesis for this is multifactorial, viz., diminution of brain volume secondary to administration of mannitol or hypertonic saline, hyperventilation, removal of space-occupying lesions, contraction of intravascular blood volume associated with acute hemorrhage, the gravitational effect of sitting position, and intraoperative drainage of CSF with the "Inverted Pop Bottle Analogy" (i.e., as CSF pours out, air bubbles migrate to the top of the cranium) [33]. This explains the accumulation of air in subdural space after slow continuous gravitational drainage of CSF in sitting position. Tension pneumocephalus may manifest during the intraoperative period with hemodynamic instability (Cushing's response) [38], convulsion, and inability to reverse after closure, while in the postoperative period as seizures, confusion, headache, and new-onset neurological deficits. If left untreated, it may cause brain herniation and even death. Management includes supine position, 100% oxygen ventilation, and immediate twist-drill aspiration of air through burr holes.

30.5.4.6 Quadriplegia (Mid-Cervical Flexion Myelopathy)

Besides a surgical complication, it can occur due to stretching of the spinal cord at C-5 level due to over flexion of the head on the neck, causing spinal cord infarction [39]. Also, persistent hypotension in the perioperative period can compromise regional cord perfusion leading to such a condition. Electrophysiologic monitoring might enable early identification of spinal cord dysfunction to minimize or avoid this complication.

30.5.4.7 Postoperative Cranial Nerve Dysfunction/Brainstem Swelling/Compression

These complications are often encountered following posterior fossa surgeries in pediatric patients.

30.5.4.8 Macroglossia

Tongue swelling may occur when a large oral airway is kept for a prolonged period of time, lead-

ing to obstruction of its venous and lymphatic drainage. Extreme flexion of the head with chin resting on the chest may further aggravate it. Extreme flexion of the neck may also lead to airway obstruction and hypoxemia or hypercapnia during the intraoperative period [40].

30.5.4.9 Airway and Swallowing Difficulties

Children with brainstem or cerebellopontine angle tumors may develop postoperative vocal cord paresis/plegia, making them susceptible to aspiration and respiratory complications leading to often emergent airway interventions. This may be prevented by assessing vocal cord movement before tracheal extubation, and in case of bilateral vocal cord paralysis, tracheostomy should be a reasonable option [41].

30.5.4.10 Posterior Fossa Syndrome (PFS)

PFS or cerebellar mutism is generally described in the pediatric age group. It can be defined as temporary loss of speech after posterior fossa surgery that is not related to cerebellar bleed, infection, degenerative, or neoplastic pathology [42, 43]. Ataxia, neurobehavioral, and emotional problems are also defined as primary symptoms apart from mutism. This usually manifests 1–2 days after surgery and may last for a day to several months. The incidence of PFS has been reported to be 8–25% in the retrospective series and even higher in prospective studies [42, 43]. Medulloblastoma, particularly located in the midline and involving vermis, has also been found to be a risk factor for the PFS as it is the most prevalent malignant post fossa tumor in the pediatric age group. However, the exact etiology of PFS is still not known, except for transient ischemia and edema, as a result of manipulation of the dentate nuclei and superior cerebellar peduncles.

30.5.4.11 Re-Exploration

Surgical re-exploration is sometimes required in cases that develop postoperative complications such as hydrocephalus, subdural hematoma formation, etc.

30.5.4.12 Reintubation

Reintubation during the postoperative period may be attributable to factors like altered sensorium, pulmonary edema, subdural hematoma (SDH) formation, and seizures due to tension pneumocephalus [44]. The incidence of reintubation in such neurosurgical patients can be as high as 16% and attributed to both anesthetic and surgical factors [45, 46].

30.5.4.13 Seizures

Postoperative seizures are rarely encountered in children after posterior fossa surgery. If presented postoperatively, seizures could be secondary to hematoma formation or tension pneumocephalus in most cases [47].

30.5.4.14 CSF Leakage/ Pseudo-Meningocele

Posterior fossa craniotomies may be complicated by CSF leak, pseudo-meningocele, and intracranial hypotension. Several factors that can predispose to CSF leak include tumor size, dural invasion of the tumor, hydrocephalus, blood in CSF, brain edema, and defective closure of the dura mater. Pseudo-meningoceles are defined as clinically symptomatic fluid collections under the skin surrounding the surgical site. MRI is useful in diagnosing this reversible complication [48]. Secondary dural closure may be performed using pericranium, muscle, glue, sealants, or fat graft to augment the dural closure. Additionally, fibrin glue or polyethylene glycol (PEG) sealants can be used to reduce the CSF leak rate [49].

30.5.4.15 Meningitis

After surgery, septic meningitis may occur due to poor postoperative care, unmanaged pre-existing ventriculitis, or infected shunt prior to surgery. This is considered a poor prognostic sign leading to higher morbidity and mortality. Aseptic meningitis is a recognized complication after posterior fossa surgery. It is often short and self-limiting [50].

30.5.4.16 Dyselectrolytemia

In general, hypokalemia and hyponatremia are the most common electrolyte disorders encountered

following intracranial surgery. Uncorrected hyponatremia is often a poor prognostic sign postoperatively. The most common postoperative factors associated with electrolyte imbalance are the use of diuretics and dehydration. Although rare, cerebral salt-wasting syndrome (CSWS) and the syndrome of inappropriate anti-diuretic hormone secretion (SIADH) may develop after posterior fossa surgery leading to hyponatremia [51–53]. These syndromes are directly related to altered mechanisms of osmolarity regulation between the brain and kidney.

30.5.4.17 Pulmonary Infection/Sepsis

The impaired gag reflex is a well-known factor to cause chest infection due to impaired swallowing, pooling of saliva in the oral cavity, and silent aspiration. Other possible factors attributable to postoperative chest infections could be a high incidence of postoperative elective ventilation, decreased sensorium, and reintubation [54]. The incidence of pulmonary infection/sepsis can be as high as 21% among these patients [45].

30.6 Conclusion

Posterior fossa space-occupying lesions are among the most critical brain lesions because of the limited space and proximity to the brain's vital structures. Almost two-thirds of all childhood brain tumors originate in the posterior fossa. Obstructive hydrocephalus is a common finding in these children that manifests as signs and symptoms of raised ICP and often requires a CSF diversion procedure before the definitive surgery. Posterior cranial fossa surgery in children poses a challenging task for both neuroanesthesiologists and neurosurgeons. It may be associated with various complications, some of which are exclusive to the surgical location. However, with a better understanding of tumor biology, progressive improvements in imaging modalities, advancement in microsurgical techniques, and anesthesia management, the survival and outcome for children with posterior fossa tumors have considerably improved.Conflict of InterestNone.

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31 Perioperative Management of Children with Traumatic Brain Injury

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Key Points

- Traumatic brain injury (TBI) in children occurs mostly secondary to motor vehicle accidents, falls, physical assaults, sports injuries, and abuse.
- Various factors that predispose children to TBI are large head-to-torso ratio, a disproportionally greater weight of the head, and thin calvarium. Pliability of the skull, less volume of cerebrospinal fluid, fewer myelinated neural tissue, higher cerebral metabolic rate, and narrow autoregulatory curve further increase the vulnerability to damage.
- Management strategies should focus on rapid diagnosis, aggressive initial resuscitation, and prevention of secondary insults such as hypotension, hypoxemia, dyscarbia, and dysglycemia.
- The primary goals of anesthetic management include providing adequate anesthesia and analgesia, optimizing surgical conditions, avoiding secondary insults, maintaining optimal cerebral perfusion pressure, and avoiding an increase in intracranial pressure.
- Appropriate multimodal neuromonitoring and multidisciplinary rehabilitation approaches should be instituted to facilitate early recovery and improve long-term outcomes.

31.1 Introduction

Traumatic brain injury (TBI) represents a global health problem causing significant disability and mortality among all age groups, particularly young children and adolescents. According to the Centers for Disease Control and Prevention, the young population most commonly affected by TBI has bimodal age distribution (0–4 and 15–19 years). Children up to 14 years of age in the United States of America (USA) constitute about half a million emergency department (ED) visits annually for TBI. TBI affects male children more commonly than females [1]. TBI in children occurs mostly due to motor vehicle accidents, falls, physical assaults, sports injuries, and abuse. Patients with Glasgow Coma Scale (GCS) score $\geq$ 13 constitute more than 80% of TBI and are classified as mild TBI. Only a small fraction (less than 10%) of mild TBI patients require surgical intervention [2]. Due to differences in brain structure and physiology, the spectrum of clinical manifestations, and severity, the management

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and outcome in children differ significantly from the adult population.

31.2 Prehospital Care

The goal of prehospital care is to rapidly stabilize the injured patient and prevent secondary injuries. Prehospital care of children with TBI requires a unique skill set and training. Data regarding pediatric prehospital care and outcomes is limited. Moderate-severe TBI should be considered life-threatening and necessitates aggressive management of airway, breathing, and circulation followed by rapid transportation of the patient to a tertiary healthcare center. Stabilization of the cervical spine should be ensured. Multiple intubation attempts in children have been associated with the delay in transport and lower GCS scores at discharge [3]. Current recommendations do not favor tracheal intubation over bag-valve mask ventilation for prehospital care [3]. However, patients with GCS ≤8, hypoxemia, hypercarbia, aspiration, or signs of elevated intracranial pressure (ICP) should be considered for tracheal intubation. Prophylactic hyperventilation should be avoided. Bleeding from the scalp wound can be significant and should be controlled by direct pressure on the wound. Fluid resuscitation is indicated in patients with hypovolemia, which usually manifests as hypotension with narrow pulse pressure, tachycardia, weak pulse, prolonged capillary refill time (>3 s), and other signs of volume depletion [4]. However, it should be remembered that hypotension is a late manifestation of shock in children. Appropriate and effective prehospital care in such critically injured children can maximize survival chances and improve neurological outcomes.

31.3 Pathophysiology

The primary brain injury (mechanical) occurs at the time of initial impact and results from displacement of the structures of cranial vault. The primary injury serves as the nidus, which evolves over minutes or hours or days and involves a cascade of cellular, vascular, and biochemical events [5, 6]. A mild injury elicits less inflammatory response than moderate or severe TBI [7, 8]. Subsequent secondary brain injury causes dysregulation of cellular functions through various mechanisms like depolarization, excitotoxicity, disruption of calcium homeostasis, free radical generation, mitochondrial dysfunction, and membrane damage, which in turn aggravates inflammation, edema, ischemia, and necrosis (Fig. 31.1) [9]. If timely and necessary interventions are delayed, intracranial hypertension can progress rapidly, leading to an accentuation of neurological deficit and herniation. Favorable prognosis following TBI can be expected if early and aggressive management is executed to limit secondary brain injury.

31.4 Neuroimaging

Computed tomography (CT) of the head is the initial and preferred imaging modality for rapid detection of intracranial injury, cerebral edema, mass effect, midline shift, and/ or herniation during the first 24 h after TBI (Fig. 31.2) [10]. CT is also particularly beneficial for evaluating bones and detecting acute parenchymal or subarachnoid hemorrhage [11]. However, obtaining CT of the head for diagnostic purposes in children with mild TBI is not routinely indicated because of the risks associated with radiation exposure. Pediatric Emergency Care Applied Research Network (PECARN, Fig. 31.3) [12] and Canadian Assessment of Tomography for Childhood Head injury (CATCH, Table 31.1) [13] criteria can be used to predict the need for head CT after mild TBI. Up to 7.5% of children seen in the ED with mild TBI suffer intracranial injury [14]. A CT scan is usually repeated in severe TBI in (1) absence of neurologic improvement; (2) persistent or increasing ICP; or (3) assessment of neurologic status is difficult (e.g., sedation, paralytic agents) [10]. Magnetic resonance imaging (MRI) is not indicated routinely in the acute evaluation of suspected or diagnosed mild TBI. Skull radiograph is not indicated for diagnosing pediatric mild TBI [14].

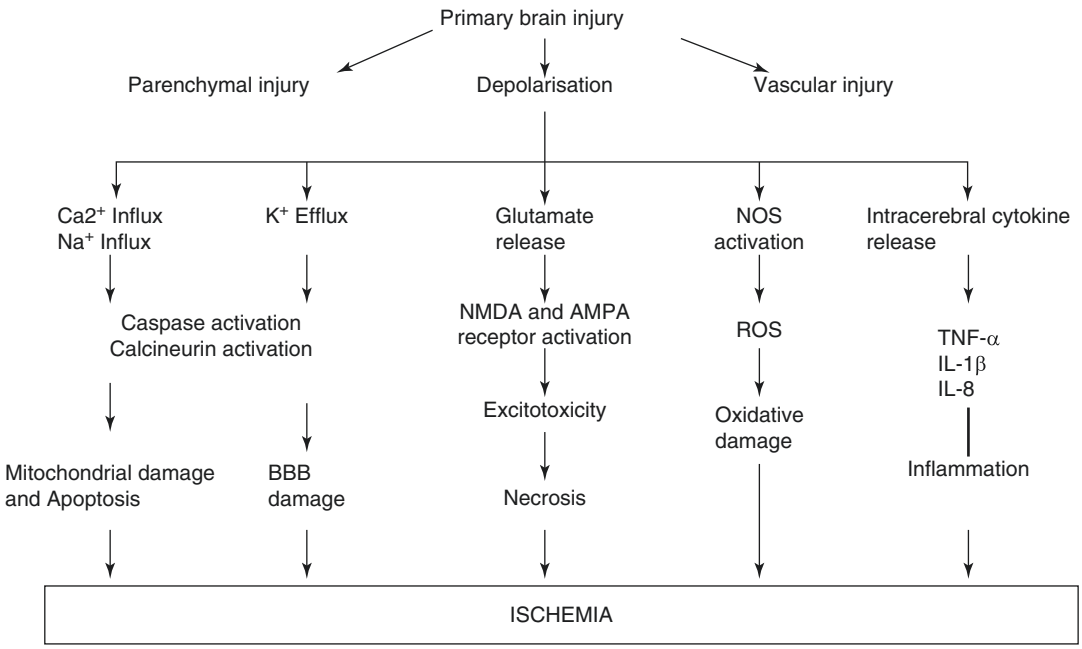

Fig. 31.1 Schematic showing pathophysiological changes during secondary injury in TBI. *NOS* nitric oxide synthase, *NMDA* N-methyl-D-aspartic acid, *AMPA* α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, *ROS* reactive oxygen species, *TNF* tumor necrosis factor, *IL* interleukin, *BBB* blood brain barrier

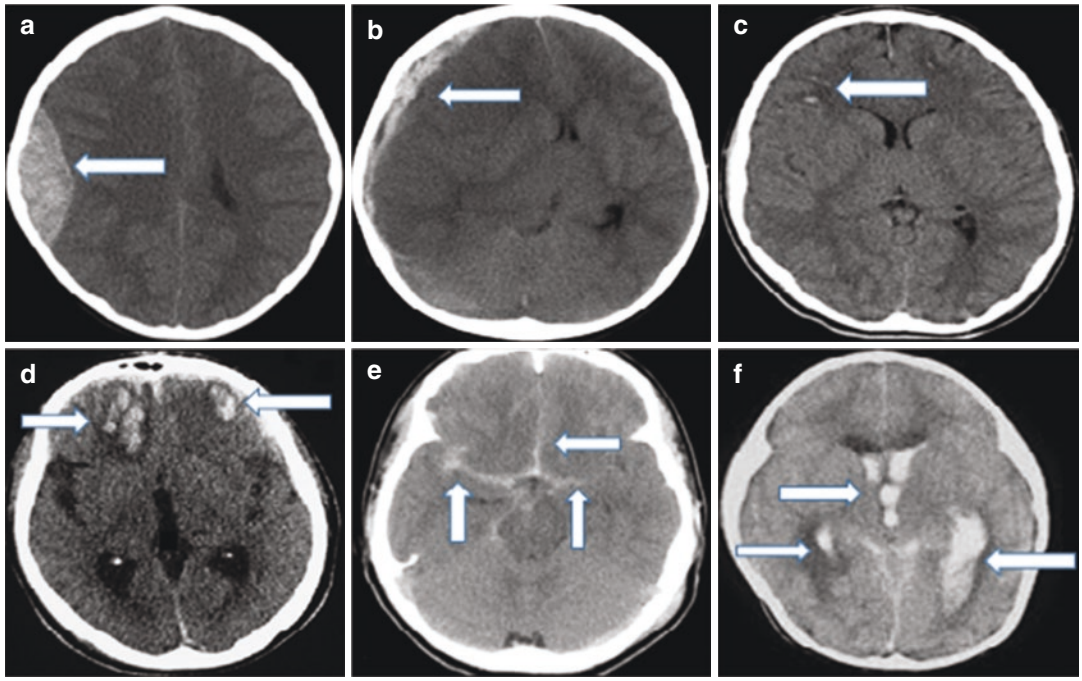

Fig. 31.2 Non-contrast computed tomographic scans of head (axial section) showing various patterns of traumatic brain injury. Arrow points (**a**) Extradural hemorrhage (**b**) Acute subdural hemorrhage (**c**) Punctate hemorrhage in diffuse axonal injury (**d**) Bifrontal contusions (**e**) Subarachnoid hemorrhage (**f**) Intraventricular hemorrhage

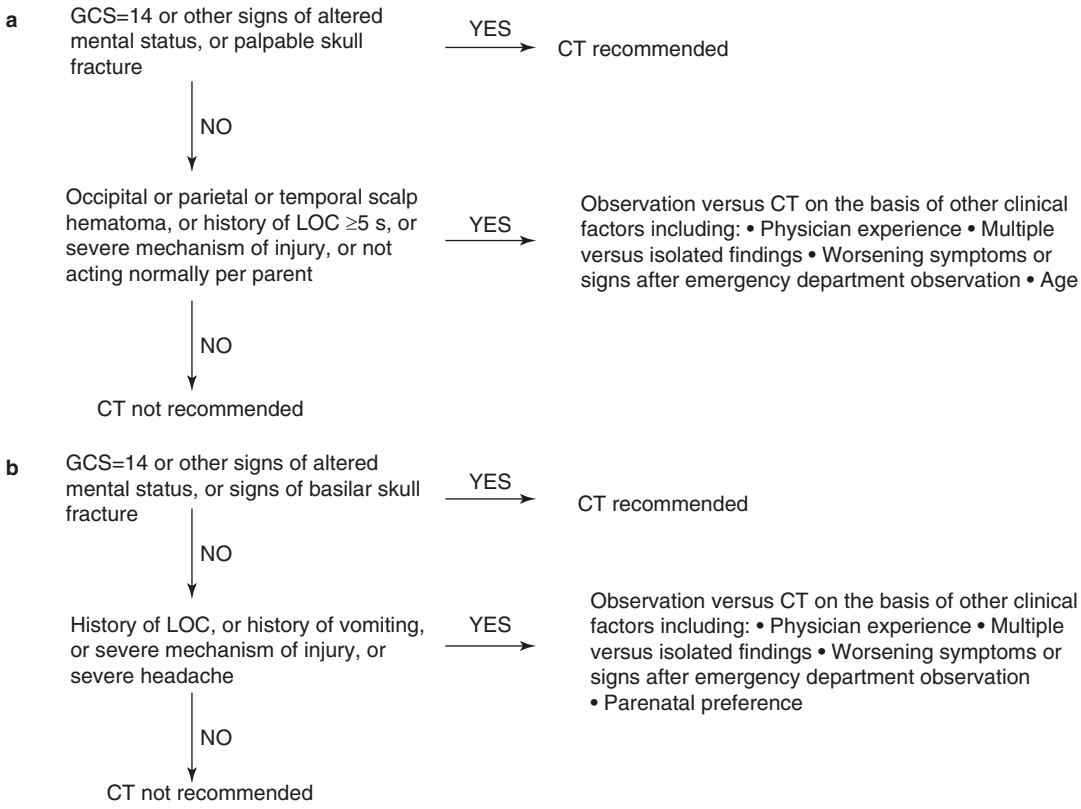

Fig. 31.3 Pediatric Emergency Care Applied Research Network: the PECARN rule. Suggested computed tomographic (CT) algorithm for pediatric TBI with GCS scores of 14–15. (**a**) Includes children less than 2 years of age, and (**b**) Includes children aged 2 years and older. Severe mechanism of injury includes motor vehicle collision with patient ejection, death of another passenger, or rollover; pedestrian or bicyclist without helmet struck by a motorized vehicle; falls of more than 3 feet or more than 5 feet for panel **b**); or head struck by a high-impact object. Patients with isolated loss of consciousness, isolated headache, isolated vomiting, and certain types of isolated scalp hematomas in infants older than 3 months, have a risk of clinically-important TBI substantially lower than 1%

31.5 Surgical Indications and Interventions

Surgical intervention in pediatric patients with TBI requires optimal anesthetic management. Common indications for the operative management in TBI are listed in Table 31.2. The perioperative period is an extension of ongoing resuscitation to restrict further injury and prevent secondary insults. As the intracranial compensatory mechanisms in children are less developed than in adults, perioperative management should be tightly regulated. The primary goals of anesthetic management should focus on providing adequate anesthesia and analgesia; optimizing surgical conditions; avoiding secondary insults such as hypoxemia, hypotension, dyscarbia, and dysglycemia; maintaining optimal cerebral perfusion pressure (CPP); and avoiding increase in ICP. To achieve the desired goals (Table 31.3), perioperative management should be carefully planned. This chapter will focus on the perioperative management of TBI in pediatric patients with various broad domains (Table 31.4).

Table 31.1 Canadian assessment of tomography for childhood head injury: the CATCH rule

CT of the head is required only for children with minor TBI and any one of the following findings:
High risk (need for neurologic intervention)
• Glasgow coma scale score < 15 at 2 h after injury
• Suspected open or depressed skull fracture
• History of worsening headache
• Irritability on examination
Medium risk (brain injury on CT scan)
• Any sign of basal skull fracture (e.g., hemotympanum, "raccoon" eyes, otorrhea or rhinorrhea of the cerebrospinal fluid, Battle's sign)
• Large, boggy hematoma of the scalp
• Dangerous mechanism of injury (e.g., motor vehicle crash, fall from elevation ≥3 ft. [≥91 cm] or 5 stairs, fall from bicycle with no helmet)

The presence of any one of the four high-risk or three medium-risk factors in the rule would identify any CT-visible brain injury with a sensitivity of 98.1% (95% CI 94.6–99.4%) and a specificity of 50.1% (95% CI 48.5–51.7%) and would require that 51.9% of patients with minor TBI undergo CT

Table 31.2 Indications for operative management in TBI

- Open, compound, depressed fracture with mass effect
- Neurological deterioration in the presence of ≥25 ml hematoma
- Hematoma measuring ≥40 ml regardless of neurological status
- Hematoma measuring 25 ml in a critical region such as the posterior fossa
- Increase in the volume of hematoma on repeat imaging
- Midline shift >5 mm
- Contralateral ventricular enlargement
- Diffuse cerebral edema
- Refractory intracranial hypertension

Table 31.3 Desired intraoperative goals in TBI

- Adequate depth of anesthesia
- Mild hyperoxygenation or at least $PaO_2 > 60$ mmHg
- Normocapnia ($PaCO_2$ 35–40 mm hg). Controlled hyperventilation only for short term control of brain bulge. $PaCO_2 \leq 30$ mmHg should be absolutely avoided. Avoidance of high PEEP.
- Cerebral perfusion pressure > 40 mmHg
- Avoid hypotension. Use of vasopressors (noradrenaline/phenylephrine) to treat hypotension.
- Normal osmolality/mild hyperosmolality
- Normovolemia
- Maintain hemoglobin at 7–10 g/dl. Fresh frozen plasma should be used to correct coagulopathy and not as volume replacement
- Random blood sugar: 80–180 mg/dl
- Avoid hyperflexion, hyperextension, and extreme rotation of neck during positioning. Prevent ocular and peripheral nerve injuries by appropriate padding.
- Avoid hyperthermia. No role of routine hypothermia
- No role of perioperative steroids
- Anticonvulsant for prevention of early post-traumatic seizure
- Prophylactic broad-spectrum antibiotic

Table 31.4 Different domains of perioperative management during TBI

- Preoperative evaluation
- Intravenous access
- Airway management
- Anesthetic medications
- Oxygenation and ventilation
- Cerebral perfusion pressure and hemodynamic targets
- Fluid and blood component administration
- Glycemic control
- Positioning
- Temperature management
- Management of intracranial hypertension
- Perioperative steroids
- Seizure prophylaxis
- Antibiotic prophylaxis

31.6 Preoperative Evaluation and Consent

A focused medical examination should be promptly conducted prior to anesthetic administration. In urgent/emergency procedures, only brief history outlined by the mnemonic SAMPLE (Signs and symptoms, Allergies, Medications, Past medical/surgical history, Last oral intake, Events related to injury) along with focused clinical examination (airway, breathing, circulation, neurological examination, extracranial injuries) may suffice [15]. Routine laboratory testing should not delay emergent procedures. Blood products should be promptly available, and hence, a type and cross-match should be ordered. Since coagulopathy is associated with trauma in general and TBI, the coagulation profile is useful in critically injured patients. Serial arterial blood gas (ABG) testing is valuable in assessing dynamic changes in hematocrit, oxygenation, and acid-base status as well as glucose levels.

The family members or close relatives of the patient should be informed about the prognosis

and goals for postoperative care of the patient. Informed consent for surgery, anesthesia, and postoperative ventilation should be taken.

31.7 Intravenous Access

Securing intravenous access in pediatric trauma patients often becomes challenging, particularly when complicated with low blood pressure (BP). A restless and uncooperative child may be challenging to manage safely. The intraosseous route can be used for initial resuscitation if there is a failure to cannulate the peripheral veins [16]. However, it demands expertise; the failure rate is as high as 16% even with trained operators [17]. Moreover, it is difficult to secure and maintain in place, especially during surgery, and can potentially malfunction at a critical time [18]. Children that shifted to operation theater (OT) without peripheral cannulation can undergo inhalation induction followed by cannulation of peripheral veins or large central veins if the need arises.

31.8 Airway Management

Given the risk of worsening brain injury and progressive cerebral edema, patients with severe TBI (GCS ≤ 8) will require urgent tracheal intubation [19]. Moreover, obtunded airway reflexes secondary to impaired neurological status necessitate securing the airway to prevent aspiration. Further, TBI patients should be presumed to have a full stomach and undergo rapid sequence induction (RSI) although recent studies have questioned the benefit of this technique [20, 21]. Additional challenges in airway management in pediatric TBI include the possibility of associated cervical spinal injury (CSI), blood and vomitus in the mouth, and laryngopharyngeal injury. All TBI patients should be presumed to have CSI unless excluded. Thus, extreme care should be taken to minimize the patient's neck movement during intubation. Video laryngoscopy with manual in-line stabilization (MILS) is very effective in minimizing neck movement. Flexible fiberoptic laryngoscopy is typically not suitable. Tracheal intubation should be performed smoothly and gently to prevent hemodynamic responses and ICP accentuation. In patients with basilar skull fractures, nasotracheal intubation should be avoided [22].

31.9 Anesthetic Drugs

Preservation of cerebral autoregulation, vasoreactivity, the coupling between cerebral blood flow (CBF) and cerebral metabolic rate of oxygen consumption ($CMRO_2$), and stable hemodynamics are the most important criteria for selecting appropriate anesthetic agent during neurosurgery. Given that there is no single ideal anesthetic agent for neurosurgery, the current practice in neurosurgical anesthesia should ensure optimal cerebral dynamics while minimizing adverse effects.

31.9.1 Induction Agents

Intravenous and volatile agents exert diverse effects on CBF, cerebral blood volume (CBV), and $CMRO_2$. Intravenous agents including thiopental, propofol, and etomidate reduce $CMRO_2$, with an associated decrease in CBF, CBV, and ICP. However, thiopental and propofol may cause a reduction in CPP secondary to systemic hypotension. In addition, with intact autoregulation, systemic hypotension is compensated by cerebral vasodilatation to maintain CBF, which in susceptible individuals might cause an increase in CBV and ICP [23]. Despite the well-known adrenal suppressive effects of etomidate, data pertaining to its unfavorable effects on survival are lacking. It affects MAP minimally; however, it increases CPP secondary to a reduction in CMR and ICP [24]. Historically, because of concerns related to its ICP-increasing effects, ketamine was avoided in patients with TBI; however, it has been shown to decrease ICP during painful interventions [25]. A systematic review that evaluated the effect of ketamine on ICP in five studies involving 101 adults and two studies involving 55 children showed that ketamine administration did not

increase ICP. Overall, ketamine reduced ICP in three studies and increased CPP and MAP in two studies. None of the studies reported adverse events related to ketamine. Data on outcomes were poorly reported. Essentially, the ICP does not increase with ketamine in sedated and ventilated severe TBI patients; in fact, it may decrease in select cases (Oxford level 2b, Grade C) [26]. Furthermore, it has also been shown that ketamine at dosages of 4 mg/kg or less does not significantly increase intraocular pressure in pediatric patients without eye injuries [27, 28].

Volatile anesthetic agents (halothane, isoflurane, sevoflurane, and desflurane) decrease $CMRO_2$; however, they increase CBF, CBV, and ICP in a dose-dependent manner by cerebral vasodilatation. In neurosurgical anesthesia, halothane is nearly obsolete. Other agents may be used in <1.0 minimum alveolar concentration (MAC) [29]. The use of nitrous oxide (N_2O) in neurosurgical anesthesia continues to be debatable given its negative effects on intracranial dynamics, specifically, increase in CBF, $CMRO_2$, and ICP. Thus, it is prudent to avoid its use in severe TBI [30–33].

31.9.2 Neuromuscular Blocking Drugs

When rapid neuromuscular blockade is required, succinylcholine or rocuronium can be used to achieve optimal intubating conditions. Concerns regarding an increase in ICP with succinylcholine have not been substantiated in systematic studies. Another known adverse effect of succinylcholine includes bradycardia and, in extreme cases, asystole, especially with repeat doses in young children (<5 years) and infants. As such, atropine is recommended as a premedication in patients receiving a second dose of succinylcholine [34]. Succinylcholine causes post-junctional membrane depolarization resulting in potassium ion efflux that produces an increase of 0.5–1.0 mEq/l in serum potassium concentration. Therefore, its use is contraindicated in patients with hyperkalemia, history of muscular dystrophy, extensive crush injuries with rhabdomyolysis, and within 48–72 h after burns or acute spinal cord injury [35]. Rocuronium, a non-depolarizing muscle relaxant, can be used as an alternative drug to achieve rapid intubating conditions. However, it has a longer duration of action. The non-depolarizing agents can be used effectively to provide surgical relaxation and ensure immobility as they lack a direct effect on ICP. It is postulated that they increase cerebral venous drainage by eliminating thoracic skeletal tone and consequently decrease ICP. However, they are not recommended routinely in the post-operative period as they are associated with increased adverse effects and unfavorable outcomes [36, 37].

31.10 Oxygenation and Ventilation

Hypoxemia (PaO_2 < 60 mm Hg) increases CBF, CBV, and ICP in a linear fashion and, thus, demands aggressive management. Application of positive end-expiratory pressure (PEEP) recruits collapsed alveoli and improves oxygenation [38]. However, few studies have demonstrated ICP accentuation with high PEEP in adult TBI patients [39, 40]. In a study of 21 pediatric patients undergoing surgery for intracranial neoplasm, Pulitano et al. did not find any significant difference in ICP after increasing PEEP from 0 to 8 cm H_2O [41]. Moreover, a large change in the intrathoracic pressure in children results in only minor change in chest wall pressure due to steep volume-pressure relationship. As such, pleural pressure is minimally affected even with a large change in ventilator pressure. This explains the higher cardiovascular tolerance of children to the application of PEEP [42]. However, current literature recommends augmenting oxygenation by first increasing the FiO_2 and inspiratory time rather than PEEP [43].

The principle of ventilatory strategy in neurosurgery is to maintain normocapnia. Worse perioperative outcomes have been observed with both hypercapnia and hypocapnia. Although hypocapnia decreases CBF by causing vasoconstriction, it also predisposes to the risk of cerebral ischemia. It is suggested that hyperventilation be used only

for short-term control of ICP and facilitation of surgical exposure during craniotomy. Prophylactic hyperventilation to a $PaCO_2$ level below 30 mmHg is not recommended within the first 48 h of TBI. Advanced neuromonitoring for assessing cerebral ischemia may be considered if hyperventilation is done (level III recommendation) [10].

31.11 Cerebral Perfusion Pressure and Hemodynamic Targets

The 2019 pediatric TBI guidelines recommend immediate intervention at an ICP ≥20 mmHg (level III recommendation) [10]. Although the target CPP in neonates and infants is not well defined, unlike adult TBI [44], the guidelines recommend maintaining CPP above 40 mmHg (level III recommendation) [10]. Chambers et al. proposed age-stratified critical levels of CPP. CPP values of 43, 54, and 58 mmHg in the age groups of 2–6, 7–10, and 11–16 years, respectively, were shown to be associated with favorable outcomes [45].

Various studies have clearly shown that even a single perioperative hypotension episode after TBI can adversely affect the outcome [46, 47]. Data from the Traumatic Coma Data Bank clearly showed an association between hypotension and increased mortality rate in children with TBI [48]. Moreover, the limits of cerebral autoregulation are not well defined in infants and children. William et al. suggested that intraoperative BP should be targeted to maintain a child's preoperative baseline BP if it was obtained without distress and with an appropriately sized cuff. However, during the unreliable recording of baseline BP, they suggested that the 50th percentile for MAP in children at the 50th percentile for height is approximately 55 mmHg and 67 mmHg at 1 and 5 years, respectively. The degree and duration of relative hypotension that can safely be tolerated remain unclear [49].

In both animal and human studies, norepinephrine has been shown to have a more consistent and predictable effect in CPP augmentation as compared to dopamine [50, 51]. Additionally, norepinephrine reduces the regional oxygen extraction fraction and consequently increases brain tissue oxygen levels [52, 53]. In a retrospective study, in severe TBI patients who received dopamine, norepinephrine, or phenylephrine, the maximal increase in MAP and CPP from baseline was noticed with phenylephrine [54]. Either phenylephrine or norepinephrine can be effectively used for optimizing blood pressure intraoperatively.

31.12 Fluid and Blood Component Administration

Perioperative fluid management in pediatric patients after TBI can impact the postoperative outcome. Concerns regarding fluid management include the type of fluid (crystalloids versus colloids), osmolarity of fluid, and liberal versus restrictive approach. Maintaining a euvolemic and isotonic or mild hypertonic state is the cornerstone of fluid management.

Typically, iso-osmolar crystalloids are recommended as the fluid of choice. Isotonic normal saline (0.9% NS) with an osmolarity of 308 mOsm/l is the most commonly used fluid for neurosurgical cases. However, large volume isotonic saline causes normal anion gap hyperchloremic metabolic acidosis (HCMA), and thus, serum chloride and acid-base status should be monitored during large-volume saline resuscitation [55, 56]. Balanced salt solutions such as plasmalyte A (osmolarity of about 295 mOsm/L) may be preferred as alternatives to isotonic saline during imminent hyperchloremia. Changes in plasma osmolality (<5%) have been shown to increase brain water content and ICP [57]. Lactated Ringer's solution is a hypoosmolar fluid (osmolarity 275 mOsm/l) that can increase cerebral edema in large volumes, although small volumes are considered safe.

During large-volume resuscitation, it is advisable to infuse colloids and/or blood transfusion to restrict the volume of crystalloids being administered. Colloids contain large molecules that remain within the intravascular compartment. They expand the intravascular volume and

stabilize the systemic BP without aggravating cerebral edema. However, there is a lack of robust data to support their use in TBI. A meta-analysis showed lower mortality with crystalloids [58]. A subgroup analysis followed by a post hoc analysis of SAFE study in adult TBI patients found increased mortality with 4% albumin compared to 0.9% saline in TBI. This was attributed to increased extravasation of albumin in areas of disrupted blood-brain barrier leading to increased vasogenic edema and also to hypotonic stress of 4% albumin (260 mOsm/kg) [59, 60]. Safe volume of hydroxyethyl starch (HES) is undetermined, although deleterious effects on kidney and coagulation have been reported [61–64].

In severe TBI, anemia can aggravate brain injury secondary to decreased cerebral oxygen delivery [65]. Acute traumatic coagulopathy is common in isolated TBI and increases the likelihood of red blood cell (RBC) transfusion. Following acute brain injury, there is release of tissue factor which activates the coagulation cascade resulting in formation of thrombin and consumption of clotting factors. Coagulopathy may be further compounded in the presence of hypothermia, acidosis, and hypocalcemia. Risk factors for acute traumatic coagulopathy in children include GCS ≤8, increasing age, higher severity of illness score, and brain contusions/lacerations [66]. Epstein et al. reported that acute traumatic coagulopathy was associated with high transfusion rates of 41% and high mortality (17 to 86%) [67]. Little is known regarding optimal transfusion practices in pediatric patients with TBI. A recent retrospective study that reviewed pediatric TBI outcomes found that 178 out of 1607 pediatric patients received RBC transfusion [68]. The authors demonstrated that RBC transfusion was associated with unfavorable outcomes and increased mortality. Therefore, they suggested that a transfusion trigger of 8.0 g/dl be considered in children with TBI. Early administration of tranexamic acid in adults within 3 h of TBI has been shown to significantly decrease head injury-related deaths in mild and moderate TBI with no evidence of adverse effects or complications (CRASH-3 trial) [69].

31.13 Glycemic Control

Hyperglycemia has been shown to worsen neurological outcome in both adult [70–72] and pediatric TBI [73–75]. Various mechanisms of hyperglycemia after TBI include catecholamine surge and cortisol release secondary to stress response, insulin resistance, and pituitary and/or hypothalamic dysfunction [76–78]. As such, it is suggested to avoid dextrose containing fluids except in cases of established hypoglycemia. On the contrary, treatment of hyperglycemia should be intensively monitored in order to prevent iatrogenic hypoglycemia [79]. Since both hyperglycemia and hypoglycemia are associated with adverse sequelae, blood glucose concentrations should be monitored intermittently during the perioperative period. A commonly acceptable range of perioperative blood glucose is between 80 and 180 mg/dl.

31.14 Positioning

Careful positioning of the neurosurgical patients requires appropriate anesthetic depth, maintenance of oxygenation and hemodynamic stability, and safeguarding of invasive monitors. Transient disconnection of invasive vascular catheters and tracheal tube is often required during the process of positioning. It is optimal to monitor at least pulse oximetry and blood pressure to avoid a complete "blackout" state [80].

During positioning, special care should be taken to avoid extreme flexion, extension, and rotation of the head to ensure optimal cerebral venous drainage [81]. The free movement of the abdominal wall should be ensured. Other less common complications include swelling of face, neck, and airway, increased airway pressures, and macroglossia leading to airway obstruction, pressure sores, and peripheral nerve damage and

should be prevented by ensuring appropriate padding and avoiding direct compression.

31.15 Temperature Management

Initial studies showed an improvement in neurological outcome following initiation of mild hypothermia in children with severe TBI [82–84]. The proposed mechanism involves hypothermia-induced reduction in $CMRO_2$, CBF, and ICP. However, recent randomized controlled trials such as Hypothermia Pediatric Head Injury Trial [85] and Cool Kids Trial [86] failed to show any improvement in neurological outcome following prophylactic initiation hypothermia in children with severe TBI. Similar results have been observed in a few other recently conducted studies [87, 88]. The 2019 pediatric TBI guidelines recommend an institution of moderate hypothermia (32–33 °C) only as rescue therapy for ICP control (level III recommendation) and avoiding it prophylactically in severe TBI (level II recommendation). Rewarming should be done gradually at a rate of 0.5 °C per hour or slower to avoid complications [10]. Various complications of induced hypothermia include hemodynamic instability, arrhythmias, hyperglycemia, coagulopathy, sepsis, and rebound intracranial hypertension during and after rewarming [89, 90].

On the other hand, hyperthermia increases metabolic demands, lipid peroxidation, inflammation, and excitotoxicity and lowers the seizure threshold and should be strictly prevented and treated aggressively [91]. Several studies have shown that hyperthermia significantly increases ICU and hospital stay duration and worsens neurological functions at 6 months after the initial injury [92, 93].

31.16 Management of Intracranial Hypertension

31.16.1 Hyperosmolar Solutions

Hyperosmolar solutions (mannitol, hypertonic saline) are effective in decreasing intracranial hypertension through two discrete mechanisms: (1) plasma expansion and resultant decrease in blood viscosity and decreased CBV due to cerebral autoregulation-driven cerebral vasoconstriction and (2) osmotic effect that draws cerebral edema fluid from brain tissue into the circulation. Either agent can be considered for intraoperative brain relaxation. However, there is a lack of robust evidence to recommend any specific hyperosmolar therapy to improve overall outcomes. In a recent prospective observational study, Shein et al. noticed that children with severe TBI, when treated with multiple drug regimens (fentanyl, mannitol, 3% HTS, pentobarbital), are known to reduce ICP; HTS was associated with the most favorable cerebral hemodynamics and fastest resolution of intracranial hypertension [94]. Effectiveness of 7.5% and 23.4% HTS in reducing ICP, augmenting CPP, and minimizing total fluid volume in children has also been shown [95, 96]. The 2019 pediatric TBI guidelines recommend the use of 3% HTS for intracranial hypertension in the bolus dose ranging from 2 to 5 ml/kg over 10–20 min (level II recommendation) and continuous infusion at a rate of 0.1–1 ml/kg/h, administered on a sliding scale (level III recommendation). A bolus of 0.5 ml/kg of 23.4% HTS (maximum 30 ml) is also suggested for refractory ICP (level III recommendation) [10]. Although recent evidence favors the use of HTS, mannitol is still commonly used in the management of intracranial hypertension in pediatric TBI (20% mannitol; 0.25–1 gm/kg). The commonly recommended upper limit of osmolality for mannitol and HTS is 320 and 360 mOsm/l, respectively [97].

Half molar sodium lactate (SL), another hypertonic agent (1020 mOsm/l), has been shown to effectively reduce intracranial hypertension in adult TBI [98, 99]. The probable mechanism of ICP reduction due to SL involves limiting cellular edema through the extrusion of chloride and water [99]. Other beneficial effects of SL infusion involve maintenance of serum chloride levels (unlike 3% HTS) [99], preservation of extracellular brain glucose levels [100], improved mitochondrial oxidative respiration [101], and attenuation of cognitive deficits following TBI [102]. However, its utility during the intraoperative period in pediatric neurosurgical patients is yet to be ascertained.

31.16.2 Barbiturate Coma

The 2019 pediatric TBI guidelines recommend high-dose barbiturate therapy in cases of intracranial hypertension refractory to medical and surgical interventions. If barbiturates are used, baseline hemodynamics should be stable. Continuous monitoring of arterial blood pressure is recommended. Cardiovascular support should be provided to maintain adequate CPP (level III recommendation) [10].

31.16.3 Decompressive Craniectomy

The 2019 pediatric TBI guidelines recommend decompressive craniectomy to treat neurologic deterioration, herniation, or intracranial hypertension refractory to medical management (level III recommendation) [10]. In adults with severe diffuse TBI and refractory intracranial hypertension, early bifrontotemporoparietal decompressive craniectomy decreased ICP and the duration of ICU stay but was associated with more unfavorable outcomes on Glasgow Coma Scale-Extended (GOS-E) at 6 months [103, 104].

31.17 Perioperative Steroids

Many studies in adults, including the multi-center CRASH study, did not show any benefit with the use of steroids in TBI [105–107]. Complications of steroids like hyperglycemia, gastrointestinal bleeding, adrenal suppression, and increased risk of infection have been shown to worsen outcome. The 2019 pediatric TBI guidelines also stated that there is no role of steroids to improve neurological outcome or lower ICP in TBI patients (level III recommendation) [10].

31.18 Seizure Prophylaxis

The incidence of post-traumatic seizures (PTS) in children after severe TBI has been reported to be as high as 19% [108]. PTS affect TBI patients through various mechanisms: increasing excitotoxicity, increasing ICP and $CMRO_2$, aggravating cerebral hypoxia, and causing fluctuations in systemic blood pressure [109, 110]. The risk factors for early PTS (≤7 days of injury) after severe TBI are younger age (<2 years), mechanism of injury (non-accidental trauma), skull fracture, GCS ≤8, and presence of a subdural hematoma [108, 111–113].

Phenytoin, if administered prophylactically, has been shown to decrease the incidence of early PTS but not late PTS (>7 days of injury) [114, 115]. The 2019 pediatric TBI guidelines also recommend the prophylactic use of anticonvulsant to reduce the incidence of early PTS (level III recommendation) but, however, could not generate sufficient evidence to recommend levetiracetam over phenytoin [10].

31.19 Antibiotic Prophylaxis

Infections are common after pediatric TBI (particularly penetrating brain injury) and increase the incidence of morbidity and mortality [116]. These include local wound infection, meningitis, ventriculitis, or brain abscess caused by the presence of contaminated foreign object including skin, hair, or bone fragments inside the brain. The severity of infection is compounded in the presence of cerebrospinal fluid leak, air sinus injury, trans-ventricular injury, or injuries crossing the midline. All TBI cases should receive broad-spectrum antibiotic prophylaxis and continued for at least 6 weeks [117].

31.20 Postoperative Intensive Care

Care in an intensive care unit (ICU) is directed toward maintaining systemic homeostasis and preventing/treating any complications. Multimodal neuromonitoring by simultaneous assessment of cerebral and systemic hemodynamics, cerebral oxygenation, and metabolism allows individualized patient care. Appropriate analgesia (multimodal approach) should be ensured to prevent harmful complications of pain. Optimizing glucose levels, temperature, electrolytes, and acid-base status, correcting

coagulation abnormalities, and ensuring optimal nutritional support should be the utmost concerns. Enteral nutritional support should be initiated early (within 72 h of injury) to improve outcome and reduce mortality [10]. Early tracheostomy is recommended to reduce the duration of mechanical ventilation, although there is no concrete evidence that it reduces the incidence of nosocomial pneumonia or overall mortality in children. Recently, the CENTER-TBI study showed that early tracheostomy (≤7 days from admission) in adult TBI was associated with a reduced length of ICU stay and better neurological outcome at 6 months [118]. Appropriate rehabilitation (multidisciplinary) should be implemented to facilitate early recovery and improve long-term outcome [119, 120].

31.21 Miscellaneous Conditions

1. **Abusive head trauma (AHT):** AHT is the most common cause of non-accidental TBI-related mortality. The American Academy of Pediatrics has defined AHT as "the constellation of cerebral, spinal, and cranial injuries that result from inflicted TBI to infants and young children." [121] With an overall incidence of around 12%, AHT is the leading cause of death under 2 years of age [122]. The risk factors include young parents, poor socioeconomic status, disturbed family environment, and prematurity or disability of the child. Children with developmental disorders are at higher risk of abuse [123].

   The presentation may vary from cerebral concussion to irreversible brain damage and/or death. Sentinel signs have been observed in 30% of infants with AHT. These include bruising (face, forehead, ear, extremity, trunk) in 80% of cases, intraoral injury (frenulum injury, tongue contusion) in 11% of cases, and fracture (including both acute and healing) in 7% of cases [124].
2. **Paroxysmal sympathetic hyperactivity (PSH):** PSH is characterized by sympathetic hyperactivity, which manifests as simultaneous paroxysmal transient increases in heart rate, blood pressure, respiratory rate, temperature, sweating, and motor (posturing) activity [125]. PSH has been described in 13–14% of children following acquired brain injury [126, 127]. Constipation, distended abdomen or bladder, increased respiratory secretions, infections, pressure sore, and just an intravenous cannulation are known triggers [128]. Since PSH is a diagnosis of exclusion, there may be a delay in diagnosis, even if the index of suspicion is high. Severe brain injury and consequent PSH in children have been associated with worse clinical outcomes, prolonged periods of hospital stay, and intensive care support [125, 129]. Commonly advocated medications are beta-blockers (propranolol), central alpha-blockers (clonidine), bromocriptine, gabapentin, benzodiazepine, medications for hyperthermia (baclofen, dantrolene), and opioids [129, 130].
3. **Growing skull fractures (GSF):** GSF is a rare complication of pediatric head trauma that is associated with cranial defect and delayed onset neurological deficits [131]. The etiopathogenesis of GSF is not fully understood, but the presence of diastatic linear skull fracture, dural and arachnoid disruption with cerebrospinal fluid leak, and underlying contusion of the brain is an invariable accompaniment. The reported incidence of GSF ranges from 0.05% to 0.6% of skull fractures in children [132]. Fall from height has been found to be the most common mode of injury in these children [133]. Their usual site is the parietal region, which presents as a cystic, non-tender swelling with an underlying palpable bony defect. Less common sites for GSF are the posterior fossa, skull base, and orbital region [134]. Early diagnosis and treatment are essential to avoid complications.
4. **Cranioplasty:** Cranioplasty is a reconstructive procedure that is mostly done after decompressive craniectomy. It provides structural, cosmetic, and physiological rehabilitation. The technique is challenging in children as compared to adults because of the growing calvarium and thin bones [135]. Autologous bone grafts are preferred in children as their

osseointegration with the growing skull has been well established [136]. However, in resource-poor healthcare settings, the storage of autologous bone at controlled temperatures is technically difficult. Again, subcutaneous pockets may not be suitable for very young children because of their limited abdominal fat thickness [137]. The current trend in practice appears to be the use of particulate bone grafts or exchange cranioplasty in infants. In older children, custom-made implants using titanium or hydroxyapatite have been used successfully [138]. Regarding the timing, it was previously suggested that cranioplasty, if done after at least 6 months, and preferably after 12 months of the craniectomy, resulted in a lower infection rate [139]. However, recent studies have favored early (<6 weeks) cranioplasty in view of reduced occurrence of bone resorption and a better outcome [140, 141].

31.22 Conclusion

TBI in children continues to increase as a cause of fatality worldwide. Apart from falls and sports-related injuries, as access to motorized transportation expands, more children are susceptible to road traffic accidents either as passengers or pedestrians. Children have unique injury patterns and responses to injury. Future developments in the management of pediatric TBI should focus on the appropriate training of prehospital healthcare providers and the development of protocols and guidelines to improve prehospital care. The development of effective neuroprotective strategies is the need of the hour. Controversies in pediatric TBI regarding surgical versus medical management, the timing of surgery, use of ketamine, blood transfusion threshold, effective anticonvulsant, invasive versus noninvasive neuromonitoring, early versus late tracheostomy, etc. should be resolved by conducting large randomized controlled trials. Attention should be paid to employ effective rehabilitation to ultimately restore quality of life and dignity after trauma.

Conflict of Interest Nil.

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Perioperative Management of Pediatric Spine Injury

32

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Key Points

- Pediatric spine injury is a devastating condition with a substantial lifelong impact on the patient, family, and society.
- Age-related differences in the pediatric spine and the growth potentials in children lead to different patterns, mechanisms, and injury levels compared to adults.
- The pediatric population is at a greater risk for spinal cord injury without radiographic abnormality than adults.
- The initial resuscitation should focus on managing respiratory and hemodynamic parameters while maintaining immobilization of the neck and/or spine to prevent secondary injury.
- Perioperative management should maintain hemodynamic and respiratory parameters, facilitate surgical conditions and neuromonitoring, prevent complications, minimize pain, and enhance early recovery.
- Early surgical intervention and stabilization of the spine can facilitate early mobilization of these children and reduce complications.
- Those who survive the acute phase of spine injury usually require long-term rehabilitation.
- Neurological recovery following spinal cord injury is thought to be better in children than adults.

32.1 Introduction

Spinal cord injury (SCI) is a devastating condition that leads to substantial complications. Although relatively less common, spinal injuries in pediatric patients are associated with higher mortality and morbidity as compared to adults [1, 2]. The anatomy and biomechanical properties of the pediatric spine are different from adults, and this makes it a different entity from adult spinal injuries [3]. The distribution of spinal injuries across various spinal segments is also different in pediatric patients compared to adults. Children are particularly prone to cervical spine injuries, and they account for 60–80% of all pediatric spinal injuries [2]. Moreover, spinal injury is more likely to be associated with traumatic brain injury (TBI) in children resulting in poorer outcomes than adults [4]. Thus, it is important to have a high degree of suspicion for prompt diagnosis and early management for better functional recovery [5].

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The chances of cervical spinal injury in children are high due to the relatively large head size compared to the trunk, weak neck musculature, and horizontal orientation of the facets. The age-related differences in children and adults and the growth potentials in children result in a difference in the incidence and presentations of spine trauma as well as in the pattern, mechanism, and levels of injury [2, 6]. Thus, it demands an understanding of the unique aspect of the pediatric spine for appropriate evaluation, diagnosis, and management necessary to reduce morbidity associated with this condition [2].

Children with unstable cervical spine injuries are more likely to have associated neurologic injury and must be treated with great caution [7]. In patients with a suspected cervical spine injury, extreme care should be taken to limit the movement of the cervical spine in order to prevent the secondary neurologic injury until definitive stabilization is ascertained [7].

32.2 Epidemiology

Spinal trauma is less common in children than adults, with an estimated incidence of 1.99 per 100,000 children in the United States [8]. Pediatric spinal injury patients constitute 1–10% of all spine injuries [9]. The reported incidence of pediatric spine injury in different studies varies depending on the cohort and the age included. Although the exact incidence is unknown, the true incidence may be underestimated as the spinal injuries may be masked by other trauma features. The coincident TBI reported with spine injury in children varies from 25% to 38.8% [10–13].

There are age-related differences in the distribution of spinal injury among children. The incidence of injury is higher at the C1–C2 level in children less than 3 years, with girls more commonly affected [14, 15]. However, the incidence of injury to the lower cervical and thoracolumbar spine increases with age, with adolescent males 4 times affected than females [16]. Motor vehicle accidents (MVAs) are the most common causes of spine injury in children among all age groups. Other causes may include fall from a height, sports and recreational injuries, pedestrian and bicycle injuries, and child abuse. Falls and abuses are relatively common in young children, while older children are often injured during MVAs and sports or recreational activities. Also, birth-related injuries (obstetric causes) may lead to spinal cord injuries in neonates with an incidence of 1 in 60,000 births [17].

32.3 Anatomy of Pediatric Spine

In humans, the spinal or vertebral column consists of 33 vertebrae (bony elements), including 7 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 4 coccygeal vertebrae. These bony elements are separated by intervertebral disks (fibrocartilaginous) and supported by ligaments. However, the bodies of lower vertebrae, i.e., 5 sacral and 4 coccygeal vertebrae, later fuse to form the bony sacrum and coccyx, respectively, reducing the number of vertebrae to 26 in the adults. The vertebral column provides attachments to muscles and supports the trunk. Also, it protects the spinal cord and nerve roots and serves as a site for hemopoiesis.

Certain anatomic and biomechanical differences exist between the immature spine of children and adults that include greater mobility of the spine owing to ligamentous laxity, shallow angulations and horizontal orientation of facet joints, immature development of neck musculature, underdeveloped spinous processes, physiologic anterior wedging of vertebral bodies, and incomplete ossification of the vertebrae (Table 32.1). Due to these anatomical differences, the pediatric spine is more prone to neurological injury without musculoskeletal damage than adults.

In children, the larger head size relative to the body results in a higher center of gravity and fulcrum of neck motion. After 8 years, the fulcrum of movement changes from C2-3 to C5-6 (i.e.,

Table 32.1 Important anatomical variations of the pediatric spine from adults

- Head is relatively larger to the body, and thus fulcrum of neck movement is located at C2–C3 in the younger children compared to C5–C6 in older children and adults.
- Weak neck muscles
- Ligamentous and joint capsule laxity
- The horizontal orientation of the facet joints in younger children
- Mild physiological anterior "wedging" of vertebral bodies
- Underdeveloped spinous processes
- Incomplete ossification of the odontoid process (depending on the age of the child)
- Presence of primary and secondary ossification center

the adult fulcrum), which is also reflected in the types and patterns of spinal injury in different age groups [9]. The upper cervical spine (from the occiput to C3) is more commonly injured in young children (<8 years), while the lower cervical and dorso-lumbar spines are more often involved in older children and adults [18].

32.4 Radiology

Based on radiographic findings, the pediatric spine injury can be broadly classified into two groups: injury with radiographic abnormalities (fracture, dislocation, subluxation) and without radiographic abnormalities (SCIWORA). The routine radiological investigations to evaluate pediatric spinal trauma patients include plain X-rays, computed tomography (CT), and magnetic resonance imaging (MRI). Usually, plain X-ray or CT is done only when there is high suspicion or neurological symptoms of spinal cord injury. It has been recommended to get spinal imaging in children who have unexplained hypotension or experience cardiac arrest, as these may suggest the presence of cervical spinal cord injury [19]. Screening imaging is not indicated in patients with low risk for cervical spinal injury as per the NEXUS (National Emergency X-Radiography Utilization Study) criteria [20]. Dynamic cervical radiographs may help diagnose ligamentous injuries without fracture, especially in the high cervical spine.

MRI can be helpful in the diagnosis of SCIWORA, which accounts for about 20% of pediatric spinal cord injuries and occurs predominantly in children younger than 8 years of age. SCIWORA is rare in adolescents and adults and is often seen in cervical and thoracic levels, but is rare in the lumbar region. It occurs due to the elasticity and flexibility of the child's spine. The pediatric spine can withstand elongation without any fracture, but the spinal cord gets injured.

One has to be careful in considering the age-related changes in maturation when viewing something abnormal in pediatric radiographs as the fusion of various parts of vertebra happens at a particular age and may be misinterpreted as a fracture. Some examples of this include pseudo-subluxation of C2 on C3, anterior overriding of atlas related to the odontoid on extension and exaggeration of the atlantodental interval (ADI), and radiolucent synchondrosis between the odontoid and C2 body [21]. Important radiological variations between pediatric and adult spine are given in Table 32.2.

32.5 Management

Spinal cord injuries in children may occur from varying modes of injuries ranging from congenital defects like Down's syndrome [23], traumatic breech deliveries, physical abuse (shaken baby syndrome) to road traffic accidents, diving injuries, and fall from heights. The mechanisms of injury include hyperflexion, hyperextension, and vertical compression injuries [24]. Almost 50% of children with spine injuries show no abnormality on spine X-ray [25]. Almost 60–80% of all pediatric vertebral injuries are in the cervical region compared to adults in whom cervical injuries constitute 30–40% of all vertebral injuries. Further, in young children, injuries to the upper cervical spine are more common and associated with higher morbidity and mortality.

Table 32.2 Important radiological variations between the pediatric and adult spine

Radiological features	Adults	Children	Implication(s)
Atlantodental interval (ADI) (distance between the anterior aspect of the dens and the posterior aspect of the anterior ring of the atlas)	Less than 3 mm	May be up to 5 mm	Normal ADI confirms that the transverse ligament is intact. ADI 3–5 mm may be normal in children
Pseudo-subluxation (caused due to the horizontally placed facet joints in younger children, which later becomes more vertical as the spine matures)	Absent	It may be normally present (anterior displacement of C2 in relation to C3 and a lesser extent C3 over C4)	Resembles ligamentous injury
Secondary ossification centers	Absent	Present (especially of spinous processes and unfused ring apophyses of vertebral bodies)	It may be confused with fractures (these should be differentiated as they appear as smooth and regular with a subchondral sclerotic line delineating the growth plate in contrast to fractures which are irregular and can occur anywhere)
Physiological wedging (wedging of the vertebral bodies)	Absent	May show mild anterior wedging of the vertebral bodies (up to 3 mm) until the endplates are fused; most clearly evident in C3 vertebrae	May be confused with a compression fracture [22]
Absence of cervical lordosis	Potentially pathological	May be normally seen in children up to 16 years when the neck is in a neutral position	The absence of cervical lordosis may not always be pathological in children
Pure ligamentous injuries without fracture	Uncommon	Quite common in children, particularly in children <10 years of age with cervical spine injuries	The absence of fracture on CT imaging or plain radiographs does not exclude injury in the pediatric cervical spine

32.5.1 Initial Management

Initial management must focus on resuscitation of the injured patient (Table 32.3). Maintaining adequate gas exchange and end-organ perfusion is fundamentals of initial management. Hypoxia and hypotension are detrimental. Once stable, a more comprehensive assessment, including a thorough neurological examination, is performed. All patients should be treated as if they have an unstable spine until proven otherwise. Spinal movement during intubation can cause secondary neurological injury. Hence, immobilization of the cervical spine before radiographic and/or clinical clearance is the standard of care [26]. Reportedly, 18% of patients with cervical spine injury need intubation within 30 min of arrival in the emergency department [27].

32.5.1.1 Immobilization of Cervical Spine

There are certain key differences in the management of pediatric and adult cervical spine injuries [7]. Children have a relatively larger head circumference that causes relative cervical flexion when placed supine on a horizontal surface [28]. Therefore, either a backboard with the trunk elevated by 25 mm should be used, or the head should be placed in an occipital recess when immobilizing the spine in children <8 years age [28].

Various techniques can be used to stabilize the cervical spine (Table 32.4), including soft and hard collars, sandbags, or supportive blocks and tape. The use of cervical traction in children has specific concerns and is rarely described in the literature. The thinner cranium increases the like-

lihood of inner cranial table penetration; lighter bodyweight provides less counterforce to traction, and more elastic ligaments and less well-developed musculature increase the potential for overdistraction. Manual in-line stabilization (MILS) is a more widely accepted technique, although it can cause poor visualization and increase intubation failure rates [29]. MILS is shown to cause significantly lesser movement during intubation than cervical collars [30].

Table 32.3 Goals of initial management

• Immobilize head and neck in all patients of trauma until spine injury is excluded
• Immobilization of the spine may be achieved by placing the patient on a spine board with neck neutral, sandbags on either side of the head, and 3-inch adhesive tape to secure the head to the spine board
• Watch for signs of respiratory compromise; tracheal intubation, if required
• Maintain mean arterial pressure (MAP) according to the age-specific targets. Avoid fluid overload and pulmonary edema
• Bradycardia, if associated with hemodynamic instability, is treated with atropine
• In the case of gastric distension, a nasogastric tube is inserted to decompress the stomach
• Frequent neurological examination (sensory, motor, Glasgow coma scale (GCS) score, pupillary response) and expeditious radiological examination
• Maintain normothermia

Table 32.4 Cervical spine immobilization techniques

Technique	Important considerations
Sandbag, blocks, tape	Effective in reducing cervical spine movement in all directions Make intubation difficult
Cervical collars	Do not completely eliminate cervical spine movement during intubation Anterior portion of the collar makes mouth opening difficult Make intubation difficult
Manual in-line stabilization (MILS)	Reduces neck movement during intubation The preferred method for intubation in cervical spine injury
Axial traction	May cause distraction, subluxation
Halo brace	Effective in limiting cervical spine movement in all directions Makes direct laryngoscopy difficult Fiber-optic intubation is preferred

32.5.1.2 Tracheal Intubation

Intubation using direct laryngoscopy causes maximum movement in the upper cervical spine at occiput–C1 and C1–C2 levels [31]. This gives rise to the possibility of aggravation of SCI during intubation. Different intubation techniques have been studied in patients with cervical spine injury; advantages and disadvantages of each of them are discussed (Table 32.5). Technically, intubation techniques that do not need direct visualization of the glottis require less extension of the cervical spine. However, the literature suggests that the maximum movement of the cervi-

Table 32.5 Techniques of tracheal intubation

Techniques	Advantages	Disadvantages
Direct laryngoscopy (DL)	Takes less time	Extension at atlantooccipital and C1–C2 levels
Video-laryngoscopy	Better visualization	Cervical motion similar to DL [33]
Fiber-optic oral intubation	Better visualization Minimal cervical movement May be performed in the awake and co-operative child; neurological assessment is possible during and after intubation	Longer time for intubation Difficult in cases where acute airway management is required Awake fiber-optic intubation is difficult in uncooperative patients
Fiber-optic nasotracheal intubation	Excellent visualization of the glottis Substantially less cervical motion Neck hyperextension is not required	Considerably time-consuming Difficult in an emergency setting Contraindicated in basilar skull fracture and craniofacial trauma
Laryngeal mask airway	May be helpful when intubation is not possible	High pressure on upper cervical vertebrae

cal spine occurs during intubation and not during glottic visualization [32–34]. Hence, the clinical benefit of using indirect techniques in cervical spine injury is not proven. Laryngeal mask airway and surgical access are part of the ASA difficult airway algorithm. These are desperate measures to prevent hypoxia when intubation and ventilation are not possible.

32.5.1.3 Management of Systemic Effects of Spine Injury

The SCI can have a multisystem presentation; Table 32.6 provides a brief overview of the systemic manifestations of SCI along with their management.

32.5.2 Medical and Surgical Management of Spine Injury

The medical management or presurgical management of pediatric spinal injuries is not as well described. The role of bolus corticosteroids has been extensively studied in adults, but there is no evidence available from the pediatric population. Similarly, the optimal mean arterial pressure is also not defined for pediatric patients. Hence, the goal for the adult population is followed in children without any level 1 evidence.

32.5.2.1 Cervical Spine Injuries

Conservative Management

Cervical spine injuries can be managed with closed reduction using traction. Halo fixation can be done in children but requires modified instrumentation. Specialized pediatric halo rings are required, and 8–10 pins are used. Less force (2- to 4-inch pounds) is used than is used in adults [36]. A CT scan of the head may be done before the halo ring placement as the areas for pin placement where the skull is sufficiently thick can be identified [37]. However, the complication rates of halo in children are more than in adults. It is estimated that up to 68% of children develop complications after applying traction like pin site infection, skull perforation, or even brain abscess [38]. Perhaps this is why halo is less commonly used these days, especially in countries with tropical weather. Another pertinent risk to be kept in mind while considering traction in children is the risk of overdistraction at the level of injury or atlanto-occipital junction. The reasons for overdistraction may include

Table 32.6 Systemic effects of spine injury

System(s)	Signs and symptoms	Management
Cardiovascular system	***Spinal shock***: Motor and sensory loss below the level of injury, loss of sympathetic autonomic function ***Neurogenic shock***: Hypotension, bradycardia, hypothermia, relative hypovolemia from increased venous capacitance due to functional sympathectomy. Absence of tachycardia because cardiac accelerator fibers arise from T1 to T4 ***Injury above T7***: Decreased adrenal response to stress, absence of tachycardic response to hypotension ***Hypovolemic shock***: Hypotension, tachycardia	Invasive hemodynamic monitoring Vasopressors (norepinephrine, phenylephrine), colloids Mean arterial pressure as per age should be maintained
Central nervous system	Raised intracranial pressure (ICP)	ICP lowering measures
Respiratory system	Airway obstruction, aspiration, flail chest, pneumothorax Poor cough decreased respiratory drive	Intubation, ventilation Chest tube $PaO_2 > 60$ mmHg [35]
Gastrointestinal system	Gastroparesis, neurogenic bowel	Nasogastric tube insertion
Genitourinary system	Neurogenic bladder	Urinary catheter
Coagulation cascade	Deep venous thrombosis (DVT), pulmonary embolism	DVT prophylaxis

ligamentous laxity, less muscle mass, and less body weight [21, 39].

Conservative or non-surgical management is followed in the scenarios of pediatric cervical spinal injury patients, as below.

Neonatal injuries: Neonates can get spinal cord injury during birth either related to an abnormal presentation like a breech presentation or due to the application of assistive devices like forceps. The most common neonatal injury locations are the upper cervical spine, followed by the cervicothoracic junction [40]. Treatment depends on the location of the injury, residual neurological function, and weight of the child. Pang and Hanley reported the use of an external immobilization device (thermoplastic molded device that contoured to the occiput, neck, and thorax) for neonates [41]. Velcro straps across the forehead and torso were used to immobilize the infants completely.

Odontoid epiphysiolysis: The synchondrosis of the C2 body and dens fuses completely by the age of 7 years and is prone to get injuries in preschool-aged children [42]. It can be diagnosed on a plain X-ray where anterior or posterior angulation of the odontoid can be made. This injury can be managed successfully by external immobilization using a halo vest or Minerva jacket. Fassett and colleagues reported that 80% of such injuries could be managed non-operatively, with fusion rates as high as 93% [43].

Atlantoaxial rotatory subluxation is commonly seen in children and can even occur following minor trauma. It often reduces spontaneously, and, if it does not, traction and external immobilization are enough in most cases [21].

Subaxial cervical spinal injuries mandate spinal immobilization for healing. This can be achieved either by external immobilization or internal fixation. External immobilization may be required in conjunction with the placement of temporary traction to restore alignment.

SCIWORA: Patients with SCIWORA may have recurrent episodes; external orthosis may be required for a prolonged period to prevent further injury.

Surgical Management

Many pediatric cervical spine trauma patients have SCI associated with vertebral column injury. These patients may require surgical decompression and fixation. There is no evidence regarding the timing of surgery in pediatric patients with SCI, unlike in adults where an early surgery has been proven to be beneficial [21]. The choice of approach (anterior or posterior) depends on the location of injury and degree of compression of the spinal cord. Moreover, the age of the patient and size of the vertebral body, pedicle, and lateral masses also play a major role in deciding the approach. It is sometimes challenging to find appropriately sized screws and cages that could be used safely in pediatric patients, especially young children.

32.5.2.2 Thoracolumbar Spine Injuries

Fractures of the thoracolumbar (TL) spine are rare in children (1–2% of all pediatric fractures). The commonest mechanism of these fractures is high-velocity trauma, the other lesser common mechanisms being a fall from height and sports trauma. Thoracolumbar fractures are rare in children less than 8 years of age due to the large head to trunk ratio, which results in predominantly cervical spinal injuries. These older children tend to have fracture patterns similar to adults, while the fractures in younger children are different.

Compression Fractures

These are the commonest TL fractures seen in the pediatric population and occur most commonly at the thoracolumbar junction. These fractures are managed conservatively with a thoracolumbosacral orthosis (TLSO) brace.

Burst Fractures

These result from axial loading when the nucleus pulposus is pushed into the vertebral body resulting in damage to the anterior and posterior column. There can be associated retropulsion of fracture fragments into the spinal canal and associated spinal cord or conus or cauda equina injury, depending on the injured spinal level (Fig. 32.1). Burst fractures can be stable as well as unstable, depending on the degree of vertebral body damage and focal kyphosis. Stable burst fractures can be managed conservatively, while the unstable ones require internal fixation in the

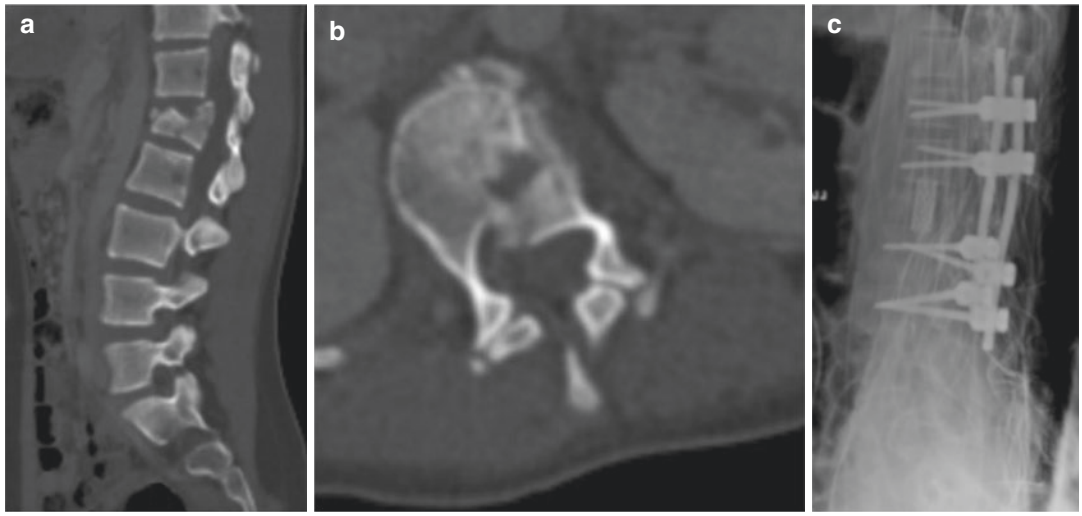

Fig. 32.1 A 13-year-old girl with a history of falls from the first floor of the house and presented with pain complaints in her lower back and weakness in bilateral lower limbs. On examination, she had an ASIA D injury with bladder involvement. A non-contrast computed tomographic (CT) scan of the lumbosacral spine (**a**) sagittal and (**b**) axial section shows L1 burst fracture with resultant kyphosis. She was taken up for L1 corpectomy and pedicle screw fixation; (**c**) postoperative image shows implants in situ

form of pedicle screws with or without anterior column support.

Flexion-Distraction Injuries

Flexion-distraction injuries are a severe form of injuries and include chance fractures. They have high chances of being associated with multiple solid organ injuries, which must be looked for and treated appropriately. These fractures can be purely osseous, purely ligamentous, or a combination of both. Fractures with osseous components alone can be managed by external immobilization like a TLSO brace, while the ones with ligamentous or disk injury will require an internal fixation using pedicle screws.

Spinous Process/Transverse Process Fractures

Blunt trauma can result in fractures of the spinous process or transverse process. Most of the time, there is no instability, and rarely they may be associated with unstable pelvic injuries or iliolumbar ligament injury. Pain control is the only treatment required for these fractures.

32.5.3 Perioperative Anesthetic Management

The children of varying ages (neonate to adolescent) present for surgery following spine trauma. The surgical options for pediatric spine injuries include traction and immobilization, vertebral fusion, laminectomy, etc. Thus, these children need to be managed based on their age and planned surgical procedures.

32.5.3.1 Preoperative Evaluation

Preoperative assessment should include the details of previous medical and surgical procedures, associated medical conditions, previous anesthetic records, and treatment history. A detailed systemic examination must be performed. Thorough neurological assessment and any preoperative deficits should be documented. The airway must be evaluated, and a plan for securing the airway may be formulated. Awake intubation, if needed and feasible, is to be explained to the patient beforehand. All routine preoperative investigations should be ordered.

32.5.3.2 Intraoperative Anesthetic Management

The important aspects of anesthetic management of acute pediatric SCI are summarized in Table 32.7.

Induction of Anesthesia

General anesthesia is the technique of choice for any spine surgery. Induction of anesthesia can be done using inhalational or intravenous (IV) agents. Propofol can be used for induction of anesthesia in children older than 3 years. Non-depolarizing neuromuscular blockers are used for intubation. Armored (reinforced) tracheal tubes reduce the risk of kinking. Intubation in a non-emergent situation may be carried out with any of the techniques described (Table 32.5). Fiber-optic-aided intubation provides better visualization and lesser movement of the cervical spine. The use of fiber-optic intubation in both awake and sleep states is acceptable [34].

Venous access must be adequate. For surgeries in prone positioning, the patient should be turned prone while maintaining the spine alignments. Care should be taken to prevent dislodgment of the lines (intravenous, arterial, and urinary catheters) during positioning. All pressure points must be adequately padded.

Maintenance of Anesthesia

Management aims to avoid spinal cord ischemia by maintaining spinal cord perfusion pressure and providing a bloodless surgical field. Venous congestion should be minimized by careful positioning and avoiding abdominal compression.

Table 32.7 Management goals of anesthesia

- Avoid secondary injury to the spinal cord
- Manual in-line stabilization (MILS) is the best technique to be used with direct laryngoscopy
- Avoid hypoxia and hypotension
- Bradycardia is treated with chronotropic agents like dopamine and hypotension with fluids and vasopressors having α-agonist action
- Judicious fluid management
- Careful extubation depending on the level of spine injury

Inhalation or IV techniques may be used for the maintenance of anesthesia. Propofol may be used for maintenance in children more than 2 months of age [44]. Remifentanil, being an ultra-short acting opioid with profound analgesia, has become a popular choice. It is being used for the maintenance of anesthesia with both inhalation and IV agents.

Intraoperatively, it is advisable to set age-specific targets for MAP and heart rate on a case to case basis. IV fluids, colloids, blood products, and vasopressors might be needed to achieve this goal. Goal-directed fluid therapy using isotonic crystalloids is commonly practiced. Blood loss may be excessive in some procedures and must be replaced; hemoglobin levels are generally targeted at 8–10 g/dL.

Adequate oxygenation with $PaO_2 > 60$ mmHg has been shown to provide some degrees of neuroprotection [45]. Normothermia and normoglycemia (blood glucose <180 mg/dL) should be maintained. Children and infants are prone to hypothermia compared to adults due to physiological differences. Operation theater temperature should be maintained at 27 °C.

Intraoperative Monitoring

Monitoring should include electrocardiography (ECG), blood pressure, pulse oximetry, capnography, anesthetic agent monitoring, temperature, and neuromonitoring (described later). Arterial blood pressure and central venous pressure monitoring may be advocated on a case to case basis, e.g., in patients with associated cardiac disease and where major fluid shifts/blood loss is anticipated. Urine output should be monitored with a urinary catheter.

Recovery and Tracheal Extubation

Early recovery and neurological assessment to determine any complication or new neurological deficits are the goals. However, the clinical condition and the nature of the surgery performed largely determine whether to extubate the trachea or continue elective mechanical ventilation during the postoperative period. Children with high

cervical injury, preoperative respiratory or cardiovascular compromise, and prolonged surgeries are some of the common reasons for postoperative ventilation [46].

Intraoperative Neuromonitoring

Intraoperative neurophysiological monitoring (IONM) is now a standard of care in spine surgery [47]. Various monitoring modalities available are wake-up test, somatosensory evoked potentials (SSEP), motor evoked potentials (MEP), and dermatomal responses.

Wake-Up Test

First described by Vauzelle et al. in 1973 [48], it assesses the anterior, i.e., motor functions, of the spinal cord [49]. It can be performed with both inhalation and IV anesthesia. A standard wake-up test is not possible in infants and small children. In this age group, alternative techniques like tetanic stimulation of lower limbs can be performed [50]. The major disadvantage of the wake-up test is that it cannot assess spinal cord function continuously during the procedure. Also, accidental extubation and air embolism on deep inspiration are practical complications.

Somatosensory Evoked Potentials (SSEP)

Baseline potentials must be recorded to document neurological dysfunction and to assess the feasibility of IONM. A decrease in amplitude of more than 50% and/or increase in latency by 10% is considered significant. Anesthetic agents, level of surgical stimulation, hypothermia, etc. interfere with SSEP. Volatile agents, cold, hypoxia, hypercarbia, and spinal ischemia suppress both SSEPs and MEPs [51].

Motor Evoked Potentials (MEP)

Transcranial MEPs (TcMEP) play a critical role in spine surgery. They are extremely sensitive to the effects of inhalational anesthetics and neuromuscular blockers [52]. Hence, muscle relaxants are to be used sparingly. Ideally, tcMEP monitoring must commence before intubation. IV anesthetic agents like propofol, ketamine, and opioids should be preferred.

Specific Intraoperative Considerations

Important considerations in pediatric spine surgeries include positioning, spinal cord monitoring, blood conservation strategies, and management of complications, including new neurologic deficits.

Positioning

With an unstable cervical spine, the risk of secondary neurological injury during positioning is high. While positioning a patient supine, the log-roll technique and a sliding board should preferably be used.

The prone position is the most commonly used position for spine surgeries. The patient lies with the face facing the floor, and chest and iliac crests are supported by bolsters or jelly rolls such that there is no compression of the abdomen. The head is placed neutral in a headrest or turned to one side. In older children and adolescents, special frames like Wilson's frame or Relton-Hall frame may be used for specific surgical procedures or special operating table, e.g., Allen® (Hillrom; United States) may be used for complex spine surgeries requiring rotation of the patient from supine to prone and vice versa under anesthesia.

Most complications associated with prone position can be prevented by meticulous attention to minute details. The endotracheal tube must be carefully secured, and all lines should be free before making the patient prone to avoid accidental extubation and dislodgement of vascular access. The eye must be taped and properly padded to prevent corneal abrasions, conjunctival edema, and postoperative visual loss. Free abdominal movement is essential to ensure adequate ventilation, reduce intra-abdominal pressure, and reduce bleeding from the epidural plexus. Macroglossia can be prevented by proper head and neck positioning.

Spinal Cord Blood Flow (SCBF)

A single anterior spinal artery supplies the anterior two-thirds of the spinal cord, while the posterior one-third is supplied by a pair of posterior spinal arteries that form a plexus. There is no collateral flow between the anterior and posterior circulations. There are watershed areas at upper

thoracic and lumbar levels making the cord vulnerable to ischemia.

Spinal cord metabolism is lower than that of the brain; SCBF is lower than cerebral blood flow (CBF). Animal data suggest that both SCBF and CBF are regulated by similar factors [53]. Spinal cord perfusion pressure is equal to the difference between the mean arterial pressure and extrinsic pressure on the spinal cord. Extrinsic pressure might occur due to tumor, hematoma, or spinal venous congestion. The autoregulation limits are 45–180 mmHg and may be affected by severe hypoxia, hypercapnia, and trauma [53].

Blood Conservation Strategies

Spine surgeries are prone to major bleeding. Adequate blood and blood products are a prerequisite for surgery. Acute normovolemic hemodilution (if feasible), antifibrinolytic agents (tranexamic acid, ϵ-aminocaproic acid) [54], good surgical technique and hemostasis, correct positioning when prone, hypotensive anesthesia (only with adequate cord monitoring), use of cell saver, intrathecal opioids, and monitor use of coagulation products are techniques that help in blood conservation.

Intraoperative Complications and New Neurological Deficits

Intraoperative complications include secondary injury to the spinal cord, pneumo- and hemothorax, blood loss, and cardiac arrest. Spinal cord injuries can occur due to direct surgical trauma to the cord, distraction injury due to instrumentation, improper positioning, and hypotension or during intubation. If a new neurological deficit is identified intraoperatively, corrective measures like removing the instrument and correction of metabolic causes should be performed. IONM remains the standard of care in spine surgeries to avoid permanent neurologic deficits.

32.5.3.3 Postoperative Management

Postoperative Pain Management

Cervical spine surgeries are associated with the least amount of pain, while thoracic and lumbar spinal fusion and instrumentation are associated with the maximum pain. Various techniques used in pediatric patients include opioids, neuraxial techniques (intrathecal, epidural), regional blocks, wound infiltration, and non-opioid analgesics [55]. Older children can use patient-controlled analgesia (PCA). Currently, a multimodal regimen involving different analgesic techniques is preferred for the management of pain.

Management of Complications

Postoperative complications include the neurologic deficit, visual loss, arachnoiditis, epidural hematoma, anemia, coagulopathy, cerebrospinal fluid (CSF) leak, atelectasis, pneumonia, urinary retention, paralytic ileus, and DVT. Anterior cervical procedures may be complicated by dysphagia, hoarseness of voice, and airway compromise due to hematoma or edema. Awareness of these complications is important for the prevention and management of postoperative complications.

Deep Venous Thrombosis (DVT)

DVT is reported in 2.3–6% of spine surgeries [56]; hypotension, hypovolemia, and hypothermia predispose it. Prolonged or multiple level surgeries and lumbar surgeries further increase the risk of postoperative DVT [57]. Mechanical prophylaxis for low-risk patients and combined mechanical and pharmacological prophylaxis for high-risk patients are advised, preferably, within 48–72 h of surgery [58].

Anterior Spinal Artery Syndrome

Anterior spinal artery (ASA) syndrome results from spinal cord ischemia in the region supplied by ASA. It generally occurs after surgeries involving aortic cross-clamping but may also occur from persistent hypoperfusion or vertebral injury. Clinical features include a motor weakness that is more than the sensory symptoms; the causative factors need to be corrected.

Postoperative Visual Loss (POVL)

POVL is reported in 0.2% cases after spine surgery [59]. Preoperative anemia, blood transfusion, use of Wilson frame, prolonged procedures (>6 h), and posterior approach surgeries are some

of the factors that predispose to POVL [60]. Postoperative visual assessment and ophthalmologic evaluation in case of the deficit should be performed.

Cerebrospinal Fluid (CSF) Leak
Dural tear as part of the surgery or inadvertently causes CSF leak. If left unrepaired, the leak can cause headaches and meningitis.

Epidural Hematoma
An epidural hematoma may occur due to trauma itself or iatrogenically. It may further be complicated by mass effect and subsequent neurologic deficits. An MRI of the spine is the preferred method to evaluate an epidural hematoma.

32.5.4 Intensive Care Management

Pediatric spine trauma patients may require intensive care unit (ICU) admission either for conservative management or after surgery. ICU management is the continuity of care, which begins early in the emergency department (ED). It has a similar focus on stabilization and secondary injury prevention with additional considerations like adrenal insufficiency, autonomic dysfunction, ongoing shock, temperature dysregulation, bowel dysfunction, neurogenic bowel and/or bladder, appropriate nutrition, and prevention of venous thromboembolism and decubitus ulcers [61].

32.5.4.1 Hemodynamic Management

Patients with acute spine injury are prone to neurogenic, hemorrhagic, and/or mixed shock, which necessitates early stabilization in the ED and subsequent management in the ICU. Neurogenic shock leads to vasodilatation and hypotension without a compensatory rise in heart rate. There is unopposed parasympathetic activity due to loss of sympathetic fibers. The risk of neurogenic shock is more with higher SCI and severe (complete) cord injury. These patients may respond to IV fluids but usually will require vasoactive/inotropic support. Drugs having both α and β agonist activity like noradrenaline, adrenaline, or dopamine will be required to maintain blood pressure and prevent reflex bradycardia. Spinal cord injury below T5 will present with hypotension without bradycardia, and drug with an α-agonist activity like phenylephrine is reasonable in such cases.

In cases of polytrauma with a spine injury, hemorrhage may lead to hypovolemic or mixed shock. Aggressive fluid resuscitation and vasopressors may be required to treat hypovolemia and hypotension and control bleeding. The treatment of hypotension is important to ensure adequate organ perfusion and prevent ischemia of the spinal cord. Since many patients with SCI present with some degree of shock, management of shock is crucial during the early stages of ICU stay. Moreover, SCI patients with neurogenic shock are at risk of developing relative adrenal insufficiency and may require hydrocortisone supplementation [62]. These patients have reduced catecholamines, and orthostatic hypotension may persist even after achieving hemodynamic stability, which gradually resolves over a period of time [63].

Bradycardia is common in high spinal cord injury due to loss of sympathetic supply to the heart and parasympathetic overactivity. These patients are also at higher risk of non-specific ST changes and other arrhythmias. A procedure like tracheal suctioning or intubation may trigger severe bradycardia (requiring treatment with atropine) or even cardiac arrest.

32.5.4.2 Respiratory Management

A significant number of patients with SCI present with respiratory compromise. This is particularly seen in patients with cervical cord injury. Depending on the severity of respiratory compromise, patients may require mechanical ventilation support. Nearly half of the patients with cervical cord injury may require prolonged mechanical ventilation [64]. The strategy of mechanical ventilation should be individualized based on the requirement and lung condition. Aggressive respiratory management is needed to prevent secondary lung infections and to wean from a mechanical ventilator. Early tracheostomy should be considered in children where prolonged mechanical ventilation is anticipated.

Tracheostomy improves respiratory care and facilitates early weaning from mechanical ventilation, thereby allowing early mobilization.

32.5.4.3 Management of Autonomic Dysfunctions

Autonomic dysfunctions (or autonomic dysreflexia) in SCI patients result from unopposed afferent stimulation distal to injury level. It is seen in 20–70% of patients with SCI above the T6 level and is unlikely to occur in injuries below the T10 level [65]. Autonomic dysreflexia usually develops weeks to months after the injury but has also been reported as early as the first day following injury.

Any stimulation below the level of injury may initiate the afferent impulse that elicits reflex sympathetic activity. This causes diffuse vasoconstriction and a rise in blood pressure. In normal individuals, this is counteracted by stimulation of baroreceptors in the carotid sinus leading to increased parasympathetic outflow, causing vasodilation and slowing of heart rate. However, in patients with SCI, the parasympathetic impulse cannot travel below the injury level, thereby leading to unopposed sympathetic vasoconstriction below the injury level, causing systemic hypertension. However, the compensatory parasympathetic response occurs above the injury level, causing bradycardia and vasodilation above the injury level.

These patients present with varied manifestations that include severe headache, visual disturbances, nasal stuffiness, anxiety, nausea and vomiting, diaphoresis, flushing, and piloerection above the injury level. The skin may be dry and pale because of vasoconstriction below the level of injury. Hypertension may be asymptomatic or severe to cause hypertensive crisis complicated by left ventricular dysfunction and pulmonary edema. Retinal detachment, seizures, intracranial bleed (hemorrhagic stroke), and death have also been reported. Common stimuli that cause autonomic dysreflexia are distension of bladder or rectum, urinary tract infections, urinary bladder catheterization, pressure ulcers, fractures, and surgical procedures below the injury level. Treatment includes control of blood pressure and removal of noxious stimuli. Blood pressure should be monitored closely, and any possible stimulus like bladder or bowel distension or infection should be treated. If the trigger cannot be identified or blood pressure remains high, pharmacological treatment with drugs having a rapid onset and short duration of action should be initiated, e.g., nitrates (sublingual), nifedipine (oral or sublingual), captopril (sublingual), IV hydralazine, labetalol (if no bradycardia), or infusions of nitroglycerine or clevidipine (with close titration of infusion using intra-arterial pressure monitoring).

32.5.4.4 Prophylaxis of Deep Vein Thrombosis (DVT)

Children with significant SCI are at risk of developing DVT and thrombo-embolization due to immobilization of limbs and body. The incidence of venous thromboembolism in the pediatric trauma population is reported to be 0.2–0.33%, and SCI is an independent risk factor for venous thromboembolism [66]. The risk of venous thromboembolism is higher in adolescents compared to infants and children. Thus, mechanical and/or pharmacological prophylaxis should be used based on the appropriateness of each patient. Early mobility decreases the risk of VTE.

32.5.4.5 Bowel and Bladder Dysfunctions

Neurogenic shock in SCI patients may result in shock bowel syndrome due to prolonged periods of bowel hypoperfusion. These patients should be managed with aggressive volume resuscitation to restore perfusion to the injured bowel. Bowel and bladder dysfunction are common in patients with SCI, ranging from incontinence to retention. An appropriate regimen for the evacuation of bowel and bladder and proper hygiene is important for providing comfort and preventing infection. Neurogenic bowel regimens may include the use of drugs like stool softeners and laxatives. Neurogenic bladder may require aseptic intermittent catheterization for retention or drugs like oxybutynin to control urinary incontinence.

32.5.4.6 Thermo-Dysregulation

Patients with SCI may manifest with altered body temperature regulation such as poikilothermia (body temperature varies according to environmental temperature) or quad-fever (fever occurring for weeks to months after injury) [67, 68]. This thermo-dysregulation is more common in high SCI patients [67].

32.5.4.7 Nutritional Care

Early enteral nutrition is the goal and should be started as early as possible. Determining each individual's appropriate calorie requirement is crucial to provide adequate nutrition and improve health and recovery. Immobility also leads to bone demineralization and osteopenia, particularly in patients with high SCI. Vitamin D deficiency is common in these patients, and it should be supplemented. The spontaneous pathological fracture may develop due to osteopenia [69].

32.5.4.8 Prevention of Decubitus Ulcers

Frequent change of patient's position at regular intervals (every 2–3 h) and air mattresses are important to prevent decubitus ulcers.

32.6 Rehabilitation

Rehabilitation in children with spinal cord injuries poses unique challenges due to the complex developmental process of the child. Thus, the approach should be age-appropriate and family-centered with the active involvement of parents in child development. Generally, the rehabilitation care following SCI is divided into acute and long-term phases [70]. In an acute setting, the goals are to prevent muscle contractures and muscle wasting, as well as to prevent pressure ulcers [71]. The long-term challenges in chronic SCI management include regaining function for daily living activities, maintaining muscle mass, and re-establishing family and community involvement [61].

The SCI in children can result in spasticity or may affect the growth and development of the skeleton requiring orthopedic correction procedures. Spasticity, caused by upper motor neuron injury, is usually managed by non-pharmacological modalities like physical therapy, hydrotherapy, as well as by drugs [5]. Physical therapy includes a range of motion exercises and passive stretching that reduces spasticity and improves the movement range over time. Hydrotherapy also helps to decrease the spasticity and lower the requirement of antispasmodic medications. Various oral drugs have been used to treat spasticity, the most common being baclofen, which acts as an agonist on GABA (inhibitory) receptors. Children with focal hypertonicity may benefit from intramuscular injections of botulinum toxin. It inhibits the release of acetylcholine from the pre-synaptic axons at the neuromuscular junctions [72]. Pediatric SCI may cause spastic hip subluxation or dislocation. This is a common sequel involving over 90% of children with SCI below 10 years of age. Moreover, injury before spine maturity may lead to spine deformity such as scoliosis, and two-thirds of these children will require surgical interventions in the later part of life [5]. Stem cell-based interventions for SCI are still in experimental stages. Animal studies have shown some benefit, but clinical studies so far have not shown encouraging results.

The primary aim of rehabilitation is to gain independence, which can be achieved either by restorative or compensatory interventions. Exercises appropriate for the child (designed/ modified according to the patient's limitations), electrical stimulation, and prostheses enhance the ability to restore independence and maintain an active lifestyle [73]. Involvement with the community and participation with diverse peer group improves the quality of life and emotional health [74].

32.7 Conclusion

Pediatric spine injury, though rare, is a devastating entity. Appropriate and timely management of these children may prevent secondary injuries and help to achieve a better outcome. The management includes maintenance of airway, circulation, and immobilization of spine in the pre-hospital setting and early resuscitation in ED

and ICU with a focus of care on treating shock, respiratory insufficiency, and stabilization of an unstable neck and/or spine while preventing the secondary injuries, simultaneously [61]. Radiology plays an important role in determining the extent of the injury and the need for surgery. However, interpretation of imaging requires an understanding of age-related differences between pediatric and adult spines. Although there is no evidence regarding the appropriate timing of surgery in pediatric patients, early surgical intervention and stabilization of the spine can facilitate early mobilization of these children and reduce complications. Perioperative management should aim at maintaining hemodynamic and respiratory parameters, facilitate surgical conditions and neuromonitoring, prevent perioperative complications, minimize pain, and enhance early recovery. Most of the children will require long-term rehabilitation to gain independence and improve their quality of life. Family and community support can play a major role in helping the child adjust and cope with long-term challenges and transform a potentially life-ending injury to a life filled with new possibilities and hope.

Conflict of Interest None to Declare.

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33 Anesthesia for Interventional Neuroradiologic Procedures in Children

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Key Points

- Anesthesia for neurointervention in pediatric patients assumes greater significance with advances in neurointervention technology, including advances in coils, catheters, embolization devices, and other equipment.
- It is challenging to provide anesthesia in a non-operating room for the pediatric patient where at one end of the spectrum there is the concern of radiation and monitoring while, at the other end, there are specific challenges that may arise during the process of intervention.
- All elective cases should ideally undergo a detailed preoperative anesthesia assessment, but sometimes an on-table evaluation is carried out due to emergency nature of the procedure. The nature of urgency of the procedure should be discussed with the radiologist, neurologist, or neurosurgeon to allow proper scheduling or resource allocation.
- The neuroanesthesiologist should provide immobility, periodic ventilatory variations, and smooth recovery with a watch on intracranial pressure.

33.1 Introduction

Interventional neuroradiology has advanced by leaps and bounds in the current decade due to advancements in both hardware and imaging. The scope of neurovascular intervention in children is important as even though pediatric brain malformations are rare (0.06–0.11%), the risk of rupture is higher than in adults [1] and is the most common cause of spontaneous intracranial hemorrhage and recurrent debilitating seizures in this age group. For the neuroanesthesiologist, it brings to the table the issues of maintaining physiology of the brain and difficulties of administering anesthesia in the unfamiliar non-operative environment along with the usual challenges of a

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pediatric patient. The commonly encountered pediatric neurointerventional procedures may be diagnostic or therapeutic (Table 33.1).

33.2 Relevant Neuroanatomy

The vascular neuroanatomy of a child is different from an adult because of the inflexibility of the vasculature and the associated physiology, which can rapidly produce symptoms or be lethal, unlike in an adult. The parent artery supplying the **anterior cerebral circulation** is the internal carotid artery (ICA), which consists of seven embryonic segments and is classified by Bouthillier [9] as C1 (cervical), C2 (petrous), C3 (lacerum), C4 (cavernous), C5 (clinoid), C6 (ophthalmic), and C7 (communicating). The variations in the ICA occur in the segmental agenesis of the embryonic segments or deviations in the course. The branches of these segments and their anatomical knowledge are important to anticipate complications during the intervention (Table 33.2). The posterior circulation is supplied by the vertebral arteries (VA) that combine to form the basilar artery (BA), which then divides into the posterior cerebral arteries (PCA) (Table 33.3).

Collateral or anastomotic pathways are vascular pathways, which provide alternate perfusion if the primary vessel is occluded. They include primary collaterals from the circle of Willis (CoW) and secondary collaterals from the ophthalmic artery (extracranial-intracranial pathways) and leptomeningeal vessels. The CoW collaterals are useful in acute and chronic cerebrovascular-occlusive diseases (CVOD). However, a complete CoW is present in only 40% of cases [10]. Extracranial-intracranial anastomosis is useful in chronic CVOD and more so when any material injected into the external carotid artery blocks the anastomosis. Leptomeningeal vessels supply the watershed zone and have a role in acute infarct of those areas during hypotensive episodes.

Table 33.1 Commonly practiced pediatric neurointerventional procedures

Diagnostic procedures	Therapeutic procedures
• Cerebral or combined cerebral and spinal angiography for [1, 2] known or suspected vascular malformations, vasculitis, moyamoya disease, intracranial hemorrhage, headache, acute stroke, intractable epistaxis • To diagnose neoplasm or infection and fluoroscopy-guided biopsy of lesions	• Embolization of congenital pial arteriovenous malformation (AVM) in the brain [2], dural AV shunts [3], the vein of Galen malformation (VOGM) [4], extracranial vascular lesions of head and neck, and spinal vascular malformations [5] • Ischemic/embolic stroke intervention within the window period [6] • Catheter-based mechanical or chemical thrombolysis in dural sinus thrombosis [7] • Intra-arterial delivery of chemotherapy (melphalan) as a treatment for retinoblastoma

33.3 Pre-Procedural Preparation of the Child

A quick pre-intervention evaluation by the anesthesiologist needs to be carried out when a child is posted for interventional procedures. Most of these interventions are carried out as daycare procedures, e.g., spinal arteriovenous fistula (AVF), intra-arterial chemotherapy for retinoblastoma, etc.

33.4 History

An important history in a pediatric patient is about fasting hours or nil per oral status. This is followed by a detailed history of the current illness. The important points in this regard are the following:

- **Cavernous malformation**: They most commonly present with seizures (45%) and cerebral hemorrhage (41%).
- **Hereditary hemorrhagic telangiectasia**: The most common presentation is epistaxis, while the central nervous system (CNS) lesions can also present with stroke, transient ischemic attack (TIA), and abscess.

Table 33.2 Internal carotid artery (ICA) segments, their branches, and supply areas with their clinical implications

ICA segments	Branches	Areas of brain supplied	Clinical importance
C4	Tentorial and inferior hypophyseal artery	Nearby cranial nerves	Anastomose with the external carotid artery (ECA)
C5	Ophthalmic artery (OA)	Eyeball, ocular muscles, etc.	When there is the regression of OA, then the entire orbit is supplied by the middle meningeal artery, and with this variant, any tumor embolization (e.g., meningioma) supplied by ECA can cause blindness
Terminal ICA divides into anterior cerebral artery (ACA) [A1 (horizontal segment), A2 (vertical segment), A3 (genu segment), and A4–A5 (terminal portions)] and middle cerebral artery (MCA) [M1 (horizontal segment), M2 (insular segment), M3 (opercular segment), and M4 (cortical branches)]	A1→small perforating branches called medial lenticulostriate arteries (out of which the largest is the recurrent artery of Heubner) A2→orbitofrontal artery and frontopolar artery A3→pericallosal and callosomarginal artery M1→medial and lateral lenticulostriate (LS) arteries, anterior temporal artery (ATA)	The superficial and deep branches supply the inferior frontal lobe, the medial surface of the frontal and parietal lobes, anterior corpus callosum, deeper cerebrum, diencephalon, the limbic structure, head of caudate, and the anterior limb of the internal capsule LS→perforating branches Supplying basal ganglia and capsular regions ATA→anterior temporal lobe	Hypoplastic A1 occurs more commonly than aplastic A1 Aplastic A1 occurs with ACom (anterior communicating artery) aneurysm where any compromise of the neck can lead to frontal lobe infarct

Table 33.3 Vertebral artery (VA) and basilar artery (BA) branches and areas supplied with their clinical importance

Artery	Branches	Areas of the brain supplied	Clinical importance
VA	PICA (posterior inferior cerebellar artery)	Brainstem, inferior cerebellar hemisphere, vermis, and choroid plexus	Occlusion of PICA (or, vertebral artery) leads to Wallenberg syndrome (neurological manifestation due to involvement of brainstem and cerebellum → vertigo, nausea, and truncal ataxia)
BA	Anterior Inferior cerebellar (AICA), superior cerebellar (SCA), posterior cerebral arteries (PCA), and brainstem perforators PCA segments are P1(pre-communicating), P2(ambient), P3 (quadrigeminal), and P4 (terminal)	AICA → anterior inferior part of cerebellum, internal auditory meatus nerves SCA→superior part of the Cerebellar hemispheres Occipital lobe, the inferior part of the temporal lobe, and various deep structures including the thalamus and the posterior limb of the internal capsule	The most important variant clinically is the "Fetal PCA" where the P1 segment is absent or hypoplastic and the PCom (posterior communicating artery) is larger than the P1 segment [and supplies blood to the PCA from the anterior circulation (or, ICA)] Therefore, in PCOM aneurysm with fetal PCom, any inadvertent block of PCom can lead to occipital infarct

- **Vein of Galen malformation (VOGM)**: They comprise 30–50% of all vascular malformations in children with an incidence of 1:25,000 [11]. Postnatally, the most common presentation is of congestive cardiac failure (CCF), pulmonary arterial hypertension (PAH) with respiratory distress, or multi-organ failure [12]. The other presentations are

hydrocephalus and macrosomia. The presence of neurological symptoms at presentation implies a poor outcome.

- **Pediatric intracranial aneurysm**: The incidence is around 0.6–4.6% [13] with major clinical symptoms of sudden severe headache, chronic headache, proptosis, hemiparesis, and unconsciousness.
- **Moyamoya disease**: The most common presentation of moyamoya disease in children is clinical features of cerebral ischemia or infarction (hemiparesis, aphasia, sensory loss, etc.), especially when these features are associated with commonly performed vigorous activities like crying, coughing, or blowing, due to reduced blood carbon dioxide ($PaCO_2$) levels. There can be symptoms related to posterior circulation ischemia, like visual disturbances [14]. Other presenting features are headache, seizures, or choreiform movements.

An overview of the distribution of vascular malformations in children based on age [15] has been described (Table 33.4). Other anesthesia-related information should include relevant antenatal histories like perinatal hypoxia, determination of gestational age, history of prior anesthesia exposure, adverse drug reactions and allergy, and immunization status.

Table 33.4 Age-wise distribution of neurovascular malformations with clinical features

Age	Clinical features	Vascular malformation
In-utero	Congestive cardiac failure (increased heart rate > 200/min, ventricular premature contraction, tricuspid regurgitation), hydrocephalus, loss of brain tissue	Pial arteriovenous malformation (AVM) of high flow nature, vein of Galen malformation (VOGM), or dural sinus malformations
Neonatal period	Multi-organ failure, congestive cardiac failure, intracranial hemorrhage, seizures	VOGM, pial AVM, dural sinus malformation
Infancy	Hydrocephalus, seizures, mental retardation, intracranial hemorrhage	VOGM, pial AVM, aneurysm, cavernoma
Childhood	Intracranial hemorrhage, progressive neurological deficits, seizure, headache	Pial AVM, aneurysm, cavernoma, dural arteriovenous shunt

33.5 Physical Examination

Physical examination should be carried out to record baseline vital parameters, hydration status of the child, airway examination, and assessment of the cardiovascular system (CVS), the respiratory system (RS), and the central nervous system (CNS). The pertinent points during airway examination include the history of chronic cold and stuffed nose, which may indicate the possibility of a high-arched palate, while a history of snoring and nasal regurgitation of liquid may indicate lower cranial nerve involvement (sensitivity to opioid, apneic episodes during recovery) [16]. Medication history includes information of any sedative causing respiratory depression that implies heightened sensitivity to these drugs. The airway examination is done as per routine practice, and any anticipated difficulty should prompt appropriate preparation. As in the operation room (OR), the neuroanesthesiologist should maintain an adequate depth of anesthesia and muscle relaxation to prevent any undue rise of intracranial pressure (ICP) during airway management [17].

The respiratory system examination should focus on identifying active infection and differentiation between uncomplicated upper respiratory tract infection (URTI) and lower respiratory tract infection (LRTI). Since it takes around 6 weeks for inflammation to resolve, a decision on delaying the intervention may be taken if respiratory tract infection is present in patients scheduled for non-emergent procedures.

The CVS examination is done based on five main aspects [18]: a) breathlessness due to heart failure and the age-related causes (the first week, left heart obstruction, e.g., coarctation or aortic

stenosis; the first month, left to right shunt, e.g., ventricular septal defect [VSD], atrial septal defect [ASD], and patent ductus arteriosus [PDA]; after the first month, rheumatic fever, dilated cardiomyopathy, myocarditis, endocarditis, arrhythmia), b) cyanosis, c) dysmorphism, d) failure to thrive, and e) scars on thorax implying previous cardiac surgery.

In the scenario of neurointervention, a diagnosis of VOGM should encourage the anesthesiologist to search for other signs of heart failure. Secondly, heart failure should prompt close monitoring of the volume of heparinized flush used during digital subtraction angiography (DSA) and interventions.

The best signs of dehydration are prolonged capillary refill time, decreased skin turgor, and abnormal respiration. In an emergency scenario, severe dehydration should be resuscitated first by isotonic crystalloids like normal saline (NS) or Ringer's lactate (RL) of about 20–60 ml/kg [19].

CNS examination should document the Glasgow Coma Scale (GCS) score, neurologic deficits, and any signs of raised ICP such as vomiting, anisocoria, depressed respiration, etc.

33.6 Investigation

Currently, the consensus is not to routinely investigate a pediatric patient during the preoperative period until it is reasonably certain that the current history and physical examination findings demand it, or it may improve the outcome of surgery [20, 21]. Certain tests like hemoglobin [22] or electrocardiogram (ECG) [23] are done only if there is any expectant blood loss (unlikely in any endovascular neurointervention) or if there is an audible murmur on auscultation. The investigations that have some merit in pediatric patients posted for endovascular neurointervention are:

1. Renal function tests due to exposure to the contrast (associated risk of contrast-induced nephropathy, CIN) and to optimize serum electrolytes (K^+) before the procedure to reduce the risk of wire-induced arrhythmias.
2. Blood grouping and cross-matching are usually done only when the patient is on anticoagulant medications [24].

33.7 Preprocedural Checklist

After the evaluation of the child, a preprocedural check should be carried out comprising of the following:

Support staff or personnel: Any procedure under moderate sedation to general anesthesia (GA) requires second help or personnel trained in pediatric life support. It is recommended that the sedation provider should be able to manage any sedation deeper than intended.

Equipment: An emergency cart should be available, comprising of all the age-appropriate devices required for the resuscitation of an apneic or unconscious patient.

Monitoring devices: All the standard American Society of Anesthesiologists (ASA) monitors such as ECG, pulse oximeter with a pediatric probe, capnometer, and size-appropriate noninvasive blood pressure (NIBP) cuff are used. A temperature probe should be used when the age of the child is less than 2 years. In situations like cerebral aneurysms where beat-to-beat blood pressure recording needs to be monitored, invasive arterial blood pressure recording can be done either at the radial artery or the side port of the femoral line used by the radiologist. The defibrillator with age-appropriate paddles should be checked.

Some newer monitoring devices that are used in intervention lab are (a) mask system with mainstream capnograph (cap-ONE from Nihon Kohden Corporation, Japan) [25] that can be used without any advanced airways; (b) piezoelectric apnea alarm sticker attached to the neck to detect lack of airflow >30 s (Masimo RRa, from Masimo Corporation, USA) [26]; and (c) electrical impedance-based spirometry (Respiratory Motion ExSpirion, from RVM, USA) [27].

A final check of informed consent and fasting status (as per ASA) [28, 29] is done. Special pre-

cautions include the availability of a lead apron, thyroid shields for protection against radiation, extra-long IV extension lines (e.g., 200 cm long) to administer drugs away from the site of the procedure, pressure bags for rapid infusion, and body warmers like forced-air warming blankets to prevent hypothermia. In-line warming devices for warming the IV infusion line are also useful to prevent hypothermia. Figure 33.1 shows a typical image of a neurointervention suite.

33.8 The Procedure of Neurointervention

The incidence of complications in pediatric patients following neurointervention is lower than in adults due to the straight vascular course (particularly in older children), lack of atherosclerosis, and high collateral flow. The incidence of neurological complications is reported at 0.9% [30] or less [31].

Due to the small radial artery, the femoral artery is the preferred route of vascular access for angiography. The arterial puncture may be difficult due to the smaller caliber of the vessel, greater mobility, superficial presence, and a higher likelihood of vasospasm. Hence, ultrasonography may be preferred in such cases, and the contralateral femoral artery may be utilized if there is a previous history of angiography. Alternatively, the umbilical artery may be used in neonates and newborns as the artery remains patent for up to 5 days.

At first, a local anesthetic infiltration is done at the presumed puncture site (especially in cooperative older children while in uncooperative or younger children, general anesthesia is administered before puncture), and the arterial access is established by a micro-puncture needle; ultrasound may be used where the arterial pulsation is feeble. A 4F (French) diagnostic catheter is commonly used; a 5F catheter may be required in the teenagers. Choice of guidewires and catheters is different in pediatric patients based on their weight (Table 33.5) [32]. A continuous warm (prewarmed saline to body temperature is used to prevent hypothermia) heparinized flush is maintained during the procedure. Usually, a bolus dose of heparin of approximately 50–100 U/kg is given, restricting the maximum dose up to 2000 U. It is followed by an infusion of heparinized flush fluid at the rate of 30 ml/h at a concentration of 3000–4000 U/l. However, in very small children, non-heparinized warm saline is also used. The maximum dose of contrast agent (isoosmolar, non-ionic contrast) used is around 4–6 ml/kg in neonates and 6–8 ml/kg in older children [33]. In most cases of angiography (diagnostic), less than 20 ml of contrast agent is used [34] with a maximum dose of 7 ml/kg [35].

Fig. 33.1 Figure shows a neuroradiologic suite with ongoing neurointervention in a child (a) interventional neuroradiologist, (b) anesthesiologist, (c) child on the intervention table, (d) multiparameter patient monitor, (e) angiography monitor, (f) protective shield for radiation exposure, and (g) image intensifier

Table 33.5 Needle, guidewire, and catheter selection based on weight of the patient

Weight (kg)	Needle size in gauge (G)	Wire size in inch	Catheter size
<7	21	0.018	4
<7	21	0.018 or 0.021	4
7–16	19	0.025	5
16–27	18	0.035	5

Since the growing nervous system is more sensitive to radiation, hence, the principle of ALARA (as low as reasonably achievable) is followed. For that, several measures are considered during the procedure such as pulsed fluoroscopy instead of continuous mode, a reduced dose of radiation per pulse/frame/road map [36], a reduced distance between patient and image intensifier, tight collimation to only the area of interest, beam angulation away from radiosensitive areas (like eyes, breasts, testes, thyroid, etc.), use of previous still image instead of live fluoroscopy for review, and low dose protocols [37]. After 1 month, a review of the patient may be undertaken if the total cumulative surface dose is greater than 2 Gy [38].

Anesthesia alerts: A careful titration of intravenous (IV) fluids infused during the procedure is done by taking into account the heparinized flush as a part of the maintenance regimen. There is a high likelihood of hypothermia in pediatric patients due to exposure to the low temperature of the suite, as well as cold flush fluid inadvertently drenching the drapes. Monitoring of body temperature along with the use of forced warming blankets and warm flushing fluids (as mentioned above) should be done routinely.

33.9 Anesthesia Technique

Anesthesia goals are smooth induction and recovery, complete immobility or neuromuscular relaxation during the procedure, maintenance of stable hemodynamics throughout the procedure, anticoagulation maintenance and reversal if required, maintaining adequate cerebral perfusion pressure (CPP), and management of complications and radiation hazards.

There is no consensus over a particular mode of anesthesia in adult patients, but general anesthesia is most commonly used in pediatric patients. The separation anxiety is high in a crying or restless child less than 5 or 6 years of age. Hence, the guardian may be allowed inside the suite at the time of anesthetic induction. For older children, adequate counseling might suffice. In the pre-induction phase, narcotics like IV fentanyl 2–3μg/kg are given to blunt the stress response followed by induction with either propofol 2.5–3.5 mg/kg or thiopentone sodium 5–10 mg/kg followed by neuromuscular relaxation with rocuronium 0.6–1.2 mg/kg, vecuronium bromide 0.08–0.1 mg/kg, atracurium 0.5 mg/kg, or cis-atracurium 0.15 mg/kg. Both total intravenous anesthesia (TIVA) and an inhalational agent may be used for the maintenance of anesthesia. A background infusion of muscle relaxant or time-adjusted boluses should be used for relaxation for immobility during intervention or image acquisition. The intraprocedural volume status should be euvolemia or slight hypervolemia, and isotonic fluids like NS or plasmalyte may be used. After reversal of the residual neuromuscular blockade at the end of the procedure, tracheal extubation may be attempted if the pre-induction GCS was normal, without any clinical or radiological evidence of raised ICP, and the procedure remained uneventful.

The femoral sheath is removed after the procedure, and the site is compressed for 15–20 min or longer as needed to prevent hematoma formation. One common practice is to use a pulse oximeter on the toe of the same limb and compress with a force slightly less than that required to obliterate the pulse wave. A pressure dressing is then applied at the site of the arterial puncture.

All children who undergo intervention under general anesthesia should be observed after the procedure in an area with a multiparameter monitor and oxygen supply with resuscitation equipment nearby. Before shifting to the wards, a safety practice is to wait till the child is awake for at least 20 min in a quiet environment [39] while maintaining oxygen saturation and airway and is normo-

thermic. All children should be kept supine with legs flat for 4–6 h to prevent hematoma formation.

33.10 Commonly Performed Neurointerventional Procedures

33.10.1 Digital Subtraction Angiography (DSA)

Unlike in adult patients, young children are frequently administered general anesthesia even during diagnostic procedures, making it the most frequent procedure to be done under general anesthesia in this patient population.

33.10.2 Intracranial Aneurysm

There are certain stark differences between pediatric and adult aneurysms with a greater male preponderance, more posterior circulation location, increased complexity, non-modifiable comorbidities, a lower rate of vasospasm, and, overall, less mortality [40] in the former. There is insufficient data to establish either clipping or coiling as the standard of treatment in children, even though there is a lean toward coiling in recent times (Fig. 33.2) [41]. A recent meta-analysis suggests similar outcomes [42]. There are limited data concerning the use of flow-diverting devices for the treatment of aneurysms in children. The major concerns of flow-diverting devices in children revolve around the durability and long-term safety of these devices, the ongoing growth of the cerebral vessels in children, and the need for prolonged antiplatelet medications.

The chief anesthesia goal is to prevent rupture through control of BP surges (recorded by invasive blood pressure) that may occur during laryngoscopy, intubation, or anytime during the procedure. Despite adequate measures, the complication may occur, as below:

- **Rupture:** Normally, once the femoral access is established, heparin is used for anticoagulation to attain an activated clotting time (ACT) of 250–300 s. If any inadvertent rupture occurs during the procedure as heralded by contrast extravasation on angiography and the sudden rise of blood pressure (due to increased ICP), the anesthesiologist might need to reverse the anticoagulation with protamine (1 mg of protamine for every 100 U of heparin). Hyperventilation may be needed to reduce the ICP. In the meantime, the radiologist either inflates the balloon (in a balloon-assisted procedure) and/or rapidly packs the rupture with the placement of coils. An external ventricular drain (EVD) can be rapidly inserted to lower the ICP.
- **Thromboembolism** risk is higher if the size of the aneurysm is >10 mm with neck >4 mm. The first sign is the development of a flow defect around the coils. Other signs like abrupt termination of the vessel, loss of arterial branch, absence of blush in the capillary phase, and stagnation of contrast may be seen [43]. The anesthesiologist should immediately increase the arterial blood pressure to improve collateral flow, while the radiologist administers glycoprotein IIb-IIIa receptor antagonists like abciximab or tirofiban, either IV or intra-arterial (IA).

33.10.3 Cerebral Arteriovenous Fistula (AVF) and Arteriovenous Malformation (AVM)

33.10.3.1 Cerebral Arteriovenous Fistula (AVF)

AVFs are usually acquired arteriovenous shunts within the dura mater involving the wall of the dural sinus or nearby cortical vein. They are distinct from AVMs, generally congenital malformations within the brain parenchyma supplied by pial arteries. Unlike in adults who present with pulsatile tinnitus, or ICH, or raised ICP, children commonly present with cardiac features (murmur, CCF, etc.). Hence, in a child presenting with CCF, only palliative embolization is carried out to reduce the failure, followed by a definitive embolization later. With supportive history, the anesthesiologist should include in the pre-

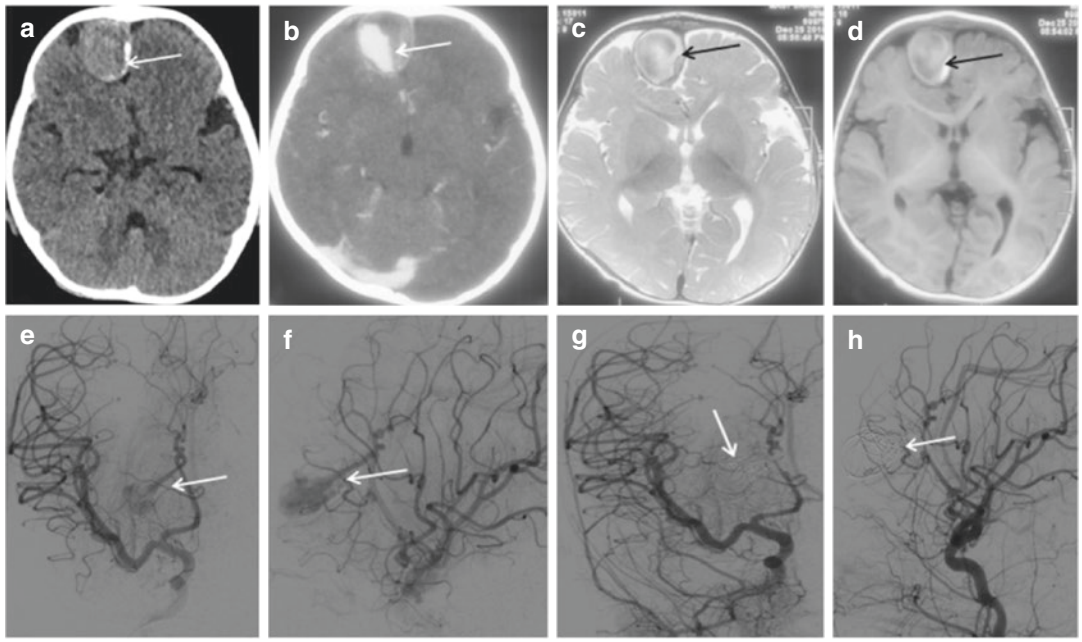

Fig. 33.2 Mycotic aneurysm of the right distal anterior cerebral artery (DACA): A 2-year-old male child presented with fever and irritability. Axial NCCT (**a**) shows a well-defined globular iso-to-mild hyperdense lesion in the right anterior frontal lobe (arrow) with a thin rim of peripheral eccentric calcification. Axial CT angiogram (**b**) shows a filling of contrast within the lesion (arrow) with peripheral eccentric thrombus suggestive of an aneurysm. Axial T2 (**c**) and T1 (**d**) show an aneurysm (arrow) in the right anterior frontal lobe near the anterior interhemispheric fissure with mass effect. Digital subtraction angiography (DSA) (**e**) anteroposterior (AP) and (**f**) lateral view confirm the aneurysm in the right DACA originating from the frontopolar artery (arrow). Post-embolization DSA AP (**g**) and lateral (**h**) show coil mass within the aneurysm with complete exclusion from the circulation (arrow) and good antegrade flow within the distal arteries

anesthesia evaluation a two-dimensional echocardiography (2D- ECHO) to rule out failure and also to identify any right-to-left shunt like patent foramen ovale (PFO) for risk of paradoxical embolization [44, 45].

33.10.3.2 Arteriovenous Malformation (AVM)

In the case of AVM, embolization is either staged (for neonates and infants) or done before surgery (for age > 1 year). The rate of obliteration is inversely proportional to the size of the nidus (<3 cm) and the number of feeder arteries (<4) [46]. The embolic materials used are either solid, like polyvinyl alcohol (PVA) particles, silicon, latex balloon, and coils, or liquid, such as n-butyl cyanoacrylate (nBCA), onyx, and fibrin glue (Fig. 33.3). In recent times, only liquid embolic materials are used for AVM embolization with other materials of mere historical importance. The most important complication during the procedure is stroke due to glue migration to an arterial feeder of the normal brain or a draining vein or hemorrhage due to perforation or venous hypertension accompanying stroke. During embolization, embolic material entry into the arterial side of the AVM may be prevented by hyperventilation. It leads to vasoconstriction in the normally autoregulated (rest of the portion other than AVM) brain and shunting of blood into the AVM (area with impaired autoregulation). Embolic material entry into the venous side of AVM may lead to venous hypertension and subsequent hemorrhage, which is the most feared complication. The embolus entry into the venous side of the AVM may be prevented by a reduction of arterial pressure (slight induction of hypotension) from the baseline values [47]. Post-

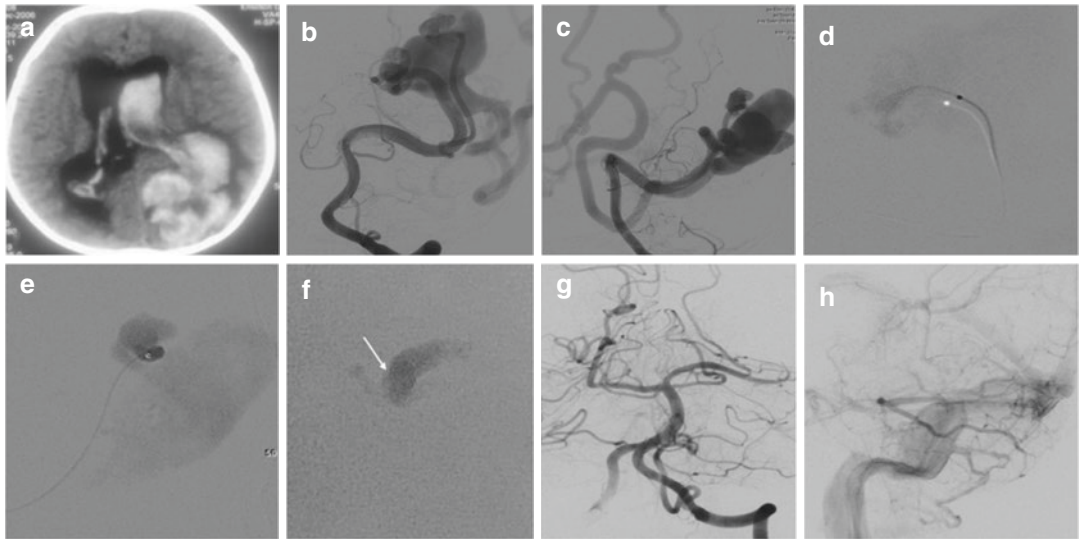

Fig. 33.3 A 7-year-old boy presented with seizures and vision disturbance. Previous CT images (**a**) during acute neurological illness at the age of 6 months show a large occipital bleed with intraventricular extension. Left vertebral artery (VA) angiogram (**b**, **c**) reveal multi-hole pial arteriovenous fistula (AVF) supplied by the left posterior cerebral artery (PCA) branches opening into a large venous sac with cortical venous reflux and venous congestion. Two separate feeders were selectively catheterized (**d**, **e**) using microcatheters and were embolized (**f**, glue cast indicated by white arrow). Control left VA angiogram (**g**, **h**) reveals a complete exclusion of the fistula

embolization, the anesthesiologist should lower the blood pressure to prevent the phenomenon of normal perfusion pressure breakthrough (NPPB). In NPPB, cerebral edema occurs when normal blood flow is restored to the ischemic bed, which has a loss of autoregulation owing to chronic ischemia. This blood pressure regulation should be made both during the patient's transport and in the post-procedure recovery area [48].

33.10.3.3 Vein of Galen Malformation (VOGM)

VOGM presents as CCF in the neonate, hydrocephalus in young children, and headache or SAH in older children. The pre-anesthesia check-up may include a 2D-ECHO. VOGMs are treated with glue (nBCA) embolization (via arterial route) in multiple stages. It is a high-flow malformation, and hence, the glue may fly off to distal parts of draining veins similar to AVM or dural AVF. Hence, hypotension is induced during glue injection (i.e., flow arrest). The choice of agent is based on the expertise of the practitioner, condition of the patient, and blood pressure goals.

33.10.3.4 Retinoblastoma and Intra-Arterial Chemotherapy

Intra-arterial chemotherapy (IAC) is also known as superselective ophthalmic artery (OA) chemotherapy, chemo-embolization, or chemosurgery. IAC is an accepted modality of treatment in group D and E intra-ocular retinoblastoma [International Classification of Retinoblastoma (ICRB)] with good clinical outcomes [49]. Generally, the OA (from femoral artery →ICA→OA→target arteries, i.e., central retinal artery [retina] and ciliary artery [choroid]) is preferred for direct instillation of chemotherapeutic agents such as melphalan (commonly), topotecan, or both. The anesthesia goals include complete immobility during the injection. Post-intubation vasoconstrictors like oxymetazoline or xylometazoline may be sprayed through the nostril on the side of the tumor to ensure that the chemotherapeutic agent stays within the OA [8]. The microcatheter is positioned at the ostia of the OA, which can be ascertained by the characteristic "blush" seen in the choroid on contrast injection with little or no run past the retina. The

chemotherapeutic agent is injected over 30 min (Fig. 33.4).

Two important phenomena require the attention of the anesthesiologist:

1. Respiratory event occurs in 29% of the cases [50]. There is a sudden drop in tidal volume with desaturation without any bronchospasm as reflected by normal capnograph and absence of wheeze when the microcatheter is in the external carotid artery (ECA) or OA even before any injection is given. It can be detected by a decrease in >10 ml of tidal volume when using pressure control ventilation (PCV). The treatment involves informing the neuroradiologist to stop and withdraw the microcatheter, ventilate with 100% oxygen, and administer adrenaline 0.5–1μg/kg boluses intravenously (IV).

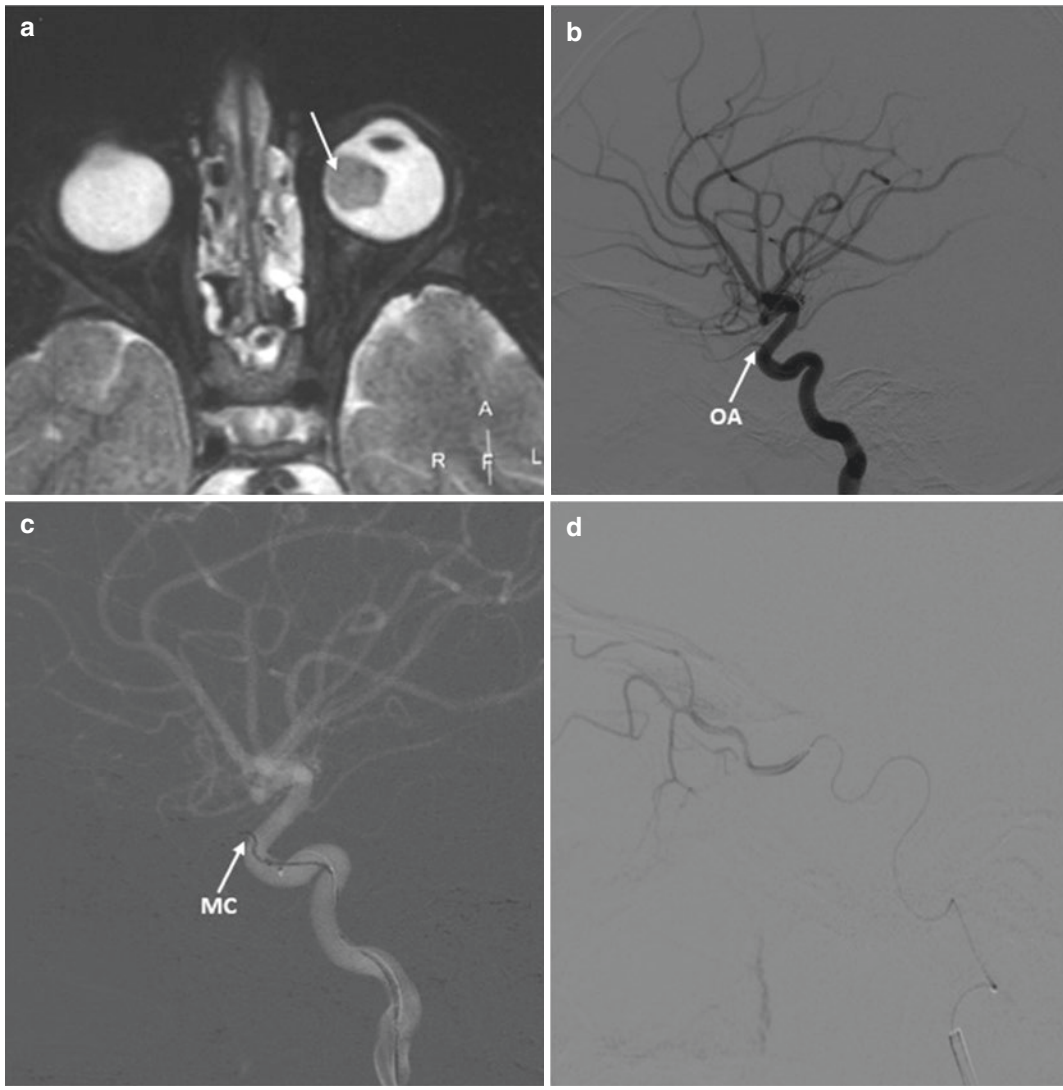

Fig. 33.4 A 4-year-old girl with left retinoblastoma: (**a**) axial T2 image shows a left retinal mass (arrow); (**b**) left internal carotid artery (ICA) angiogram in lateral view: arrow shows left ophthalmic artery (OA), (**c**) roadmap showing superselective access of the left OA with a microcatheter (MC), (**d**) microcatheter angiogram of the OA: chemotherapeutic agents are injected through the microcatheter selectively into the OA

2. Hemodynamic events usually follow the respiratory event in which there is a sudden onset of hypotension and bradycardia when there is the catheter in OA or ICA. Prior administration of adrenaline during the respiratory event prevents its occurrence. The treatment is also adrenaline. Both the events are explained by the "diving reflex" or the "trigemino-cardiac reflex (TCR)" in which the afferent is carried by the ophthalmic division of the trigeminal nerve via the anterior ethmoidal nerve while the efferent limb comprises the vagus nerve [51].

33.10.4 Spinal DSA and Vascular Interventions

Spinal vascular malformations in children are rare, congenital lesions and complex to treat (Fig. 33.5). Involvement of the spinal cord may cause venous congestion and hemorrhage leading to myelopathy. This may present with pain, neurological deficits such as paraplegia, and bladder and bowel involvements [52]. The various presentations and approaches in pediatric patients differ from adults in the following aspects [53]:

1. Clinically, children are more likely to present acutely due to hemorrhage.
2. Genetic syndromes (especially when age is less than 2 years) like hereditary hemorrhagic telangiectasia (HHT) or somatic nonheritable mutation [spinal arteriovenous metameric syndrome (SAMS)] are more likely associated with children.
3. Anatomically, children commonly present with high-flow lesions in intradural (intramedullary or perimedullary), extradural, and paraspinal locations, whereas dural locations are more common in adults.
4. Cervical and thoracic regions are more commonly affected in children.
5. The arteries are more tortuous; hence, instead of the over-the-wire catheter, flow-directed microcatheters are used, and consequently, instead of coils, more often n-butyl cyanoacrylate (NBCA) or small particles such as polyvinyl alcohol (PVA) beads are used.

The decision of endovascular intervention depends on the severity and rapidity of disease progression and the presence of features of a high risk of re-rupture on DSA like pseudoaneurysm with ruptured AVM, nidal aneurysm, or venous outflow obstruction. Generally, the outcome is good

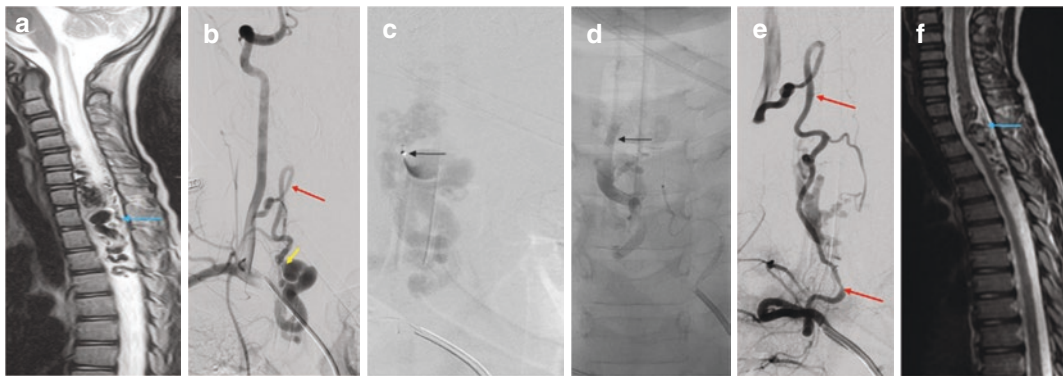

Fig. 33.5 Spinal cord pial macrofistula; a 7-year-old girl with acute onset paraparesis; (**a**) MRI showed multiple dilated vascular flow voids (blue arrow) with extensive cord edema, (**b**) DSA shows macrofistula at the upper dorsal level (yellow arrow), fed by radiculo pial artery (red arrow) from right vertebral artery, (**c**) superselective microcatheter angiography with tip of microcatheter (black arrow) close to the fistulous point for glue injection, (**d**) native image shows glue cast (black arrow); (**e**) post glue embolization, check angiogram shows preservation of the spinal axis (red arrow); (**f**) follow-up MRI shows disappearance of flow voids and cord edema. The child improved significantly 1 month after embolization

(around 60%) [54] with intervention. General anesthesia is used for both DSA (to reduce motion artifact) and intervention. Post-intervention, they are managed in the pediatric intensive care unit (PICU) or neurointensive care unit with the goals of maintaining baseline blood pressure and euvolemia.

33.11 Iodinated Contrast Media (ICM)

Usually, hypo-osmolar (monomer) or iso-osmolar (dimer) (290 mOsm/kg H_2O, e.g., iodixanol) iodinated contrast agents are preferred over hyperosmolar agents [55] for interventional neuroradiologic procedures. Hypo-osmolar ICMs have 2–3 times of plasma osmolality (600–800 mOsm/kg H_2O), e.g., iohexol (Omnipaque), iopamidol (Isovue), iopromide (Ultravist), and ioversol (Optiray), whereas hyperosmolar agents have 5–8 times of plasma osmolality. The reactions to contrast may be anaphylactic, which are IgE-mediated fatal reactions, characterized by tachycardia, hypotension, laryngeal edema, etc. Anaphylactoid or idiosyncratic reaction via complement system activation through histamine and/or serotonin may occur; the symptoms may range from minor (urticaria, pruritus) to moderate (laryngeal edema, bronchospasm) or even severe (hypotension, shock, cardiac arrest). Physiochemotoxic reactions are non-immunologically mediated reactions depending on ionicity, volume, osmolality, and route of administration of the contrast agents and may present with nausea, flushing, and *contrast-induced nephropathy (CIN)*. To prevent these, a set of questions can be asked during the pre-anesthetic check to identify the subset of patients who are more likely to have the abovementioned reactions. Patients with a history of previous allergic reactions to ICM, shellfish, and povidone-iodine, asthma (increases risk by 6 times), and thyroid disorders are at an increased risk of allergic reactions [56]. Some patients with increased risk of CIN or *contrast-induced acute kidney injury (CI-AKI)* are renal transplant recipients; patients with a single kidney, with renal malignancy, on dialysis, with diabetes mellitus, and with high blood pressure requiring medication; those who have undergone surgery in the past 6 weeks; and patients with risk factors for chronic kidney disease (renal dysplasia, chronic glomerulonephritis, etc.), acute illness, ICM exposure within the previous 2 days, and the use of metformin.

CIN/CI-AKI is defined as a decline of kidney function represented by either a 25% increase in serum creatinine from baseline or a 0.5 mg/dl (44μmol/l) increase in its absolute value within 48–72 h after IV administration of contrast agent [57]. CIN in the pediatric population has been reported variedly in literature as uncommon [58] to as high as 10.3% [59]. The mechanism [60] of ICM-induced CIN can be by direct cytotoxic effects (proximal renal tubular cell vacuolation), oxidative damage to cells, renal artery vasoconstriction [increased plasma levels of asymmetrical dimethylarginine (ADMA) which inhibits nitric oxide (NO)] causing outer medullary ischemia/hypoxia, etc. As mentioned above, when there are risk factors for CIN, then some preventive measures that can be employed are using iso-osmolar non-ionic contrast medium, withdrawal of nephrotoxic agents especially if eGFR <60 ml/min, a gap of at least 48–72 h between any two contrast studies, stopping of metformin and restarting 48 h later, and minimizing the volume of contrast administration which has been set variedly in different studies ranging from 2 ml/kg [61] to 5 ml/kg [2] while in some the net volume has been fixed as per the number of vessels studied e.g., 2.5 ml/vessel [62] by using saline mixed contrast (50% each) during angiography and using 1–2 ml/vessel. Prophylactic intervention includes pre-procedure hydration by saline 4 ml/kg for an infant or 6 ml/kg for children 6 h before DSA [63]. Still, it is not found to be effective [64] (similarly for N-acetylcysteine [65], sodium bicarbonate [66]).

33.12 Allergic Reactions

For patients with moderate to severe risk of allergic reactions, prior history of cutaneous reactions, upper airway edema, or cardiovascular collapse, the following prophylactic regimen [67] may be used before ICM administration

Table 33.6 Prophylactic drug regimen in pediatric patients with risk of contrast allergy as per elective or emergency case

	Drugs	Dosage	Timing of administration
Elective cases	Diphenhydramine	1.25 mg/kg PO (up to 50 mg)	1 hour before giving contrast
	Prednisone	0.5–0.7 mg/kg PO (up to 50 mg)	At 13, 7, and 1 h prior to giving contrast
	Diphenhydramine	1.25 mg/kg PO (up to 50 mg)	1 hour before giving contrast
	Hydrocortisone	2 mg/kg IV	At 5 and 1 h prior to giving contrast

Table 33.7 Suggested steps in the event of an intra-procedural anaphylactic reaction

i. Recognition of the event, inform the interventionalist and stop the procedure
ii. For cutaneous reactions like urticaria or pruritus (moderate to severe), non-selective antihistamines, like diphenhydramine, either orally or intravenously (IV), may be used (1 mg/kg IV or PO slowly over 1–2 min)
iii. If there is a cardiac arrest, then the pediatric advanced life support (PALS) algorithm [68] should be followed
iv. For bronchospasm, inhaled salbutamol 100μg/puff (6 puffs <6 y, 12 puffs >6 y), IV salbutamol infusion (1–5μg/kg/min), magnesium sulfate 50 mg/kg over 20 min (maximum dose of 2 g), aminophylline 10 mg/kg over 1 h (maximum dose of 500 mg), hydrocortisone 2–4 mg/kg (maximum dose of 200 mg)
v. For shock/ hypotension, a crystalloid bolus of 20 ml/kg is given
vi. Adrenaline: (IV dose) • Bolus: Dilution 1 mg in 50 mL = 20μg/ml – Moderate anaphylaxis: 0.1 ml/kg or 2μg/kg – Life-threatening anaphylaxis: 0.2–0.5 ml/kg or 4–10μg/kg Dose to be repeated every 1–2 min, if unresponsive • In the absence of IV access, IM adrenaline 1:1000 1 mg/ml lateral thigh <6 y = 0.15 mL (150μg), 6–12 y = 0.3 ml (300μg), >12 y = 0.5 ml (500μg) may be used and repeated every 5 min as required • Adrenaline infusion: 1 mg adrenaline in 50 ml (20μg/ml) started at 0.3 ml/kg/h (0.1μg/kg/min) and titrated to maximum 6 ml/kg/h (2μg/kg/min)

(Table 33.6). In the event of an anaphylactic reaction, the necessary steps may be followed (Table 33.7); it includes the recommendations of pediatric advanced life support (PALS) algorithm in case of cardiac arrest [68].

33.13 Radiation Hazards

All personnel including the pediatric patient present inside the radiology suite are prone to adverse effects of radiation exposure. Children are vulnerable as there is a greater risk of radiation-related cancer in children than adults. Usually, children have a high mitotic rate in the cells during the growing phase and are more susceptible to radiation-induced DNA damage. Associated congenital syndromes in these children may prevent recovery of the damaged DNA leading to cancerous conditions. Therefore, to prevent radiation exposure, the number of imaging studies should be minimized, or alternative modalities like ultrasonography or magnetic resonance imaging may be utilized for imaging whenever possible. Other strategies may include shielding the child with lead, use of pulsed fluoroscopy, reducing space between the child and image receiver, and optimizing the distance between the child and radiation source [69].

33.14 Conclusion

The successful anesthetic management of various neurointerventions in the radiology suite depends on a thorough understanding of the pathophysiology of various disorders, the critical steps of the procedure, taking leadership to update the interventional suite environment as per anesthesia requirement, and training of the staff. Even though pediatric neurovascular malformations are rare and complex, the outcome is good with meticulous endovascular techniques. As children have a long life expectancy, every effort should be made to facilitate an uneventful neurointervention by performing smooth induction and emergence from anesthesia and providing continual immobility during the procedure. It is important to remain vigilant during critical steps of the neurointervention and provide a good environment for post-procedure observation.

Conflict of Interest Nil.

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Neuroanesthesia at Remote Locations

34

Gentle Sunder Shrestha and Pradip Tiwari

Key Points

- The number of diagnostic and interventional procedures performed under anesthesia outside operation theater is increasing.
- The unfamiliarity of anesthesiologists with the environment, equipment, procedure, and assistance, as well as medically complex patients, can result in reduced patient safety.
- Pre-procedural patient evaluation and preparation and adequate monitoring are critical to provide safe anesthetic care.
- Adequately trained anesthesia providers, with standard monitoring, proper record keeping, and careful titration of drug effects to achieve a recognized sedation endpoint, are key to maximizing patient safety.
- The presence of a strong static magnetic field, high-frequency electromagnetic waves, darkened room, loud acoustic noise, radiofrequency heating, unintentional projectiles, and restricted patient access creates unique challenges for providing anesthesia in MR units.
- The physical obstacle of the imaging equipment, the distance from the patient, and exposure to ionizing radiation are the challenges for delivering safe anesthesia for CT scan.

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34.1 Introduction

Remote site is defined as any location at which an anesthesiologist is required to provide general or regional anesthesia or sedation away from the main operation theater suite and/or anesthesiology department and in which it cannot be guaranteed that the help of another anesthesiologist will be available [1]. Anesthesiologist is frequently involved in anesthetizing children with neurological disorders undergoing therapeutic and diagnostic procedures. These procedures are steadily increasing every year.

The goals for procedural sedation/ anesthesia are the following:

- "Do No Harm."
- It can be achieved when the child is managed by an adequately trained anesthesia provider, with standard monitoring modalities, proper record keeping, and careful monitoring after the procedure until discharge criteria have met.
- Minimize pain and discomfort.
- Minimize the anxiety of the child and family.
- Abolish movement to improve safety for invasive procedures and to optimize imaging studies.

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34.2 Challenges

Anesthesia at remote locations may pose a significant risk for the patient [2]. Providing anesthesia in pediatric neurological patients outside the operating room creates a new set of challenges for anesthesiologists. Decreased safety can result from the following factors [3]**:**

- **Patient:** Children scheduled to undergo anesthesia at remote locations require special consideration because of the physiological differences. A full appreciation of physiological, anatomical, and pharmacological characteristics is key to safe anesthesia (Table 34.1). Children may be too sick or too frail patient with complex medical conditions. In emergencies, little to no information about the patient may be available, and patient preparation may not be adequate. Children with depressed level of consciousness and raised intracranial pressure (ICP) possess unique challenges of maintaining cerebral perfusion, avoiding hypercarbia and hypoxia.
- **Environment:** Unfamiliar location, lack of adequate space for anesthesia equipment and drugs, energy hazards, and compromised assessment of the child increase the risk of complications during the procedure.
- **Equipment:** Unfamiliar equipment layout, inconvenient location of anesthesia equipment and drugs, and new technologies may render the delivery of quality anesthesia difficult. Equipment may also be less well maintained.
- **Assistance and communication:** Support and medical personnel in a remote location may not be familiar with the equipment and drugs needed for safe anesthesia. Working with an individual whom anesthesiologist has not met before and who may not appreciate a fine line between a stable case and a potentially dangerous case may be dangerous.
- **Procedure**: Complexity of procedure, the unfamiliarity of the procedure, and longer duration are the challenges for safe anesthesia.

Table 34.1 Characteristics of children that differentiate them from adults [3]

Physiological	Increased heart rate and metabolic rate Decreased blood pressure Increased respiratory rate and chest compliance Decreased lung compliance and functional residual capacity Cardiac output is heart rate dependent. An elevated ratio of body surface area to body weight Elevated body water content Impaired thermogenesis Less efficient respiration
Anatomical	Less complaint ventricles Transitional circulation Immature sarcoplasmic reticulum Small diameter airways Larger tongue in relation to the oropharynx Larynx more cephalic Epiglottis short, stubby, and omega-shaped Funnel-shaped larynx Prominent tonsils and adenoids Smaller veins and arteries Lesser glycogen stores
Pharmacological	A large volume of distribution for water-soluble drugs Reduced total plasma protein Reduced renal clearance Immature hepatic biotransformation Higher minimum alveolar concentration Immature neuromuscular junction Rapid induction from inhaled anesthetics

34.3 Pre-Procedural Assessment and Preparation

Pre-procedural evaluation and preparation are critical to providing safe and qualified anesthetic care. This includes a thorough understanding of anesthetic techniques and the radiological procedure, preparation of the anesthetizing location and familiarities, and patient preparation.

34.4 Preparation of Patient

The children should be screened for coexisting medical conditions before the procedure; medical conditions should be optimized. A comprehensive medical history and a focused physical examination should be performed. The ASA Practice Advisory for pre-anesthesia evaluation, an evidence-based guideline that explains all aspects of preoperative assessment and testing, should be followed [4]. Inadequate pre-assessment is frequently attributed to sedation-related adverse events and, hence, poor outcomes. Appropriate pre-procedural consultation with a medical specialist and/or anesthesiologist decreases the incidence of adverse outcomes. Informed consent should incorporate detailed information about the planned procedure, potential risks of the procedure, and sedation/anesthesia. ASA fasting guidelines should be followed to avoid the risk of aspiration [5].

Children with increased risk of pulmonary aspiration, depressed consciousness level, raised intracranial pressure (ICP), the possibility of airway obstruction, history of sleep apnea, conditions where increased partial pressure of arterial carbon dioxide ($PaCO_2$) could cause harm, renal or hepatic dysfunction, severe cardiac comorbidities, and a severe pulmonary disorder, premature infants, and uncooperative children are at increased risk of sedation-related complications.

34.5 Premedication

Premedication is usually not required for young infants; however, older children may need premedication. Numerous agents can be used as sedative premedication. Commonly used drugs include midazolam, temazepam, dexmedetomidine, ketamine, and opioids. Midazolam, clonidine, and ketamine are available as an oral formulation. Intranasal dexmedetomidine is an alternative for a child refusing oral premedication. Topical local anesthesia should be used before IV cannulation. Topical lidocaine-prilocaine, liposomal lidocaine, tetracaine gel, and amethocaine gel may be used depending on availability.

34.6 Preparation of Anesthesia Location

The limitations of working in the relative "resource limitation" of the non-theater or non-hospital setting, possible lack of skilled operating department practitioners and/or assistants, and familiar equipment should be recognized. The preparation that is not different than the standard operation theater should be ensured. The proper functioning of the anesthesia machine, monitors, types of equipment related to airway, resuscitation, and safe patient care must be established. ASA standards for basic anesthetic monitoring should be adhered to [6]. The ASA has developed standards for non-operating room anesthesia (NORA) described in Table 34.2 [7].

34.7 Anesthetic Techniques

Anesthetic techniques in the remote location depend on the child's age, underlying neurological condition, drug tolerance, anticipated procedure, and procedure length (Table 34.3). This ranges from monitored anesthesia care (MAC) and conscious sedation to general anesthesia (GA). MAC is an anesthesia service in which an anesthesiologist will participate in the care of a patient undergoing a therapeutic or diagnostic procedure [8]. Sedation is a drug-induced depression of consciousness, a continuum ultimately ending up in GA. While increasing sedation level from minimal sedation through moderate sedation and deep sedation to GA, the physiological system is increasingly depressed. The likelihood of adverse events increases as the level of seda-

Table 34.2 Remote location requirements

- A reliable oxygen source (preferably piped from central source) sufficient for the length of the procedure with a backup supply (equivalent to full E-type oxygen cylinder)
- A source of suction that meets operating room standards
- If inhalation anesthetics are administered, the system for scavenging waste anesthetic gases should be adequate and reliable
- A self-inflating hand resuscitator bag can provide at least 90% and provide positive pressure ventilation, adequate anesthesia drugs, all supplies and equipment needed for the intended anesthesia care, and sufficient monitoring equipment that adheres to the "standards for basic Anesthetic monitoring"
- An anesthesia machine with equivalent functions to that employed in operating rooms is required if inhalation anesthesia is to be provided
- Adequate electrical outlets. "Wet location" should have either electric circuits with ground fault circuit interrupters or isolated electric power
- Adequate lights to the patient, monitoring equipment, and anesthesia machine
- Space sufficient to accommodate required equipment and personnel and to allow easy access to the patient, monitoring equipment, and anesthesia machine
- An emergency cart with emergency drugs, a defibrillator, and other equipment necessary to provide cardiopulmonary resuscitation
- Trained staff to support the anesthesiologist and a reliable means of two-way communication to request assistance
- Building and safety codes and facility standards, if they exist, they should be observed
- Appropriate post-anesthesia care should be provided

Adapted from ASA Guidelines 2018

Table 34.3 Common indications and anesthetic considerations of procedures in remote location

Procedure	Common indication	Anesthetic considerations
CT scan	Trauma, ICH, bone lesion, hydrocephalus, seizures, tumors	– Physical obstacle due to imaging equipment – Distance to the patient – Hazards of ionizing radiation – Exposure to ionizing radiation
MRI	Seizures, vascular lesions (aneurysms, AVMs, hemangioma), CNS inflammation, developmental delay, tumor and staging, sensorineural hearing loss, hypotonia, metabolic disorders	– Screening for ferromagnetic object – MR-safe/ MR-conditional anesthesia equipment – Planning for emergencies – Hearing protection
Gamma knife	Treatment of tumors, arteriovenous malformations, and trigeminal neuralgia	– Absolute immobility while in frame
PET/ SPECT scan	Diagnosis and staging of CNS tumors, identification of seizure foci	– Minimize the effect of the anesthetic drug in cerebral circulation and metabolism – Avoid dextrose containing intravenous fluid
ECT	Severe depression, mania, catatonia	– Amnesia and muscle relaxation – Control of hemodynamic changes of ECT

CT computed tomography, *MRI* magnetic resonance imaging, *PET* positron emission tomography, *SPECT* single-photon emission computed tomography, *ECT* electroconvulsive therapy, *ICH* intracerebral hemorrhage, *AVM* arteriovenous malformation, *CNC* central nervous system

tion increases, and it may not always be possible to predict how an individual will react. Hence, the practitioner should be able to rescue patients whose sedation level becomes deeper than initially intended or develop unanticipated complications. Titrating a drug to effect is key to achieve a recognized sedation endpoint with maximal patient safety. Children may require more sedation and GA as they cannot endure long and/or uncomfortable procedures. The ASA defines four different levels of sedation (Table 34.4) [8]. General anesthesia with endotracheal intubation may be safer than deep sedation in some patients (e.g., infants, obstructive sleep apnea) and procedures on prone position, MRI, and poor access to patient's airway. Laryngeal mask airway (LMA) may be an alternative and easy airway management tool.

Many drugs (Table 34.5), single or in combination, can be used to achieve the required sedation level. Alternative routes like intranasal,

Table 34.4 Depth of sedation provided during remote location neuroanesthesia

	Minimal sedation-anxiolysis	Moderate sedation/ analgesia (conscious sedation)	Deep sedation/analgesia	General anesthesia
Responsiveness	Preserved response to verbal stimulation	Purposeful[a] response following tactile or verbal stimulation	Purposeful[a] response to repeated or painful stimulation	Unarousable to any stimulus
Airway	Intact	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Intact	Sufficient	May be sufficient	Frequently insufficient
Cardiovascular function	Intact	Usually preserved	Usually preserved	May be impaired

[a]Reflex withdrawal from a painful stimulus is not considered a purposeful response

Table 34.5 Commonly used drugs for remote location neuroanesthesia [9]

Drug	Dose	Onset of action (min)	Duration of action (min)	Comments
Chloral hydrate	PO or PR: 30–100 mg/kg	20–30	60–150	No intrinsic analgesia, unpredictable effect, CNS depression with repeat dosing and impaired liver function, gastric irritation, no antagonist
Midazolam	IV: 0.05–0.1 mg/kg (maximum 0.4 mg/kg) *IM: 0.1–0.2* mg/kg PO: 0.5 mg/kg IN: 0.2–0.6 mg/kg PR: 0.3–0.5 mg/kg	2–5 15–20 15–30 10–20 15–30	30–60 45–90 60–90 30–60 60–90	Excellent anxiolysis; combination with opioids may produce respiratory depression; Antagonist: Flumazenil
Fentanyl	IV: 1–4 μg/kg	2–3	20–60	Good analgesia; respiratory depression when combined with midazolam; chest wall rigidity when pushed rapidly; Antagonist: Naloxone
Ketamine	IV: Loading dose: 1–2 mg/kg Maintenance: 0.25–1 mg/kg q10–15 min IM: 2–5 mg/kg	2–5 5–10	15–60 15–60	Dissociative anesthesia may increase bronchial and salivary secretions, good analgesia, emergence hallucinations in children >10 years
Propofol	IV: Loading 1–1.5 mg/kg Maintenance 0.25–0.5 mg/kg every 3–5 min; or infusion of 50–150 mg/kg/min	1–2	5–10	Rapid induction of general anesthesia; can cause apnea
Sevoflurane	Inhalation: 2–3%	–	–	May cause airway obstruction and laryngospasm contraindicated in intracranial hypertension
Dexmedetomidine	IV: 0.5–1 μg/kg loading; 0.2–0.7 μg/kg/h infusion PO: 2.6 μg/kg	10 30–45	85	Anxiolysis, sedation, and analgesia don't depress respiration, may cause airway obstruction
Remifentanil	IV: 0.5 μg/kg bolus; 0.1 μg/kg/min	1–2	2–4	Ultra-short acting can be used in combination with propofol, midazolam, etc.

transmucosal, rectal, and intramuscular routes can be used for children without IV access requiring a lesser sedation level.

34.8 Complications

Complications of neuroanesthesia at remote locations range from common post-anesthetic complications to death. Airway obstruction and respiratory depression due to oversedation are not an uncommon complication. Unintended intubation, difficult bag and mask ventilation, wheezing, desaturation, and aspiration are also encountered. Similarly, IV-related complications, inadequate anesthesia, vomiting, and hypothermia are seen. Equipment malfunction, nerve injury, eye injury, hemorrhage, and death are reported. Allergic reactions to contrast or drugs, radiation injury, and unintentional projectiles are also seen.

34.9 Post-Procedural Care

Children recovering from all forms of sedation should receive care in an appropriately staffed and equipped post-procedural care area. Following the procedure, standard post-procedural care must be achieved even if alternative sites lack dedicated recovery facilities and personnel. The standard of care should be the same as the care provided in the main operating suites. Children should be observed until they are at or near their baseline level of consciousness and are no longer at risk for cardiopulmonary depression or airway compromise. The designated care provider should monitor and record the vital signs, along with continuous pulse oximetry monitoring.

Post-anesthesia care may be provided in the units that are at some distance from the anesthetizing location. The principles of safely transporting the patient should be followed. Problems like the emergence delirium, agitation, pain, airway obstruction, and hemodynamic instability should be anticipated. Nausea and vomiting should be prevented as the Valsalva maneuver resulting from it increased intracranial pressure. Largely the procedures at the remote sites are performed on a daycare basis. Discharge criteria should be established and followed for all daycare cases.

34.10 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a type of scan that uses a magnetic field and radio waves, to produce detailed images of organs and tissues of the body. MRI is increasingly used for diagnostic procedures as well as for therapeutic interventions. The continuous presence of the strong static magnetic field, time-varied magnetic field, high-frequency electromagnetic waves, and restricted patient access creates unique challenges for providing anesthesia in MR units. Other challenges are darkened room, loud acoustic noise, radiofrequency heating, and unintentional projectiles.

Currently, the magnetic field's strength in the scanner used is 1.5 to 3 Tesla (T). One Tesla (T) is the equivalent of 10,000 Guess (G); the earth's magnetic field is only 0.5G [10]. Thus, any ferromagnetic material brought in proximity of the MRI scanner can become a projectile due to the strong, attractive force created by the scanner. Even a small projectile can injure or kill someone in their path.

34.11 MRI Scanner Design [10, 11]

The ASA and American College of Radiology have delineated zones to describe the physical plan of the MRI suite (Fig. 34.1).

- ***Zone I***: This is the area outside the MR environment. It is freely accessible to the general public. Through this area, patients, healthcare professionals, and other employees can access the MR site.
- ***Zone II***: This is the buffer zone between public-accessible zone I and strict-controlled zone III. Patients are received in this zone and are kept under the supervision of MR person-

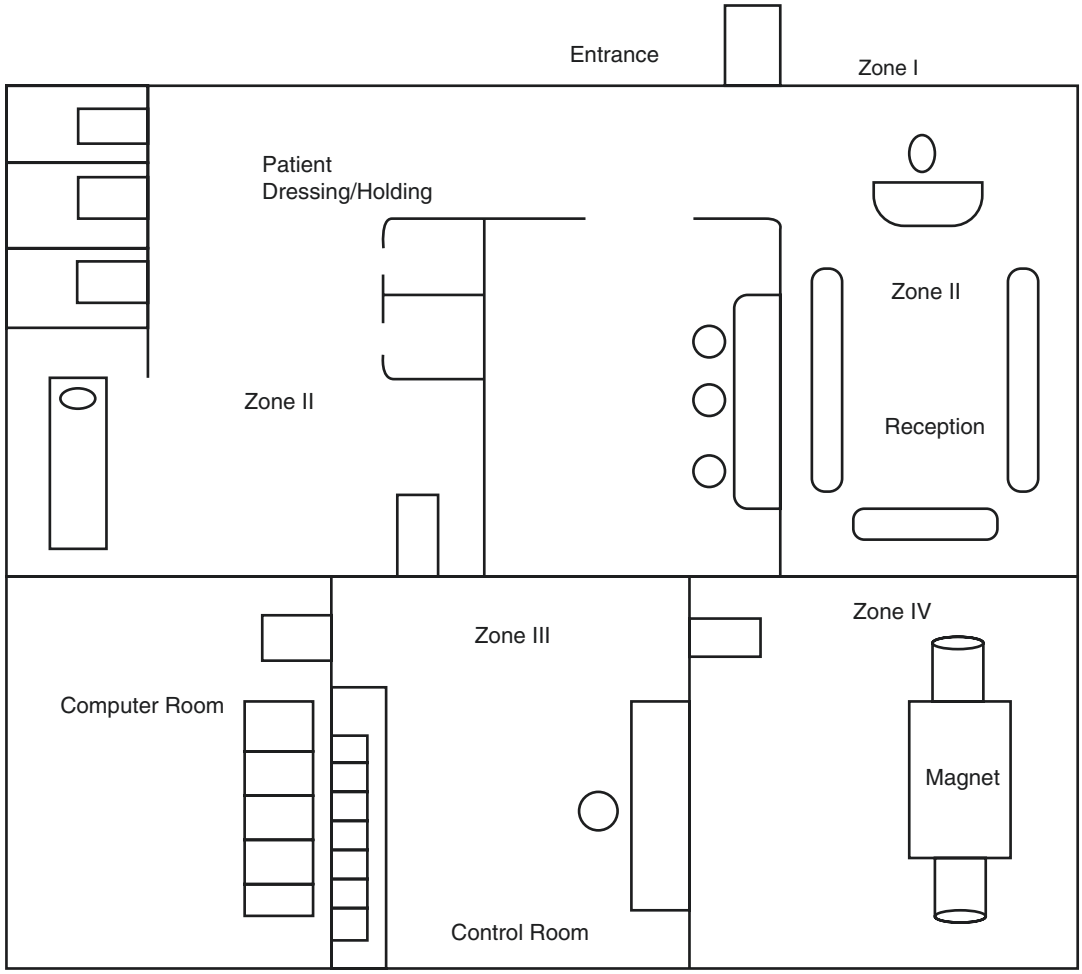

Fig. 34.1 Layout of MRI suite. These are named as zones I through IV with increasing magnetic field exposure

nel. In this zone, answers to MR screening questions and patient histories are obtained. The zone should include an area for the induction of anesthesia and/or management of recovery from anesthesia. It should be equipped with a defibrillator, airway equipment, wall and backup oxygen supplies, suction, code cart, and appropriate drugs.

- ***Zone III***: It is the restricted zone just outside the magnet room. Unrestricted access by unscreened non-MR personnel or ferromagnetic objects can result in various complications due to the interactions between the ferromagnetic objects and the MR environment. All MR-unsafe objects should be removed before entry to zone III.
- ***Zone IV***: This zone contains the scanner magnet and is always located within zone III. All equipment and monitors used in this zone should be MR safe and/or conditional.

34.12 Anesthetic Considerations for MRI

MRI suite is usually noisy and claustrophobic. Complex scans and whole-body scans usually take 20 minutes to 1 hour. Anesthesia is usually required for children and infants to keep motionless during that period. The American College of Radiology and the Joint Commission on Accreditation of Healthcare Organizations have

Table 34.6 Practice advisories for magnetic resonance imaging

- Education:
  - Safety education regarding the physical environment of the MRI scanner
  - Magnet hazards in zone III and IV
  - Limitations and challenges of monitoring
  - Safe response to code blue
- Screening of anesthesia care provider for the presence of ferromagnetic objects
- Patient screening:
  - High-risk medical condition
  - Implanted ferromagnetic devices and objects (pacemaker, cardioverter defibrillator, nerve stimulator, prosthetic valves, surgical clips, orthopedic implants)
  - Embedded foreign bodies (iron filings, permanent eyeliner tattoo)
- Preparation
  - Determination and implementation of an individualized anesthetic plan
  - Optimal positioning of equipment and personnel
  - Plan for the management of emergencies
- Patient management
  - Monitoring: Similar to standards for basic anesthesia monitoring, MR-safe/MR-conditional monitors, provision of remote monitoring
  - Anesthetic care: MR-safe/MR-conditional anesthesia equipment and pumps, light levels of anesthesia is usually adequate
  - Airway management: Appropriate prior airway plan and prior plan to address common airway issues during the procedure
- Management of emergencies:
  Medical emergencies:
  - Initiate CPR whenever indicated
  - Remove the patient out of zone IV
  - Call for help
  - Transport the patient to a previously identified safe area for resuscitation

  Fire, projectile emergencies, and quench
- Post-procedural care:
  - Similar to ASA standards of post-anesthetic care
  - Oral and written discharge instructions

developed standards, guidelines, and recommendations for the MRI suite, and the ASA formulated specific practice advisory (Table 34.6) [12]. The pre-procedural assessment should focus on identifying patients and personnel who have ferrous implants or fragments, surgical clips, cochlear implants, pacemakers, and prosthetic valves.

Most MRI studies are associated with minimal patient discomfort. Patients should receive the same monitoring as suggested by ASA standards for basic anesthesia monitoring. The equipment used in the MRI suite are classified as MR safe, MR conditional, and MR unsafe. MR-safe equipment do not constitute additional MR hazards, while MR-unsafe equipment constitute hazards in the MR environment. The safety of MR-conditional equipment depends on the different properties of the MR environment. Monitors and anesthesia equipment used in zone III and IV must be MR safe/conditional. Frequently light sedation is sufficient, but sedating a child can be difficult and unpredictable. General anesthesia is preferred in sick children and children with raised ICP. The anesthesia induction should be done in a dedicated anesthetic room located outside of the 5 Gauss line. Anesthesia machine used in zone IV should be MR safe or conditional. When MR-safe equipment are not available, IV anesthetic agents and inhalational agents can be delivered using additional circuits or tubing from the equipment in zone III. RF generators produce very loud noises (>90 dB). Hearing protection is mandatory for both the child and healthcare personnel present in the scanning room [13]. Medical emergencies must be anticipated, and a plan must be in place. The recovery of patients undergoing sedation and/or GA should be consistent with the ASA standards of post-anesthesia care [14].

34.13 Management of Emergencies during MRI

The emergencies in the MRI suite include medical emergencies, projectiles, quenching, and fire. When a pediatric patient suffers cardiac arrest in zone IV, cardiopulmonary resuscitation (CPR) should be initiated as indicated; the child should be removed from zone IV and transported to a previously designated area for resuscitation. The resuscitation area, usually in zone II, should be located close to zone IV. Quenching is the rapid, almost explosive, escape of liquid helium and the accompanying loss of superconductivity. A large volume of helium gas is generated; if not properly vented, quench fills zone IV leading to asphyxia. Quenching may occur due to a system

fault or deliberate action to shut down the magnetic field. When quench occurs, the child should be immediately removed from zone IV, and oxygen should be administered.

34.14 Computed Tomographic Scan

The challenges for anesthesiologists for sedation and/or anesthesia during computed tomographic (CT) scan include physical obstacle of the imaging equipment, the distance to the patient, the hazards of ionizing radiation, and exposure to ionizing radiation. Interference in monitoring is not a problem in CT scans. Chemotoxic reactions of contrast agents, renal toxicity, and allergic reactions are additional concerns for contrast-enhanced CT scans (Table 34.7) [15]. Most of the diagnostic scans can be performed without sedation or minimal sedation. Complex interventions require deeper sedation or even GA.

Chemotoxic reactions are caused by the physiochemical effects of contrast agents on organs and vessels. These reactions are dose and concentration dependent. The clinical presentations of contrast reactions may vary depending on the severity (Table 34.8). The incidence of acute adverse reaction to contrast is 5–8% [16]. Severe life-threatening reaction occurs in 0.05–0.1% of injections of conventional contrast media. Otherwise, non-life-threatening and self-limiting, chemotoxic reactions may become life-threatening in unstable children.

34.15 Neuroradiologic Procedures

Anesthesia is increasing requested for different neuroradiological procedures, both diagnostic and therapeutic. Cerebral angiography, embolization, and sclerotherapy of vascular lesions and balloon-occlusion of vascular malformation, as well as radiation therapy to various CNS tumors, have unique anesthetic considerations. The details of these procedures are discussed elsewhere in this book.

Table 34.7 Chemotoxic effects of intravascular contrast

Effects	Mechanism
Vascular changes	
Hypervolemia	Increased plasma osmolality
High cardiac output	Increase in plasma osmolality
Local pain or inflammation	Alteration in vascular permeability
Formation of microthrombus	Alteration in vascular permeability
Increase in blood flow	Dilatation of vessels
Hypotension	Dilatation of vessels
Cerebral changes	
Dilated external carotid artery	Hyper-osmolality
Alterations in systemic blood pressure	Stimulation of chemoreceptors, hyper-osmolality, and sodium load
Fluctuations in heart rate	Stimulation of chemoreceptors
Tachypnea	Stimulation of chemoreceptors
Increased blood-brain barrier permeability	Hyper-osmolality
Variations in neuro-electrical activity	High concentration of ions
Cardiac changes (specific to coronary angiography)	
Dilated coronary artery	Hyper-osmolality
Decrease in heart rate	
Conduction abnormalities	
Ventricular fibrillation	Calcium ion binding
Myocardial depression	Calcium ion binding
Renal changes	
Sustained renovascular constriction leading to decreased blood flow	Hyper-osmolality
Proteinuria	Increase in glomerular permeability
Osmotic diuresis	Non-reabsorbable solutes
Toxic effects on renal tubules	Probable molecular toxicity

Table 34.8 Classification of severity of contrast media reactions

Minor	Moderate	Severe
Vomiting (minimal)	Faintness	Anaphylactic shock
Urticaria (limited)	Vomiting (severe)	Cardio-respiratory arrest
Pruritus	Urticaria (profound)	Seizures
Diaphoresis	Facial edema	Pulmonary edema
Nausea	Airway edema	
	Bronchospasm (mild)	

34.16 Gamma Knife Radiosurgery

Gamma knife radiosurgery is a treatment modality in which radiotherapy is delivered to a very precise area of the brain. This procedure is used to treat brain lesions such as tumors, arteriovenous malformations, and trigeminal neuralgia. Head should be absolutely immobile during the entire length of the procedure because of the use of a stereotactic frame and localization of the treated area to within 1.2–1.3 mm of spatial error (Fig. 34.2). A stereotactic frame will be placed around the head, and MRI brain scans will be done with the external frame in place. The child needs to be absolutely immobile while in the stereotactic frame (Fig. 34.3). Any movement during this time may result in the failure of imaging and skull fracture. Displacement of the pin in the skull might result in epidural or subdural hematoma as well.

The anesthetic technique depends on the length and type of procedure and the patient's comorbidities. Discussion between anesthesiologists, radiologists, and neurosurgeon is key to determine the optimal anesthetic regimen. The discussion should also include the expected length of the procedure, site of the procedure, the expected level of procedural stimulation, and positioning. The procedure requires deep sedation or GA. There is no definitive evidence to suggest the superiority of one anesthetic agent or technique over another. General anesthesia is preferred over sedation as pediatric sedation carries risks such as desaturation, airway obstruction, aspiration, need for emergency intubation, and seizures [17]. As in the other areas outside operation theater, the communication between anesthesiologists and proceduralists is essential, to ensure optimal patient management.

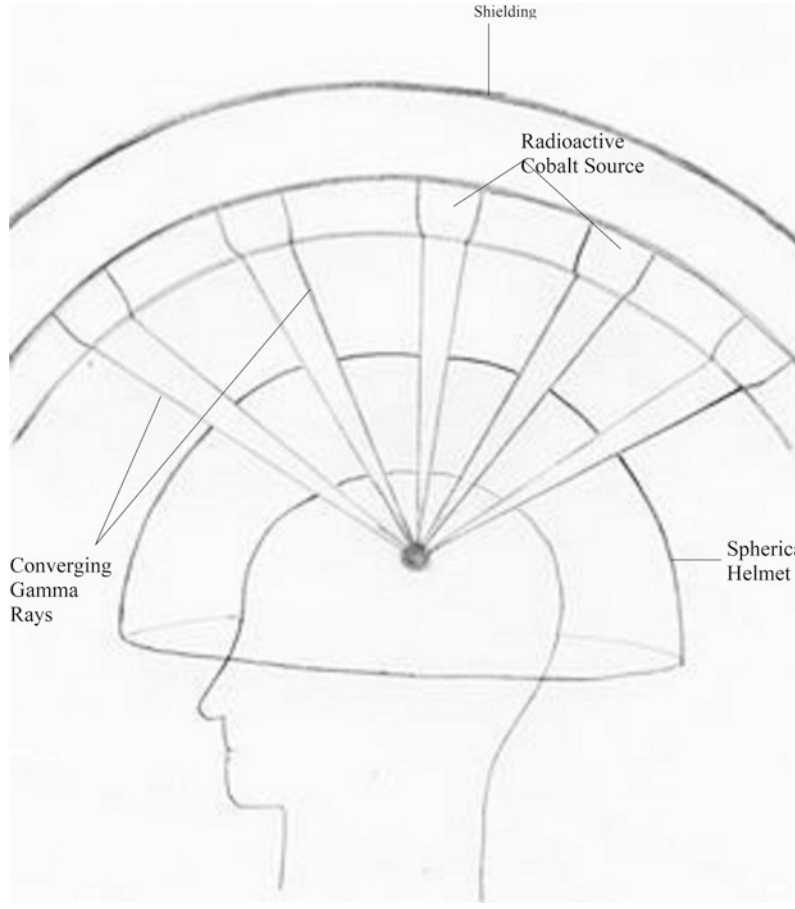

Fig. 34.2 An illustration of the principles of gamma knife radiosurgery. Gamma ray beams converge at the intended target to deliver a therapeutic dose of radiation

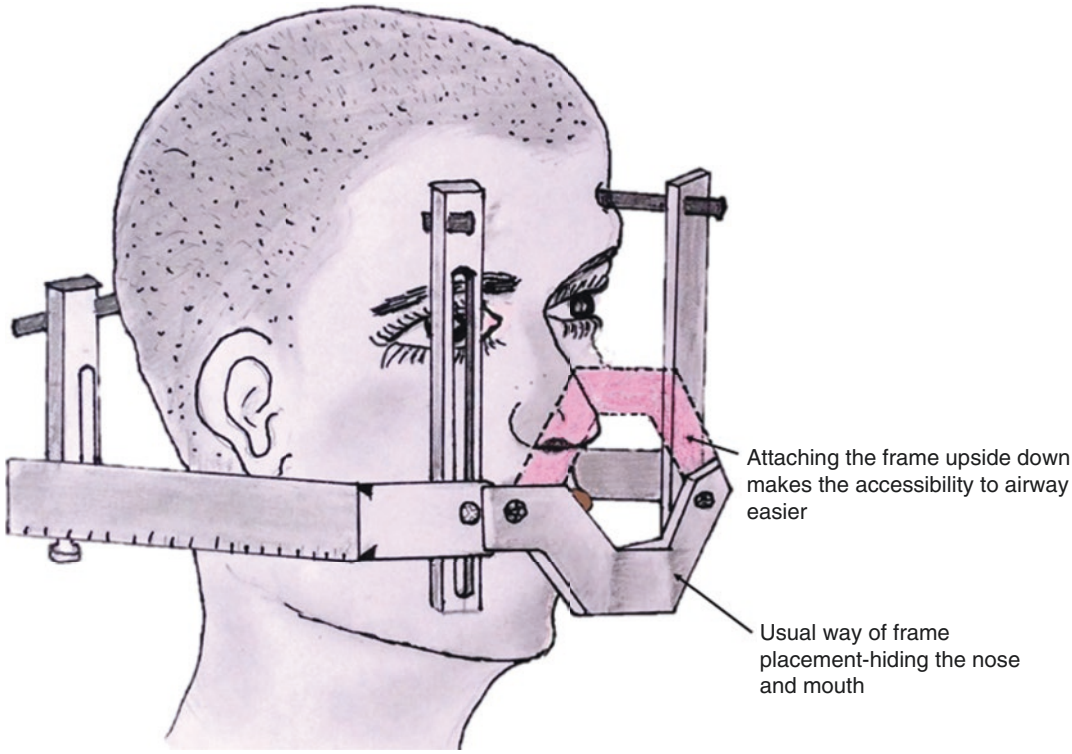

Fig. 34.3 Schematic diagram of the stereotactic radiosurgery frame applied to a child. The anterior arch in front of the face should be placed as inverted "U," as shown by dotted pink shadow to get better airway exposure

34.17 Positron Emission Tomography and Single-Photon Emission Computed Tomography

Positron emission tomography (PET) is a modality to study physiological and pharmacological processes as they occur in the living brain by injecting radioactive compounds. PET scan assesses regional blood glucose uptake and metabolism. Single-photon emission computed tomography (SPECT) is a nuclear medicine technique that maps the regional cerebral blood flow. SPECT scans are used to identify epileptic foci and for evaluation of brain injury and suspected brain inflammation. PET scans are commonly used to distinguish benign from malignant neoplasms, staging the malignancy, determining the response to therapy, and distinguishing scar from residual neoplasm [18]. The PET/ SPECT scan obtained in an anesthetized and stressed child might not correctly represent the awake properties of the brain. Anesthetics can alter the neurophysiological parameters, including cerebral blood flow (CBF) and cerebral metabolism, affecting the kinetics of PET/ SPECT tracers. Also, alteration of hemodynamics due to anesthesia can indirectly influence PET/ SPECT findings; physiological parameters should be monitored and maintained closer to baseline. Both hyper- and hypoglycemia should be avoided as blood glucose levels can affect cerebral function by modulating neuroprotective mechanisms and properties of the blood-brain barrier.

34.18 Electroconvulsive Therapy (ECT)

Electroconvulsive therapy (ECT) induces generalized, tonic-clonic epileptic seizures and several physiological changes. It causes transient activation of parasympathetic activity followed by

more prominent sympathetic activation. Cerebral metabolic rate (CMR) increases, which results in a marked increase in CBF and ICP. There is also increased intraocular and intragastric pressure. The anesthetic requirements for ECT include amnesia and muscle relaxation for and control of hemodynamic changes and related complications. Earlier, ECT used to be administered without general anesthesia (GA), leading to emotional trauma and morbidities. Currently, GA is utilized with propofol (common), methohexital, or thiopentone as induction agents, and muscle paralysis is achieved, preferably with succinylcholine administration. The use of GA for ECT has improved the tolerability of patients, also reducing the morbidities.

In children and adolescents, ECT is being used to treat major psychiatry illnesses such as severe and medication-resistant depression, schizophrenia, bipolar disorder, and catatonia. ECT has been commonly utilized among children between 12 and 17 years to counter severe psychosis, suicidality, symptoms refractory to pharmacotherapy, catatonic symptoms, and self-injurious behaviors [19]. However, no report is available on the use of ECT in children less than 6 years of age. Minor adverse effects such as headache, nausea/vomiting, and amnesia have been reported, which are transient yet common, after ECT. Some patients may end up with severe complications like cardiac arrhythmias and prolonged seizures. Nevertheless, ECT has been increasingly utilized as a treatment modality in children.

34.19 Conclusion

The need for anesthesia and sedation for pediatric patients in a remote location is increasing. Providing anesthesia to a pediatric patient with a neurological disorder is not without risk. Pre-procedural patient evaluation and preparation, trained anesthesiologists, adequate monitoring, and familiarity with the equipment and location are critical for providing safe and qualified anesthetic care.

Conflict of Interest Nil.

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35 Anesthesia for Children with Neuromuscular Diseases

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Key Points

- Neuromuscular disorders (NMDs) are a heterogenous group of conditions characterized by myopathy due to the involvement of muscle, peripheral nerve, or neuromuscular junction.
- They are rare, mostly inherited, with multisystem involvement and associated with serious anesthesia-associated complications.
- Children with NMDs are at risk for respiratory complications owing to poor airway tone, bulbar dysfunction, poor cough with an insufficient clearing of secretions, chronic lower airway disease due to aspiration, and sleep-disordered breathing.
- Cardiac myocyte involvement leads to the development of cardiomyopathy and heart failure.
- Malignant hyperthermia, propofol infusion syndrome, and anesthesia-induced rhabdomyolysis are the major anesthesia-related complications in these children.
- Succinylcholine is contraindicated in any patient with NMD.
- Increased sensitivity to nondepolarizing muscle relaxants may result in the prolonged neuromuscular blockade and, hence, mandates judicious use in conjunction with neuromuscular monitoring.
- A preoperative discussion with a neurologist and meticulous planning are essential to manage a "floppy" child with undiagnosed myopathy successfully.

35.1 Introduction

Neuromuscular disorders (NMDs) are a heterogenous group of conditions characterized by myopathy due to the involvement of peripheral nerve, neuromuscular junction, or muscle [1]. Children with diagnosed or undiagnosed NMDs pose unique challenges to an anesthesiologist owing to their multisystem involvement and increased susceptibility to severe, often fatal anesthesia-related complications. The combined incidence of NMDs is estimated to be 160/100000 [2]. As they are rare, NMDs are not subjected to extensive research. Most of the literature available is based on anecdotal reports and retrospective studies [2, 3]. A majority of NMDs are inherited [4]. Anesthesiologists cater to these

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children as a part of diagnostic workup (e.g., muscle biopsy or magnetic resonance imaging), disease-related surgical procedures (e.g., scoliosis surgeries), incidental surgeries, or in intensive care scenarios. A thorough understanding of the pathophysiology of the disease process and anesthetic implications are critical in the perioperative management of these patients.

NMD refers to many disorders, and discussing all of them in detail is beyond the scope of this text. This chapter focuses on common disorders that have significant anesthetic implications. Moreover, there are several reports of asymptomatic children with undiagnosed myopathies, who develop serious complications while they receive anesthesia for routine surgery. Knowledge of NMDs and their clinical presentation will help anesthesiologists identify undiagnosed myopathy features and direct the patients for further evaluation before proceeding with a non-emergent surgery.

35.2 Classification of Neuromuscular Diseases in Children

The term NMD encompasses more than 70 diagnoses with often overlapping phenotypes [2]. A detailed classification is given in Table 35.1 [5]. However, for simplicity, these can be broadly grouped as myasthenic syndromes (problems with the release of acetylcholine or its action), channelopathies (disorders relating to sarcolemma), dystrophies, myotonias (abnormalities in myofibrils), and mitochondrial myopathies. It is critical to emphasize that overlap in the phenotype exists.

The prejunctional disorders are characterized by the upregulation of acetylcholine receptors and, hence, associated with the possibility of severe hyperkalemia after succinylcholine administration. Junctional disorders like myasthenic syndromes show sensitivity to nondepolarizing muscle relaxants and resistance to succinylcholine. However, it is the postjunctional disorders that are implicated in serious adverse reactions in response to anesthesia. Currently, there is no general consensus available related to the anesthetic management of these patients.

Table 35.1 Classification of neuromuscular diseases (NMDs)

Prejunctional disorders	A. Motor neuron disorders a. Amyotrophic lateral sclerosis (ALS) b. Spinal muscular atrophy (SMA) c. Friedreich's ataxia B. Peripheral neuropathies
Junctional disorders	a. Myasthenia gravis b. Lambert-Eaton syndrome
Postjunctional disorders	A. Progressive muscular dystrophies a. Dystrophinopathy: Duchenne's and Becker's muscular dystrophy b. Limb-girdle muscular dystrophies c. Facioscapulohumeral muscular dystrophy e. Oculopharyngeal muscular dystrophy B. Congenital muscular dystrophies C. Congenital myopathies a. Central core myopathy (Shy-Magee syndrome) b. Multiminicore or multicore myopathy c. Nemaline rod myopathy d. Myotubular myopathy e. Myosin storage myopathy f. Sarcotubular myopathy D. Myotonias a. Myotonic dystrophy: DM1 and DM2 b. Non-dystrophic myotonias: myotonia congenita, paramyotonia congenita, and Schwartz-Jampel syndrome E. King-Denborough syndrome F. Metabolic myopathies a. Mitochondrial cytopathies b. Diseases of carnitine pathway c. Myoadenylate deaminase deficiency d. Glycogenosis type 5 e. Familial periodic paralysis

DM1 myotonic dystrophy type 1, *DM2* myotonic dystrophy type 2

A brief outline of myasthenic syndromes, muscular dystrophies, myotonia dystrophica, mitochondrial myopathies, and spinal muscular atrophy (SMA) are described in this chapter. Other disorders like cerebral palsy and brachial plexopathy that can present with clinical mani-

festations similar to NMDs are also briefly described. General and disease-specific anesthetic considerations pertaining to these disorders are discussed, along with an approach to undiagnosed myopathies.

35.2.1 Myasthenic Syndromes

Myasthenic syndromes particularly involve neuromuscular junction resulting in impaired neuromuscular transmission by affecting either release of acetylcholine (Ach) or its action on the postsynaptic membrane [6]. Of these, 10% occur in children less than 16 years of age. While myasthenia gravis (MG) in adults is an acquired disease, this is not always the case in children. Myasthenic syndromes can be classified into three groups: transient neonatal MG, juvenile (autoimmune MG), and congenital myasthenic syndromes (Table 35.2) [7–9].

Table 35.2 Myasthenic syndromes

Transient myasthenia gravis	• Seen in babies born to mother with MG; 20–30% of them develop clinical signs • **Mechanism:** Passive transfer of acetylcholine receptor (AChR) antibodies across the placenta • **Presentation:** Ptosis, facial weakness, poor cry, suckling and swallowing difficulties, and respiratory distress • **Onset:** Within 72 hours of birth; usually resolves in 5 weeks. Good response to anticholinesterases
Juvenile myasthenia gravis	• Female predominance • **Mechanism:** Autoimmune destruction of AChRs in postsynaptic membrane • **Presentation and clinical course** similar to adult-onset MG. Predominantly ocular symptoms; benign course. Managed with anticholinesterases and steroids similar to adult-onset myasthenia gravis
Congenital myasthenic syndromes	• **Mechanism:** Genetic mutations resulting in decreased neuromuscular transmission. Various types of mutations present at presynaptic, synaptic, and postsynaptic levels. All of them present with fatigable weakness • Genetic testing is necessary for diagnosis. Need to be differentiated from myopathies (due to the possibility of overlapping signs) • Response to anticholinesterases depends on the type of mutation

35.2.2 Channelopathies

As the name suggests, this group of genetic disorders is characterized by dysfunction of voltage-gated/ligand-gated channels on the postsynaptic membrane or sarcolemma [6]. Some categorize these under metabolic myopathies, e.g., chloride ion channel defect in myotonia congenita and calcium and sodium channel defects in hypo- and hyperkalemic periodic paralysis, respectively.

35.2.3 Muscular Dystrophies

Muscular dystrophies refer to more than 30 genetic diseases that result in defective synthesis or regeneration of contractile proteins [10]. They are characterized by weakness due to muscle degeneration. The complete absence or presence of abnormal dystrophin or other glycoproteins results in dissociation of muscle cell contraction from the surrounding connective tissue. Ineffective contraction leads to muscle weakness. Sarcolemmal instability leads to degeneration and atrophy. Most of the degenerated muscle is eventually replaced with fat and connective tissue [6]. Duchenne's muscular dystrophy (DMD) is the most common and most severe form of muscular dystrophy; its clinical features are summarized in Table 35.3 along with those of *Becker's muscular dystrophy* [2, 4, 11].

35.2.4 Myotonic Syndromes

Myotonic syndromes are a set of diseases characterized by the presence of myotonia regardless of the mechanism. Myotonia is a "slow relaxation of muscle following a voluntary (e.g., hand grip) or stimulated (percussion or electric) contraction."

Table 35.3 Muscular dystrophies

Type	Inheritance/genetic defect/incidence	Clinical features	Common surgeries
Duchenne's muscular dystrophy	X-linked recessive Characterized by absent dystrophin 1:3500	Most commonly encountered myopathy in the operating room and most severe dystrophy. Male predominance Presents in early childhood (2–6 years of age) Clinical features depend on the age of presentation Up to 90% have a positive family history. **Clinical features:** Proximal muscle weakness Progressive weakness, wheelchair-bound by 10–13 years Joint contractures (due to limb disuse) Scoliosis in 60–90% of patients (owing to truncal motor weakness) Pseudohypertrophy of calf muscles is the hallmark (muscle bulk replaced by fat) Gower's sign **Other system involvement:** Restrictive pulmonary disease (spine abnormalities and involvement of respiratory muscles) 30% have cardiac manifestations by 14 years; ECG changes (70–80%; poor R-wave progression, deep q-waves in lateral leads) and conduction defects (~48%) Cardiomyopathy (100% by 18 years) Mitral valve prolapse due to degeneration in papillary muscle Usually, die of cardiorespiratory failure by 30 years of age **Management:** Glucocorticoids, gene therapy, and cardiorespiratory support	• Muscle biopsy • Contracture release • Tendon transfer • Correction of spine deformities • Scoliosis surgery is the most common major surgery in this subgroup of patients
Becker's muscular dystrophy	Reduced amount of dystrophin	Milder disease than Duchenne's muscular dystrophy Less severe weakness Presentation in the second decade Milder disease progression Life span can extend till fifth decade Cardiac involvement is rare <16 years of age. But 75% of patients have ECG abnormalities	–

Other triggers are cold temperature and pharmacological agents like succinylcholine. Myotonia dystrophica (with its two subtypes DM1 and DM2) continues to be described as a disease associated with myotonia despite the abundant evidence of its multisystem involvement. In fact, muscle stiffness or myalgia is not a common complaint in this group compared to those presenting with non-dystrophic myotonias i.e., myotonia congenita, paramyotonia congenita, and potassium-associated myotonias (these are essentially channelopathies). The salient clinical features of myotonia dystrophica and myotonia congenita are described in Table 35.4 [12–14].

35.2.5 Mitochondrial Myopathies

These are characterized by inborn errors of metabolism, mainly affecting adenosine triphosphate (ATP) production in mitochondria due to defects in the respiratory chain with an incidence of 1:5000 live births [4]. Defects in nuclear DNA (encodes 85% of protein subunits in mitochondria) follow the mendelian inheritance pattern. They are seen in most pediatric mitochondrial myopathies, whereas defects in mitochondrial DNA (encodes 15% of protein subunits) are seen in adults. At least ten common disorders are described in the literature with varied clinical presentations (Table 35.5).

Table 35.4 Myotonia dystrophica (DM)

Types	**DM1 and DM2** DM2 is seen in adults. It doesn't have a congenital form
Inheritance/genetic defect/incidence	Autosomal-dominant inheritance Unstable repeat expansion disorder Delayed inactivation of sodium channels after an action potential is responsible for myotonia. DM1: CTG nucleotide repeat on chromosome 19
Clinical features	• Three types depending on the age of presentation **Congenital DM1** - Almost always have a maternal inheritance with an aggravated presentation in the newborn due to genetic phenomenon "anticipation" (with each mitosis, the number of repeats increases, making it very unstable) • Born as floppy babies due to generalized hypotonia; tone gradually improves in early childhood. By 10 y, 75% have clinical myotonia. (Absent before 3–5 years of age) • *Multisystem involvement* • Weak cry and impaired sucking and swallowing • Facial diplegia with open tent-shaped mouth • Mental retardation and delayed speech • Aspiration pneumonia and sleep-disordered breathing • Cardiomyopathy and conduction abnormalities • Gastrointestinal manifestations (reflux and gastroparesis) • Endocrinal and psychiatric disorders and cataract **Childhood-onset DM1**—uneventful neonatal period. Moderately delayed early motor development. No typical facies. Speech and learning difficulties, cognitive defects, and psychosocial issues present. Cardiomyopathy and arrhythmias appear in the second decade **Adult-onset DM** is the classical form of DM1
Common surgeries	Muscle/organ biopsies CTEV correction (present in 50%) Inguinal hernia repair Gastrostomy and tracheostomy during later stages of life

DM1 myotonic dystrophy type 1, *DM2* myotonic dystrophy type 2, *CTEV* congenital talipes equinovarus

35.2.6 Spinal Muscular Atrophy (SMA)

SMA is a progressive NMD characterized by degeneration of spinal anterior horn cells and brainstem nuclei [15]. Prominent clinical features are hypotonia, respiratory insufficiency, bulbar dysfunction, and sleep-disordered breathing. It can also be associated with autonomic dysfunction. Of the four types, type 1 presents in infancy and rarely survives to adolescence; SMA types 2 and 3 are present later in life, and type 4 is an adult-onset SMA. Apart from diagnostic, orthopedic procedures, these children require tracheostomy, gastrostomy, fundoplication, and scoliosis surgeries. Most of the complications in these patients are related to the respiratory system as their cardiac function is usually normal.

35.3 Anesthetic Considerations

Children with NMDs have special perioperative requirements and are best managed with a multidisciplinary approach. Anesthesiologists provide anesthetic care for these children in two different scenarios: (A) child with diagnosed or suspected muscle disease and (B) asymptomatic or mildly symptomatic child with undiagnosed or undefined myopathy for routine surgery.

35.3.1 Anesthetic Considerations for Diagnosed NMDs

35.3.1.1 General Considerations

- **Concerns related to respiratory system involvement:** Patients with NMDs are at risk for respiratory complications owing to poor

airway tone, bulbar dysfunction, poor cough (due to thoracic and abdominal muscle weakness along with bulbar dysfunction) with an insufficient clearing of secretions, and chronic lower airway disease due to aspiration [2, 16]. Decreased chest wall compliance with or without the presence of scoliosis and other chest wall deformities, sleep-disordered breathing, and diminished hypercarbia response are also often seen. Additional considerations are tongue hypertrophy leading to upper airway obstruction or intubation difficulties in DMD and gastroesophageal reflux (due to abdominal muscle spasticity and esophageal incoordination) in case of cerebral palsy. Preoperative evaluation of these children should include assessment of baseline oxygen saturation in room air, arterial blood gas (ABG) analysis, and pulmonary function tests (PFTs). Less than 50% forced vital capacity predicted postoperative respiratory complications and vital capacity less than 680 ml predicted daytime hypocapnia in patients with DMD [17, 18]. Preoperative noninvasive ventilation (for patients at risk of hypoventilation) and incentive spirometry (for patients with ineffective cough) could be employed to optimize their respiratory status. Opioids and anesthetic agents are to be judiciously administered and titrated to effect. Children with respiratory compromise might need tracheal extubation on noninvasive ventilation (NIV) or require postoperative ventilation. Chest physiotherapy, adequate pain control, and assisted airway clearance with chest physiotherapy and cough assist devices, along with judicious fluid balance and nutritional support, are essential for good outcomes.

Table 35.5 Mitochondrial myopathies

Genetic defect	Clinical features
• Defects in protein subunits of the respiratory chain • In adults, defects in I and III complexes • In children, defects in I and IV complexes and multiple combinations can be seen	• Can present at any age **Childhood**—More severe, multiorgan involvement • Organ involvement depends on the tissue distribution of defective DNA • Severity depends on the relative concentration of normal and defective DNA in those tissues • **CNS:** Encephalopathy, seizures, stroke associated with hemiplegia, ataxia, and bulbar palsy • Myopathy (varying severity, from exercise intolerance to generalized hypotonia) • Hearing and visual loss • **Gastrointestinal:** Bowel dysmotility and swallowing problems • Cardiomyopathy (20% incidence, contributing to mortality of 70% below 30 years) • **Respiratory involvement** (aspiration) • Nocturnal desaturation and increased opioid sensitivity **Others** • Hepatic and renal involvement • Hypoglycemia and anemia

- **Concerns related to cardiovascular system involvement:** Along with striated muscle, most NMDs can also affect cardiac myocytes. Due to muscle weakness, it is difficult to elicit a history of breathlessness or comment on NYHA status. Heart failure with cardiomyopathy could present with nonspecific symptoms like weight loss, abdominal pain, sleep disturbance, fatigue, and decreased urine output [19]. Similarly, chest pain could be musculoskeletal or cardiac in origin. Hence, careful examination and thorough evaluation in conjunction with a cardiologist are essential for preanesthetic evaluation. Preoperative vitals should be recorded. Resting tachycardia and hypotension at baseline indicate the occurrence of possible severe intraoperative hemodynamic perturbations, especially with major surgeries like scoliosis correction. Careful examination for the presence of murmur, gallop, peripheral edema, and hepatomegaly is needed. Dependent edema is not helpful as it can occur due to no ambulation as well [19]. Needless to say, preoperative ECG is mandatory for documentation of rhythm and acts as a baseline to compare and observe

new changes during the intra- and postoperative period. Echocardiography (resting echo and dobutamine stress echo to evaluate the response of cardiac muscle to intraoperative stress) and Holter monitoring are advocated as per necessity. Cardiac MRI provides information regarding the extent of myocardial fibrosis involvement in these patients. These findings may precede the left ventricular dysfunction and, hence, sometimes advocated in patients with DMD and BMD.

- **Regional anesthesia and NMD:** Cardiorespiratory complications, opioid sensitivity and sleep-disordered breathing, and probability of fatal anesthesia-related complications in children with NMDs make regional anesthesia (as a sole anesthetic technique or in conjunction with general anesthesia) a safer choice. Hence, it should be considered while formulating an anesthetic plan. Younger age, cognitive impairment (even older children might be uncooperative), contractures, and the presence of spine abnormalities (kyphoscoliosis) can make it technically challenging. Meticulous examination and documentation of preoperative neurological deficits are imperative. Regional anesthesia is preferably avoided in rapidly progressing NMD (differentiation between disease progression and the effect of the blockade can be difficult) [20]. Attention to the technique and use of adjuncts like ultrasound should be employed as injuries from needles/catheters and toxic effects of local anesthetics could exacerbate the preexisting nerve damage [21]. Sympathetic blockade due to neuraxial block can exacerbate preexisting autonomic dysfunction and can be detrimental in children with severe cardiac dysfunction; hence, caution should be exercised [20]. Nevertheless, regional anesthesia should be preferred and employed wherever feasible in this patient population.
- **Malignant hyperthermia (MH) susceptibility:** MH is a pharmacogenetic disorder characterized by a hypermetabolic state induced by a defect in calcium homeostasis that results in sustained contracture in skeletal muscles. Its incidence in children is 1:15,000 [4]. Inheritance is autosomal dominant—several of the genetic mutations on chromosome 19 in the area coding for ryanodine receptor (ryanodine controls the release of calcium from the sarcoplasmic reticulum, defects lead to excessive calcium release).

The only NMDs with definite MH susceptibility is King-Denborough syndrome, central core disease, multiminicore disease, and Evans myopathy [2, 6]. Variants of RYR1 and certain variants of CACNA1S and STAC3 genes are associated with MH susceptibility (e.g., periodic paralysis and nemaline myopathies with these gene variants are MH susceptible) [22]. However, MH-like symptoms are seen in many NMDs in response to volatile agents and succinylcholine. It is now established that DMD does not have MH susceptibility, and the symptoms described in the literature are due to rhabdomyolysis.

Caffeine-halothane contracture test is the gold standard for diagnosing MH [4]. With the advent of dantrolene, mortality has drastically decreased from more than 60% to 1.4% by 2000. It is a hypermetabolic crisis presenting with tachycardia, tachypnea, increased end-tidal carbon dioxide ($EtCO_2$), increased oxygen consumption, acidosis, hyperkalemia, muscle rigidity, rhabdomyolysis, and hyperthermia [23]. The triggers for MH are succinylcholine and volatile agents (halothane>isoflurane). Though considered weak triggers, MH reactions continue to occur with desflurane and sevoflurane [4]. Children with MH susceptibility should be scheduled as the first case of the day (minimum volatile concentration in ambient air). The anesthetic station should be flushed for 10 min with more than 10 l/min fresh gas flow to minimize the inhalational anesthetic concentration to less than 10 ppm (with the ventilator switched on after changing soda lime and breathing circuit). Newer workstations might require longer flush times. UK Malignant Hyperthermia Registry issued guidelines recommending 90-second flush before attaching activated charcoal filters to both the limbs [24]. Use of

activated charcoal filters eliminate the necessity of longer flush times and renders anesthesia machine volatile free in less than 3 minutes [25, 26]. Earliest sign of MH is the rapidly increasing $EtCO_2$ [4, 23]. Metabolic and respiratory acidosis along with tachycardia, electrolyte imbalance, and rhabdomyolysis occurs which, if left untreated, may progress to severe hyperthermia, disseminated intravascular coagulation, cardiac and renal failure, and death. Intravenous dantrolene is the definitive treatment for MH. It inhibits ryanodine and thereby the excessive release of calcium from the sarcoplasmic reticulum. Each dantrolene vial contains 20 mg of the drug and 3 gm of mannitol and sodium hydroxide adjusted to pH, which needs to be reconstituted with 60 ml of sterile water. The reconstituted solution turns orange. The usual dose of dantrolene is 2.5 mg/kg as a rapid intravenous bolus. Its complications include muscle weakness, gastrointestinal symptoms, respiratory failure, and chronic phlebitis (slow infusions). Repeat dosing can be given if symptoms reappear. There is no role of preoperative dantrolene [4]. Patients with suspected MH need muscle biopsy, genetic testing, and an identification bracelet.

- **Anesthesia-induced rhabdomyolysis (AIR)** is a phenomenon observed in patients with muscular dystrophy characterized by skeletal muscle breakdown and release of myoglobin, creatinine kinase, and potassium leading to acute life-threatening hyperkalemia after exposure to triggers like succinylcholine or volatile anesthetics [3]. Dystrophin-glycoprotein complex is responsible for maintaining the integrity of sarcolemma during and after muscle contraction. Its absence makes sarcolemma unstable, resulting in its chronic tearing and destruction [3, 4]. Succinylcholine-induced depolarization and fasciculations are implicated with the occurrence of rhabdomyolysis, whereas the mechanism of the volatile agents causing rhabdomyolysis is still unclear. It is postulated that volatile anesthetics make sarcolemma unstable so that any superimposed insult on the already unstable membrane precipitates lysis. Several reports in the literature support this hypothesis. They have evidenced a greater number of complications in the recovery room where volatile agents' concentration is minimal but could have been triggered by factors such as shivering, rigidity, and agitation [6, 10, 27]. It is commonly seen with younger children (<8 year old) due to active destruction and regeneration of muscle bulk compared to the older children and adolescents where the muscle fibers are fibrotic and no longer regenerating [4]. All volatile agents have been implicated in rhabdomyolysis (halothane>sevoflurane>isoflurane), and the minimal safe concentration to use in the patients is not known [4]. Aggressive management of hyperkalemia, hemodynamic support, hydration, and diuresis to prevent myoglobin precipitation in renal tubules is vital [4].
- **Propofol infusion syndrome (PRIS):** All the anesthetic agents are known to affect mitochondrial function, with the prompt restoration of function on discontinuation, but propofol is of particular concern due to the risk of PRIS [2]. Mechanism of PRIS involves impairment of mitochondrial oxidation and transport of free fatty acids, which is similar to the pathophysiology of mitochondrial disorders. Concerns have been expressed about an association between mitochondrial disease and susceptibility to PRIS, which could occur with lower doses and shorter infusion times than normal individuals (the usual implicated dose is >4 mg/kg/h for >48 h). Hence, it is prudent to avoid or restrict its use to very brief procedures in patients with mitochondrial myopathies [4, 6].

35.3.1.2 Disease-Specific Anesthetic Considerations

Most important anesthetic considerations for the common neuromuscular disorders are summarized in Table 35.6 [3, 4, 10–13, 15, 19, 27–31]. Other less frequent NMDs that a neuroanesthesiologist frequently encounters are summarized along with considerations below.

35.3.2 Disorders with Clinical Manifestations Similar to NMDs

35.3.2.1 Cerebral Palsy

It is a spectrum of neurological disorders affecting movement and posture due to injury to the developing brain [32]. These children present with varying degrees of the motor, sensory, and cognitive impairment. Multiple fetal, maternal, and acquired factors have been implicated in its etiology [4, 32, 33]. Clinical presentation of these children and important anesthetic considerations are outlined in Table 35.7 [4, 32–34].

35.3.2.2 Brachial Plexopathy

Birth injury (due to extensive stretch during delivery) and traumatic brachial plexus injury are the

Table 35.6 Anesthetic considerations in neuromuscular diseases

Disorder	Anesthetic considerations	Anesthetic plan
Duchenne's muscular dystrophy (DMD)	DMD is the most severe muscular dystrophy • In DMD – Early childhood→ongoing skeletal muscle damage →rhabdomyolysis, and hyperkalemia in response to triggers are the main concerns – Late adolescence and adulthood→cardiac and respiratory failure are concerns • Possible difficult airway due to progressive fibrosis of masseter muscle (restricted mouth opening) and neck muscles (affecting flexion and extension) • Cardiomyopathy could be undiagnosed as they are wheelchair bound and rarely exert. Preop echo mandatory for diagnosis • Restrictive lung disease, upper airway dysfunction, and sleep apnea. Need preoperative pulmonary function tests. If preoperative forced vital capacity is below 50%, patient might need postoperative mechanical ventilation [10] • On long-term glucocorticoids as a part of the management	• Regional can be safely administered. But it can be challenging due to spine abnormalities • No susceptibility to MH • AIR with succinylcholine and inhaled anesthetics (halo>sevo>iso). Minimal safe concentration not known. Cardiac arrest was reported with even <10 min of volatile-based anesthesia The prudent option is TIVA. There is minimal risk with brief inhalational induction till IV line is secured • Upregulation of endorphin receptors→ increased opioid sensitivity. Titrate opioids carefully • NDMR for induction. Can have prolonged action and high chances of residual paralysis. Use in conjunction with TOF monitoring. No adverse effects with sugammadex • Use potassium free crystalloids. Colloids are safe • **Recovery:** Defer extubation in case of concerns for respiratory depression. High chances of postoperative apnea **Postoperative pain:** NSAIDs can trigger rhabdomyolysis. Use regional techniques wherever possible. Caution with opioids
Mitochondrial myopathies	• Multisystem involvement. Thorough preoperative evaluation, including hepatic and renal function tests and echocardiography • Bowel dysmotility, gastroesophageal reflux along with bulbar palsy→ high risk of aspiration. Anti-aspiration prophylaxis • Preoperative optimization of respiratory function. Treat aspiration-associated infections, and assess for and treat airway reactivity. NIV for OSA and nocturnal desaturation • In patients with lactic acidosis, avoid excessive fasting and lactate-containing solutions	• Volatiles can be used. No risk of rhabdomyolysis. However, caution with cardiomyopathy and ventricular dysfunction • Increased sensitivity to opioids • Succinylcholine is contraindicated • TOF monitoring during NDMR usage. Both sensitivity and resistance to NDMR are possible • Caution with propofol. Even standard doses can cause acidosis mimicking PRIS • Avoid lactate-containing solutions **Recovery** • Might require prolonged postoperative ventilation

(continued)

Table 35.6 (continued)

Disorder	Anesthetic considerations	Anesthetic plan
Myotonia dystrophica (DM)	• Swallowing difficulties and aspiration pneumonia • Cardiomyopathy and conduction abnormalities • High risk for aspiration. Anti-aspiration prophylaxis and modified RSI **Myotonia and considerations** • Triggers can be physical (hypothermia and shivering, electrocautery, surgical stimulation) or pharmacological (succinylcholine, etomidate, methohexital) • Myotonic contractures can interfere with positioning and intubation • Administration of muscle relaxant or regional anesthesia does not prevent myotonic contracture (defect lies in the muscle, not in nerve or neuromuscular junction) • Mexiletine and phenytoin should be handy for its management • Maintain temperature and avoid shivering	• Myotonic contractures can result in an incomplete neuraxial blockade • No susceptibility to MH. Inhalational agents can be used (caution with effects on myocardial contractility). Agents with a faster recovery profile are preferred • Titrate IV agents and opioids to effect. Increased sensitivity was reported • Pain during propofol injection and etomidate can precipitate myotonia • NDMR can be given. Consider dose titration and monitoring. (Muscle wasting is present; even small doses can prolong recovery) • Use of neostigmine is controversial due to a case report mentioning severe muscular weakness after NMB reversal. However, whether the weakness was due to DM or an excessive dose of neostigmine could not be ascertained [30]. This finding was not confirmed in any of the other studies. It is generally agreed that neostigmine does not produce untoward reactions in DM **Recovery and postoperative period** • Respiratory muscle weakness and need for postoperative ventilation. (Majority of anesthetic complications are respiratory; worsening of respiratory symptoms should be anticipated.) • Extreme caution with the use of opioids. NSAIDs are safe. Prolonged postoperative ileus is expected
Spinal muscular atrophy (SMA)	• Cardiac function is usually normal, except in cases of very severe pulmonary hypertension. Preoperative testing is not mandatory • Difficult airway due to joint contractures, cervical spine immobility, and reduced mouth opening have been reported [31]. • There is no risk of MH susceptibility in SMA [15]	• All anesthetic agents can be safely used without any adverse effects • Motor neuron degeneration can cause dysregulation of acetylcholine receptors; succinylcholine should be avoided • As with other NMDs, NDMR should be titrated to effect and in conjunction with neuromuscular function monitoring (increased sensitivity and prolonged action can be seen) **Recovery and postoperative concerns** • Prolonged emergence and need for postoperative mechanical ventilation should be anticipated [15, 31] • Agents that could suppress postoperative respiratory drive should be avoided

MH malignant hyperthermia, *NDMR* nondepolarizing muscle relaxants, *NIV* non invasive ventilation, *OSA* obstructive sleep apnoea, *TIVA* total intravenous anesthesia

common mechanisms of brachial plexopathy in the pediatric population. Risk factors for birth injuries include shoulder dystocia, large birth weight, assisted deliveries, prolonged labor, and breech presentation [35, 36]. Children with obstetric brachial plexus injuries should be evaluated for injuries to the phrenic nerve and clavicle, intracranial hemorrhage, and torticollis, all of which bear

Table 35.7 Clinical features and management of cerebral palsy

Clinical features	Seizures (30%) Joint contractures Gastroesophageal reflux and aspiration Chronic pneumonia and reactive airway disease Anemia (nutritional deficiency, multiple surgeries, associated blood loss, and chronic diseases like pneumonia/aspiration) Platelet dysfunction Decreased clotting factors Scoliosis (20%)
Common surgical procedures	Baclofen pump insertion Dental surgeries Orthopedic surgeries and contracture release Nissen's fundoplication for gastroesophageal reflux disease Scoliosis correction Dorsal rhizotomy
Anesthetic considerations	• Multiple preoperative medications (anticonvulsant, antispasticity, anti-reflux) • Baclofen should not be stopped abruptly to avoid withdrawal • Gastroesophageal reflux and bulbar palsy can lead to chronic pneumonia, failure to clear secretions, and reactive airway disease. A full course of preoperative antibiotics along with bronchodilators to treat wheeze might be required • Anti-aspiration prophylaxis • Positioning challenges due to chronic contractures and kyphoscoliosis • Difficult airway owing to temporomandibular joint dysfunction along with dental caries and the loose tooth should be evaluated • Patients with cerebral palsy do not mount a hyperkalemic response to succinylcholine. (Minimal upregulation of extra-junctional acetylcholine receptors. A probable theory is that the muscles were never fully developed and hence cannot mount a significant hyperkalemic response to succinylcholine.) • Baclofen and dantrolene can cause delayed recovery of NMB. But patients with cerebral palsy can demonstrate resistance to NDMR. Hence, monitoring is advised • Pain difficult to assess. More sensitive to opioids (OSA and nocturnal desaturation and upregulation of endorphin receptors might be the cause) • Little subcutaneous fat and the altered threshold for shivering due to neurocognitive dysfunction. Hence, difficult to maintain temperature perioperatively. Aggressive measures are required • Risk of extensive blood loss (platelet deficiency and dysfunction along with decreased clotting factors in the setting of anemia)

NMB neuromuscular blockers, *NDMR* nondepolarizing muscle relaxants, *OSA* obstructive sleep apnea

significant perioperative concerns [35]. Traumatic brachial plexus injuries are rare in children with a prevalence of approximately 0.1%, the most common cause being motor vehicle accidents. They are often associated with a head injury and upper extremity vascular lesions [37].

Type of injury and severity determines the presentation and extent of recovery [35]. Diagnostic modalities include myelography, MRI, CT scan with myelography, and nerve conduction studies [36, 38]. There can be neurological recovery with minor injuries, but persistent palsy requires microsurgical intervention. Surgical management options include nerve transfer, tendon and muscle transfers, and nerve grafts/conduits (mainly in obstetric palsies) [38]. Level of injury determines the surgical plan. Nerve grafts can be used for reconstruction in case of postganglionic rupture. However, nerve root avulsions require nerve transfer [35].

Both diagnostic procedures and surgical intervention in young children require anesthesia. Anesthetic concerns for brachial plexus repair include long-duration surgery, intraoperative neuromonitoring (muscle relaxants should be avoided), and respiratory complications (owing to preoperative coexisting phrenic nerve palsy, atelectasis, the possibility of delayed weaning,

and ineffective postoperative physiotherapy due to the thick plaster cast after surgery) [35].

35.3.3 When to Suspect NMDs in Asymptomatic or Mildly Symptomatic Children

Although the anesthesia fraternity is well primed to anticipate and prevent anesthesia-related critical events with patients with diagnosed NMDs, undiagnosed myopathies still remain a challenge. It has been observed that the vast majority of complications occur in patients with undiagnosed myopathy, especially related to DMD and other dystrophinopathies [39]. In an ideal scenario, anesthesiologist should bear in mind the cues suggesting the possibility of myopathies, e.g., progressive weakness of limbs, frequent muscle stiffness or cramps during exercise and at rest, episodes of cola-colored urine especially after exercise, hypotonia (floppiness) in the neonatal period, family history of hereditary myopathies, evident bone malformations (hip, palate, spine, foot, chest), enlarged firm calves, slow relaxation after voluntary contraction, and raised serum creatine phosphokinase (CPK) [3, 40]. It should be noted that some of the abovementioned symptoms/signs could result from neuropathy or motor neuron disease. Hence, the absence of other causative pathology should be established before attributing these to undefined myopathy.

Elective surgery should be withheld in children with suspected symptoms, and expert consultation should be sought for further evaluation. Genetic testing, biochemical analysis, and muscle biopsy, along with meticulous clinical examination, are mandatory before proceeding with any elective surgery.

35.3.4 Considerations for Children with Suspected Myopathy for Muscle Biopsy (or Emergency Surgery)

The estimated risk of rhabdomyolysis or MH in a child with undiagnosed myopathy is ≤1.09% [6, 41]. Nevertheless, management of a "floppy" child with an undiagnosed myopathy is complicated for several obvious reasons. These patients should have a thorough preoperative evaluation of cardiac and respiratory disease, aspiration risk, difficult airway assessment, and minimum fasting time. It is worth to note that previous uneventful anesthesia with volatile anesthetics does not guarantee safety as fatal AIR has been reported in the literature in patients with prior uneventful inhalational agent-based anesthetics [6, 42].

Muscle biopsies are usually carried out under local anesthesia in adults and older children. However, infants and younger children require regional anesthesia with sedation or general anesthesia (GA). Regional anesthetic techniques (commonly spinal anesthesia) have been successfully employed in patients with undefined myopathy [28, 43].

When GA is planned, it is prudent to discuss with the primary physicians (pediatrician and/or neurologist) regarding the most probable diagnosis based on clinical features and laboratory investigations before formulating an anesthetic plan. Volatile agents should be used with great caution in patients with elevated creatinine kinase, history of DMD, or similar pathology with increased risk of AIR. Caution is advised as there are cardiac arrest reports in patients with dystrophy with as short as <10-minute exposure to volatile anesthetics [28]. Elevated lactates suggest mitochondrial myopathies, which increases the chance of PRIS[3], and therefore, volatile agents are an option in these patient groups. It is however risky to set store on preliminary suspicions alone. Discrepancies between prebiopsy diagnosis and post-biopsy findings have been reported in about 22% of patients in a retrospective study [28]. Prior genetic testing to exclude susceptible variants of RYR1, as well as CACNA1S and STAC3, has been suggested to obtain more information about MH susceptibility [22]. Nevertheless, succinylcholine is contraindicated in any child with undefined myopathy. It is advisable not to use propofol if mitochondrial enzyme analysis is required from the biopsy specimen.

Regional anesthesia should be the first choice in a child with undiagnosed myopathy. If not feasible, total intravenous anesthesia (TIVA) without succinylcholine appears to be the logically safe option for these patients for diagnostic procedures. However, the anesthesiologist should be aware that this approach does not guarantee the absence of anesthesia-related complications as rhabdomyolysis has been reported with non-triggering anesthetics and in fasted individuals [27]. Unexpected MH deaths have also been reported without volatile anesthetic use [44]. Hence, regardless of the anesthetic technique used, vigilant monitoring to enable early detection and treatment of complications is mandatory for the safe conduct of anesthesia. These procedures should never be conducted as day-care procedures as complications like AIR could occur in the immediate postoperative period. In addition, these patients mandate strict cardiac and respiratory disease postoperative monitoring. It is advisable to monitor these patients in the intensive care unit (ICU) or high dependency unit (HDU) during the immediate postoperative period.

35.4 Chronic Pain Management in Children with NMD

Chronic pain is an important ailment in patients with NMDs, contributing significantly to disease burden and quality of life [45]. Literature states that more than 70% of parents of children with DMD reported chronic pain in their children [46]. Studies conducted in the adult population show that NMDs are associated with chronic pain commonly involving the lower back and legs, often reporting severe intensity [47]. Characterized pain is mostly musculoskeletal [45], but neuropathic pain is also described in Charcot-Marie-Tooth disease disorders [48, 49]. There is insufficient literature to characterize chronic pain in pediatric NMDs.

Significant delays in referral to pain clinic have been reported in the pediatric population [50]. Older children can self-report pain, but recognizing chronic pain in infants and younger children is difficult and requires careful evaluation. Diagnosis involves recognizing pain behaviors and utilization of pain assessment tools [51]. Multimodality approach involving physical and psychological therapy along with pharmacological interventions are necessary to manage chronic pain in the pediatric population [52].

35.5 Stem Cell Therapy

Significant functional impairment caused by NMDs is responsible for the poor quality of life with no promise of a cure. Degeneration of muscle/nerve/neuromuscular junction is often irreversible. However, as specific defective gene/proteins responsible for these inherited disorders have been identified, there has been great interest in utilizing them as targets of therapy [53]. Gene therapy targets the defective gene (replacing or repairing it) or modifying other genes (unrelated to the actual genetic defect) to induce growth modulating agents (facilitate muscle regeneration) and anti-inflammatory agents (that modulate immune response) [53]. The combination of stem cell and gene therapy shows the promise of a treatment for degenerative NMDs.

Many stem cell therapy applications have been explored in muscular dystrophies, amyotrophic lateral sclerosis, myasthenia gravis, cerebral palsy, and other conditions like spinal cord injury, Friedreich's ataxia, and spinocerebellar ataxia [54–56]. Genetic modification of stem cells by incorporating corrective genes has shown promising results in animal studies involving muscular dystrophies [57]. However, the results are yet replicated to the same extent in clinical trials [54].

The process of stem cell harvesting and transplantation can be carried out under local anesthesia in adults. However, young children and even older children with cognitive impairments are uncooperative and require general anesthesia or monitored anesthesia care with sedation [58]. It is unclear whether the type or duration of anesthesia can affect the stem cell yield [59]. Nonetheless, it is logical to avoid nitrous oxide for stem cell harvesting. In vitro studies showed that amide local anesthetics induce time- and

dose-dependent cellular apoptosis, and also, adhesion of mesenchymal stem cells effects seemingly minimal with ropivacaine [60–62]. Hence, caution is warranted during concurrent administration with local anesthetics. Apart from perioperative care, the anesthesiologists' skills may also be sought in case of intrathecal, epidural, or caudal delivery of stem cells [63]. Currently, the preferred way of stem cell delivery in NMDs is the direct injection into the target tissues. However, a lot of research is underway, and newer gene-editing techniques can open up new avenues for muscle/tissue regeneration enabling other methods of delivery [57].

35.6 Conclusion

Due to their unique anesthesia requirements and association with severe life-threatening complications, meticulous planning and careful conduct of anesthesia are mandated in children with NMDs. Hence, the anesthesiologist should familiarize themselves with the pathophysiology of various NMDs and their anesthetic considerations to provide optimal anesthetic care. Vigilant monitoring and early recognition of life-threatening complications ensure prompt treatment and a safe perioperative course.

Conflict of Interest None to declare.

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Regional Anesthesia for Neurosurgery in Children

36

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Key Points

- Regional techniques are gaining popularity as anesthesia and analgesia modalities in children in several clinical scenarios.
- Scalp nerve blocks are used as anesthetic techniques for awake brain surgery as well as analgesia for other craniofacial procedures.
- Most of the nerve blocks can safely be performed with the use of ultrasound guidance.
- Regional techniques in children with preexisting neurological conditions can be challenging and should be considered on a case-to-case basis.
- Regional anesthesia should be avoided in children with documented tethered spinal cord syndrome, diastematomyelia, or spina bifida with associated cutaneous lesions, multilevel vertebral body involvement, neurologic deficits, or bowel or bladder dysfunction.
- Neurologic injury attributable to regional anesthesia procedures may be caused by direct trauma, neurotoxicity, or ischemia.

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36.1 Introduction

Regional techniques find use as anesthesia and analgesia modalities in children with several clinical scenarios. As anesthesia techniques, nerve blocks are integral to performing awake craniotomy, and some spinal procedures, while as analgesia techniques, they contribute to postoperative analgesia after several neurosurgical procedures. Regional techniques have been well established in the adult population for a long time, but they are gaining popularity among children only recently. As experience grows and expertise develops, these techniques, several advantages with relatively fewer risks, are getting more acceptance among the pediatric anesthesiologists. The principles of these regional techniques are shared with adults, but few salient points stand out, which have been discussed in detail through this chapter. Although less commonly encountered in children, preexisting neurological conditions may have a bearing on utilizing the regional techniques for anesthesia or analgesia. There is an increasing number of children with previous neurosurgery, presenting for a follow-up or an unrelated medical intervention, who may be a candidate for the regional techniques; this aspect is described from the pediatric perspective in the latter part of this chapter.

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36.2 Neurosurgical Indications in Children

The common neurosurgical conditions in children, for which regional anesthesia techniques may be indicated have been listed (Table 36.1) and described below.

36.3 Regional Anesthesia for Awake Craniotomy: Scalp Block

Awake craniotomy is a well-established procedure for the neurosurgical management of brain lesions located near or within critical cortical and subcortical regions. These range from the areas involved in language, to those regulating motor functions, resulting in a significant deficit if the surgical accuracy were to be compromised. This is only complicated further by variations in the organization of these areas in the brain, and the possible distortion due to the tumor mass. To tackle these problems, cortical mapping via direct stimulation in an awake patient has come to be the gold standard to enable maximal resection of the lesions, while minimizing the risk of neurological damage [1]. It goes without saying that the patient's understanding of the procedure and cooperation are critical to achieving this. The technique is increasingly being used to resect supratentorial eloquent lesions and epileptogenic foci, and in pediatric patients with dystonia undergoing deep brain stimulation (DBS) [2].

The regional anesthesia techniques are an important aspect that one needs to be familiar with, before venturing into awake brain surgery. These techniques are described below for awake brain surgery, craniofacial procedures, and placement of vagal nerve stimulators. These can be administered safely to children of all ages, provided the safe doses and volume of local anesthetic agents are adhered to. Various nerve blocks of the scalp and face, are increasingly used to provide intraoperative as well as postoperative analgesia for pediatric head and neck surgeries (Table 36.2). These nerve blocks have become popular in maxillofacial, otorhinolaryngologic, and plastic surgeries of the face and scalp. However, performing these nerve blocks as a part of the anesthetic technique has primarily been limited to neurosurgery to facilitate awake brain surgery. With the growing popularity of ultrasonography for peripheral nerve blocks, more anesthesiologists are gaining the expertise in performing these blocks as well, more so as some of these nerve blocks also find a place in the management of chronic pain.

Table 36.1 Neurosurgical indications of regional techniques in children

• Craniotomy for awake brain surgery
• Postoperative pain management of craniofacial procedures
• Vagal nerve stimulator placement
• Repair of neural tube defects
• Spine surgeries

Table 36.2 Common head and neck nerve blocks in children along with their indications

Type of block	Indications
Supraorbital/ supratrochlear	Frontal scalp incisions for craniotomy, scalp nevi excision, dermoid excision, and ventriculoperitoneal shunts
Infraorbital	Cleft lip repair Endoscopic sinus surgery
Greater palatine	Cleft palate repair
Auriculotemporal	Temporoparietal incision of the scalp
Mental nerve	Lower lip surgery
Greater occipital nerve	Posterior fossa surgery Occipital neuralgias
Superficial cervical plexus	Tympano-mastoid surgery Ear surgery Anterior cervical incisions like vagal nerve stimulator placement Thyroid surgery

In children, nerve blocks of the head and neck region are safe and performed using well-described and easily identified anatomical landmarks. The safety margin is higher, considering the fact that these nerves are mainly sensory and usually terminal branches with a lower risk of nerve damage than the motor nerve blockade for extremity surgeries. The local anesthetic volume needed for performing these blocks is low, which reduces the potential for its toxic effects [3–5].

Irrespective of the approach used, anatomical or ultrasound guided, it is vital to be aware of the dermatomal distribution of the nerves supplying different areas. The primary sensory nerve supply of the head and neck region is through the three branches of the trigeminal nerve, i.e., the fifth cranial nerve (Fig. 36.1) and cervical nerve roots C2–C4 (superficial cervical plexus) providing sensory supply to the occipital and postauricular area (Figs. 36.1 and 36.2). Blockade of one or more of these nerves provides effective analgesia if appropriate divisions are identified based on the planned surgical procedure. The analgesic effect continues well into the postoperative period, possibly reducing opioid consumption. A good regional anesthetic technique prevents hemodynamic changes during pinning for head fixation, as a part of the surgical position as well as the noxious stimulus of the surgery. These nerve blocks, along with the recommended volumes of local anesthetics, have been enumerated in Table 36.3.

36.3.1 Equipment

Weight-based calculation of the dose and total volume of a local anesthetic (LA) to be used is mandatory for every single child. Evidence suggests a rapid rise in the systemic levels of levobupivacaine and ropivacaine when used in regional blocks than other drugs, albeit without signs of cardiovascular or central nervous system toxicity. The dose and type of LA used for blocks must be recorded and communicated with the surgeon to ensure that the surgical supplementation carried out for the skin, temporalis fascia, and dura mater does not exceed the maximum allowable dose. Drugs used for scalp block (children and adults) include bupivacaine, levobupivacaine, and ropivacaine in varying concentrations, with or without epinephrine [6]. Epinephrine (1:200000) is usually added to the LA mixture to increase the total amount of LA that can be used, to decrease

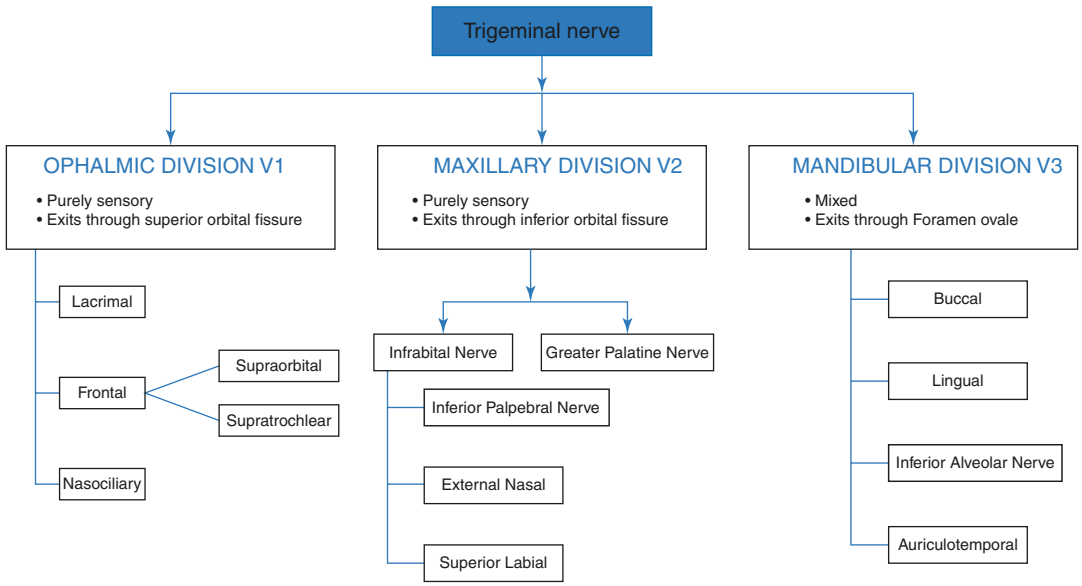

Fig. 36.1 Main branches of the trigeminal nerve: "the great sensory nerve of head and neck"

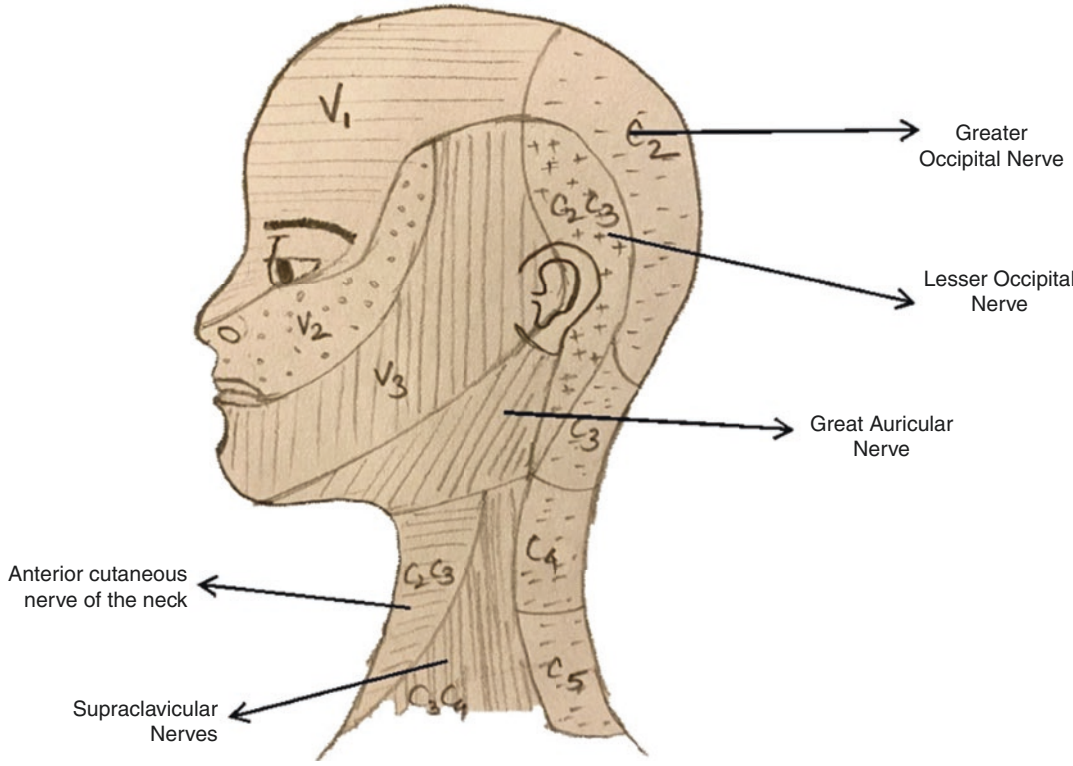

Fig. 36.2 Sensory supply of the head and neck

Table 36.3 Nerves blocked for awake craniotomy and local anesthetic volume (based on the age of the child)

Nerve blocked	Local anesthetic volume required
Supraorbital nerve	1–1.5 ml
Supratrochlear nerve	1 ml
Zygomaticotemporal nerve	1–3 ml
Auriculotemporal nerve	1–2 ml
Lesser occipital nerve	1–2 ml
Greater occipital nerve	1.5–3 ml
Greater auricular nerve	0.5–1 ml

localized bleeding, to reduce the systemic absorption and toxicity of the drug, and to maximize the duration of action. The anesthesiologist should always be on the lookout for features of systemic absorption like tachycardia and hypertension, with epinephrine containing solutions or inadvertent intravascular injection. Literature suggests an improvement in the quality of blocks with the addition of either dexamethasone (8 mg) or magnesium sulfate (500 mg) or both in adult patients [7]. However, no such information has been recorded in pediatric patients.

The preferred needle size is 27G to 30G, and very low volumes of local anesthetic are injected (Table 36.3). For USG guidance, a high-frequency linear probe of 10 MHz or more is the probe of choice. The blocks are generally performed after general anesthesia (GA) is induced, utilizing the asleep phase of "asleep-awake-asleep" technique, with full monitoring in place [8].

36.3.2 Technique

The scalp block includes infiltration of local anesthetics to seven nerves on each side (Fig. 3). This is an anatomical block and hence requires a lesser volume of the drug than a ring block would, reducing the possibility of toxicity. A ring block also has the disadvantage of not providing anesthesia deep to the temporalis fascia [9]. At the end of the scalp block, further LA infiltration

may be needed for the pin insertion sites as well as the incision site for craniotomy (field block).

- ***Supraorbital Nerve: A Branch of V1 Distribution of the Trigeminal Nerve.***

  The supraorbital nerve, with the accompanying vessels, emerges from the supraorbital foramen. On palpation, it is felt as a notch on the superior orbital rim. It divides into a deep and superficial branch. The deep branch courses superiorly and laterally in the loose areolar tissue between the galea and the pericranium and runs parallel to the superior temporal line of the skull. It provides sensory supply to the scalp, piercing the galea near the coronal suture and dividing into its terminal branches. The medially located superficial division divides near its origin into multiple branches that pierce the frontalis muscle and pass cephalad to supply the forehead and up to 3.5 cm of the frontal scalp.

With the child in a supine position, the supraorbital notch is easily palpated by running a finger from the midline laterally along the eyebrow or orbital rim. The needle is inserted into the supraorbital notch perpendicularly, and 1–1.5 ml of the local anesthetic is injected into the space after careful aspiration. Firm pressure is applied after the injection.

The supraorbital notch can also be identified with a high-frequency linear transducer and placing it above the orbital rim. The bone appears as a hyperechoic linear edge with an underlying dark shadow. The notch is visualized as a "bone gap" or a "discontinuity in the bone." Ultrasound can also be useful in locating any vessels in the vicinity using color Doppler function, thereby preventing intravascular injection of the local anesthetic. Ultrasound guidance is also useful to avoid nerve damage and injection into the foramina, where relevant.

- ***Supratrochlear Nerve: A Branch of V1 Distribution of the Trigeminal Nerve.***

  The supratrochlear nerve exits the orbit through a notch at the superior orbital rim, above the trochlea, and medial to the supraorbital notch. Most of the skulls (97%) possess bilateral supratrochlear notches; variations observed include bilateral foramina (1%), a notch on one side, and a foramen on the other (2%). Immediately after the exit, the nerves penetrate the corrugator and the frontalis muscle, supplying cutaneous sensation to the nasal bridge, medial upper eyelid, and medial forehead.

  To block the supratrochlear nerve, the needle is withdrawn to skin level after blocking the supraorbital nerve and directed a few millimeters medially toward the apex of the nose. A further 1 ml is injected after aspiration.

  Besides frontal craniotomies, blockade of these two nerves also helps in upper eyelid surgery, frontal ventriculoperitoneal (VP) shunt placement, Ommaya reservoir insertion, and plastic surgeries like excision of pigmented nevus in the anterior scalp, dermoid cysts, and benign tumors with skin grafting.

- ***Zygomaticotemporal Nerve: A Branch of V2 Distribution* of *the Trigeminal Nerve.***

  The zygomaticotemporal nerve passes through the temporalis muscle and enters the temporalis fascia, innervating a small area of the forehead and the temporal area. Therefore, the local anesthetic infiltration is to be done deep and superficial to the temporalis muscle. Anatomical landmarks include the lateral edge of the supraorbital margin where infiltration begins and is continued to the distal aspect of the zygomatic arch.

- ***Auriculotemporal Nerve: A Branch of V3 Distribution of the Trigeminal Nerve.***

  It innervates the temporal areas, the auricle, and the scalp region above the auricle. The local anesthetic is injected about 1 cm anterior to the auricle, behind the superficial temporal artery, which is palpable just above the posterior part of the zygoma.

- ***Lesser Occipital Nerve: A Branch of the Second or Third Cervical Spinal Nerve.***

  The innervation of the posterolateral part of the scalp, posterior to the auricle, is by the lesser occipital nerve. Sensory blockade of this nerve is performed by infiltration of local anesthetic subcutaneously behind the auricle,

starting from the top down to the earlobe and along the superior nuchal line to the greater occipital nerve.

A case of sudden unconsciousness during a lesser occipital nerve block has been reported in an adult with an occipital bone defect due to previous posterior fossa surgery [10]. Although no such event has been described in pediatric patients, an occipital nerve block is better avoided in the presence of a bone defect, due to the possibility of an inadvertent subarachnoid injection.

- ***Greater Occipital Nerve: A Branch of the Second Cervical Spinal Nerve.***

  Arising from the first and second cervical vertebrae, the greater occipital nerve ascends upward to innervate the skin over the posterior part of the scalp. The sensory supply can extend up to the vertex and over the auricle. Anatomically, it can be located by palpating the occipital artery, which is a branch of the external carotid artery. The artery can be felt approximately 3–4 cm lateral to the external occipital protuberance, along the superior nuchal line. The nerve is usually present medial to the occipital artery. The midpoint of a line drawn between the mastoid process and the occipital protuberance, is taken as a guide to block this nerve in children, whereas in infants, it has been suggested that a distance equal to the width of the medial three fingers of the patient from the occipital protuberance is a better landmark [11]. Best performed with the child in a lateral or prone position, 3 ml of local anesthetic drug is infiltrated using a "fanning" technique at this point to block the greater occipital nerve.

  The USG-guided technique, similar to the one described in adults, uses a linear probe of 10 MHz or more. An in-plane approach is described using the obliquus capitis as a landmark. The probe is initially placed over the spinous process of the C1 vertebra in the midline and then moved caudally to identify the bifid C2 vertebra. The probe is now rotated laterally and then moved laterally to identify the obliquus capitis muscle. In this position, the greater occipital nerve lies superficial to the muscle and can be blocked easily.

  The other indications of greater occipital nerve block described in children include postoperative analgesia following occipital craniotomies, cranioplasties, posterior parietal VP shunts, and occipital neuralgia.

- ***Greater Auricular Nerve: A Branch of the Second and Third Cervical Spinal Nerves.***

  It is the largest of the ascending branches from the upper cervical nerve roots. It emerges from the posterior border of the sternocleidomastoid muscle and divides into anterior and posterior branches. The great auricular nerve innervates the skin over the parotid gland, mastoid process, and the auricle. Blockade of this nerve is performed by injecting the local anesthetic 2 cm posterior to the auricle at the level of the tragus.

36.4 Regional Anesthesia for Craniofacial Surgery

Craniofacial surgery in the pediatric population includes surgery for craniosynostosis and cleft lip and palate surgery. These procedures pose several anesthetic challenges in terms of difficult airway management, prolonged duration, significant blood loss, and the need for postoperative ventilation. Several such procedures are carried out in very young infants, in whom postsurgical pain is difficult to assess and managed only with opioids. The addition of regional anesthetic techniques, in the form of nerve blocks of the scalp and face, provides excellent intraoperative and postoperative analgesia, also reducing opioid consumption [12, 13].

Some of the surgical procedures for craniosynostosis include strip craniectomy, cranioplasty, total vault reconstruction, minimally invasive endoscopic surgery, fronto-orbital remodeling, and posterior calvarial vault expansion. The use of scalp nerve blocks has been described to reduce blood loss during craniofacial surgery and perioperative analgesia [13]. Although definite evidence for the former is lacking, reduced

requirements of intraoperative opioids have been noticed. Other advantages include hemodynamic stability, increased time to need for rescue analgesia, and reduced doses of rescue analgesia in the postoperative period [14].

Scalp block, like many nerve infiltration methods, is a pre emptive method of analgesia [15]. Suppression of the inflammatory cascade at the surgical site or even its reversal is hypothesized to occur with a scalp nerve block. When given postoperatively, a longer duration of action is achieved. Adequate measures to control pain in the immediate postoperative period help prevent chronic post-craniotomy pain, although evidence in this regard is limited [16, 17].

Use of scalp block with or without additional infiltration around the surgical site has also been reported in excision of scalp nevi in children, resulting in complete blockade of nociception at the wound site for a few hours [18]. Performing a supraorbital and supratrochlear nerve block has also been found useful in midline dermoid excisions.

A modified technique, described as the "extended scalp block" which involves infiltration around the supraorbital, supratrochlear, auriculotemporal, and posterior auricular nerves, can be used in patients undergoing neurovascular reconstruction surgery (moyamoya disease). The benefits reported are maintenance of stable hemodynamic parameters along with a reduction in the requirement of inhalational anesthetic agent, hence reduced effect on cerebral perfusion pressure [19].

36.5 Regional Anesthesia for Vagal Nerve Stimulator Implantation: Neck Block

Vagus nerve stimulation (VNS) is a nonpharmacological treatment for pharmaco-resistant epilepsy. VNS is increasingly used for various indications among adults. Though the results have been favorable, limited evidence is available in the form of case series in children. It finds particular benefit in patients with multifocal epileptogenic zones or those who are difficult to localize and, hence, difficult to manage with surgery. The rationale of VNS therapy is that repetitive stimulation of the vagus nerve can inhibit the hypersynchronous cortical activity that is associated with seizure activity. As adjunctive therapy, it has also been observed to improve attention, cognition, behavior, mood, and quality of life besides reducing seizure burden [20].

While vagal nerve stimulator placement has been carried out successfully under regional or local anesthetic in adults, children need GA for the procedure. However, regional anesthesia techniques may be used to provide analgesia at the wound site. A combination of superficial and deep cervical plexus block is needed for regional anesthesia, whereas only superficial cervical plexus block is sufficient for analgesia [21].

36.5.1 Anatomy and Technique

The superficial cervical plexus is derived from the C2 to C4 nerve roots and is purely sensory. It is seen to wrap the belly of the sternocleidomastoid muscle at the cricoid level, where it divides into four branches, innervating the skin over the shoulder in a cape-like distribution.

With the patient in a supine or semi-recumbent position and the head turned to the opposite side, a horizontal line drawn from the cricoid cartilage to intersect the posterior border of the sternocleidomastoid is identified. At this point, 1–3 ml of local anesthetic solution is injected subcutaneously while avoiding the external jugular vein, which lies in close proximity. Older children may need higher volumes like 5–15 ml. A deep injection should be avoided to prevent a deep cervical plexus block, resulting in complications like paralysis of the recurrent laryngeal nerve, hemidiaphragmatic palsy, and Horner's syndrome due to unilateral sympathetic ganglion blockade.

USG guidance may be used to perform this block. The position is similar to the landmark technique, with adequate exposure of the neck and upper chest. The transducer is placed on the lateral part of the neck, over the sternocleidomastoid at its midpoint, corresponding to the cricoid

cartilage. The transducer is then moved posteriorly till the posterior edge tapering off could be visualized. At this point, it is useful to try to identify the brachial plexus or the interscalene groove. The cervical plexus may be seen as a small collection of hypoechoic nodules, superficial to the prevertebral fascia overlying the interscalene groove. Either the in-plane or out-of-plane technique can be used for needle insertion. After negative aspiration, 1–2 ml of local anesthetic agent is injected. Once the correct spread is visualized, the rest of the volume can be injected to envelop the plexus.

36.6 Regional Techniques and Preexisting Neurologic Disease

Anesthetic management of children with preexisting neurologic diseases poses unique challenges. Surgical trauma, tourniquet pressure, improper patient positioning, or anesthetic techniques may result in new neural injuries and postoperative neurologic deficits, making its evaluation difficult. Independent of the anesthetic technique employed, progressive neurologic diseases such as multiple sclerosis may worsen in the perioperative period. In these cases, the most logical and conservative approach would be to avoid regional anesthesia. However, the benefit of regional anesthesia and analgesia in high-risk cases must be considered on a case-by-case basis. Whenever used, a meticulous technique, including the use of image guidance wherever feasible, must be employed to minimize the risk of further neurologic injury.

The ***double crush syndrome***, first proposed by Upton and McComas in 1973, is a general term referring to the coexistence of dual compressive lesions along the course of a nerve, wherein the presence of a proximal lesion apparently renders the nerve vulnerable to further injury when there is a distal compression [22]. Both the proximal and distal insults, however minor or subclinical, act synergistically to cause a clinically significant and potentially permanent nerve injury. It was initially described in patients with concomitant cervical radiculopathies and median or ulnar neuropathies and later extended to include injury even from non-compressive mechanisms. These include toxic (chemotherapeutics, local anesthetic agents), metabolic (aging, diabetic neuropathy), ischemic (tourniquet related), or traumatic (surgical traction, needle/catheter placement) etiologies. The presence of a preexisting neurological condition, whether neuraxial or peripheral, is thought to be an additional mechanism by which minor or subclinical symptoms interact, resulting in new or worsening neurologic deficits.

36.7 Neural Tube Defects

Neural tube defects (NTDs) are congenital anomalies of neural development that primarily affect the cranium or spine. Clinical presentation varies from cranial defects (e.g., anencephaly, exencephaly, encephalocele), open spinal dysraphism, and closed spinal dysraphism [23]. Anecdotal reports suggest using epidural analgesia or spinal anesthesia during labor and delivery of a child in a parturient with spina bifida cystica and subsequent surgical correction. It has been opined to exercise caution while performing neuraxial blockade in such children; it could be technically challenging as there may be an unpredictable spread of the drug, and there is an associated risk of inadvertent dural puncture.

To perform the neuraxial blockade under these clinical circumstances, it is recommended that the site of needle insertion should be at a level above the original lesion (isolated spina bifida occulta) due to the limitations in local anesthetic spread [24]. It is not uncommon for patients with spina bifida to present with cutaneous manifestations like a tuft of hair, sinus or subcutaneous lipoma, and neurologic symptoms including autonomic dysfunction in the form of bladder or bowel involvement. Such children tend to have tethered spinal cord syndrome or diastematomyelia, which contraindicates the application of neuraxial techniques. Since complications have been reported after neuraxial procedures in children with previously unrecognized neurologic problems, it is important to be vigilant and

observe for cutaneous signs and examine for deficits before attempting such procedures.

Another condition in children where inadvertent dural puncture can occur with a caudal block or cause incomplete spinal anesthesia is dural ectasia [25–27]. It refers to an abnormal widening or ballooning of the dural sac, most commonly observed within the lumbosacral region of the spinal cord. Conditions associated with dural ectasia include Marfan syndrome (63–92%), Patau syndrome (trisomy 13), Ehlers-Danlos syndrome, neurofibromatosis type I, and ankylosing spondylitis.

At present, there are no definitive recommendations for the safety of neuraxial blockade in children with NTDs due to the wide spectrum of abnormalities, their associated risks, and a lack of proper and large-scale evidence. But regional anesthesia should be avoided in children with prior sensorimotor neurologic deficits, bladder or bowel involvement, documented TCS, diastematomyelia, spina bifida with associated cutaneous lesions, or radiological evidence of involvement of multiple vertebral levels. If regional procedures are to be considered in patients with NTDs (e.g., isolated spina bifida occulta, prior meningomyelocele repair), radiographic imaging should be undertaken to rule out complex findings and then a decision made after a comprehensive risk/benefit analysis. The risk of technical difficulties, extensive cephalad spread of local anesthetic, sacral sparing, inadvertent dural puncture, and neurologic injury should be highlighted to the parents/legal guardian. If the neuraxial blockade is performed under these clinical conditions, the needle insertion site is kept at a level above the vertebral abnormality or site of prior surgical repair.

The role of USG-guided neuraxial procedures in children has been well established for caudal epidural injection but has specifically not been studied in children with preexisting neurological conditions. The evidence for lumbar neuraxial procedures is even more scarce. One randomized study evaluated USG guidance for epidural catheter placement in children aged 0–6 years, but these children were otherwise neurologically healthy [28]. Therefore, despite ultrasound-suggested increased speed and accuracy of the procedure, the extent of its benefits may be limited in children with spinal anomalies.

36.8 Brain Tumors, Aneurysms, and Arteriovenous Malformations

Administration of spinal or epidural anesthesia in children with preexisting intracranial masses or vascular lesions such as brain tumors (primary or metastatic), saccular aneurysms, or arteriovenous malformations (AVMs) increases the risk of neurologic compromise. Cerebral herniation, infarction, or subarachnoid hemorrhage (SAH) may occur as a result of changes in intracranial pressure (ICP) and mean arterial pressure (MAP) due to neuraxial blockade. Dural puncture is contraindicated in patients when there is evidence of increased ICP like cerebral edema, midline shift, or obliteration of the fourth ventricle. In such cases, dural puncture causes a leak of cerebrospinal fluid (CSF) under pressure and results in herniation. The drop in CSF pressure due to dural puncture acutely increases the aneurysmal transmural pressure (MAP-ICP) gradient, causing a rupture and SAH. Rupture of an occult AVM coincident with dural puncture has been reported during an attempt for epidural anesthesia [29]. Due to the risk of accidental dural puncture, epidural and caudal anesthesia are contraindicated in patients with raised ICP. Also, ICP may increase further by the injection of local anesthetic solutions into the epidural space. However, neuraxial anesthesia may be considered in patients with surgically repaired vascular malformations with minimal or no risk of neurologic complications.

36.9 Epilepsy

Epilepsy is a recurrent seizure disorder that affects 0.5–1% of the population. Epilepsy may be idiopathic, typically beginning in childhood, or presenting intracranial pathologic conditions like neoplasm, trauma, infection, or stroke.

Children with seizure disorder undergo several surgical procedures safely under anesthesia, and various regional techniques in seizure disorders have been described. Precautions during the performance of regional anesthesia procedures include measures to minimize the systemic levels of LA by selecting appropriate volume and dose, addition of vasoconstrictors, and also slow and incremental injection through a short-bevel needle with a frequent aspiration to prevent intravascular injection, and considering the possibility of continuous infusion of a low volume of the drug through a catheter. In addition to precautionary measures, these patients must be continuously monitored for early warning signs of local anesthesia systemic toxicity (LAST). Seizures are one of the central nervous system manifestations of LAST and can occur even with the intravascular injection of very small amounts of the drug [30]. The likelihood of CNS side effects is amplified with hypoventilation leading to hypercapnia and acidosis, all of which may occur due to oversedation. CNS toxicity leading to seizures can occur in the postoperative period if infusions of LA are not carefully managed and monitored.

36.10 Neurosurgical Complications After Regional Techniques

Neurologic injury resulting from regional anesthesia occurs due to various mechanisms like trauma, neurotoxicity, and ischemia. Permanent neurologic injury due to direct needle- or catheter-induced trauma, though rare, is possible. These pressure effects from an epidural or spinal hematoma after a lumbar puncture (diagnostic or therapeutic) also contribute to the neurologic complications. The paresthesia technique has also been postulated as one of the factors for neurologic injury after brachial plexus block but without any conclusive data for evidence [32]. The overall incidence of persistent paresthesia has been estimated to be 0.08% after spinal anesthesia and 2% after brachial plexus block [31, 32]. Needle-bevel configuration influences the frequency and severity of peripheral nerve damage during regional anesthesia; increased incidence of complications is observed using long-beveled needles, highlighting the importance of minimizing direct needle trauma in patients risk for neurologic complications [33, 34]. Neurologic deficits after regional anesthesia may directly result from LA toxicity, indicating the potential neurotoxicity of anesthetic solutions [35–39]. Patients with underlying nerve dysfunction tend to have a decreased LA requirement and a decreased threshold for neurotoxicity [37]. Hence, the general agreement is that LA administered in clinically appropriate doses and concentrations does not cause nerve damage. Rather, the prolonged exposure to high concentrations of LA solutions causes permanent neurologic deficits [40].

Neural ischemia may occur due to systemic or local vascular insufficiency. Spinal cord ischemia in the watershed areas (between radicular arteries) occurs due to systemic hypotension associated with spinal anesthesia (or even without), causing flaccid paralysis of the lower extremities (anterior spinal artery syndrome). Theoretically, the addition of vasoconstrictors like epinephrine or phenylephrine to the local anesthetic may result in local ischemia, especially in patients with the microvascular disease [36, 41]. Clinical studies have failed to provide adequate evidence against the use of such vasopressors, with only isolated case reports that suggest other risk factors as well [42]. The Neural Double Crush patients with preexisting neurological conditions may be at increased risk for regional anesthesia-related nerve injury.

Studies regarding risk factors for the development of neurologic injury after regional anesthesia are scarce. Several disorders of the central and peripheral nerves may require further evaluation to identify and provide information regarding ideal anesthetic techniques. The largest series of neuraxial anesthesia in the patient with a preexisting CNS condition included 139 patients [43], post-polio syndrome and multiple sclerosis being the most common disorders. The majority of these patients had sensorimotor deficits at the time of the blockade. The significant finding in the study was that no patient developed a new or worsening neurologic deficit during the postoperative period, as compared to the preoperative findings (0.0%; 95% CI 0.0–0.3%).

36.11 Epidural and Spinal Anesthesia After Major Spine Surgeries

Previous spinal surgery has been considered as a relative contraindication to the use of regional anesthesia. Chronic back pain and fear of exacerbation of preexisting back problems are the major reasons for patient refusal for neuraxial anesthesia. Technically, performing spinal or epidural anesthesia becomes difficult due to postoperative anatomical changes making needle or catheter placement more complicated. The changes include injury to ligamentum flavum resulting in adhesions within or obliteration of the epidural space affecting the spread of the LA, leading to an incomplete or "patchy" block. The possibility of dural puncture is increased, and when required, the subsequent intervention with epidural blood patch also becomes difficult due to altered anatomy. The usually performed midline or paramedian approaches for needle placement in a spinal segment that has undergone bone grafting and posterior fusion is not possible. It can be accomplished at unfused segments only. With epidural anesthesia, a false loss of resistance has been reported to occur frequently. Anecdotal reports suggest that epidural anesthesia may be successfully performed in patients who underwent previous spinal surgery. However, successful catheter placement on the first attempt is possible in only 50% of patients, even when an experienced anesthesiologist is carried out. Complications include inadvertent dural puncture, traumatic needle placement, and unsuccessful placement of epidural needle/catheter, especially if the spinal fusion is between L5 and S1.

36.12 Conditions Mimicking Spinal Canal Stenosis in Children

Morquio's disease (MPS IV) is the most common mucopolysaccharidosis syndrome (MPS) compatible with longevity. The major neurosurgical presentation in this condition is a shortened spine with platyspondyly and odontoid hypoplasia leading to C1–C2 instability with cervical myelopathy requiring surgical stabilization of the C1–C2 junction. MPS IV is due to a deficiency of the enzyme galactose-6-sulfatase, which leads to imperfect processing of keratan sulfate. The other major clinical presentations include severe short stature, marked bilateral hip coxa vara, acetabular dysplasia with a waddling gait, and genu valgum. Anesthetic considerations in these patients include a difficult airway due to cervical spine instability. Performance of neuraxial blocks also becomes difficult due to the associated kyphosis and scoliosis. Even when successfully performed, neuraxial blocks may be ineffective due to the abnormal accumulation of glycosaminoglycans in the epidural space.

Epidural lipomatosis is another condition that can present a situation for challenging neuraxial block. The cauda equina is normally mobile within the CSF; it may move about as the child changes posture. The dural sac and CSF cushion generally ensure the correct placement of the spinal needle, minimizing the risk of accidental traumatic nerve injury. Epidural lipomatosis with or without a small spinal canal leads to reduced CSF volume and a less movable cauda equina, resulting in nerve injury after the administration of spinal anesthesia. Post-spinal neuropathies are usually transient, but paresthesia and pain at injection may increase the risk of long-term damage. Diagnostic methods like electromyography (EMG) are unreliable because EMG measures only large nerve fiber signals, and it may take up to 3 weeks before a nerve injury can be confirmed.

36.13 Neuraxial Blocks in Patients with Preexisting Baclofen Pumps

Intrathecal baclofen (ITB) pumps are increasingly used in children with cerebral palsy (CP), spinal cord injury, and upper motor neuron disorders to treat spasticity and dystonia. Though medical management of hypertonicity with these agents improves comfort, ease of care, and function for these children, additional corrective orthopedic procedures are often necessary to

improve gait and mobility. These orthopedic procedures include osteotomy, muscle-tendon lengthening, and foot-realignment procedures. Ambulatory children between ages 6–10 years often undergo several of these procedures in one setting, a practice known as single-event multilevel surgery (SEMLS) that may result in significant postsurgical sciatic nerve stretch. Epidural anesthesia can be used for perioperative pain management for these procedures.

Anesthesiologists are wary of placing epidural catheters in patients with intrathecal catheters. Concerns include accidental damage to the intrathecal catheter or pump apparatus, infection, risk of intrathecal migration of the epidural catheter, and exaggerated epidural response. A few cases reports in the literature report uneventful placement of epidural catheters in patients with ITB pumps for labor analgesia and orthopedic procedures [44]. Safe placements of epidurals with concurrent ITB pump for SEMLS and femoral osteotomy have been reported [45]. The balance deficit found in children with CP is mainly caused by muscle tone imbalance (spastic agonist and weak antagonist).

It is imperative to determine the entry level of the intrathecal catheter to avoid damage to the ITB catheter with epidural placement. Epidurals may be sited above or below the level of the intrathecal ITB insertion site. Surgical interventions around the neuraxis may cause the epidural space scarring and result in misdirected epidural catheters and patchy blocks. Real-time fluoroscopic placement of epidural catheters seems to be the best course in these patients with the potential for difficult placement and catheter malposition.

Post-procedure cross-sectional imaging, for either postsurgical or dedicated epidural catheter evaluation, may be used to confirm catheter course and tip position as well as related complications. As compared to computed tomography (CT) scan, magnetic resonance imaging (MRI) better characterizes soft tissues, including potential spinal cord insults. Of note, the normal appearance of injectate may mimic other causes of fluid collection, particularly abscess. CT scan more noticeably displays small-caliber epidural catheters, which may be augmented by nonionic radiographic contrast material. Both modalities may be limited by metal artifacts related to the ITB pump and/or spinal fusion hardware.

CSF leak is a rare but clinically significant complication of ITB pump placement, estimated to occur in approximately 5% of patients. In a case series of patients with CRPS-related dystonia treated with ITB pump, there was a high incidence of post-dural puncture headache (PDPH) even in the absence of CSF leak [46]. In more than half of these patients, symptoms were noted to persist beyond the typical time frame, in one case for as long as 36 months despite two attempts for an epidural blood patch. For these infrequent complications, the response to an epidural blood patch has been found to be variable.

In conclusion, epidural blocks in patients with baclofen pumps should be considered on a case-to-case basis. The protocol should include serial neurologic documentation in collaboration with rehabilitation medicine and orthopedic surgery teams. LA infusions could be diluted down to facilitate neurologic examinations in the postoperative period. Potential synergism of adjuvants and baclofen with local anesthetics should be considered. Sciatic stretch is a real concern in patients with limb-lengthening procedures. Routine epidurograms should be considered to verify the epidural catheter position.

36.14 Local Anesthesia Toxicity

Local anesthetic systemic toxicity (LAST) is not a very common complication, but it is potentially fatal in children when it occurs. The estimated incidence is 0.76–1.6:10,000, with a majority of the complications that occur in infants. It is essential to be well versed with the maximum safe doses of various local anesthetic preparations (Table 36.4) even though the minimum effective dose should be used. Early CNS signs and symptoms in children may be masked by concomitant GA and delay the diagnosis. Early CNS toxicity may also be mistaken for poor analgesia in infants and children with special needs. The potency of the anesthetic agent, pharmacoki-

Table 36.4 Common local anesthetic preparations with their recommended maximum doses and duration of action

Agent	Maximum dose (mg/kg)	Duration of action (min)
Procaine	10	60–90
2-chloroprocaine	20	30–60
Tetracaine	1.5	180–600
Lidocaine	5	90–200
Bupivacaine	2.5	180–600
Ropivacaine	2.5	180–600
Levobupivacaine	2.5	180–600

Table 36.5 Local anesthetic toxicity in children: key points

- It may be due to inadvertent vascular injection, excessive absorption, or accidental overdose.
- Neonates at high risk: immature hepatic metabolism
- Infants: increased volume of distribution, decreased LA binding proteins, longer elimination half-life, and reduced plasma cholinesterase
- On suspicion, stop the injection and call for help.
- Symptomatic treatment; benzodiazepines for seizures, epinephrine for hypotension (up to 1 μg/kg), treat arrhythmias but avoid vasopressin, calcium channel blockers, and beta-blockers
- Monitor and correct acidosis, hypercarbia, and hyperkalemia.
- Administer 20% intralipid emulsion; bolus of 1.5 ml/kg followed by infusion @ 15 ml/kg/h (0.25 ml/kg/min) to a maximum dose of 12 ml/kg, along with supportive resuscitation

netic properties like rate of biotransformation and penetration through the blood-brain barrier, and acid-base status of the patient (hypercapnia and acidosis decrease the convulsive threshold by up to 50%) are the factors affecting CNS toxicity. Though multiple reasons are suggested for aggravation of LAST in children, recent data from pediatrics registries suggests an overall low incidence in children than adults [47]. The factors attributed to low incidence include the use of lower volumes of drugs; administration of LA under GA, thereby increasing seizure threshold; and a lower burden of comorbidities [48]. The key points about local anesthetic toxicity in children are summarized in Table 36.5, and additional reading of the guidelines by the *Association of Anaesthetists of Great Britain and Ireland (AAGBI)* is recommended. Basic life support with prompt administration of intralipid emulsion (bolus of 20% solution 1.5 ml/kg followed by infusion at the rate of 15 ml/kg/h) immediately after airway management is the cornerstone of management.

36.15 Conclusion

Regional anesthesia techniques improve the postoperative experience of both children and parents or caregivers and facilitate the efficient use of hospital facilities. The safety and efficacy of most of these techniques have been established in children as well, and therefore, anesthesiologists must become skilled in performing these procedures. Training in the acquisition of ultrasound imaging and needling skills and knowledge of pediatric anatomy and physiology should be an integral component of specialty training. In children with preexisting neurological conditions, a careful case analysis of the risk-benefit ratio can help deliver the standard care within the confines of patient safety.

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Part III

Postoperative Care and Miscellaneous Topics

37 Recovery and Postoperative Care in Children Undergoing Neurosurgery

Sangeetha R. Palaniswamy and Sriganesh Kamath

Key Points

- Children undergoing neurosurgery pose inherent challenges during recovery and in the postoperative period.
- Uniqueness in airway anatomy, systemic physiology, and some neurosurgical pathologies necessitates modification in the anesthetic techniques and perioperative care.
- Poor preoperative neurological status, surgery involving vital cranial structures, significant bleeding, perioperative hemodynamic fluctuations, postoperative respiratory insufficiency, and new-onset neurological deficits may necessitate postoperative intensive care unit management.
- Delay in recovery beyond the window of anticipation should trigger a sequence of investigative and therapeutic measures.
- Specific pediatric neurosurgical conditions present with distinct postoperative issues. Thorough understanding and careful management are essential to achieve desirable recovery and good clinical outcomes.

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37.1 Introduction

Pediatric neurosurgery forms about one-third of the total neurosurgical procedures in most tertiary care centers. Good anesthesia care in children undergoing neurosurgery should incorporate essential principles of both neuroanesthesia and pediatric anesthesia. Postoperative recovery is an important component of perioperative management in children undergoing neurosurgical procedures. Early and smooth recovery is essential to assess neurological function and avoid perturbations in systemic hemodynamics and resultant intracranial dynamics. This chapter discusses various aspects of recovery from anesthesia and general principles of early postoperative management relevant to anesthesiologists in children undergoing neurosurgery.

37.2 Physiological Changes During Recovery After Neurosurgery

Catecholamine release, sympathetic nervous system activation, and increased oxygen consumption are prominent physiological changes during the recovery phase [1]. Systemic hypertension is defined on an individualized basis, depending on the child's baseline blood pressure (BP). Figure 37.1 demonstrates the interplay of

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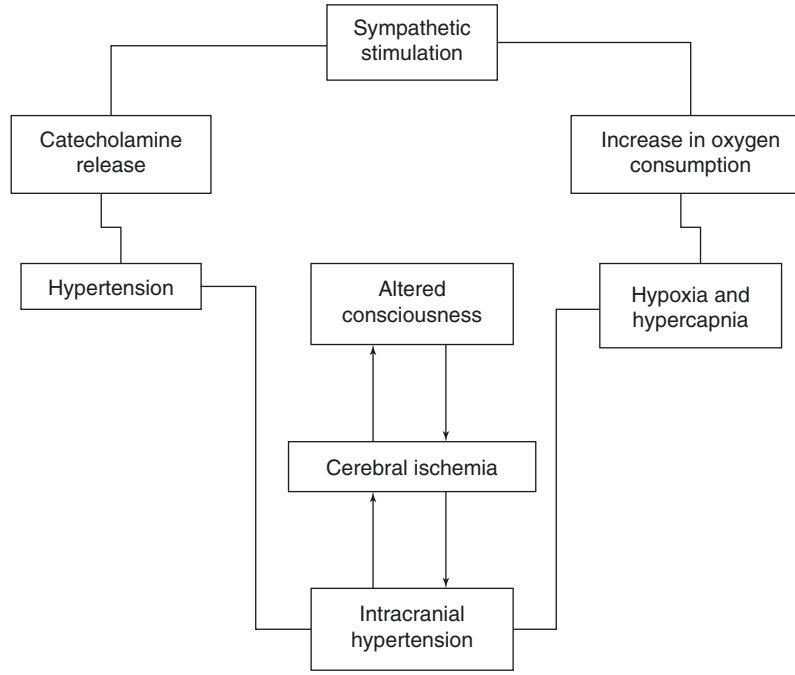

Fig. 37.1 Basic interplay of cardio-respiratory system in neurological recovery during emergence

cardio-respiratory systems in neurological recovery during emergence from anesthesia.

37.3 Enhanced Recovery After Surgery (ERAS) Pathways

The goal of ERAS pathways is to achieve enhanced recovery and good postoperative outcomes by implementing multiple processes together that maintain patient's physiology close to normal in the perioperative period. Preoperative counseling, avoiding prolonged fasting, liberal use of regional anesthesia, opioid-sparing analgesic approach, appropriate and judicious use of intravenous fluids, maintenance of normothermia, and early mobilization are key interventions to promote enhanced postoperative recovery after neurosurgery in children. The benefits of ERAS pathways include reduced complications such as postoperative nausea and vomiting (PONV), pain, shivering, bladder and bowel dysfunction, and increased satisfaction. Early discharge from intensive care unit (ICU) and hospital, reduced healthcare costs, and lower rates of redo surgery, readmission, and mortality [2].

37.4 Implications of Poor Recovery in Children

Poor recovery indicators such as hypertension, tachycardia, airway obstruction, laryngospasm or bronchospasm, seizures, emergence agitation (EA), slowed recovery, etc. are associated with delayed discharge from postanesthesia care unit (PACU), additional investigations and interventions, and long-term behavioral changes [3]. Hence, efforts to improve recovery time and quality should begin before surgery, continue during the intraoperative period, and extend into the PACU.

37.5 Impact of Anesthetic Management on Postoperative Recovery

The postoperative recovery is predominantly impacted by the quality of intraoperative management during neurosurgery. Anesthetic drugs greatly influence the recovery profile. Spine surgeries serve as a better model than cranial surgeries to study the influence of anesthesia on

recovery. The recovery profile is attributable primarily to the anesthetic management in this population, unlike cranial surgeries, where recovery is likely to be influenced by intracranial pathologies and neurosurgical factors [4].

In a study comparing isoflurane and sevoflurane anesthesia in children undergoing spinal dysraphism surgery, authors observed shorter time to extubation (6.4 vs 10.7 min), emergence (7.8 vs 12.8 min), and achieving full Aldrete score (13.9 vs 20.3 min) with sevoflurane. There was no difference for other recovery attributes such as EA, discharge time from the PACU, or time for first analgesia requirement in the postoperative period [5]. In another study by the same group where sevoflurane was compared with desflurane anesthesia in 60 children for spinal dysraphism surgery, shorter time for emergence and extubation was seen with desflurane (2.75 vs 8 min and 3 vs 5.5 min, respectively) when compared to sevoflurane. There was no difference in other recovery characteristics [6].

The use of adjuvants, such as dexmedetomidine during surgery, also provides advantages during recovery from anesthesia. In a randomized controlled trial (RCT) involving 36 children, the impact of intraoperative dexmedetomidine on recovery characteristics was evaluated after surgery for spinal dysraphism. Children who received dexmedetomidine had lower pain scores, lower agitation scores, and faster time achieving full modified Aldrete score after surgery. Similarly, postoperative opioid consumption was lower, time to the first analgesic requirement was longer, PONV was lesser, and heart rate and BP were better maintained with dexmedetomidine when compared to placebo [7].

Despite increasing neurophysiological monitoring, few centers still perform intraoperative wake-up tests to assess neurological function during spine surgeries. It is important that the wake-up is smooth to minimize major perturbations in cardio-respiratory physiology. When combined with sevoflurane anesthesia, low-dose dexmedetomidine provided hemodynamic stability and good wake-up condition in 60 children during scoliosis surgery [8].

In cranial surgeries, smooth and early recovery is warranted to avoid intracranial adverse events and facilitate quick neurological assessment. The choice of anesthetic technique plays an important role in achieving favorable recovery. In an RCT comparing isoflurane, sevoflurane, and desflurane anesthesia in 60 patients undergoing supratentorial surgeries for brain tumors, the emergence and extubation times and the time for reaching an Aldrete score of nine were significantly shorter with desflurane and sevoflurane than with isoflurane. Other variables, such as hemodynamics and postoperative shivering or vomiting, were similar to all anesthetics [9].

There are many situations where general anesthesia may not be appropriate in children undergoing craniotomies for pathologies involving eloquent brain areas. In these children, intraoperative clinical or electrophysiological assessments necessitate either awake surgery or asleep-awake-asleep pattern of anesthesia. Use of dexmedetomidine or a combination of dexmedetomidine, ketamine, remifentanil, and nicardipine provides smooth transitions between asleep-awake-asleep conditions and facilitates neuropsychological assessments and electrophysiological monitoring during surgery [10–12]. However, dexmedetomidine as a sole agent may be inadequate in children undergoing stereotactic procedures, and supplementation of additional anesthetic such as propofol can complicate recovery [13].

37.6 Assessment of Recovery

After surgery, recovery characteristics are usually assessed in terms of time to extubation, quality of extubation, time to spontaneous eye opening and following verbal commands, and hemodynamic changes during extubation. Postoperative recovery is also evaluated in terms of occurrence or otherwise of PONV, shivering, pain, EA or delirium, cognitive dysfunction, and change in neurological, respiratory, and hemodynamic status compared to the preoperative period.

37.7 Desired Recovery Profile

Early recovery from anesthesia and extubation is preferable in most scenarios provided children fulfill the extubation criteria. The success of extubation in children undergoing neurosurgery is dependent on anesthetic, surgical, and patient factors, and these should be met (Fig. 37.2). When early extubation is considered, an approach suggested in Fig. 37.3 may be preferred in children undergoing neurosurgery. Occasionally, planned delayed recovery and extubation might be necessary for exceptional situations to minimize complications and improve outcomes. In either scenario, the following characteristics are considered as desirable for a good recovery.

- *Stable respiratory parameters*: No coughing, patient-ventilator asynchrony, retching, desaturation, airway obstruction, hypo- or hypercarbia, etc.
- *Stable cardiovascular parameters*: Sinus rhythm, acceptable intravascular volume, heart rate and BP, adequately replaced blood loss.
- *Favorable neurological and psychomotor recovery*: No EA, return of consciousness without new neurological deficits.

37.8 Dilemmas in Decision-Making

37.8.1 Early Versus Delayed Recovery

Recovery from anesthesia occurring within the initial few minutes after surgery is generally described as early recovery. If the recovery is over several minutes to hours after surgery, it would be late or delayed recovery. The pattern of recovery (early vs delayed) should be individualized with consideration of multiple factors, namely, patient-related (clinical status, primary pathology, co-existing congenital anomalies, ease of securing the airway), surgery-related (elective/emergency nature of the surgery, intermediate to major risk surgery, surgery close to vital centers, cranial nerves, major blood vessels, and vascular sinuses), perioperative course (hemodynamic and metabolic status, degree of fluid shift, the requirement of blood transfusion), and anticipated complications unique to different pathologies. The advantages and disadvantages of early versus delayed recovery are enumerated in Table 37.1.

Early recovery may be suitable in children with normal preoperative sensorium, easy air-

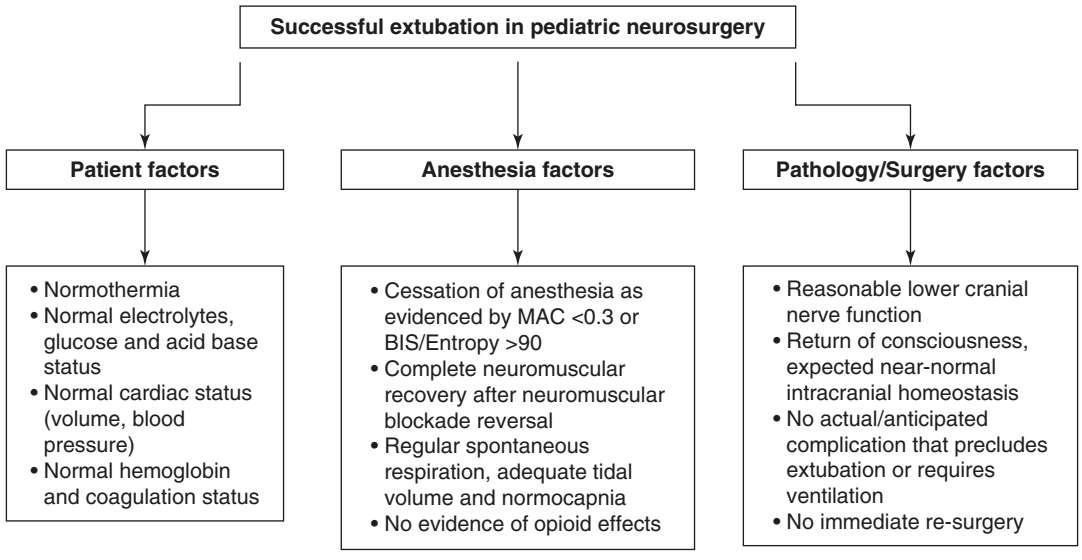

Fig. 37.2 Factors contributing to successful extubation in children undergoing neurosurgery

Fig. 37.3 Suggested approach for extubation and recovery after pediatric neurosurgery

Table 37.1 Advantages and disadvantages of early and delayed recovery and extubation after neurosurgery in children

Early recovery	Delayed recovery
Advantages • Rapid neurological assessment possible • Early detection and management of complications • Avoids problems with intensive care and prolonged intubation and ventilation • Avoids sedation needs, agitation, and pain • Avoids coughing and bucking and resultant systemic and intracranial stress response	*Advantages* • Provides opportunity to stabilize systemic hemodynamics and intracranial homeostasis • Reduced chance of pain and agitation • Facilitates invasive monitoring, oxygenation and ventilation, and intensive care • Avoids secondary insults in the event of complications in the immediate postoperative period
Disadvantages • Hemodynamic perturbations and their impact on injured/operated nervous tissue • Increased possibility of pain and agitation • Possibility of adverse cardio-respiratory events and secondary brain insults • Need for multiple quick interventions in case of complications	*Disadvantages* • Early neurological assessment not possible • Inability to detect complications early and intervene early • Problems associated with sedation, intensive care, and prolonged ventilation • Coughing, bucking and airway spasm with resultant systemic/intracranial stress response

way, uneventful perioperative course, and an uncomplicated surgical technique not involving critical areas. Patients with stable cerebral parameters such as apparently normal cerebral blood flow (CBF), cerebral metabolic rate (CMRO2) and intracranial pressure (ICP), absence of seizures, and good lower cranial nerve function and normal systemic homeostasis such as normotension (age-appropriate), normoxia, normothermia, and normal metabolic parameters are also candidates for early recovery.

Planned delayed recovery may be warranted for those requiring postoperative ventilation due to anticipated and inadvertent perioperative adverse events or in whom neurological and cardio-respiratory recovery is expected to occur over a prolonged timeframe. It is prudent to delay extubation following prolonged (>6 h) extensive surgery with major blood loss, fluid shifts, and hypothermia, or where a significant risk of cerebral ischemia is possible due to excessive retractor pressure or involvement of major blood vessels, and when airway edema is likely due to excessive neck flexion, as in sitting or prone position. Planned delayed recovery provides time for achieving cardiovascular, metabolic, and thermal stability, optimization of oxygenation and ventilation, and amelioration of edema associated with neural tissue handling.

37.8.2 Awake Versus Deep Extubation

Awake extubation is ideal in pediatric neurosurgery if accompanying surges in hemodynamic parameters can be minimized. This helps in avoiding unnecessary adverse airway events and should be considered in children with a difficult airway. It also ensures ability of the child to protect airway from secretions or obstruction as consciousness would have returned to preoperative status.

Deep extubation avoids agitation, coughing, hemodynamic activation, and consequent disturbance in the intracranial homeostasis. However, deep extubation might lead to loss of airway and respiratory insufficiency in a yet-to-be fully recovered child and potentially subject it to risk of hypoxia, hypercapnia, and pulmonary aspiration [14].

37.8.3 Postoperative ICU Versus Ward Care

Most children have a good recovery after neurosurgery, can be extubated in the operating room, and shifted to a ward with a facility for physiological monitoring. In children without significant pre-existing neurological or systemic physiological derangements, ward care is appropriate if surgery is minor and uneventful. However, vigilant monitoring at least in the initial 24 h is warranted as acute adverse events are known after intracranial surgery.

Few children need transfer to ICU after elective neurosurgery for invasive monitoring and mechanical ventilation. Reasons include poor preoperative neurological status, adverse perioperative event, prolonged surgery, or extensive neuronal handling. ICU stay permits longer, more frequent, and vigilant monitoring and care of these patients.

Rarely, transfer to ICU after initial shifting to the ward may be required to manage complications. Children with primitive neuroectodermal tumors and those undergoing repeat craniotomy are more likely to require transfer to ICU after initial admission to the ward [15]. A balanced approach and well-documented protocol help transfer patients between ICU and ward, when required.

Care in the pediatric ICU (PICU) involves close monitoring of cardiovascular, respiratory, and neurological function. The readiness of weaning from sedation, mechanical ventilation, hemodynamic support, and other measures such as anti-edema and antibiotic therapy should be assessed daily and tailored to the individual patient or as per PICU protocols.

37.9 Common Issues and Their Management During Recovery

Recovery and care in the postoperative period after neurosurgery require added vigilance in children. Systematic assessment of cardio-respiratory and neurological system, timely and appropriate administration of due medications and anticipation, prevention, and management of

potential complications are key components of perioperative care that should be continued during recovery and in the immediate postoperative period. The common postoperative issues after pediatric neurosurgery and their management are enumerated in Table 37.2 and discussed below.

Table 37.2 Common postoperative complications after pediatric neurosurgery

System	Complications
Cardiovascular	Brady- or tachycardia, arrhythmia, hypo- or hypertension, cardiac arrest
Respiratory	Desaturation, apnea, hypo- or hypercarbia, airway obstruction, laryngo- or bronchospasm, pulmonary aspiration, pulmonary edema
Neurological	Seizures, delayed or non-awakening, agitation, new-onset behavioral changes, neurological deficits, raised intra cranial pressure, pain
Miscellaneous	Hypo- or hyperthermia, dyselectrolytemia, hypo- or hyperglycemia, anemia, coagulation disorders

37.9.1 Unintended Delayed Recovery

One of the undesirable components of recovery from anesthesia after neurosurgery is delayed awakening. Recovery is termed as "delayed" when there is an unprecedented lag exceeding the expected time to awakening from anesthesia (usually 20–30 min), defined in the context of an otherwise uneventful procedure.

Several anesthetic, surgical, and patient factors contribute to delayed awakening after neurosurgery in children. The causes for delayed recovery, approach to diagnosis, and management options are shown in Fig. 37.4. Anesthetic causes include inappropriately timed or excessively dosed anesthetic drugs apart from the selection of anesthetic technique itself. Other intraoperative factors include unstable cardiovascular and respiratory status, acidosis, hypothermia, and glucose and electrolyte abnormalities. Surgical causes include stroke, operative or remote site hematoma, venous air embolism, cerebral edema, or pneumocephalus [16]. Non-

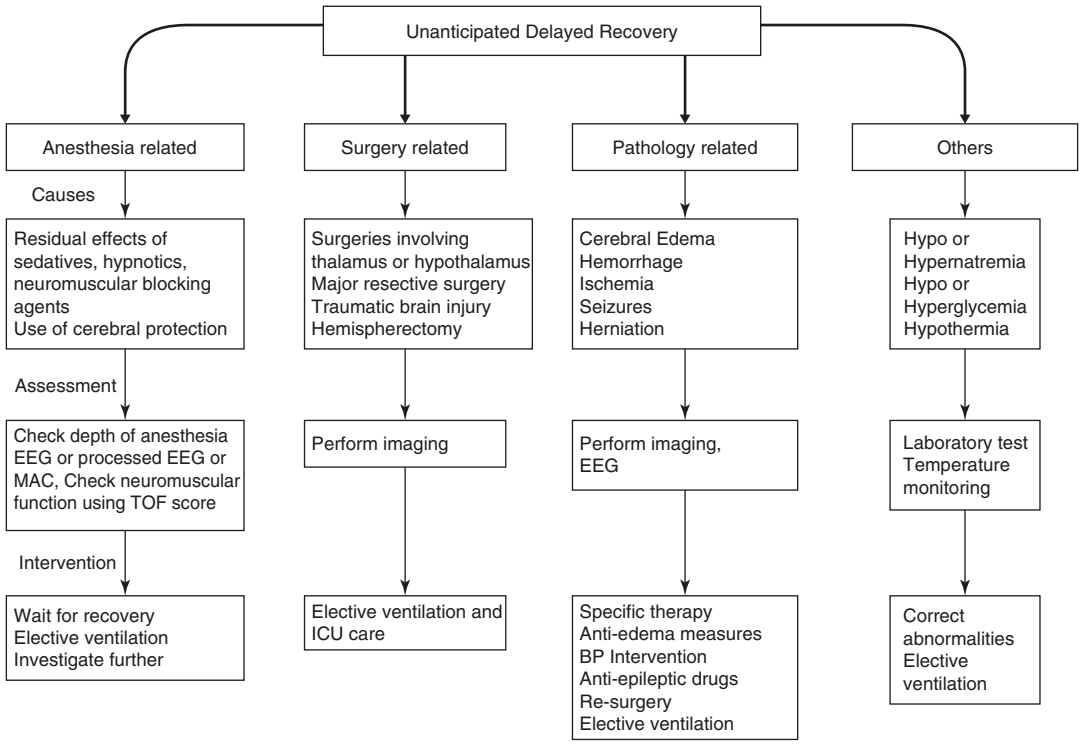

Fig. 37.4 Causes for delayed recovery, approach to diagnosis, and management options

awakening after anesthesia and bradycardia, hypertension, and irregular respiration have been reported from tension pneumocephalus following infratentorial surgery [17]. It is important to use age-appropriate minimum alveolar concentration (MAC) of volatile anesthetics during neurosurgery in children. Inappropriate MAC can result in under-dosing or over-dosing and affect recovery from anesthesia [18].

37.9.2 Emergence Agitation

This represents a constellation of myriad components, emergence delirium (ED), pain, discomfort, anxiety, and PONV, leading to excessive motor activity threatening both self-harm (removal of indwelling catheters, cannulas, and drain tubes) and a predicament for parents and attending healthcare workers. EA is mostly seen with sevoflurane and desflurane. Prophylactic use of fentanyl (1–2 μg/kg), clonidine (1–3 μg/kg), dexmedetomidine (0.1–0.25 μg/kg), or ketamine (0.25 mg/kg) [19] has shown to reduce EA.

37.9.3 Delirium

ED and postoperative delirium (POD) are a spectrum of postoperative cognitive dysfunction (POCD) with varied incidence depending on several factors. A simple behavior assessment scale, the Pediatric Anesthesia Emergence Delirium (PAED) scale, helps in the diagnosis of ED in children [20]. Predisposing factors include younger age, preoperative anxiety, perioperative electrolyte imbalance, volatile anesthetics, and intracranial surgery (mostly of the frontal region). The use of above mentioned drugs (fentanyl, clonidine, dexmedetomidine, ketamine) administered toward the end of surgery have shown to minimize ED and POD. However, these drugs can delay recovery and discharge from PACU. Apart from pharmacological interventions, ED can be better managed by the reunion of children with their parents [21].

37.9.4 Hemodynamic Complications

The most common hemodynamic changes during emergence and recovery after neurosurgery in children are tachycardia and hypertension. These are seen as a consequence of awakening from anesthesia and can also be a manifestation of pain. Age-appropriate BP targets must be established and maintained using antihypertensive drugs such as labetalol to avert breach of surgical hemostasis and cerebral hyperemic or hemorrhagic complications [22].

Hypotension is rare and is more likely due to reduced intravascular volume from inadequate fluid or blood administration during surgery. Fluid boluses and transfusion correct hypotension from these causes. Bradycardia may be a sign of intracranial hypertension, the cause of which should be ascertained and acted upon. It may be the only manifestation of skull pin-induced extradural hematoma [23]. Unexplained bradycardia should warrant immediate work-up for prompt diagnosis and management.

Brainstem surgeries can result in persistent hemodynamic perturbations, which can continue during recovery and in the postoperative period. Knowledge of the underlying pathophysiological process avoids unnecessary anxiety and overzealous correction of numerical parameters. The greater resting vagal tone in children renders them susceptible to trigemino-cardiac vagal reflex during craniosynostosis surgeries [24].

37.9.5 Respiratory Complications

Upper airway obstruction is a common problem in children after neurosurgery. Obesity, obstructive sleep apnea (OSA), prolonged surgery in the flexed neck position, and deep extubation predispose to airway obstruction. Manifestations include noisy breathing, tracheal tug, sternointercostal respiratory excursions, and desaturation. OSA is commonly seen in children with Cushingoid features, craniofacial anomalies, and craniosynostosis. Nursing in the lateral position with neck extension, triple airway maneuver (head-tilt, chin-lift, and jaw-thrust), and oral air-

way placement help maintain airway patency and relieve obstruction in most patients. Rarely, reintubation may be necessary. Unattended hypoxia can quickly worsen to cardiac arrest as children have a low functional residual capacity, which results in rapid desaturation.

Post-extubation stridor could be due to laryngeal edema from repeated or traumatic intubation or a snuggly fitting tracheal tube. It can restrict airflow across the narrow subglottic region in children. Nebulized adrenaline results in vasoconstriction and bronchodilation and improves symptoms in these children.

Laryngospasm is common in children during the perioperative period. Airway manipulation in hyper-reactive airway (from recent upper respiratory tract infection), noxious stimulus during lighter plane of anesthesia, and trickling of blood and secretions during extubation can precipitate laryngospasm. Removal of the irritant stimuli and oxygen administration with positive pressure usually help resolve this complication. Occasionally, propofol (0.8 mg/kg), succinylcholine (1 mg/kg) with atropine (0.02 mg/kg), and re-intubation may be required to curtail an unresolved laryngospasm [25].

Pulmonary edema can occur from respiratory obstruction due to high inspiratory negative intrathoracic pressure generated against an obstructed glottis. Measures to relieve obstruction and positive pressure ventilation help in the management of negative pressure pulmonary edema.

Respiratory insufficiency or apnea episodes are occasionally seen after posterior fossa surgeries, in those with neural tube defects with associated brainstem dysgenesis, or in preterm infants. Careful monitoring and reassessment of neuromuscular function are pre-requisites before further investigation. If opioid-associated respiratory depression is suspected, it should be reversed with intravenous naloxone 0.01 mg/kg (repeated every 2–3 min, if required), and pain is further managed with non-opioid analgesics.

37.9.6 Pain Management

Pain is common after neurosurgery, especially after infra-tentorial or spine surgery. Various scales have been used for its assessment in children. Multimodal analgesia should be provided to minimize postoperative pain and reduce side effects of analgesics. Loco-regional analgesia such as scalp block [26], incision and pin site local anesthetic infiltration for craniotomy, and epidural, caudal, and erector spinae plane block [27] for spine surgery provide pre-emptive analgesia which continues into the early postoperative period and facilitates pain-free recovery from anesthesia. Systemic drugs such as paracetamol, non-steroidal anti-inflammatory drugs, opioids, and co-analgesics (lignocaine, dexmedetomidine, and ketamine as infusion or oral gabapentinoids in older children) also help in preventing and managing postoperative pain. In older children, patient-controlled analgesia with opioids (fentanyl or morphine) can be practiced and is effective and safe [28]. Non-opioid analgesia is an attractive option in the adult neurosurgical population [29]. Similar benefits are likely in children and may be considered for pain-free recovery without opioid-related side effects.

37.9.7 Postoperative Nausea and Vomiting

PONV is a common complication after neurosurgery in children with a reported incidence of 24–66% [30, 31]. A higher incidence (73%) is observed in children undergoing posterior fossa surgery. Younger children and those receiving desflurane are more likely to develop PONV [32]. Other risk factors described in adults such as female gender, surgery for craniopharyngioma or involving cranial nerves and spine, prolonged surgical duration, and inhalational anesthesia could also contribute to PONV in children [33]. PONV results in discomfort and increased ICP and contributes to intracranial hyperemia and bleeding with adverse consequences. Prophylactic administration of ondansetron (0.1 mg/kg), or granisetron (10–80 μg/kg), minimizing opioid dose, and using intravenous anesthesia technique reduce PONV. Metoclopramide (0.25 mg/kg) and dexamethasone (0.15 mg/kg) can be used to treat PONV. However, perioperative steroids can lead to intestinal perforation, complicating the postoperative course [34].

37.9.8 Hypothermia

Hypothermia, defined as a core temperature less than 36 °C, is common in the perioperative period in children undergoing neurosurgery, with at least 50% developing it in the absence of active warming [35]. Greater body surface area to weight ratio, cold ambient temperature, inadequate warming, prolonged surgery, and large quantities of fluid administration predispose children to hypothermia [36]. Hypothermia results in shivering and increased oxygen consumption in the postoperative period. Treatment includes active warming, oxygen supplementation, and drugs such as pethidine (0.5 mg/kg), clonidine (1.5 μg/kg), and dexmedetomidine (0.5 μg/kg).

37.9.9 Seizures

Postoperative seizures in children could be a continuation of pre-existing seizures from intracranial pathology or de novo after surgery due to handling of the brain. All anti-epileptic drugs should be continued in the perioperative period, and additional doses may be administered when significant blood loss occurs to maintain their plasma levels. In children undergoing neurosurgery with no prior seizures, the incidence of perioperative seizure was 7.5%. Supra-tentorial tumor surgery, age < 2 years, and hyponatremia were associated with the occurrence of seizures [37]. Postoperative seizure occurrence was not related to brain incision, while hyponatremia significantly contributed to postoperative seizures in another study [38].

37.10 Specific Conditions and Postoperative Issues

The general principles of managing pediatric patients during the recovery phase mandate further specialized care that caters to the specific underlying primary neurosurgical pathology.

37.10.1 Tumor Surgery

Major surgery can result in hypothermia, massive blood loss, and significant fluid shifts with the requirement of continued ventilator support. The transfusion to body volume ratio can be high in children, with potential for complications such as life-threatening hyperkalemia, acidosis, and hypocalcemia [39]. Diffuse bleeding, hypotension, and brain bulge could be unusual manifestations of transfusion reaction [40]. Identifying the cause and correcting transfusion-associated complications should take precedence. A planned delay in recovery may be preferred.

Children undergoing infratentorial surgeries require vigilant monitoring as rapid decompensation can occur after handling the brainstem and lower cranial nerves. Surgeries close to the brainstem can cause edema or injury and contribute to apnea, vocal cord palsy with stridor, abnormal respiration, and hemodynamic disturbances.

Cerebellar mutism encompassing reduced speech, hypotonia, and ataxia is a rare transient postoperative complication commonly seen after 1 to 2 days of posterior fossa surgery [41]. It is not associated with loss of consciousness or cranial nerve dysfunction. It is thought to be due to vascular disturbances and damage to the dentato-thalamo-cortical pathway from manipulation of cerebellar region around the fourth ventricle [42].

Postoperative neurological deficit (POND) is a commonly encountered complication after pediatric neurosurgery. Monitoring of changes in the evoked potentials (motor, somato-sensory, brainstem auditory) can predict and prevent POND after cranial and spine surgeries [43].

Dysphagia is an under-recognized manifestation after posterior fossa surgery in children and can lead to complications such as pulmonary aspiration, pneumonia, airway interventions, and sepsis. Dysphagia is associated with younger age, aggressive tumors, and higher hospital resource utilization [44].

Craniotomies in atypical positions (sitting, lateral, or prone), an predispose to *glossal and pharyngeal edema* precluding early on-table extubation and possibility of postoperative airway obstruction. Peripheral nerve injuries are likely with prolonged surgeries in abnormal positions if adequate precautions and careful examination are not performed [45].

Children undergoing craniopharyngioma surgery are predisposed to metabolic, hemodynamic, and electrolyte disequilibrium. Delayed

recovery can occur from frontal lobe manipulation during surgery, electrolyte disturbance, or non-convulsive seizures. The pre-existing or surgery-associated hypothalamo-pituitary dysfunction can cause hypo- or hyperthermia and diabetes insipidus (DI) anytime during the perioperative period. Preoperative anticipation and preventive strategies contribute to the amelioration of the intensity of these changes during emergence. The incidence of DI can be as high as 70–90% and is diagnosed with serum sodium >150 mEq/L, serum osmolarity >300 mosm/kg, urine output >4 ml/kg/h, and urine osmolarity <300 mosm/kg. Management includes administration of hypotonic fluids such as 0.2% or 0.45% saline alone or with dextrose for both replacement and maintenance and vasopressin infusion at 0.5–1 mU/kg/min titrated to urine output of <2 ml/kg/h. The presence of disturbed thermoregulation and behavioral and memory disturbances often heralds unfavorable outcomes in these children [46–48].

37.10.2 Epilepsy and Functional Surgery

Most children with medically refractory seizures are evaluated and considered for surgical management. The common procedures performed include focal lesion resection, disconnective surgeries (hemispherotomy, corpus callosotomy), and vagal or direct brain stimulation. Antiepileptic medications, seizures, and disconnection surgeries can delay recovery. Acute postoperative seizures in children herald a poor prognosis; hence, intraoperative supplementation of anti-epileptic medication is warranted, especially if significant blood loss has occurred [49]. Older children can undergo awake surgery for the treatment of their seizure disorder. Recovery from sedation is better, and postoperative complications are less. However, apnea can occur, and constant vigilance is needed throughout the perioperative period [50]. Children undergoing hemispherotomy for refractory seizures can develop postoperative hyperthermia, which poses a diagnostic dilemma and requires unconventional management [51].

Children with severe dystonia undergo deep brain stimulation to manage their drug-resistant manifestations. The intraoperative electrical recording is important to place the stimulating electrode correctly. Titration of anesthetic agent with depth of anesthesia monitoring and appropriate selection of drugs not only helps in uneventful intraoperative management but also provides smooth recovery and postoperative course [52].

37.10.3 Neurovascular Surgery

Ischemic complications are common in children undergoing neurosurgery, especially for vascular pathologies. The most common neurovascular surgery in children is for moyamoya disease (MMD). Vascular bypass or encephalo-duro-arterio-myo-synangiosis (EDAMS) procedures are done to enhance CBF in MMD. These children are vulnerable to postoperative ischemic complications, especially from crying (due to shivering, pain, hunger, and parental separation), induced hyperventilation, and hypocapnia or hypotension. Predictors for postoperative ischemic complications in MMD are preoperative infarction, younger age, higher Suzuki grade, and posterior cerebral artery occlusion [53]. POND is common (13% incidence) and secondary to cerebral ischemia in children undergoing surgery for MMD. A prolonged hospital course is seen in younger children and those with longer anesthesia duration and POND [54]. Ensuring smooth, non-agitated, and pain-free recovery and postoperative period is important to prevent new-onset POND. Hence, adequate multimodal analgesia using scalp block and systemic drugs, temperature management, and early parental involvement are vital in these patients. In contrast, hypercapnia can induce cerebral steal phenomenon, worsening the CBF across the diseased blood vessels. Low-dose dexmedetomidine during extubation results in comfort, normocapnia, and absence of pain and ischemic complications [55].

The intracranial arterio-venous malformation is another indication for neurovascular surgery in children. A perioperative seizure is common and is associated with adverse outcomes. Seizure can

be detected by using electroencephalogram or cerebral oxygen monitoring as seizure increases oxygen extraction resulting in cerebral deoxygenation [56]. Management of seizures and pain and maintaining lower BP levels in the immediate postoperative period are important aspects of postoperative care to prevent hyperemia-related complications.

37.10.4 CSF Diversion Procedures

Surgeries for hydrocephalus include cerebrospinal fluid (CSF) diversion techniques such as endoscopic third ventriculostomy (ETV), external ventricular drain (EVD) placement, or ventriculo-peritoneal (VP) shunt surgery. These children do not present significant challenges as ICP reduces after the procedure, and recovery and postoperative process are generally smooth and uncomplicated. However, rarely, complications can occur such as inadvertent cerebral injury, pneumothorax, failure of technique, CSF over-drainage and its complications, and bowel perforation which require close monitoring and appropriate intervention. If CSF diversion is made for posterior fossa pathology, lower cranial nerve function should be considered in the decision-making regarding extubation and postoperative care.

37.10.5 Craniosynostosis

Cranial remodeling surgeries are commonly performed to repair craniosynostosis, complicating the airway, craniofacial growth, and cerebral homeostasis. Vigilant monitoring for signs of raised ICP consequent to cranial remodeling is desirable. If ICP is monitored during surgery, it should be continued in the postoperative period. Significant blood loss requiring massive blood transfusion can complicate postoperative course with hypothermia, hemodynamic imbalance, and delayed recovery. Syndromic association with co-existent airway compromise and cardio-respiratory involvement necessitates a careful evaluation of extubation and postoperative care [57].

37.10.6 Cranio-Vertebral Junction Anomalies

Corrective procedures for atlanto-axial dislocation, Arnold-Chiari malformation, and upper cervical spinal pathology involve proning and handling of the cervico-medullary junction and structures close to the patient's airway. After observation in the ICU, a planned delayed recovery should be considered, and extubation performed after confirmation of adequate spontaneous breathing. Syndromic associations (Down's syndrome and Klippel-Feil syndrome) can have congenital cardiac and airway anomalies that require careful consideration during recovery [58].

37.10.7 Spine Surgery

The postoperative course of corrected scoliosis can be complicated by neurological injury, massive blood transfusion, and multiple levels of instrumentation, necessitating the use of multimodal analgesia [59]. Co-existing muscular dystrophies or neuromuscular scoliosis may complicate pre-existing reduced forced vital capacity and congenital heart disease (CHD). These patients need mechanical ventilation before their pulmonary function improves to acceptable levels. Tracheostomy should be considered if longer course of mechanical ventilation is anticipated. Intravenous, interpleural, or epidural infusion of local anesthetic and/or opioids provides effective postoperative analgesia with minimal side effects [60]. Children with meningomyelocele and encephalocele often have associated non-neurological congenital malformations and defective temperature regulation [61]. These factors should be considered during extubation and recovery along with careful positioning to

avoid pressure on the operative site after surgery. Caring in the lateral position and strict aseptic precautions avoid the risk of meningitis in the postoperative period.

37.10.8 Brain Trauma Surgery

Pediatric trauma resulting in intracranial hematoma or contusion with significant midline shift may necessitate emergent surgery. Compromised intracranial compliance and disturbed cerebral autoregulation are common after surgery, contributing to cerebral ischemia or postoperative edema. The intraoperative goals of systemic and cerebral homeostasis should be continued in the postoperative period. Prevention of secondary brain injury is necessary by avoiding and treating hypotension, hypoxia, hypoglycemia, hyperglycemia, and hyperthermia.

37.10.9 Neuroendoscopy

Endoscopic choroid plexus coagulation and ETV are performed for managing obstructive hydrocephalus. Inadvertent injury to the pituitary gland, hypothalamus, or fornix and manipulation of third ventricular floor can predispose to cranial nerve palsies, delayed recovery, hematoma from injured ependymal veins, CSF leak, electrolyte imbalance, memory disturbance, hypothermia, cognitive dysfunction, cardiac arrhythmias, and neurogenic pulmonary edema [62].

37.10.10 Surgery for Neuro-infections

The incidence of perioperative complications is high in children with cyanotic CHD undergoing brain abscess surgery. Avoiding tachycardia in the perioperative period is important in these children to minimize complications [63]. Position-related desaturation should be borne in mind after anesthesia for brain abscess surgery in children with cyanotic CHD. Careful monitoring should be continued in the postoperative period [64].

37.10.11 Neuroradiologic Interventions

Most diagnostic imaging procedures are safely performed under sedation with either dexmedetomidine or propofol infusion. Post-procedural recovery is smooth with both techniques, and these patients can be discharged the same day without any adverse effects from procedure or anesthesia [65]. Rarely, in syndromic patients where respiratory adverse events are known, such as Joubert syndrome, the selection of appropriate anesthetic techniques helps smooth recovery and avoidance of peri-procedural complications [66].

Children undergoing interventional neuroradiological procedures, however, require general anesthesia. Safe and smooth emergence should be aimed, as done after surgery. Neurological status, hypothermia, contrast or protamine reactions, and puncture site hematoma should be carefully monitored after the procedure. Endovascular treatment is commonly performed for neurovascular pathologies such as vein of Galen malformation (VOGM) or AVMs in children. Cerebral oxygen monitoring helps detect peri-procedural complications and predicts the success of the neurointervention [67]. Post-procedural recovery and management are crucial in preventing complications in these children. This is especially true after embolization of VoGM where high-output congestive cardiac failure and pulmonary hypertension may require close monitoring and management in pediatric neuro-ICU. Post-embolization complications are high (38%) and include seizures, thrombosis, infarction, hydrocephalus, cerebral hyperperfusion with consequent hemorrhage and edema, and cardiac failure [68]. BP control with antihypertensive drugs, sedation and reduction in pulmonary vascular resistance with morphine, and careful fluid and temperature management should be considered in the post-procedural period [69].

37.10.12 Neurosurgery in Children with Syndromic Associations

Children with neurosurgical pathologies are likely to be associated with syndromes, making their perioperative management, including recovery from anesthesia, challenging. Children with Down's syndrome undergo neurosurgical interventions for atlanto-axial instability, MMD, stroke, and seizure disorders. These children can pose problems during recovery and in the postoperative period due to interplay between anesthesia, neurosurgical pathology, intracranial surgery, and inherent multisystem involvement [70]. Pediatric patients with Marfan's syndrome may require neurosurgical intervention for the management of cerebrospinal leak or sacral meningocele. Monitoring for adverse respiratory and cardiac events is needed in the postoperative period [71]. Children with Crouzon's and Apert's syndrome who present for surgery for craniosynostosis correction often have associated cardiac and airway anomalies and require special attention during recovery and postoperative phase [72, 73]. Multisystem involvement, significant blood loss, and airway difficulty are common in children with Klippel-Trenaunay syndrome [74]. These factors should be considered during perioperative care and recovery from anesthesia.

37.11 Discharge from PACU

Specific criteria for discharge of children from PACU after neurosurgery are unavailable. A period of 30 min of observation in the PACU allows reasonable time for assessment and stabilization of physiological parameters and is desirable after extubation. Stable cardio-respiratory parameters, return of protective airway reflexes, recovery of consciousness to preoperative levels, control of pain and PONV, and absence of active surgical bleeding are essential before children are discharged to the ward. Parental presence in the PACU may be encouraged to reduce crying and negative behavior [75, 76].

37.12 Conclusion

Recovery from anesthesia and postoperative management requires special considerations in children undergoing neurosurgery. Preoperative preparation and intraoperative management also affect recovery. After anesthesia, good recovery entails planning, preparation, and performance of safe and swift extubation as soon as possible. While early and smooth recovery is the norm in pediatric neurosurgical patients, planned delayed extubation and recovery may be desirable in certain situations. Both neurosurgical and pediatric considerations determine postoperative care after neurosurgery in children.

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38 Postoperative Pain Management of Pediatric Neurosurgical Patients

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Key Points

- Pain after neurosurgery usually results from skin incision and meningeal irritation after craniotomies and muscle dissection and cerebrospinal fluid loss after posterior cervical and spine surgeries.
- Balanced multimodal strategies including opioids, non-opioid adjuncts such as muscle relaxants, and opioid-sparing medications such as acetaminophen and non-pharmacological approaches need to be accounted for individual variability and surgery specific requirements.
- Monitoring, especially for sedation and respiratory depression, is important when using opioids through patient or proxy-controlled analgesia as it can confound neurological assessments.
- Physicians should pay attention to the development of persistent post-craniotomy pain, which has a reported incidence of 23–80% after posterior fossa procedures.
- Future studies are needed to optimize pediatric-specific dosing regimens for tailored safe and effective postoperative analgesia to minimize the use of opioids wherever possible.

38.1 Introduction

Healthcare providers commonly underestimate pain after pediatric neurosurgery [1, 2]. The notion that the brain parenchyma lacks nociception shaped the impression that post-craniotomy pain was minimal [3]. In particular, young children are thought not to experience or recall noxious stimuli to the same extent as adults do [4]. Furthermore, pain assessment in children who are unable to communicate appropriately can be difficult, especially for providers not experienced in pediatric care. In addition, out of concern for the risks associated with analgesics after neurosurgery, providers tend to avoid pursuing therapies. The administration of opioids and other drugs with side effects, including sedation, vomiting, and miosis, can confound the postoperative neurologic exam. Hypercapnia resulting from respiratory depression can worsen intracranial pressure [5]. Finally, NSAIDs have generally been avoided due to platelet dysfunction consequences and increased intracranial bleeding [6].

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However, recent evidence suggests a significant incidence of severe pain and inadequate pain relief after neurosurgery [1, 2, 7]. Poorly managed postoperative pain, in general, is associated with adverse outcomes [5]. Several well-recognized hospitals now routinely incorporate multimodal therapy when managing pain after pediatric neurosurgery, safely achieving low postoperative pain scores [8].

Consequently, the perception and management of pediatric postoperative neurosurgical pain are changing. This chapter reviews the current understanding of pain after pediatric neurosurgery and pharmacologic and non-pharmacologic therapies. It also discusses the approach to pain assessment in children to help guide providers who do not routinely care for children.

38.2 Pain Pathophysiology in Neurosurgery

Multiple nerves innervate the scalp (Fig. 38.1). The ophthalmic division of the trigeminal nerve innervates the forehead and anterior scalp. Its maxillary and mandibular divisions innervate the skin anterior to the ear. The greater occipital nerve mediates sensation to the posterior scalp, vertex, and skin over the ear. The lesser occipital nerve innervates the dermatome posterior to the ear. Finally, it is thought that the third occipital nerve may provide sensation to the posterior aspect of the scalp [9, 10].

The supratentorial dura mater receives branches from each of the three divisions of the trigeminal nerve. Innervation of the infratentorial

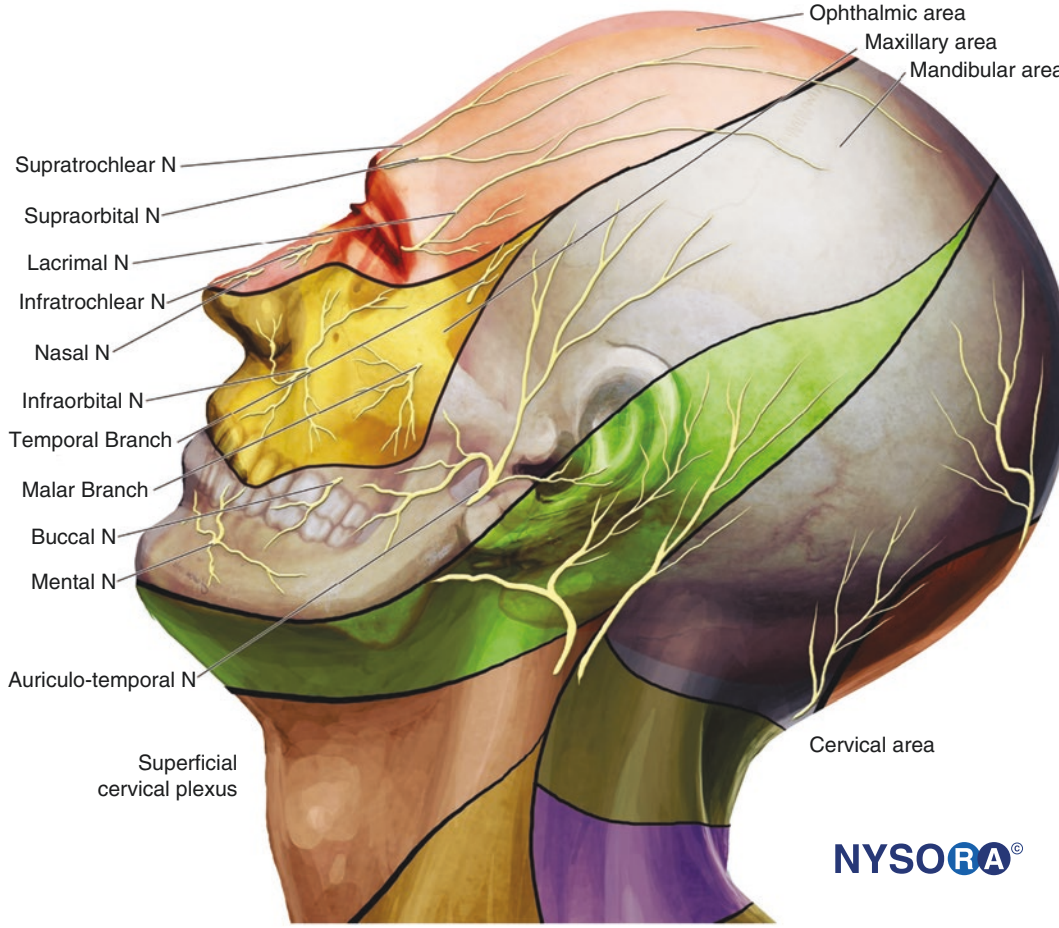

Fig. 38.1 Innervation of the scalp. *Source*: NYSORA.com

Table 38.1 FLACC pain scale [16]

Behavior	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting, back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams, sobs, frequent complaints
Consolability	Content, relaxed	Reassured by touching, hugging, or being talked to, distractible	Difficult to console or comfort

dura mater involves contributions from the hypoglossal nerve, vagus nerve, and first three cervical nerves [11]. When the intracranial dura mater is stimulated, pain is induced and referred to as the ophthalmic and mandibular division territories. Stimulation of the pia mater was recently shown to produce referred pain in the ophthalmic division [3].

Surgical trauma to overlying soft tissue and peri-cranial muscles accounts for a significant amount of pain. Suboccipital and subtemporal craniotomies involve resecting posterior cervical, occipitalis, and temporalis muscles, resulting in higher incidence of muscle spasm than other approaches [9]. Meningeal irritation from bone dust can also contribute to post-craniotomy pain [5]. Finally, cerebrospinal fluid leakage can lead to loss of cushioning effect on the brain parenchyma and stretching of the meninges and cranial nerves resulting in headaches [12]. A pounding or pulsating sensation, similar to that of tension headaches, is a common finding in post-craniotomy pain [13]. The headache is often felt superficial, suggesting a somatic origin, likely caused by surgical trauma to overlying soft tissue and peri-cranial muscle [1].

After spinal surgery, sources of pain may include the vertebrae and intervertebral disks, nerve roots and dura, and ligaments and muscles. These structures are innervated by the dorsal rami of spinal nerves. Pain may be due to mechanical irritation, compression, inflammation, neuropathic, or muscle spasms. The severity of postoperative pain correlates with the degree of surgical dissection [14].

38.3 Pain Assessment in Children

Children may be unable to self-report pain if they are too young, too distressed, or developmentally delayed with cognitive and communicative deficits. Assessment of postoperative pain requires observation of a child's behavior or the use of pictorial scales. For assessing postoperative pain in the hospital in children and adolescents aged 3–18 years, the *Face, Legs, Arms, Cry, Consolability (FLACC) scale* is recommended (Table 38.1) [15, 16]. The scale is widely used in children aged 2 months to 18 years. However, it has been consistently shown that unlike parents, healthcare professionals frequently underestimate pain in children and pain scores are lower in developmentally delayed children [17]. Additionally, for postoperative pain at home, the Parents' Postoperative Pain Measure (PPPM) is recommended due to high reliability and consistency. Fifteen items are scored 0 or 1, and it has a low burden [15]. For older and normally developed children (7–17 years), the Numerical Rating Scale (NRS) for pain intensity is an appropriate and validated pain indicator [18].

38.4 Multimodal Analgesia After Neurosurgery/Spine Surgery

Multimodal analgesia involves utilizing various medications, techniques, and non-pharmacologic therapies that differ in their sites and mechanisms throughout the nervous system. Multimodal therapy results in additive or synergistic effects, providing more effective pain relief

than single-modality interventions [19]. Multimodal analgesia can potentially minimize adverse events by reducing opioid requirements as well [20, 21]. Clinicians should offer multimodal analgesia for managing postoperative pain in children and adults. Providers must recognize that multiple potential combinations are possible and appropriate, considering the surgical procedure, patient preference, and individual factors [19]. With the recent emphasis on opioid minimization and enhanced recovery after surgery (ERAS) protocols, especially for spine surgeries, multimodal analgesia (MMA) regimens are popular [22, 23] and cost-effective [24, 25]. It is imperative to understand the indications, risks, and benefits of the different components of MMA regimens to further create new evidence-based protocols.

It is important to appreciate that opioids still have the primary role in postoperative analgesia. Their use will be discussed first, followed by the different components of MMA.

38.4.1 Opioids

Opioids, in general, act mainly on the mu-receptors to mediate analgesia. However, each opioid acts at multiple opioid receptors with different affinities, yielding different clinical effects [26]. Opioids that are commonly administered in the immediate perioperative period include intravenous (IV) fentanyl, hydromorphone, and morphine. These are given either as-needed (pro re nata [PRN]) or through patient-controlled analgesia (PCA) device, and it remains unclear if either method is safer or more effective than the other [4]. Despite using different opioid delivery methods among major institutions such as PRN, PCA, or nurse-controlled analgesia (NCA), the same degree of pain relief and parental satisfaction can be achieved [8]. The doses commonly administered are outlined in Table 38.2.

38.4.2 Patient-Controlled Analgesia

Patient-controlled analgesia (PCA) provides a mechanism for self-titrating the opioids providing superior pain control and patient satisfaction [27]. PCA offers superior pain control and improved patient satisfaction for patients undergoing complex spine surgeries, posterior fossa surgeries, and supratentorial intracranial surgeries without any increase in opioid-related

Table 38.2 Commonly used analgesic drugs and dosage intervals [43, 65]

Drugs	Oral	Intravenous
Oxycodone	0.1 mg/kg Q3–4 h	N/A
Morphine	0.3 mg/kg Q4–6 h	0.1 mg/kg Q2 h
Hydromorphone	0.05 mg/kg Q4–6 h	5–10 μg/kg Q4–6 h
Fentanyl	N/A	1–2 μg/kg
Methadone	0.1–0.2 mg/kg Q12–24 h	0.1 mg/kg Q12–24 h
Acetaminophen	10–15 mg/kg Q6–8 h, max dose 75 mg/kg	10–15 mg/kg Q6–8 h, max dose 75 mg/kg
Ketorolac	N/A	0.5 mg/kg (max dose 15 mg) Q6–8 h
Dexamethasone		0.1–1 mg/kg Q6–8 h
Diazepam	0.05–0.1 mg/kg Q4–6 h (max 5 mg/dose)	0.05–0.1 mg/kg Q4–6 h (max 5 mg/dose)
Methocarbamol	15 mg/kg Q8 h	15 mg/kg Q8 h
Baclofen	2.5–5 mg Q6–8 h	
Gabapentin	3–5 mg/kg Q8 h	N/A
Dexmedetomidine	N/A	0.5–2 μg/kg bolus; 0.2–0.7 μg/kg infusion

Patient-controlled analgesia (PCA) dosing guidelines				
Drug	PCA dose	Lockout time interval	Continuous infusion rate	Breakthrough pain loading dose
Morphine	20 μg/kg	7 min for patient-controlled and 10–15 min for parent/nurse controlled PCA	0–20 μg/kg/h	50 μg/kg q4–6 h
Hydromorphone	4–5 μg/kg		0–3 μg/kg/h	10 μg/kg q4–6 h
Fentanyl	0.25 μg/kg		0–0.15 μg/kg/h	0.5–1 μg/kg/h

Table 38.3 Treatment of opioid side effects [4]

Drug	Indication	Route	Dose
Ondansetron	Nausea/emesis	IV/PO	0.15 mg/kg
Diphenhydramine	Itching/nausea	IV/PO	0.5–1 mg/kg
Hydroxyzine	Itching	PO	0.25–0.5 mg/kg (oral)
Nalbuphine	Itching/urinary retention	IV	0.01–0.02 mg/kg every 4 h
Naloxone [34]	Over-sedation, itching, respiratory depression	IV/IM	1–2 μg/kg (for over-sedation); 10–20 μg/kg (for life-threatening respiratory depression); 0.25 μg/kg/h IV infusion (itching)

adverse events [28, 29]. Developmentally normal 6–7-year-old children will be able to associate pain relief with pressing a button when explained. In children, less than 6 years of age or with developmental delay, either nurse-controlled analgesia (NCA) or nurse plus parent-controlled analgesia (NCA + P) with longer bolus intervals can be utilized as an alternative to PRN bolus regimens. Basic PCA setup with drugs and dosages are described in Table 38.2. Typically, morphine PCA is utilized at the rate of 0.01–0.03 mg/kg intermittent boluses at the interval of 7–10 min. For NCA, the interval limit should be set at longer intervals of 10–15 min. The alternatives to morphine include hydromorphone, fentanyl, and butorphanol if contraindication or side effects for morphine exist.

When a child can tolerate oral medications, oxycodone is commonly prescribed. Unlike codeine, oxycodone is not a prodrug and, therefore, not subject to variable morphine production due to CYP450 2D6 (CYP2D6) isoenzyme inter-patient variability [30]. Weight-based doses and dosing intervals for a selection of opioids are mentioned in Table 38.2.

Common side effects of opioids include constipation, itching, nausea, and vomiting, some of which can be especially distressing in children. Adverse effects of opioid analgesia include sedation and respiratory depression. These clinical signs may be mistaken for or contribute to increased intracranial pressure, respectively, during the postoperative period [31]. While the incidence of opioid-related adverse events in hospitalized children is low (0.11–0.41%), these risks must be recognized as they can increase postoperative morbidity [32]. Risk factors in hospitalized children include the age of less than 1 year, both obesity and being underweight, and a history of obstructive sleep apnea, prematurity, and developmental delay [33]. Exercising caution with opioid administration is highly stressed in an attempt to minimize complications. Titration to the individual response after opioid administration is essential due to variable pharmacokinetics, pharmacodynamics, and pharmacogenomic factors [32]. The dosing of agents prescribed to treat opioid side effects is described in Table 38.3. One must be cognizant of the sedating effects of diphenhydramine and hydroxyzine [4]. Nalbuphine, an opioid agonist-antagonist, can be used for pruritus while also providing a degree of pain relief. However, its ceiling analgesic effect makes its use for pain relief difficult for moderate to severe pain [30]. Naloxone is a competitive opioid antagonist used mainly to reverse opioid-induced respiratory depression or sedation [34].

The types of opioids used intraoperatively can impact postoperative pain. Remifentanil is a frequently used opioid during spine surgery as it does not interfere with neuromonitoring and its short duration of action [35]. However, it may increase postoperative opioid requirements due to acute opioid tolerance in surgeries such as pediatric scoliosis surgery, where analgesic requirements generally exceed those for other procedures [36]. Methadone is a mu-opioid agonist and an N-methyl-D-aspartate (NMDA) receptor antagonist [37]. It reduces pain scores and opioid consumption after major spine surgery. In children undergoing spine surgery, 0.25 mg/kg methadone IV before surgical incision followed by 0.1–0.15 mg/kg/h for 4 h was deemed to ensure adequate plasma concentrations [38].

38.4.3 Acetaminophen

Acetaminophen is a ubiquitous non-opioid analgesic in pediatric practice. Its central analgesic effect is mediated through the activation of descending serotonergic pathways [39]. Proposed primary mechanisms of action include COX-3 enzyme inhibition and acting as a cannabinoid agonist and NMDA antagonist in the spinal cord [40]. It has demonstrated opioid-sparing potential across numerous studies [41]. Oral, IV, and rectal formulations are available [42]. Acetaminophen has an excellent safety profile. Weight-based dosing is adjusted for the child's age to minimize hepatic toxicity. Regardless of the route of delivery, the maximum daily dosing is 75 mg/kg [43].

Regarding the route of delivery, the IV form is associated with higher Cmax concentrations and better analgesia than the oral form [44]. In adolescents undergoing spine surgery, IV acetaminophen decreases postoperative opioid consumption and, with fewer opioid-related side effects, improves oral intake. It may reduce the duration of hospital stays. Rectal bioavailability tends to be relatively low and variable [45].

38.4.4 Non-steroidal Anti-inflammatory Drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) mediate analgesia through COX-2 inhibition [46]. While their use demonstrates an opioid-sparing effect and decreases PONV during the postoperative period in children [47], the literature on NSAID use after pediatric intracranial surgery is sparse. A meta-analysis demonstrated reduced postoperative pain up to 24 h after brain surgery in adults when using NSAIDs [48]. However, NSAIDs have been avoided after intracranial surgery due to COX-1 enzyme-mediated platelet dysfunction [49]. Even small amounts of bleeding can cause mass effect and compression in specific neurosurgical procedures [4]. Of the NSAIDs commonly used, ibuprofen has demonstrated minimal effect on platelet function and has been advocated for use after neurosurgery in children [6, 50].

The use of COX-2 selective inhibitors, devoid of antiplatelet effects, and risk of postoperative bleeding have been suggested [5]. While parecoxib administration has reduced opioid consumption after tonsillectomy in children, the literature lacks studies focusing on pediatric neurosurgery [51]. Furthermore, parecoxib administration at dural closure after craniotomy in adults failed to show a clinical benefit [52]. Finally, NSAIDs have decreased postoperative opioid consumption in posterior spine fusion surgery without demonstrating increased bleeding [35]. Thus, it appears that short-term exposure to NSAIDs, including low-dose ketorolac (<110 mg/day), is not associated with an increased incidence of nonunion after spinal fusion [53]. The conventional use of ketorolac 0.5 mg/kg/dose IV every 6 h for a total of six doses was shown to reduce pain scores and morphine consumption and improve activity on postoperative days 1 and 2 after spine fusion [54].

38.4.5 Antidepressants

Antidepressants may provide postoperative analgesia in neurosurgery by relieving neuropathic pain. This includes the tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin and norepinephrine reuptake inhibitors (SNRIs). Examples of drugs used include amitriptyline, venlafaxine, and duloxetine. In addition to neuropathic pain, treating any concomitant depression can improve patients' perception of pain [55]. The evidence for the use of an antidepressant in postoperative pain is limited [56]. High-quality studies need to be conducted to assess their clinical efficacy definitively.

Furthermore, antidepressants can have multiple adverse effects. SSRIs are associated with increased perioperative bleeding [57]. Starting postoperative amitriptyline can cause increased sedation. Finally, many of the antidepressants are known to cause serotonin syndrome [30].

38.4.6 Gabapentinoids

Gabapentin and pregabalin are the most common gabapentinoids used in pain management. Both

bind to presynaptic voltage-gated calcium channels, leading to decreased calcium influx and ultimately inhibit the neurotransmitter release [5]. They have been used to treat complex regional pain syndrome, diabetic neuropathy, and postherpetic neuralgia [58]. Many studies in adults demonstrate reduced postoperative pain with perioperative gabapentin [5]. Preoperative gabapentin can decrease postoperative opioid consumption in adolescents, but pediatric studies are few in neurosurgery [4]. These drugs can contribute to increased postoperative sedation. Studies in children undergoing spine fusion show a positive impact [59–61]; however, a meta-analysis in adults did not support the use of preoperative gabapentinoids [62]. Pregabalin's impact on postoperative pediatric pain remains unclear, with studies showing conflicting results on postoperative pain or opioid consumption after scoliosis surgery in adolescents [63, 64]. When used, gabapentin is started preoperatively and given for 5 days as 10–15 mg/kg per day divided every 8 h for children [65].

38.4.7 Muscle Relaxants

There are many muscle relaxants with different mechanisms of action. Commonly used benzodiazepines include lorazepam and diazepam. Non-benzodiazepine muscle relaxants include baclofen, cyclobenzaprine, and methocarbamol. Muscle relaxants may help alleviate muscle spasms related to manipulating the peri-cranial muscles and may be the mainstay of analgesia after posterior fossa decompression and occipital craniotomies. However, sedation is a potential side effect. Optimal dosing for these drugs has not been investigated [4].

38.4.8 Alpha-2 Agonists

Commonly used alpha-2 agonists in pain management are clonidine, tizanidine, and dexmedetomidine. Alpha-2 receptors can be found in the central nervous system, including the dorsal horn and the locus ceruleus. Alpha-2 receptor activation leads to reduced neural firing by decreasing calcium influx and reduced norepinephrine release. Less activity in the ascending noradrenergic pathways and reduced substance P formation in the spinal cord result in sedation and analgesia. Because these drugs bind to alpha-1 receptors, bradycardia and hypotension may develop [66].

Clonidine improves postoperative pain in children when given before surgery at a dose of 4 μg/kg per os (PO) [67]. Tizanidine has a shorter duration of action and lesser hemodynamic changes [66]. Research into tizanidine's utility in pediatric postoperative pain is lacking. Dexmedetomidine is highly selective for alpha-2 receptors. Both intraoperative boluses (0.3–2.0 μg/kg) and infusions (0.2–0.7 μg/kg/h) reduce emergence delirium, PONV, and, after certain outpatient surgeries, postoperative opioid consumption [65]. In neurosurgery patients in the perioperative setting, it also demonstrated reduced pain scores and perioperative opioid consumption [68]. With any alpha-2 agonist, postoperative sedation can be a possible side effect.

38.4.9 Corticosteroids

Corticosteroids inhibit the synthesis and release of proinflammatory mediators. Corticosteroids have been shown to reduce postoperative pain and opioid consumption, as well as reduce PONV and hospitalization [4, 69]. Single intraoperative administration of dexamethasone ranging from 0.15 to 1.0 mg/kg has been shown to reduce postoperative pain in children undergoing tonsillectomy [70]. Further studies are needed to determine the optimal dosing for postoperative pain relief. For the antiemetic effect, dexamethasone is given at 0.1 mg/kg doses in children [43]. From a surgical perspective, it reduces intracranial edema after neurosurgery. It is routinely given after intracranial surgery and may help reduce postoperative pain as well [4].

38.4.10 NMDA Antagonists

The N-methyl-D-aspartate (NMDA) receptors play a role in mediating windup, tolerance, and opioid-induced hyperalgesia [71]. NMDA receptor antagonists reduce opioid tolerance and reduce central hypersensitivity [5, 71]. Methadone, in particular, offers long-lasting analgesia even after a single dose and reduces postoperative opioid consumption and pain scores in comparison to other opioids [72]. As methadone can increase the QT interval, a screening electrocardiogram before administration is recommended to evaluate the interval. Regular electrocardiograms must be performed if treatment is continued postoperatively. The recommended pediatric methadone dose is 0.1 mg/kg [43].

Ketamine has multiple binding sites, but the NMDA receptor is the primary site of action. Its psychotropic effects preclude its use in intracranial surgery. Furthermore, several studies investigating perioperative ketamine infusions in children for spine fusion failed to demonstrate an opioid-sparing effect [73, 74]. However, scientific societies on pain in the United States have established guidelines for perioperative use of ketamine and recommend a low-dose IV ketamine bolus with a maximum dose of 0.35 mg/kg followed by a subanesthetic infusion of 0.15 to 1 mg/kg/h titrated to the lowest effective dose [75].

38.4.11 Non-pharmacologic Therapy

There are numerous non-pharmacologic therapies aimed to reduce acute postoperative pain. Behavioral interventions commonly include distraction, play, cognitive-behavioral therapy (CBT), and active relaxation training. Non-behavioral interventions include acupuncture, massage, and music therapies [76].

Many studies show reduced postoperative pediatric pain scores from non-pharmacological therapy [77], likely through the release of endorphins. Acupuncture therapy has even demonstrated therapeutic benefit in infants. Furthermore, when a pilot pediatric inpatient acupuncture program was incorporated into managing various painful conditions, both chronic and acute, it was met with positive feedback and high demand from patients and families, suggesting an appropriate use for pediatric pain [78].

CBT adheres to the principle that thoughts, emotions, and behaviors are intimately connected and that one's perception has a significant impact on behavioral, physiological, and emotional responses. CBT has an established role in managing chronic pain in children and adolescents [79]. Overall, more studies on behavioral therapies and acute postoperative pediatric pain, including neurosurgical patients, are needed.

38.4.12 Nerve Blocks

Utilizing regional anesthetic techniques in children when applicable is strongly encouraged as a component of multimodal analgesia to reduce postoperative opioid requirements [19]. Local anesthetics reversibly block the conduction of neural impulses by acting on sodium channels and preventing the passage of ions and, subsequently, the generation of the action potential [4]. Different scalp blocks, including the supraorbital, greater, and lesser occipital nerve blocks, have utility in various procedures, depending on the location of the incision [5]. Even skin infiltration of local anesthetic before incision reduces postoperative opioid requirements [80]. These blocks have demonstrated efficacy in procedures such as craniosynostosis surgery, craniotomies, and scoliosis surgery (erector spinae block) [80–82]. A detailed description of individual nerve blocks is discussed elsewhere in this book.

38.4.13 Preemptive Analgesia

Preemptive analgesia primarily refers to the initiation of antinociceptive therapy before the onset of painful stimuli with a goal of preventing central sensitization and central hyperexcitation of

the pain pathways and the central nervous system. Fentanyl by continuous infusion during neurosurgical procedures has been shown to be effective in minimizing postoperative analgesic requirements in pediatric patients [83]. Preemptive analgesia with preoperative oral NSAID, supraorbital and infraorbital perineural blockade, and local anesthetic infiltration along the incision improves pain scores and reduces postoperative analgesic requirement in frontotemporal craniotomy [84]. An acceptable regimen would include: (1) preoperative oral acetaminophen, pre-incision scalp nerve blocks, or local anesthetic infiltration based on the location of the incision; (2) an intraoperative infusion of a short-acting opioid (fentanyl or remifentanil) to ensure analgesia during surgery; and (3) scheduled IV acetaminophen along with intermittent PRN bolus doses of long-acting narcotic either by PCA or NCA to minimize the postoperative onset of inflammatory pain.

38.4.14 Special Considerations

Patient-related and surgery-related factors should be taken into consideration while managing postoperative pain in children. For example, while children undergoing certain surgeries such as posterior fossa decompression are associated with nausea and muscle tightness, they especially benefit from muscle relaxants and less from opioids. Also, anxious children may benefit from benzodiazepines and/or dexmedetomidine infusions, especially after laminectomies for tethered cord repair, where surgical concerns may dictate that they stay supine for up to 72 h after surgery. Continuous monitoring of oxygen saturation, respiratory rate, and end-tidal carbon dioxide (using nasal capnometry) has been recommended for safety while using opioid PCA for all patients. It may especially benefit children undergoing neurosurgery where there is an increased risk of subsequent elevation in ICP (with respiratory depression) and pupillary size changes secondary to overzealous use of opioids [85, 86].

38.5 Chronic Postsurgical Pain and Persistent Post-craniotomy Pain

Chronic postsurgical pain (CPSP) is defined as pain lasting longer than 3 months after surgery, which is localized or referred in relation to the surgical area; the other possible causes of pain are excluded [87, 88]. Based on the same criteria, persistent post-craniotomy headache (PPCH) has been defined by the International Classification for Headache Disorders (ICHD-3) as a headache with onset within 7 days of a craniotomy and lasts longer than 3 months duration without any other causes for the headache [89].

The incidence of post-craniotomy pain varies widely based on the location and pathology. In general, posterior fossa procedures and acoustic neuroma excision surgeries were reported to have a higher risk of developing persistent post-craniotomy pain with a reported incidence ranging between 23 and 80%. Supratentorial surgeries were reported to have 6–12% incidence of chronic headache after 2–12 months after surgery.

Preoperative pain, anxiety, and surgical duration may increase the risk of developing chronic pain [90]. Also, pain catastrophizing, sleep disturbances [91], and depression [92, 93] play a role in shaping maladaptive pain coping responses and influence the development of CPSP. It is important to identify and address the preoperative risk factors to minimize the risk of CPSP.

Modifications in surgical techniques could help reduce the risk of persistent post-craniotomy pain, including performing a craniotomy instead of a craniectomy when possible, replacement of the bone flap at the end of the surgery, duraplasty rather than direct dural closure to prevent tension on the dura mater, avoidance of fibrin glue, and excessive drilling of the posterior auditory canal to minimize the risk of aseptic meningitis [9].

The most common presenting complaint could be chronic tension headaches from pericranial muscle tension, intermittent migraine headache, or cervicogenic headache due to positioning during surgery in patients undergoing posterior

fossa surgery with underlying degenerative disk disease. Excessive CSF leak can cause orthostatic headaches, and the overuse of analgesics can lead to a rebound headache.

Chronic pain could lead to restrictions in daily activities and increased healthcare service utilization and affects sleep, appetite, and school attendance [94]. It increases the risk of anxiety, depression, and somatic complaints both in the patients and the parents [95]. CPSP leads to significant functional disability, poor quality of life [96, 97], loss of school days, and increased healthcare costs.

Treatment is based on the type and etiology of the pain and includes both non-pharmacological and pharmacological treatments. Non-pharmacological methods such as physiotherapy, supportive neck collars, acupuncture, TENS, cryotherapy, radiofrequency ablation, and cognitive behavior therapy can be useful adjuvants.

Pharmacological treatments include analgesics such as acetaminophen, NSAIDs, and mild opioids. Topical analgesics such as capsaicin can be used over painful scar tissues for symptomatic relief. Trigger point injections with local anesthetics and long-acting particulate steroids can be useful in cervicogenic headaches. Botox (botulinum toxin A) injections can provide short-term relief for pain secondary to increased muscle tension. Gabapentin is useful in neuropathic pain, including associated hyperalgesia and allodynia over scar tissue [98]. Sodium valproate is shown to be effective in migraine-like headaches in post-craniotomy and posttraumatic head injury patients [99]. Carbamazepine and lamotrigine are the other anticonvulsants used as second-line treatment for persistent headaches [100]. Sumatriptan (5-HT1 agonist) is effective in persistent headaches after acoustic neuroma excision and migraine-type headaches [101].

38.6 Role of Genetic Factors and Epigenetics for Postoperative Pain

Opioids have narrow therapeutic indices and significant inter-patient variability in response, leading to adverse side effects like respiratory depression and sedation [102–104]. Genetic variations influence both opioid pharmacokinetics and pharmacodynamics [105]. There is evidence that genetic factors are linked to increased risk for acute and chronic postsurgical pain after some surgeries like spine fusion [106–108]. In addition, gene-environmental interactions have also been identified as influencing acute to chronic postsurgical pain transitions after spine surgery in children [109].

38.6.1 Opioid Pharmacogenomics

- **Genetic Influences on Opioid Pharmacokinetics**: Most oral opioids (oxycodone, tramadol, codeine, hydrocodone) are metabolized by CYP2D6 enzyme to a more active metabolite. CYP2D6 enzyme is controlled by a highly polymorphic gene *CYP2D6* whose variants affect activity of the enzyme resulting in several metabolizer phenotypes such as poor, intermediate, normal, and ultra-rapid (UM). Several case reports of deaths in children after tonsillectomies [110–112] and an infant of a mother who was prescribed codeine [113, 114] as well as children prescribed weight-based tramadol [115, 116] have been attributed to their *CYP2D6* UM phenotype leading to high concentrations of the active metabolite [117–119]. This has led to advisories on the administration of codeine and tramadol in children who are less than 12 years old, especially in those with obstructive sleep apnea [113, 120, 121]. This is an important aspect influencing opioid choice and prescribing to children after surgery.
- **Genetic Influences on Opioid Pharmacodynamics:** Genetic influence on opioid pharmacodynamics is mostly due to gene variants resulting in altered opioid receptor numbers or structure, altered transport of opioids into and out of the central nervous system, and altered cofactor influences like endocannabinoids. Polymorphism on mu-receptor gene OPRM1 has been shown to result in opioid resistance due to decreased opioid receptor density [122, 123]. The variants of ATP-binding cassette sub-family B member 1 (*ABCB1*), a surface phosphor-glycoprotein

which acts as an opioid efflux transporter at the blood-brain barrier (BBB), significantly alter the cerebral concentration of opioids. Children with certain *ABCB1* polymorphism had higher incidence of respiratory depression leading to prolonged hospital stay after tonsillectomy [124]. The relevance of ABCB1 polymorphism in postoperative pain management neurosurgical patients with compromised BBB is unknown.

- **Epigenetic Effects on Acute and Chronic Postsurgical Pain**: Epigenetics is the study of non-structural genetic factors that may affect gene expression and are modifiable by environmental factors [125]. Epigenetic regulatory mechanisms "activate" or "silence" genes through DNA methylation, histone modification, and miRNA interference [125]. In children undergoing spine fusion, blood DNA methylation at the promotor of OPRM1 gene region was associated with higher-risk CPSP [126]. It was postulated that inhibition of transcription factor binding by DNA methylation might decrease *OPRM1* gene expression, resulting in a decreased opioid response and, hence, increased pain responses. Chidambaran et al. investigated whole blood DNA methylation profiles using epigenome-wide association approaches and identified genomic pathways underlying CPSP and anxiety sensitivity [90, 127]. Since environmental modulation affects epigenetics, these findings indicate non-pharmacological approaches (diet, exercise, mindfulness) might help decrease the risk for CPSP after spine surgery [128].
- **Clinical Implications**: Genomic technologies are becoming more cost-effective and, therefore, could, in the future, be a roadmap for the use of the "right opioid" in the "right dose" for the "right patient." Not only can this assist in bypassing the problems associated with our present trial and error strategies of opioid dosing, but it would also allow risk stratification via genetic risk signatures [129]. In addition, understanding the genetic pathways could guide preventive and therapeutic approaches. Epigenetic markers could serve as biomarkers but also guide the development of epigenetically programmed drugs [130]. Recent advances in gene-editing technology and individual gene-targeted approaches offer promising avenues to develop individualized, safe, and effective acute and chronic pain management regimens after major surgeries.

38.7 Conclusion

Safe and effective pain management is the foundation for a quicker postoperative functional recovery. While there is a diverse menu to choose from, one must consider the risks and benefits of current multimodal therapies and select targeted therapies commensurate to the intensity and nature of the pain. It is also prudent to recognize surgical factors in addition to individual factors while treating pain in children. Awareness, screening, follow-up, and management for post-craniotomy headache and chronic postsurgical pain are critical to prevent disability and psychological comorbidities from chronic pain as the child grows into adulthood with socioeconomic consequences for society. Improved screening for patients at risk of poor pain coping, preoperative targeted risk-optimization, and minimization of opioids using non-pharmacological therapies and individualized multimodal regimens are all important for safe and effective postoperative pain management in this unique patient population.

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39 Postoperative Respiratory Complications and Ventilatory Strategies in Pediatric Neurosurgical Patients

Devika Bharadwaj and Keshav Goyal

Key Points

- Non-intubated postoperative children undergoing neurosurgery should be monitored vigilantly for complications due to hypoventilation and airway obstruction.
- The indications for postoperative ventilation include preoperative conditions, intraoperative complications, and postoperative complications.
- The goals of acute respiratory distress syndrome (ARDS) management are to optimize oxygenation and ventilation while protecting the lungs from ventilator-induced lung injury.
- Neurogenic pulmonary edema (NPE) is a type of acute pulmonary edema that occurs after a sudden neurological insult.
- The main objectives of elective postoperative ventilation in pediatric patients include facilitating oxygenation, removing carbon dioxide, decreasing work of breathing, and maintaining respiratory muscle strength while aiming for early weaning from ventilation.
- Standard weaning criteria are not always appropriate in neurosurgical patients; airway patency and cough ability may be assessed before extubation.
- Early tracheostomy may be considered for children who require prolonged ventilation due to poor neurological outcome.

39.1 Introduction

The early postoperative pulmonary complications (PPCs) in neurosurgical patients include pneumonia, bronchitis, atelectasis, and respiratory failure, with an incidence of about 23% [1]. Respiratory complications have been observed in 4% of patients after pediatric neurosurgical procedures [2]. Prevention and management of postoperative respiratory complications continue to be a major challenge for a neuroanesthesiologist and neurointensivist. Due to the urgent and emergent nature of respiratory complications, an anesthesiologist must be well prepared to anticipate, prevent, and manage such complications in various pediatric neurosurgical scenarios. This chapter highlights specific considerations of respiratory pathology and the care of postoperative pediatric patients in neurosurgery.

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39.2 Postoperative Respiratory Complications in Non-ventilated Children

Providing adequate oxygenation and ventilation is essential to maintain the balance of oxygen delivery to the brain, adequate cerebral blood flow, maintenance of cerebral perfusion pressure, and intracranial pressure (ICP) in patients after neurosurgery. There is an ongoing need for assessment and decision-making for non-intubated patients after surgery. A pediatric patient with falling oxygen saturation may require intubation and ventilation on an urgent basis. This is because of two key differences in respiratory physiology compared with adults, i.e., smaller functional residual capacity and higher oxygen consumption, increasing the risk of hypoxia in pediatric patients [3]. Postoperative respiratory complications in non-ventilated patients can be broadly classified into hypoventilation and airway obstruction.

1. **Hypoventilation**

   Hypoventilation in the immediate postoperative period could be due to the residual effect of opioids, hypothermia, metabolic alkalosis (due to mechanical ventilation), muscle weakness (due to electrolyte imbalance, the residual effect of muscle relaxant), and hindered diaphragmatic movement due to pain [4]. Atelectasis is common after general anesthesia. It can be prevented by using a low fraction of inspired oxygen (FiO_2) and continuous positive airway pressure after tracheal extubation, or if required, the same strategy may be continued in the ICU [5].

   Several neurosurgical conditions such as neonatal hydrocephalus, spinal dysraphism including myelomeningocele, encephalocele, tumors such as choroid plexus papilloma, teratoma, astrocytoma, glioblastoma, and craniofacial anomaly due to craniosynostosis require surgery in tiny children [6]. Both preterm and term infants have irregular and periodic breathing patterns making them prone to severe apnea. Moreover, premature babies have immature peripheral and central chemoreceptors leading to impaired response to hypercarbia and hypoxia. While hypercarbia stimulates respiration, hypoxia can lead to sustained respiratory depression in small children. In contrast, older children and adults can increase their tidal volume and respiratory rate in response to hypoxia and hypercarbia [7]. Both central and obstructive sleep apnea is common in children with repaired myelomeningocele and Chiari II malformations. This could also be due to spinal lesions or brainstem abnormalities [8, 9]. Excessive neck movements should be avoided in such patients, and they should be monitored closely as they are prone to develop apnea in the postoperative period.

   Changes in the respiratory pattern can also be a sign of neurological deterioration though it may be a late sign. Respiratory irregularity should raise suspicion of raised intracranial pressure (ICP). A child with raised ICP often presents with abnormal posturing, anisocoria, bradycardia, irregular breathing pattern, hypertension, sixth nerve palsy, and papilledema [10]. Such patients should be intubated, and urgent measures to lower the intracranial pressure should be undertaken while investigating the cause of the rise in ICP in the postoperative period. Mass lesions such as hematoma or edema increased cerebral blood volume, and CSF flow disturbances are common causes of postoperative intracranial hypertension [11]. Tracheal intubation should be performed using a rapid sequence induction technique if not already intubated (Fig. 39.1).

   Pediatric spine injuries are most common at the cervical level (60–80%) [12]. Injuries of the upper cervical spine (C1–C4) are twice as common as the lower cervical spine (C5–C7) [13]. Changes in the respiratory pattern are seen in these patients due to the involvement of the phrenic nerve (C3, C4, and C5). Injuries occurring above C3 cause complete denervation of the diaphragm, chest, and abdominal wall musculature. These patients have to use accessory muscles for respiration and may require emergency intubation. As the

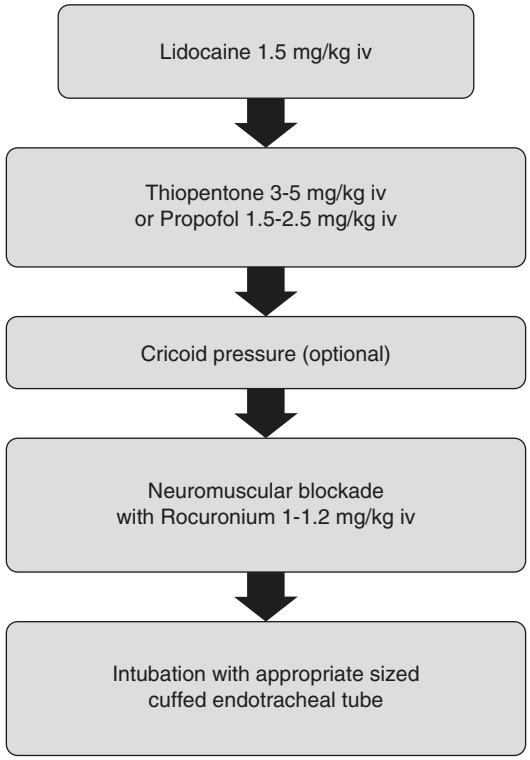

Fig. 39.1 Rapid sequence induction (RSI) technique

level of injury goes below C3, the phrenic nerve function is partially retained. In the injuries above T1 vertebral segment, there is a loss of intercostal and abdominal wall muscle function. This causes the abdomen to protrude with every diaphragmatic contraction during inspiration with minimum air movement. These patients are effectively managed in a supine position without the head of the bed elevation to help the abdominal contents push the diaphragm up, helping them mechanically for contraction. This helps to improve the tidal volume in these patients. The abdominal binder uses this principle to force the viscera inward and diaphragm upward, even in upright and semi-recumbent positions [14].

2. **Airway Obstruction**

The type of neurosurgery determines the risk of postoperative airway obstruction in a pediatric patient. Children operated for craniosynostosis can develop facial edema leading to airway compromise. Extubation should be deferred in such children by 24–48 h until edema resolves [15]. The second most important surgery, after which extubation should be avoided immediately, includes craniovertebral junction anomaly. Post anterior-posterior approach, particularly the transoral approach, these children can develop pharyngeal edema. Another factor responsible for pharyngeal edema is the prone position maintained for a prolonged duration during posterior fixation. It is recommended that these children should be extubated 12–24 h after surgery postoperatively [16]. Posterior fossa craniotomy is another leading cause of respiratory compromise postoperatively. Intraoperative respiratory center and lower cranial nerve damage can cause apnea and airway obstruction postoperatively. Moreover, airway edema can be observed postoperatively, leading to respiratory compromise [17]. Awake craniotomy is now being performed in pediatric patients as well [18]. Such patients should be closely monitored in the postoperative phase for respiratory complications.

Care of a postoperative pediatric patient with a difficult airway can be challenging. These cases can present with upper airway obstruction in the postoperative period, particularly due to the residual effect of anesthetics after surgery [19]. Neurosurgical conditions such as hydrocephalus [20], myelomeningocele (MMC) [21], syndromic craniosynostosis [22], scoliosis [23], and cervical spine injury [24] can be associated with difficult airway due to the nature or location of the neurosurgical lesion. Children with obstructive sleep apnea (OSA) are also at increased risk of postoperative respiratory complications. These patients are especially sensitive to opioids given in the postoperative period due to the central alteration of opioid receptors [25]. Postoperative airway obstruction can be overcome with airway maneuvers such as neck extension, mouth opening, jaw thrust alone, or a combination. It can be prevented by nursing the child in a lateral position with neck extended [26]. The

pediatric nasal airway can be of great help in the postoperative period in these patients. It is a practice for institutions to keep an emergency intubation trolly with equipment for alternative techniques of intubation such as fiber-optic bronchoscope, laryngeal mask airway, and video laryngoscope with the pediatric blade at the bedside for emergency management of airway obstruction of postoperative cases with a difficult airway. This ensures a prompt response as hypoxia in pediatric patients can quickly deteriorate due to smaller functional residual capacity and higher oxygen consumption [27, 28].

39.3 Postoperative Respiratory Complications in Ventilated Children

39.3.1 Indications for Ventilation

The decision to admit children to a neurocritical care unit is often based on the preoperative condition, intraoperative course, and postoperative condition of the patient. **Elective ventilation** in pediatric neurosurgery is generally practiced after posterior fossa tumor [29], craniovertebral junction anomaly [16], craniosynostosis [15], traumatic brain injury [30], and scoliosis [31]. The indications for elective ventilation in these conditions are summarized in Table 39.1.

Table 39.1 Indications for elective ventilation in pediatric neurosurgery

Diagnosis	Indications for postoperative elective ventilation
Posterior fossa tumor	• Impaired lower cranial nerve function • Intraoperative brainstem manipulation • Postoperative airway edema
Craniovertebral junction anomaly	Soft tissue/pharyngeal edema
Craniosynostosis	• History of obstructive sleep apnea • Hydrocephalus • Intraoperative major blood loss or venous air embolism
Traumatic brain injury	Glasgow Coma Scale score ≤ 8 before surgery
Scoliosis	Severe restrictive lung disease

Intraoperative complications during pediatric neurosurgery can be neurosurgical (78%) or anesthetic (22%). The highest intraoperative complication rates have been observed during cerebrovascular surgery (7.7%) and tumor surgery (7.4%) [32]. Diffuse tumor bleed leading to hemodynamic instability requiring intraoperative blood transfusion has been observed as the most frequent complication [32]. Other surgical factors likely to influence the decision to delay extubation include large tumor resection with midline shift, surgery duration >6 h, intraoperative brain swelling, injury to lower cranial nerves, new-onset neurological deficits, and convulsions during emergence. Intraoperative systemic factors that lead to delayed extubation after neurosurgery include hypothermia, hypotension/hypertension, hypovolemia, hematocrit <25%, hypoxia or hypercarbia, ineffective spontaneous ventilation, hypoosmolality, disorders of coagulation, and residual neuromuscular blockade [33]. Factors influencing the decision to delay extubation after multilevel spine surgery performed in the prone position include surgery duration, number of operative spinal levels, the total volume of crystalloid, and blood administered intraoperatively [34].

Postoperative respiratory or neurological complications may also require emergency intubation of postoperative patients. Neuroemergencies observed in the pediatric neurocritical care unit include intracranial hypertension and compromised cerebral perfusion, seizures and status epilepticus, cerebral ischemia from embolic and thrombotic stroke, infectious and noninfectious CNS inflammation, and hypoxic injury [35]. These patients should be considered for endotracheal intubation and mechanical ventilation if any of the following is observed [36].

- Poor airway protection.
- Irregular respiration.
- Cerebral edema with Glasgow coma score < 9.

- Features of respiratory failure due to neuromuscular weakness such as tachypnea, dyspnea, use of accessory muscles of respiration, forced vital capacity <20 ml/kg.

39.3.2 Common Respiratory Pathologies in Ventilated Patients

1. **Atelectasis**

   Atelectasis is observed in 90% of patients after general anesthesia. Atelectasis causes damage in two ways: stretch dependent and stretch independent. The stretch-dependent injury occurs due to excessive stretching in the non-atelectatic portions of the lungs; most of the tidal volume shifts to the ventilated lung units causing overinflation of the non-atelectatic lung. Stretch-independent damage occurs from increased risk of infection due to impaired alveolar macrophage function and hypoxia. Atelectasis can cause systemic hypoxemia as well due to increased pulmonary shunting. Localized hypoxia in alveoli occurring due to atelectasis can induce inflammation in the lungs. On the other hand, alveolar hyperoxia occurring in ventilated portions of the lungs can worsen atelectasis by causing absorption. This leads to further damage from the formation of reactive oxygen species. These factors contribute to acute lung injury (ALI). In ventilated patients, atelectasis can be a result of using low tidal volume for mechanical ventilation. This can be easily prevented by applying appropriate positive end-expiratory pressure (PEEP) [5].
2. **Ventilator-Associated Pneumonia**

   Ventilator-associated pneumonia (VAP) is defined as hospital-acquired pneumonia that develops in patients who have been mechanically ventilated for 48 h or longer [37]. In pediatric patients, VAP is the second most common cause of nosocomial infection after blood infection and accounts for about 20% of all nosocomial infections in the pediatric intensive care units (PICU). VAP has been observed in 6–10% of patients who were ventilated in the PICU [38].

   Early-Onset vs. Late-Onset VAP: Based on the onset, VAP can be classified into early and late VAP. Early-onset VAP is defined as pneumonia that develops within 4 days of mechanical ventilation. Antibiotic-sensitive pathogens usually cause it. Late-onset VAP is defined as pneumonia that occurs after 4 days of intubation. It is caused by hospital-acquired multidrug-resistant (MDR) bacteria [39]. Bacteria causing early-onset VAP include Streptococcus sp., especially *Streptococcus pneumoniae*, *Haemophilus influenzae*, and methicillin-sensitive *Staphylococcus aureus* (MSSA). Gram-negative bacilli such as *Escherichia coli*, *Klebsiella pneumoniae*, Proteus species, Serratia marcescens, and Enterobacter species also cause early-onset VAP. Common organisms implicated to cause late-onset VAP include methicillin-resistant *S. aureus* (MRSA), *Pseudomonas aeruginosa*, Acinetobacter, and extended-spectrum beta-lactamase-producing bacteria (ESBL) [40]. Early and late VAP differ in their pathogenesis, outcome, and treatment as well. Late-onset VAP has been associated with higher mortality than early-onset pneumonia [41, 42]. This classification has been challenged recently after some comparable etiologies have been found in patients with early- or late-onset VAP [43–46]. This may be due to the rise in MDR pathogens in various clinical settings across the world.

   Risk Factors: Several risk factors have been identified for VAP in pediatric and neonatal settings. The external factors include reintubation, mechanical ventilation, patient transport, previous antibiotic therapy, bronchoscopy, immunosuppressive therapy, and enteral feeding. Internal factors predispose to VAP include young age (<1 year), airway trauma, tracheal/subglottic stenosis, tracheostomy, gastroesophageal reflux, immunodeficiency, use of neuromuscular blockade, genetic syndromes, and female gender. The main risk factors of VAP in

ventilated neonates include low birth weight babies, mechanical ventilation, duration of ventilation, reintubation, tracheostomy, use of enteral feeding, and absence of stress ulcer prophylaxis in treatment [47].

Pathogenesis: An important unavoidable factor for the development of VAP is the presence of an ETT or a tracheostomy tube in situ, which interferes with the functional mechanisms responsible for the clearing of secretions such as cough and mucociliary action [48]. The pooling of secretions in the oropharynx is common in intubated patients with depressed consciousness due to impaired voluntary clearance of secretions [49]. These secretions are rich in harmful organisms. Continuous macro-aspiration and microaspiration of contaminated oropharyngeal secretions occur around the endotracheal tube cuff. The normal oral flora proliferates and trickles around the endotracheal tube to form an antibiotic-resistant biofilm, which finally reaches the lower airways [48]. The critically ill patients are immunocompromised and mount a poor response to these pathogens, which eventually leads to pneumonia [50].

The second common cause of VAP in intubated patients is the aspiration of gastric contents. Healthy individuals are protected from swallowed bacteria as they get easily destroyed by gastric acid in the stomach. Aspiration of gastric microorganisms can occur in ventilated patients despite the presence of an inflated endotracheal tube cuff. However, recent studies suggest that the gastropulmonary route is not a major pathogenic route for VAP development. Another infection source leading to VAP in intubated patients is the use of contaminated respiratory equipment such as bronchoscopes and endoscopes [51]. Disinfection before use and between use in patients is essential to prevent VAP and cross infection between patients.

Diagnosis: Several respiratory pathologies can mimic VAP. Acute respiratory distress syndrome (ARDS), atelectasis, and pulmonary edema can have a clinical presentation similar to VAP. Suspicion of VAP should be high when there is an unexplained change in the clinical status of the patient such as fever, falling oxygen saturation, increased oxygen or ventilation requirements, signs of respiratory distress, metabolic acidosis on arterial blood gas analysis, and change in the nature or volume of respiratory secretions [52]. The Centers for Disease Control and Prevention, United States, has given VAP surveillance criteria, better-called ventilator-associated events (VAEs), to offer a broader and more objective method of assessing complications of mechanical ventilation for uniform reporting and comparison between hospitals. VAE definitions are now being used across clinical settings as an indicator of performance. In a study on neurocritically ill patients, the prevalence of VAE was reported as 13 per 1000 ventilator days [53]. VAE uses a three-tier classification to include complications related to mechanical ventilation (Fig. 39.2) [54].

- Ventilator-associated condition (VAC).
- Infection-related VAC (IVAC).
- Possible or probable VAP.

This change in approach to VAP offers three main advantages. Firstly, it allows identifying patients with serious complications that were not included in previous definitions. Secondly, the new definitions are based solely on an objective criterion which allows comparison of VAP rates across all hospitals. Thirdly, the IVAC metric will help analyze data on antibiotic usage between institutions. This information will help identify institutions prescribing excessive antibiotics and help reduce antibiotic resistance and *Clostridium difficile* infections [54]. The new definition of VAE has been adopted in critical care of adult patients since january 2013. Its modification is now being considered for pediatic patients.

Prevention: Implementation of a pediatric ventilator bundle is considered as a practical approach for achieving better patient outcomes by reducing VAP rates, days on the ventilator, antibiotic usage, duration of critical care stay,

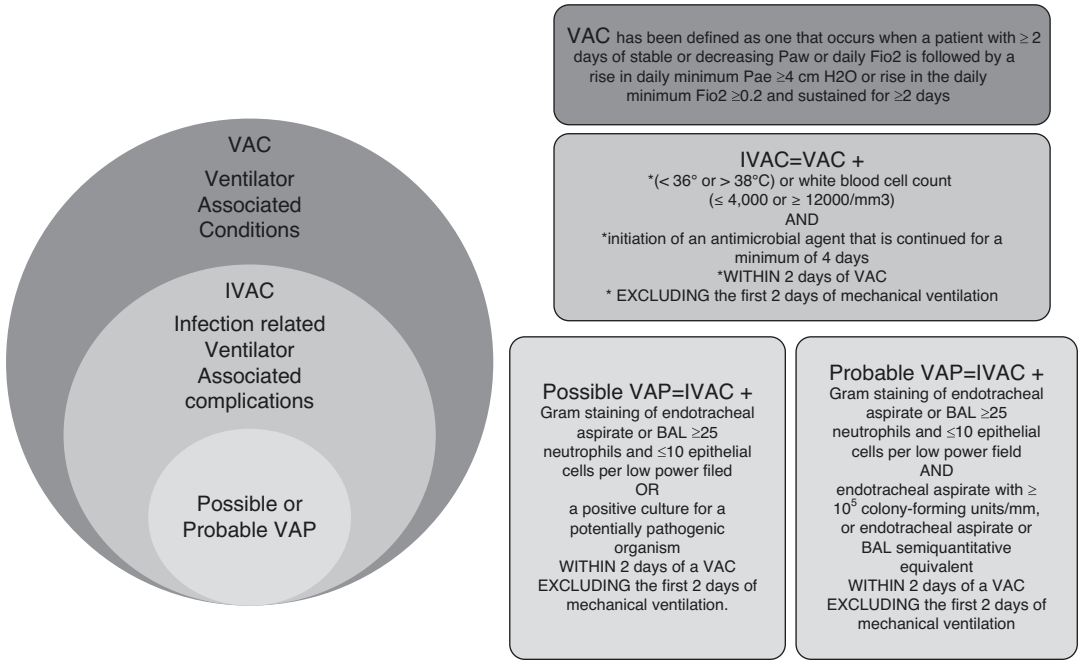

Fig. 39.2 New definitions of ventilator-associated pneumonia (VAP). Adapted from: Willson DF, Hall M, Beardsley A et al; Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Pediatric Ventilator-Associated Events: Analysis of the Pediatric Ventilator-Associated Infection Data. Pediatr Crit Care Med. 2018;19(12):e631–e636

and hospital costs [55]. A care bundle is defined as implementing a group of evidence-based interventions that, when applied together, provide better outcomes than when performed individually. Various combination of interventions such as hand hygiene with alcohol-based hand rub, use of gown and glove while handling endotracheal tube, the elevation of the head end of the bed, use of chlorhexidine for oral care, stress ulcer prophylaxis, maintaining endotracheal tube cuff pressure, use of orogastric tube for gastric decompression, and avoiding unnecessary endotracheal tube suctioning has been shown to reduce VAP rate [56].

Treatment: The microorganism type causing VAP in pediatric patients varies with geographical location. Gram-negative bacteria contribute to most cases of VAP in pediatric patients with exceptionally high contributions from Asian patients. The most common pathogens are *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae*. In Europe and North America, VAP due to gram-positive bacteria such as *Staphylococcus aureus* is more common. Due to such wide variation in the prevalence of organisms causing VAP, the American Thoracic Society has highlighted the need to monitor and maintain a local record of bacterial resistance in intensive care units using antibiograms. This ensures appropriate empirical therapy while culture results are pending and decrease inappropriate antibiotic prescriptions for VAP [57].

Due to the lack of pediatric guidelines on VAP, VAP management principles in adult patients are often extrapolated to management in pediatric patients. The initial antibiotic prescription is empirically based on previously maintained hospital data of prevalent organisms and antibiotic sensitivity. Empirical therapy should be decided after considering the patient's risk factors for infection with MDR bacteria, recently received antibiotics by the patient, and the local antibiotic resistance patterns [58]. Risk factors for colonization with antibiotic-resistant gram-negative organisms include younger age, previous intensive care admissions, and use of intravenous antibiotics

in the past year [59, 60]. Premature infants (increased risk of Staphylococcus epidermidis infections) and immunocompromised patients (need for empirical antifungal therapy) shall be noted [61]. Monotherapy has been recommended for early-onset VAP, while combination therapy is advised for patients with late-onset VAP or patients with severe illness. Empirical therapy should be judiciously decided (discontinued or altered) based on clinical status and appropriate culture results [58].

The neurocritical patients are a unique subset of critical care patients as they are particularly vulnerable to pneumonia due to the high rate of dysphagia and aspiration [62]. The microbiology of VAP in these patients often includes anaerobic flora. A retrospective study of 57 neurologically impaired children with aspiration or tracheostomy-related pneumonia, better outcome, and the antibiotic response was observed when treated with ticarcillin-clavulanate or clindamycin effective against penicillin-resistant anaerobic bacteria as compared to patients treated with ceftriaxone alone [63].

3. **Pediatric Acute Respiratory Distress Syndrome**

Pediatric acute respiratory distress syndrome (PARDS) in postoperative ventilated patients remains a challenge due to high morbidity and mortality. Acute respiratory distress syndrome (ARDS) is an independent risk factor for longer intensive care, hospital stays, poor neurological outcomes, and increased mortality [64]. ARDS is seen in 1–10% of pediatric intensive care patients [65–67]. ARDS is characterized by disruption of the alveolar epithelial-endothelial barrier due to direct injury to the alveolar epithelium (e.g., pneumonia) or indirect injury to the capillary endothelium (e.g., sepsis). Disruption of the alveolar endothelial barrier causes the accumulation of protein-rich fluid in the alveoli. Clinically, these changes manifest as restrictive-type lung disease with features of bilateral radiographic opacities and hypoxemia. ARDS must be differentiated from cardiogenic edema [68].

Characterization of acute lung injury (ALI) or ARDS in pediatric patients has been based on adult definitions given in the 1994 American-European Consensus Conference (AECC) and subsequently revised in 2012 (Berlin definition). In 2015, Pediatric Acute Lung Injury Consensus Conference (PALICC) defined ARDS in pediatric patients. This definition differs from adult definitions of ARDS in two ways. Firstly, any new parenchymal infiltrates (unilateral or bilateral) are included in the baseline criteria for the diagnosis of PARDS. Secondly, pulse oximetry can be used to diagnose PARDS if arterial blood oxygenation measurements are not available. Oxygenation index (OI) is defined as $[(FiO_2 \times \text{mean airway pressure} \times 100)/PaO_2]$. Oxygenation saturation index (OSI) defined as $[(FiO_2 \times \text{mean airway pressure} \times 100)/SpO_2]$ have been suggested to assess and classify hypoxemia as mild, moderate, or severe rather than the PaO_2/FiO_2 (P/F) ratio in all children treated with mechanical ventilation [69]. The PARDS criteria given by PALICC is given in Table 39.2.

Lung Protective Ventilation: ARDS management aims to treat the underlying cause and provide optimal oxygenation and ventilation. It is equally important to protect the lungs from ventilator-induced lung injury. Lung protective ventilation helps to avoid volutrauma and barotrauma (caused by overdistension of alveoli), minimize atelectrauma (due to repeated opening and closing of alveoli), and minimize biotrauma caused by damaging effects of circulating biochemical mediators on the lung [68]. PALICC guidelines recommend using low tidal volumes for ventilation in patients with PARDS. The tidal volume of 3–6 ml/kg predicted body weight (PBW) is recommended for patients with poor respiratory system compliance, while the tidal volume of 5–8 ml/kg PBW is recommended for patients with preserved respiratory compliance. It has been recommended to limit the inspiratory plateau pressure to 28 cmH_2O, allowing for slightly higher plateau pressure (up to 32 cmH_2O) in children with

Table 39.2 PARDS criteria (PALICC guidelines)

PARDS baseline criteria			
Age	Exclude patients with perinatal-related lung disease		
Timing	Within 7 days of known clinical insult		
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload		
Chest imaging	New infiltrates (unilateral or bilateral) consistent with acute pulmonary parenchymal disease		
PARDS severity stratification			
	Mild	**Moderate**	**Severe**
OI	$4 \leq OI < 8$	$8 \leq OI < 16$	$OI \geq 16$
OSI	$5 \leq OSI < 7.5$	$7.5 \leq OSI < 12.3$	$OSI \geq 12.3$

Special considerations

1. Noninvasive ventilation

- Total face mask bilevel ventilation or CPAP ≥5 cm H_2O
- PaO_2/FiO_2 ratio ≤ 300
- SpO_2/FiO_2 ratio ≤ 264

2. Cyanotic heart disease, chronic lung disease, and left ventricular dysfunction

- No specific OI or OSI cutoff
- Has baseline criteria and deterioration in oxygenation not explained by an underlying illness

PARDS pediatric acute respiratory distress syndrome, *PALICC* Pediatric Acute Lung Injury Consensus Conference, *OI* oxygenation index, *OSI* oxygenation saturation index, *CPAP* continuous positive airway pressure, *OI* FiO_2 X M_{Paw} X 100 /PaO_2, FiO_2 fraction of inspired oxygen, M_{Paw} Mean airway pressure, in mmHg, PaO_2 Partial pressure of oxygen in arterial blood, in mmHg, *OSI* FiO_2 X M_{Paw} X 100 /SpO_2, FiO_2 fraction of inspired oxygen, M_{Paw} Mean airway pressure, in mmHg, SpO_2 Oxygen saturation as measured by pulse oximetry

increased chest wall elastance [69]. Another important strategy is to apply PEEP. PEEP keeps the alveoli open at the end of expiration, thus preventing atelectrauma caused by the reopening of collapsed alveoli with each breath. This has an overall effect of improving ventilation-perfusion matching and oxygenation [70]. PALICC has recommended PEEP of 10–15 cm of H_2O in patients with severe PARDS titrated to oxygenation and hemodynamic response. PEEP more than 15 cm of H_2O should be used carefully to maintain plateau pressure below 28 cm of H_2O. Due to a lack of outcome data regarding the superiority of any mode of ventilation to the other, PALICC has not recommended any particular mode of ventilation in pediatric patients. To minimize the potential toxicity of ventilatory support required for oxygenation and ventilation of PARDS patients, permissive hypoxemia and hypercapnia have been recommended. PALICC has recommended oxygen saturation goals 92–97% for mild PARDS and 88–92% along with PEEP >10 cm H_2O for severe PARDS [69]. PARDS ventilatory management, according to PALICC guidelines, is summarized in Table 39.3.

Permissive Hypercarbia: Permissive hypercapnia is a necessary evil when using low tidal volumes. This strategy can be detrimental in neurosurgical patients. Hypercapnia can be detrimental in brain-damaged patients as hypercarbia-induced vasodilatation can lead to an increase in intracranial pressure [71–74]. PALICC has recommended not to use permissive hypercarbia in pediatric ARDS patients with raised intracranial pressure [69].

Adjuvant Approaches: The routine uses of corticosteroids, inhaled nitric oxide (INO), exogenous surfactant, prone positioning, and neuromuscular blockade are not recommended for routine purposes. INO should be reserved for patients with documented pulmonary hypertension and significant right ventricular dysfunction. 0for patients with documented pulmonary hypertension and significant right ventricular dysfunction. Prone position ventilation should be considered in children with severe PARDS. Use of sedation with a goal-directed protocol is recommended to ensure patients tolerate mechanical ventila-

Table 39.3 Lung protective ventilation in PARDS (PALICC guidelines)

Therapy	PALICC guidelines
Tidal volume	3–6 ml/kg if poor compliance 5–8 ml/kg if normal compliance
Plateau pressure	≤28 cm H_2O 29–32 cm H_2O if poor compliance
Permissive hypoxemia	Mild PARDS with PEEP <10 cm H_2O:SpO_2 target 92–97% Severe PARDS with PEEP>10 cm H_2O:SpO_2 target 88–92%
PEEP	10–15 cm H_2O titrated to oxygenation and hemodynamics For PEEP >15 cm H_2O in severe cases, limit peak airway pressure. PEEP can be used with careful, incremental titration for recruitment
Permissive hypercapnia	pH 7.15–7.30 Exceptions: Intracranial hypertension Severe pulmonary hypertension Congenital heart disease Hemodynamic instability Significant ventricular dysfunction

PARDS pediatric acute respiratory distress syndrome, *PALICC* Pediatric Acute Lung Injury Consensus Conference, *PEEP* positive end-expiratory pressure

tion [69]. If sedation is not adequate to achieve effective mechanical ventilation, titrated (minimal yet effective) doses of neuromuscular-blocking agents should be considered.

4. **Neurogenic Pulmonary Edema**

Neurogenic pulmonary edema (NPE) is defined as acute pulmonary edema after a sudden neurological insult [75]. It has been reported in both adults and children after CNS disorders such as brain tumors, traumatic brain injuries, infections, and seizures [76]. NPE is relatively uncommon in children as compared to adults. NPE can be acute onset (within 30–60 min of CNS insult) or delayed onset (12–72 h after CNS insult) [77].

Signs and Symptoms

The symptoms and signs of NPE are nonspecific. Symptoms such as dyspnea, tachypnea, tachycardia, pink frothy sputum, and basal crackles have been observed in patients of NPE. Chest x-ray shows diffuse bilateral infiltrates in lung fields [78]. Arterial blood gases reveal hypoxemia (low PaO_2), a PaO_2/FiO_2 ratio < 200 [79]. NPE must be differentiated from other cardiorespiratory conditions such as congestive heart failure, aspiration pneumonia, ARDS, and ventilation-induced lung injury (VILI) [78]. The NPE is a diagnosis of exclusion and requires exclusion of cardiopulmonary edema in the setting of neurological injury. Davison et al. [75] have proposed criteria for the diagnosis of NPE, which includes the presence of bilateral infiltrates, PaO_2/FiO_2 ratio < 200, no left atrial hypertension, CNS injury severe enough to cause significantly increased ICP, absence of other common causes of ARDS such as aspiration, massive blood transfusion, and sepsis.

Pathogenesis: Blast theory is the most common theory of pathophysiological mechanisms leading to NPE. Neurological insults that cause a sudden and severe increase in ICP are at greatest risk for NPE. Neurological insult is followed by sympathetic overactivity believed to originate from trigger zones (hypothalamus and medulla) activated by the sudden increase in intracranial pressure or decreased cerebral blood flow [80]. Systemic vasoconstriction shifts the blood from systemic to pulmonary circulation resulting in increased pulmonary hypertension and increased pulmonary capillary hydrostatic pressure. The increase in hydrostatic pressure causes damage to the capillary endothelium, which leads to the accumulation of protein-rich intravascular fluid into alveolar spaces manifesting as pulmonary edema [81].

Treatment: NPE often resolves in 24–72 h [82]. The main focus of management is to treat the underlying neurological insult. Measures such as decompression and clot evacuation, osmotic diuretics, antiepileptics, tumor resection, and steroids should be used to reduce intracranial pressure [75]. Most patients with NPE require hemodynamic and respiratory support. Treatment options include vasoactive compounds (dobutamine, norepinephrine), diuretics, fluid supplementation, supplemental oxygen, and mechanical ventilation [81]. Positive pressure ventilation should be considered if a patient's oxygen saturation level remains <90% even with supplemental oxygen [76]. Medications such as alpha-adrenergic blockers,

angiotensin receptor antagonists, steroids, and milrinone have been tried in NPE, but their efficacy has not been established [81, 83]. ECMO has also been tried in NPE unresponsive to conventional therapies [81].

39.3.3 Ventilatory Management in Pediatric Neurosurgical Patients

Pediatric neurocritical care (PNCC) is a unique subset of pediatric critical care. Mechanical ventilation is a common critical care intervention in pediatric neurocritical care, and patients may require prolonged mechanical ventilation >96 h in 11–46% of cases depending on the diagnosis [84]. Most children require mechanical ventilation for airway protection and preventing aspiration due to low GCS [85]. Moreover, neurological emergencies such as cerebral edema and raised intracranial pressure can be managed with ventilation to improve neurological outcomes [30]. From a respiratory point of view, the main objectives of ventilation include facilitating oxygenation, clearance of carbon dioxide (CO_2), decreasing work of breathing, and maintaining respiratory muscle strength while aiming for early weaning from ventilation [86].

Pediatric mechanical ventilation practices are often derived from personal experiences and experience from adult and neonatal ventilation. In 2017, the European Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) gave recommendations for use in ventilated pediatric patients [87]. This section aims to provide a practical guide to ventilator settings in pediatric neurocritical care while including recent recommendations on pediatric mechanical ventilation.

1. Select ventilator mode as **a pediatric or infant** as appropriate.
2. Select **volume- or pressure-controlled** ventilation: The commonly utilized modes for pediatric ventilation are pressure control ventilation (PCV), volume control ventilation (VCV), and pressure-regulated volume control ventilation (PRVC). Generally, PCV is chosen for neonates and infants while volume modes are preferably used in larger children [88]. When using PCV mode, the clinician must set the respiratory rate, inspiratory time, and inspiratory pressure on the ventilator. The tidal volume delivered is determined by the inspiratory pressure and varies with lung compliance and airway resistance [89, 90]. This means that worsening compliance and airway resistance results in low tidal volumes. In patients with normal lungs with normal compliance, an event such as endotracheal tube blockade due to kinking or secretions can increase airway resistance and decrease the tidal volume significantly [90]. This is why it is emphasized to monitor the delivered tidal volume on the ventilator and ensure whether it is appropriate for the patient.

   In contrast, VCV ventilation requires the clinician to set the respiratory rate, inspiratory flow rate, tidal volume, and PEEP. The ventilator delivers a fixed flow of air until the desired tidal volume is achieved. This means that worsened compliance may lead to higher airway pressures [91]. PRVC mode utilizes a set inspiratory time, tidal volume, and a range of allowed pressures. If the resultant tidal volume is very high, the next breath is delivered with less pressure. However, if the delivered volume falls short of the set tidal volume, the next breath is delivered with higher pressure [89].

   There is no data to support the superiority of one mode of ventilation over the other in neurosurgical pediatric patients. Irrespective of the mode used, the goals of ventilation must be met. It has been recommended that in pediatric patients, physiologic tidal volumes must be used, and Vt >10 mL/kg ideal body weight should be avoided [87]. In patients with PARDS, tidal volume of 3–6 mL/kg if poor compliance and 5–8 mL/kg if preserved compliance should be used [69].

   The plateau pressure (P_{Plat}) should be limited to ≤28 cm H_2O, and delta pressure (i.e., the difference between end-inspiratory and

end-expiratory pressure) should be <10 cm H_2O if there is no lung pathology in critically ill pediatric patients on mechanical ventilation. P_{Plat} should be limited to ≤28–32 cm H_2O in restrictive lung disease (e.g., ARDS) and ≤ 30 cm H_2O in patients with obstructive lung disease (e.g., asthma) [87].

3. **I:E ratio:** This is the ratio of the time the ventilator spends in inspiration: time spent in expiration during one breath. It is usually set at 1:2; however, in neonates, the I:E ratio can be increased as much as 1:1 to allow for higher respiratory rates in neonates. There are no specific guidelines for values of I:E ratio that must be set.
4. **Inspiratory time (Ti):** This is the time over which one breath is delivered. As a practical guide, following values can be used:

<1 year	Ti = 0.6–0.8 s
1–5 years	Ti = 0.8–1.0 s
5–12 years	Ti = 1.0–1.2 s
>12 years	Ti = 1.2–1.5 s

This parameter can be adjusted by changing I:E ratio and breath cycle time.

5. **Breath cycle time:** This is the total time for one breath cycle. It includes the total duration of both inspiration and expiration. It can be calculated from I:E ratio and Ti. For example, if I:E ratio is 1:2 and Ti of 1 s has been chosen, then expiratory time will be 2 s, resulting in a breath cycle time of 3 s. If you want an I:E ratio of 1:2 and you want a Ti of 0.8 s, the expiratory time will be 1.6 s, resulting in a breath cycle time of 2.4 s.
6. **Respiratory rate:** Respiratory rate must be set according to physiologically normal respiratory rate according to age [92].

0–1 year	30–60/min
1–4 years	24–40/min
4–6 years	22–34/min
6–12 years	18–30/min
12–20 years	12–16/min

For ventilator modes such as Synchronized Intermittent Mandatory Ventilation (SIMV) that allow patients to take spontaneous breaths, the actual respiratory rate is the sum of mandatory rate (set on the ventilator) and spontaneous breaths (breaths generated by patient effort). For example, on SIMV mode, if the set respiratory rate is 12 per minute, and the patient generates 8 breaths per minute, then the actual respiratory rate of the patient is 20 per minute. Spontaneous breathing during ventilation has the advantage of allowing better ventilation, reduced risk of muscular atrophy, and diaphragmatic dysfunction [87]. This can be particularly useful for postoperative patients with neurological deficits such as muscle weakness and phrenic nerve injury. In patients with restrictive lung disease, it has been recommended that a higher RR must be set to compensate for low tidal volume and maintain minute ventilation within the normal range [87].

7. **Positive-end expiratory pressure (PEEP):** The purpose of applying PEEP is to prevent atelectasis due to alveolar collapse by keeping the alveoli open during expiration. Physiological data in children without lung injury suggests using PEEP 3–5 cm H_2O [87]. In patients with PARDS, PALICC recommends oxygen saturation goals 92–97% for mild PARDS and 88–92% and PEEP >10 cm H_2O for severe PARDS [69].

Previously, concerns have been raised regarding the use of PEEP in patients with raised intracranial pressure. PEEP causes transmission of intrathoracic pressure directly to the cranium through valveless spinal venous plexus. However, this effect is more pronounced clinically with PEEP of more than 20 cmH2O. High PEEP should also be avoided in circumstances of hypovolemia as it reduces venous return and, hence, reduces cardiac output with consequent effects upon cerebral perfusion [93].

8. **The fraction of inspired oxygen (FiO_2):** High FiO_2 can cause hyperoxic lung injury. Hence, FiO_2 should be kept as low as possible. Application of FiO_2 > 0.70 for several days leads to progressive lung injury, depending on the concentration and duration for which it is used [94]. Similar to practice in adult patients, after intubating the trachea

of a pediatric patient, initial FiO_2 should be set at 100% to tide over hypoxia that may have occurred during intubation, and then quickly titrate it down to maintain SpO_2 of 92–97% [95].

9. **Trigger:** With controlled ventilation modes, the variable is time, and breaths are time triggered, not patient triggered. It means that depending upon the respiratory rate (breaths/minute) set on the ventilator, the ventilator calculates the time after which the breath has to be triggered/initiated. The patient cannot trigger the ventilator to initiate a breath. On the other hand, in modes of mechanical ventilation that allow spontaneous or assisted breaths, patients can initiate breaths by achieving a preset pressure or flow trigger. *Flow triggering* uses a continuous inspiratory baseline flow and continuously measures the expiratory flow. A breath is initiated when the difference between inspiratory flow and the expiratory flow reaches a set trigger value [96].

   The problem of auto triggering can be overcome by using a *pressure trigger*, but it is at the cost of increased work of breathing. When pressure is used for the trigger, the patient has to breathe against a closed valve present in the inspiratory circuit, which increases the work of breathing. The pressure-triggered mode works by detecting a drop in the airway pressure that occurs when the patient tries to inspire [96].
10. **Pressure support (PS):** PS can be used along with modes that allow patients to take spontaneous breaths, for example, SIMV and PRVC. As these modes allow the patient to breathe spontaneously, all such breaths get supported with PS. However, tidal volume and inspiratory time are not fixed/guaranteed with these breaths.

39.3.3.1 Monitoring Ventilator Settings

The monitoring of ventilated patients is essential because neurosurgical patients deteriorate rapidly and unpredictably. In addition, continuous evaluation allows assessment of clinical recovery and prognostication. In a consensus statement issued by the Neurocritical Care Society and the European Society of Intensive Care Medicine, it has been recommended that systemic pulse oximetry and end-tidal capnography should be monitored in all mechanically ventilated patients, supported by arterial blood gases measurement. Monitoring brain oxygen in patients at risk of cerebral ischemia and/or hypoxia using brain tissue ($PbtO_2$) and/or jugular venous bulb oximetry ($SjvO_2$) has been recommended [97]. Other monitoring modalities such as ICP monitoring, CPP monitoring, transcranial Doppler, and microdialysis can also be utilized on a case-by-case basis to guide ventilation settings to achieve a favorable neurological outcome.

39.3.4 Respiratory Care of Pediatric Neurosurgical Patient on Mechanical Ventilation

Attention to simple practices in critical care can go a long way in determining outcome in ventilated patients. Following are the key recommendations of the Pediatric Mechanical Ventilation Consensus Conference (PEMVECC) for the care of pediatric patients on mechanical ventilation [87]:

- Endotracheal tubes (ETT) with high-volume low-pressure cuff are recommended for use in all children. It has been recommended that cuffed ETTs do not increase post-extubation stridor risk if cuff pressure is maintained $\leq$20 cm H_2O and can be used safely in pediatric patients. Cuff pressure should be routinely monitored using cuff-specific devices.
- Dead space apparatus should be minimized using appropriate circuits and swivels. Adding components after the Y piece should be avoided as it increases dead space.
- Routine use of hand ventilation should be avoided in pediatric patients. If hand ventilation is required, pressure measurement and pop-off valves should be used.

- Routine endotracheal suctioning is not recommended. The routine installation of isotonic saline before endotracheal suctioning is also not recommended.
- Chest physiotherapy has not been recommended as a standard of care due to a lack of sufficient data. However, the use of cough-assist techniques has been strongly recommended for patients with neuromuscular diseases on noninvasive ventilation to prevent failure and endotracheal intubation.
- Humidification has been recommended in ventilated patients; however, there is insufficient data to recommend any particular type of humidification.
- It is recommended that the head end of the bed should be kept elevated to 30–45°.

39.3.5 Weaning and Extubation

The decision to extubate in pediatric neurocritical care is often based on subjective clinical assessment. The key determinants of successful extubation include the resolution of the patient's underlying pulmonary and neurological processes and hemodynamic stability. A patient can be considered hemodynamically stable if he has good tissue perfusion, vasopressor agents are not being used or used in low doses, and there is an absence of decompensated cardiac insufficiency or arrhythmias. Moreover, oxygenation status of the patient should be favorable, i.e., PaO_2 should be more than 60 mmHg with $FiO_2 \leq 0.4$ and PEEP of 5–8 cmH_2O [98].

Weaning Protocol in Pediatric Patients: The most common method of weaning used in pediatric patients is a gradual reduction of ventilator support. SIMV mode can be used for weaning by simply reducing the mandatory respiratory rate set on the ventilator. PSV mode can be used for weaning by gradually reducing the inspiratory pressure. PSV can be used along with SIMV during weaning. Extubation can be performed after the ventilatory support has been successfully tapered down or after successful daily spontaneous breathing trials (SBT) (30 min–2 h) [99]. The standard weaning criteria used in non-neurological patients take into account parameters to assess the patient's respiratory muscle strength and the ability to maintain oxygenation with minimal ventilator support. The decision of extubation based solely on such standard weaning criteria may not be appropriate in neurosurgical patients [100]. The following are some additional considerations before extubation in neurosurgical patients.

Airway Patency: Neurosurgical patients are likely to have a higher incidence of airway compromise. Cervical spine surgery causes significant facial and laryngeal edema as it is performed in the prone position, and large amounts of fluids are given intraoperatively. Such patients are prone to develop stridor and can even require reintubation. Reintubation in such patients can be challenging due to the associated difficult airway after spine fixation surgery. Cuff leak test is a useful bedside technique to assess airway edema before extubation in these patients. For patients on ventilation modes that allow spontaneous breaths, a "cuff leak" of <110 mL between inspiratory and expiratory volumes has been shown to predict post-extubation stridor development in adults. There is no such value defined in children. However, in a retrospective study by Mhanna et al., the air leak test was found to have a low sensitivity when used as a screening test to predict post-extubation stridor in children <7 years of age [101]. Postoperative patients after posterior fossa surgery may also have issues maintaining airway patency due to the loss of airway reflexes [14]. We follow a routine practice of assessing a patient's cough reflex before considering extubation in such patients.

Airway Secretions: Glasgow Coma Scale (GCS) is one of the most commonly used criteria that influence extubation in neurocritical care. Due to this, patients with GCS ≤ 8 have remained intubated. It is believed that patients with low GCS are unable to maintain airway patency. However, this practice has been challenged by some recent data that considers the presence and nature of airway secretions to play a significant role in determining the success of extubation trial. Using neurological status as an important consideration for extubation has been observed to

delay extubation. Colin et al. [102] reported that patients that had extubation delayed based on a GCS ≤8 had higher VAP rate, higher costs, and worse outcomes as compared to a group that was immediately extubated. It was observed that the presence of the patient's spontaneous cough and requirement of endotracheal suctioning more than hours was associated with successful extubation. Ko et al. [100] used the FOUR Scale score to distinguish those at risk for extubation failure. Still, they did not find any specific score that could distinguish successful extubation from failed extubation. Tanwar et al. [103] reported significantly higher successful extubation rate and lower reintubation rate and lower VAP rates, duration of ICU stay, and ventilation when modified airway care score was compared against the discretion of attending neurointensivist. Hence, individualized decisions should be taken based on the overall patient's clinical condition and hospital settings.

39.3.6 Role of Tracheostomy in Pediatric Neurocritical Care

Tracheostomy is not a common procedure in pediatric ICUs. Adult tracheostomies are usually performed in 1–2 weeks of ventilation. There is no similar consensus regarding the timing of tracheostomy in ventilated pediatric patients [104]. The time for insertion of a tracheostomy tube in pediatric intensive care is, on average, 14.4 days of endotracheal intubation in the United States while it is 21 days in Canada [105, 106]. Though the timing for considering tracheostomy may vary on an institutional basis, we consider early tracheostomy for all pediatric patients expected to receive prolonged ventilation due to poor neurological outcome. Early tracheostomy offers the following benefits to pediatric patients expected to require prolonged ventilation [107, 108]:

- Increases patient comfort.
- Decreases requirement of sedation.
- Facilitates pulmonary toilet.
- Facilitates weaning from mechanical ventilation.
- Reduces incidence of VAP.
- Reduces ICU and hospital stay.

Percutaneous tracheostomy has mostly replaced the traditional surgical tracheostomy in adult patients as the procedure is simple to perform and can be done bedside in experienced hands. However, the experience with percutaneous tracheostomy in pediatric patients (especially in young children and infants) remains limited due to safety concerns and technical limitations [104].

39.4 Conclusion

Understanding and knowledge of common respiratory pathologies in postoperative pediatric patients help prevent and manage respiratory complications after neurosurgery. Optimal ventilation and oxygenation of these patients can improve the neurological outcome.

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Brain Death and Organ Donation in Children

40

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Key Points

- There is a worldwide increase in demand for organs for transplantation.
- Initial guidelines released for the management of brain-dead organ donors were not specific for the pediatric population, and hence, it led to update of existing guidelines with recommendations specific for pediatric age group.
- Clinical criteria are sufficient to diagnose brain death in children, and ancillary tests are only supplementary to the neurological examination.
- Several pathophysiological changes occur after brain death, which may lead to impairment of multiple organ functions.
- Aggressive hemodynamic support with age-specific consideration is important in managing pediatric brain-dead donors to improve the success of organ retrieval.

40.1 Introduction

With the improvement in supportive medical care for critical illnesses, the demand for transplantation organs is increasing worldwide. In the USA, about 112,000 people were waiting for a transplant in 2019, with the total number of transplants done being only 39,718 with 19,267 donors [1]. The organ donation rate in India is one of the lowest globally, with 0.86 per million population compared to the countries like the USA, where the rate is about 31.96 per million population [2]. Although the exact statistics of patients waiting for transplantation are not available in India, the number far exceeds the organs available for transplantation. The live donor transplantation alone cannot match the demand for organs. Hence, the only way to increase the availability of the organs is by retrieving organs from brain-dead patients and cadaveric organ donors.

As in adults, the diagnosis of brain death in infants and children is established by careful medical history and detailed neurological examination. The guidelines for determining brain death in adults have been updated and published periodically [3–5]. However, to date, there are no universally accepted criteria for the determination of brain death in adults or children [6–9]. A consensus report of the ad hoc committee of Harvard in 1968 was the first to define cerebral death as a new criterion of death [10]. The American Neurological Association (ANA) in 1975 reviewed the Harvard criteria of 1968 about children. They concluded that the existing criteria could be inapplicable for children under 5 years of age. There were indications that the

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immature nervous system could survive significant periods of electrocerebral silence. The conclusion was based on a case report by Green and Lauber (1972), who described a 5-year-old child who became comatose after severe liver failure [11]. In 1977, a retrospective collaborative study on brain death was performed with strict criteria that all appropriate diagnostic and therapeutic procedures, including a toxicological screening, be performed to determine the cause of brain death [12]. However, a conclusion could not be arrived based on the age specificity of their criteria and its relation to eventual death. The Uniform Determination of Death Act was adopted as part of the President's Commission report in 1981. The commission concerning pediatric brain death recommended caution while applying neurological criteria to determine brain death in children less than 5 years. There were no age-specific guidelines in the report [13]. A special task force for determining brain death was gathered in 1987 to recommend guidelines specific for children [14]. These consensus-based guidelines were developed because the preexisting guidelines of the President's Commission failed to address the criteria to determine brain death in children adequately. Recommendations were made on age-related observation periods and the requirement for specific neurodiagnostic tests for children younger than 1 year.

Although there is a general agreement on the practice of these guidelines [15, 16], there are still criticisms about their application, particularly in young infants [17, 18]. The older 1987 task force guidelines were recently updated in 2011 [19] by another special task force; various pediatric societies endorsed it.

40.2 Definition of Brain Death

According to the Uniform Determination of Death Act 1981 [20], death can be defined in two ways. "An individual who sustains (a) irreversible cessation of respiratory and circulatory functions, or (b) irreversible cessation of all the functions of the brain, including the brain stem" is dead.

40.3 Epidemiology of Brain Death in Children

In the USA, the incidence of brain death was found to be approximately 2.06% of all hospital deaths [21]. The incidence of established brain death is not known in India. The southern Indian states like Tamil Nadu and Kerala (data from MOHAN foundation) lead in the declaration of brain death and, subsequently, organ donation. Most of these patients are adults, with very few pediatric patients declared as brain dead.

40.4 Etiology of Brain Death

Brain death is commonly observed in adolescent children and is less common in infants and newborns. Hypoxic-ischemic injury is the most common cause of brain death in infants and younger children, whereas traumatic brain injury (TBI) is the leading cause in older children [22]. The various etiologies of brain death are listed in Table 40.1.

40.5 Brain Death Determination in Children

As in adults, the clinical criteria are sufficient for establishing brain death in infants and children. There are some physiological and anatomical differences in children that require consideration in the brain-death declaration. Neonates and infants have open fontanelles and patent sutures, which prevent an abrupt increase in intracranial pressure (ICP), decreasing the reliability of cer-

Table 40.1 Etiology of brain death in children

• Traumatic brain injury
• Intracranial hemorrhage
• Gunshot wound
• Asphyxia
• Cardiovascular disease
• Drowning
• Seizures/status epilepticus
• Drug associated
• Sudden infant death syndrome

tain ancillary tests such as radionuclide cerebral blood flow (CBF) studies. A pupillary examination can be difficult in neonates and smaller infants. Small airways in neonates can affect apnea testing if tracheal insufflation is used [22].

40.6 Neurological Examination

Neurological examination is divided into three parts for the diagnosis of brain death.

- Irreversible coma.
- Absence of brainstem reflexes.
- Apnea testing.

40.6.1 Prerequisites of Neurologic Evaluation

There are some confounding factors which mimic the clinical manifestation of brain death (Table 40.2). The patient should be evaluated for these factors and treated before proceeding for further neurologic evaluation.

- Hypoxia, hypotension, hypothermia, and metabolic disturbances can affect the neurologic evaluation, and hence, these factors should be corrected beforehand.
- The patient should not be under the effect of sedatives, hypnotics, opioids, neuromuscular blocking agents, and anticonvulsants. The medication chart should be verified about the dosage and timing, and the drugs should be discontinued for an amount of time based on their half-lives. When in doubt, the plasma levels of each drug should be determined before proceeding for neurologic evaluation. When the drugs' levels are higher than the therapeutic range, the brain death diagnosis should not be attempted. Even when the drug levels are lesser than the therapeutic range, ancillary or confirmatory tests should be performed to establish brain death if there is doubt about their effects.
- Neurological examination may be unreliable immediately following cardiopulmonary resuscitation. Hence, neurologic evaluation for brain death should be postponed for a period of at least 24–48 h.

Table 40.2 Clinical conditions mimicking brain death

• Hypothermia
• Hypotension
• Hypoxia
• Metabolic disturbances
• CNS sedatives
• Antiepileptics

40.6.2 Coma

"Establishing the irreversible nature of coma" is the first step of neurological examination during brain-death diagnosis. There must be sufficient clinical and/or radiological evidence for serious irreversible brain injury. There is an absence of any response (eye-opening or motor movements) to painful stimuli (GCS 3/15). However, spinally mediated reflexes may be present, which should be carefully distinguished from cortical-mediated motor activity.

40.6.3 Assessment of Brainstem Reflexes

The patient should be evaluated for the presence of brainstem reflexes. All the brainstem reflexes will be absent when brain death occurs.

- Bilaterally dilated or mid-position pupil with absent light reflex.
- Absent cough, gag, sucking, and rooting reflexes.
- Absent corneal reflex.
- Absent oculo-vestibular reflex (caloric test).

Before performing a cold caloric test, the patency of the ear canal and intactness of tympanic membrane should be verified. Then the head end of the bed is to be elevated to 30°. The ear canal is irrigated with 10–50 ml of ice-cold water, and any movements in the eyes is noted. In patients with brain death, the movement of the eyes will be absent. This test should be repeated on the other side as well.

40.6.4 Apnea Test

Documenting apnea is one of the most important tests for establishing the diagnosis of brain death. The prerequisites for conducting an apnea test include a relatively stable patient with good oxygenation status along with the minimum requirement of positive end-expiratory pressure (PEEP), the core temperature > 36 °C, and blood pressure in the normal range for the age (Table 40.3). Under controlled conditions, when the patient is disconnected from the ventilator, the resultant hypercapnia will stimulate the respiratory center with the initiation of breathing. The detailed procedure for carrying out apnea testing is shown in Fig. 40.1. After a period of apnea of 8 min, the $PaCO_2$ of more

Table 40.3 Blood pressure targets according to the age of child

Age of the child	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Neonate	60–90	35–60
Infants	80–95	50–65
Toddlers	85–100	50–65
6–10 years	90–115	60–70
Adolescent (12–15 years)	110–130	65–80

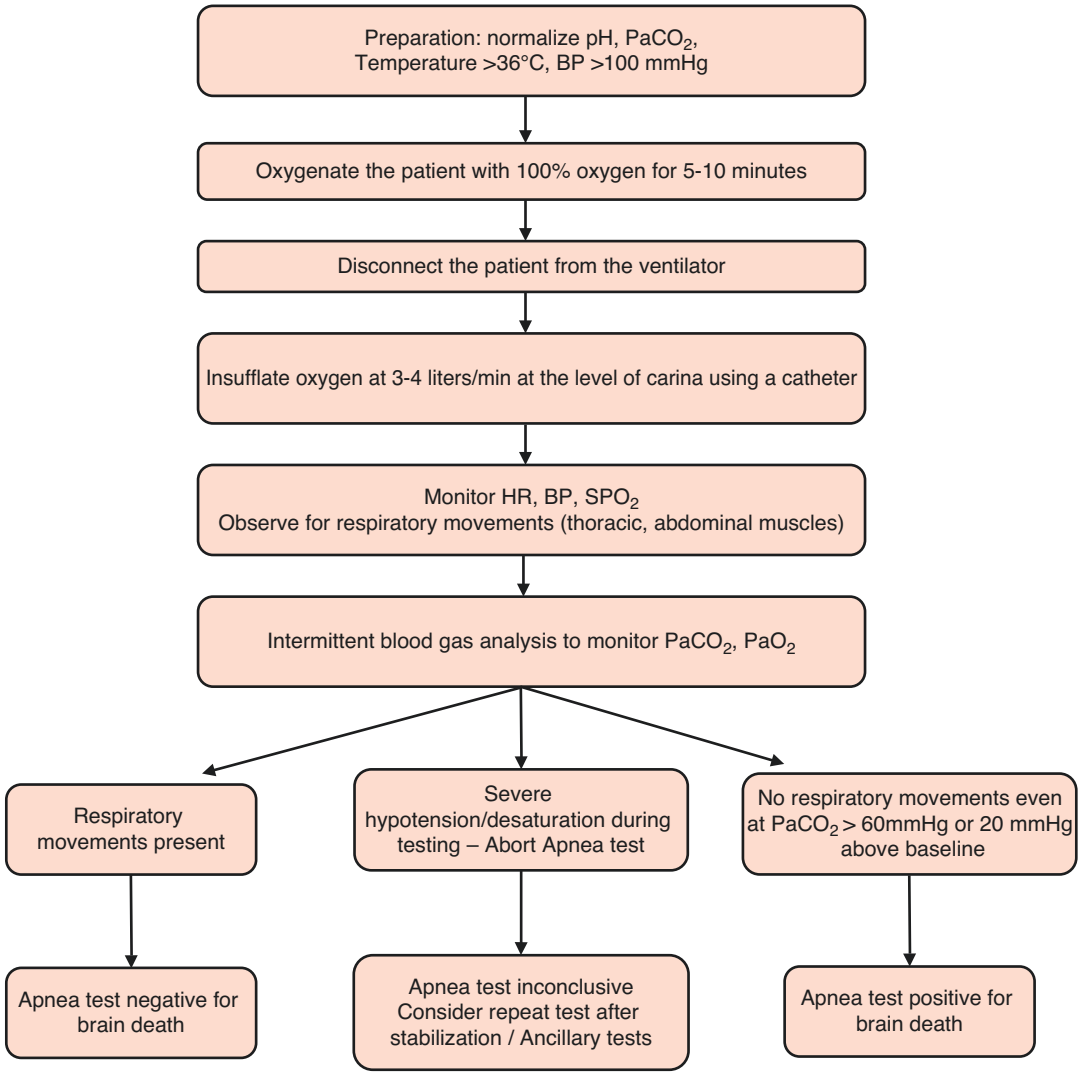

Fig. 40.1 Steps for apnea test

than 60 mmHg or 20 mmHg above the baseline is consistent with brain-death diagnosis. Although very rare, cases have been reported describing irregular breaths or minimal breathing effort in children with $PaCO_2$ more than 60 mmHg, who otherwise satisfied all other criteria for brain death [19]. Apnea testing is not recommended in children with chronic hypoxemia due to cyanotic congenital cardiac disease with the right-to-left shunt [22].

40.7 Number of Examinations and the Observation Period

In newborns, the brain is immature, and it is also difficult to carry out the detailed neurological examination in the sedated and intubated patients. Hence, it is important to have a longer observation period as compared to older children and adults. Based on the available literature, the special task force (2011) recommends performing two neurological examinations, including apnea testing with an observation period of 24 h for neonates (>37 weeks to 30 days) and 12 h (>30 days to 18 years) for infants and children between two examinations [19, 23, 24]. The first examination checks whether the child has met the clinical criteria for the diagnosis of brain death, and the second examination confirms the diagnosis of brain death. When there is a need for a reduction in the observation period, ancillary tests may be carried out for establishing the diagnosis of brain death.

40.8 Brain Death Determination in Preterm Neonates

Data concerning the diagnosis of brain death in preterm neonates is limited. The neurological examination of the preterm neonate for meeting criteria for brain death is difficult as some of the brainstem reflexes are not fully developed in these subsets of patients. Moreover, the level of consciousness in a sedated and intubated preterm neonate is difficult to be assessed. As there is insufficient data to make a conclusion regarding neurological examination and period of observation, the determination of brain death in the preterm neonate has been excluded from the current 2011 guidelines [19].

40.9 Number of Physicians Required for Diagnosing Brain Death

A single physician can diagnose brain death; however, in India, as per the Transplantation of Human Organs Act (THOA) 1994, brain death needs to be certified by four physicians for the purpose of organ procurement for transplantation [25]. The team includes the patient's treating physician, the in-charge doctor for the hospital where the patient is being treated, a neurologist or a neurosurgeon, and an independent specialist approved by the competent authority. In the case of the nonavailability of a neurosurgeon or neurologist, an anesthesiologist or intensivist can certify brain death for the procurement of organs (THOA Amendment 2011). The multidisciplinary committee, under the American College of Critical Care Medicine, which revised and updated the 1987 task force recommendation, suggests that two different attending physicians should be involved in the diagnosis of brain death. They should ensure that the diagnosis is based on the currently established criteria for brain death, there are no conflicts of interest in establishing the diagnosis, and there is consensus by at least two physicians involved in the care of the child that the criteria are met.

40.10 Ancillary Tests

Clinical criteria are alone sufficient for establishing the diagnosis of brain death. However, in some cases, ancillary testing may be required for confirmation of brain death; they are as below:

- When all the components of the neurological examination and apnea testing cannot be performed due to the medical condition of the patient.

- If there is uncertainty about the test and results.
- If suspected medication effects.
- To reduce the observation period between the two tests.

When the ancillary tests are to be performed, similar to the neurological examination, parameters like hypotension, hypoxia, and metabolic disturbances should be corrected. Pharmacologic agents like barbiturates, benzodiazepines, and opioids can affect the test; hence, these drugs should be discontinued based on their half-lives. A variety of tests are available, and each test has its own advantages and limitations. The point to remember here is ancillary tests cannot replace the clinical examination; that is why these tests are named ancillary rather than confirmatory tests.

Electroencephalogram (EEG) is widely available and, in association with clinical parameters, can be used to diagnose brain death. EEG should be isoelectric for 30 min with no electrical activity of more than 2 μV for establishing brain death. Performing EEG in pediatric patients, as well as its interpretation, poses a unique challenge due to greater artifacts, shorter interelectrode distance, and reduced cortical potential in preterm neonates [26]. EEG may be affected by the central nervous system (CNS)-depressant drugs like barbiturates, benzodiazepines, etc. The physiologic parameters like hypothermia and hypotension may also affect the EEG recording.

Four-vessel angiography is, by far, considered the "gold standard" for the diagnosis of brain death. The criteria for brain death using four-vessel angiography include filling external carotid arteries confirming proper contrast delivery and absence of flow in internal carotid arteries beyond the level of the clinoid process, in vertebral arteries beyond dural penetration, and no flow in internal cerebral veins. The disadvantages of this test are that it is invasive, unstable patients need to be shifted to radiology suite, and the study period is prolonged.

Radionuclide Imaging: Several radionuclide studies have been used in the past to demonstrate the cessation of intracranial circulation [27]. Most centers use single-photon emission computed tomography (SPECT) scanning with Technetium^{99} HMPAO (hexamethyl propylene amine oxide) as an isotopic agent. Technetium^{99} HMPAO is lipophilic and also enables inspection of cerebral parenchyma perfusion in stable imaging. Several studies have evaluated the efficacy of radionuclide imaging in diagnosing brain death and are found to be accurate and reproducible [28–31]. This technique has been compared to other techniques like CBF studies [26, 32–34]. This imaging technique is more useful when a drug-induced suppression of EEG is suspected.

Computed tomographic (CT) angiography and perfusion have been used in adults to establish the diagnosis of brain death [35, 36]. No such studies are available in pediatric patients. Nevertheless, CT angiography appears to be a promising tool for determining brain death in the future.

Magnetic Resonance Imaging (MRI) and Angiography (MRA): The MRI can give additional details, which help diagnose brain death. These include brain herniations, absent vascular flow, poor gray and white matter differentiation, and no intracranial enhancement on contrast. Non-visualization of the internal carotid artery beyond the supraclinoid area indicates absent intracranial circulation [37] and signifies brain death.

Transcranial doppler (TCD) may be utilized for establishing brain death. The absence of intracranial flow or short systolic peaks indicates malignant intracranial hypertension and cerebral circulatory arrest (CCA). However, to confirm CCA with TCD, prior recording of flow velocities in the intracranial vessels is necessary. The insonation of vessels is not possible in 10–30% of patients due to thick temporal bones. Some studies have shown a high rate of false-negative results, low specificity, and sensitivity when used for brain-death confirmation [38–40]. The advantage of TCD is it is noninvasive and can be used as a bedside monitor.

Positive emission tomography (PET) scan has been used in the literature to diagnose brain death [41]. The main disadvantages of PET are its limited availability and cost. Hence, it fails to

offer additional advantages over other standard ancillary tests.

Xenon computed tomography (Xenon CT) can be used for both quantitative and regional measurements of CBF. There is a good level of agreement between CBF measurement and EEG for the diagnosis of brain death. However, this technique is routinely not available, and also it requires shifting the patient to a radiology suite.

40.11 Physiological Changes Following Brain Death

The brain is the master organ controlling all the other organs of the body. With irreversible brain damage, several physiological changes are noticed in the organs (Fig. 40.2).

40.11.1 Management of Brain-Dead Organ Donor

Once the decision for organ procurement is made following consultation with families, the entire focus of patient management shifts toward vital organs preservation for transplantation. Strategies to decrease the ICP are discontinued, and efforts are made to provide optimal perfusion to the vital organs. Aggressive donor management in the intensive care unit (ICU) is associated with improved organ retrieval [42, 43]. This also leads to a better quality of organs and improved graft function following transplantation [42–44]. Age-specific optimal hemodynamic targets should be achieved in pediatric organ donors (Table 40.4) [45].

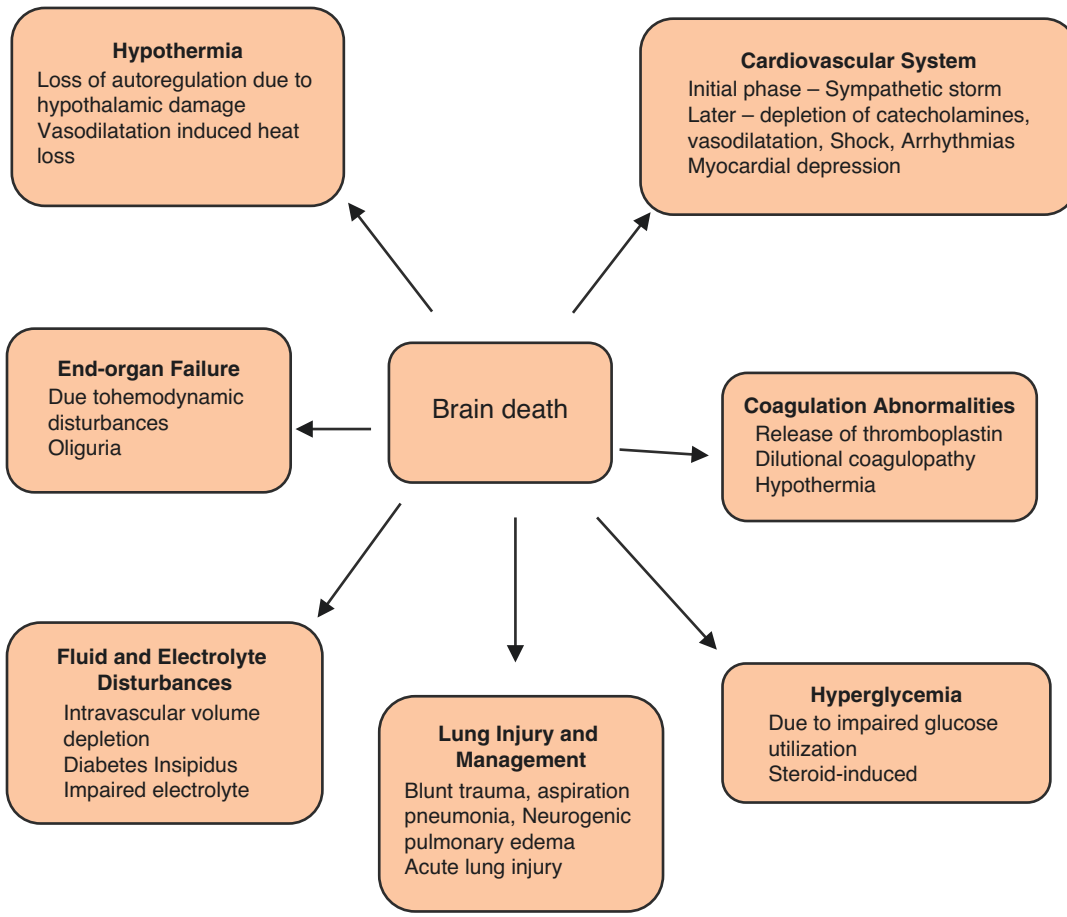

Fig. 40.2 Changes following brain death

Table 40.4 Goals for optimizing hemodynamics in pediatric brain-dead organ donor

Parameters	Targets
Hemodynamic support	Systolic blood pressure appropriate for age CVP 4–12 mmHg Dopamine <10 μg/kg/min
Oxygenation and ventilation	PaO_2 > 100 mmHg FiO_2 0.4 $PaCO_2$ 35–45 mmHg Arterial pH 7.3–7.45 Tidal volume 8–10 ml/kg
Electrolytes	Serum sodium 130–150 meq/L Serum potassium 3–5 meq/L Serum glucose 120–140 mg/dl Ionized calcium 0.8–1.2 mmol/L
Urine output	0.5–3 ml/kg/h
Temperature	Core body temperature 36–38 °C

The management of hemodynamics is more complex in a patient with brain death. Rise in ICP following brain death leads to an autonomic or sympathetic storm. Various other complications that occur following brain death include hypotension (81%), diabetes insipidus (DI) (65%), cardiac arrhythmias (25%), pulmonary edema (18%), coagulation abnormalities (28%), and metabolic acidosis (11%) [46].

40.11.2 Sympathetic Storm

Malignant increases in ICP leads to cerebral ischemia. This causes a massive release of catecholamines. Although it is transient, it can lead to increased myocardial stress, myocardial ischemia, and end-organ failure. Treatment with antihypertensives is generally not necessary. However, if required, short-acting antihypertensives such as esmolol, labetalol, sodium nitroprusside, or hydralazine may be used. These drugs should be used judiciously with titration to the response. Longer-acting antihypertensives may compound the problems of hemodynamic management once the phase of sympathetic storm passes off; hence, these agents should be avoided.

40.11.3 Hypotension

Hemodynamic parameters vary with age and should be considered during the management of a pediatric organ donor. Hypotension after brain death can be due to multiple factors. After brain death, the sympathetic flow decreases, leading to loss of sympathetic tone and profound vasodilatation. This results in a sudden onset of hypotension. Patients with raised ICP receive osmotic diuretics, hypertonic solutions, and diuretics to manage cerebral edema. Additionally, many centers follow fluid restriction for the management of raised ICP. All these interventions may cause intravascular volume depletion resulting in hypotension. The DI following brain death can further reduce intravascular volume. The associated increases in urine output due to DI can cause hypovolemia, further contributing to hypotension.

Any sign of ongoing blood loss (external, gastrointestinal, urinary) should be checked and treated. Hypotension can occur secondary to certain medications, including beta-blockers and antihypertensives, which need to be discontinued. The management of these children includes the restoration of intravascular volume and maintenance of optimum blood pressure to the age, with or without the use of vasopressor or inotropic agents and hormone replacement therapy.

Hypernatremia may occur due to concurrent DI and should be treated with crystalloids with balanced salt content. Ringer's lactate and 0.45% saline are frequently used. 0.9% normal saline may cause hyperchloremic acidosis and increases renal vascular resistance. Excessive administration of the IV fluids containing 5% dextrose may lead to severe hyperglycemia and hypothermia. Colloids are avoided as resuscitation fluids as their use is associated with renal failure, delayed graft function, and coagulation abnormalities [47, 48]. A central line may be ensured in all patients for monitoring of central venous pressure (CVP). The optimal volume status to be achieved in a brain-dead organ donor is controversial; it also depends upon the

organ to be harvested. In lung transplantation cases, a significant increase in the alveolar-arterial oxygen gradient was seen in those who achieved a CVP of 8–10 mmHg compared to those whose CVP was maintained at 4–6 mmHg [49]. Some of the studies recommend a CVP of 10–12 mmHg in cases where abdominal organs alone are procured, a CVP of less than 8 mmHg if lungs are to be harvested, and a CVP of 8–10 mmHg in cases where both abdominal and thoracic organs need to be harvested [50]. In all these cases, a target of euvolemia is important for the maintenance of hemodynamics. Dopamine and adrenaline infusions may also be titrated to the desired effect. Additional serum lactate levels and mixed venous oxygen saturation (SvO_2) can be used as myocardial performance indicators. Hormone replacement therapy with a combination of methylprednisolone, thyroid hormone, and vasopressin has been recommended to improve hemodynamics, especially in cases where ejection fraction is less than 40% [51].

40.11.4 Arrhythmias

The patients may develop arrhythmias during a sympathetic storm or following brain death. Prolonged hypotension secondary to arrhythmia leads to decreased cardiac output, myocardial ischemia, and metabolic acidosis. Electrolyte abnormalities in these children can induce arrhythmias. These arrhythmias should be managed according to standard protocols.

40.11.5 Fluid and Electrolyte Disturbances

These are prevalent associations in brain-dead patients. The commonly encountered scenarios include dehydration, DI, hypernatremia, hypokalemia, and hypocalcemia. Prompt correction of these abnormalities is essential for optimal organ perfusion and retrieval of good quality organs.

40.11.6 Diabetes Insipidus

Hypothalamic dysfunction results in decreased antidiuretic hormone resulting in increased urine output, increased serum osmolality, and hypernatremia. The resultant hypovolemia may lead to cardiovascular collapse. Hypernatremia is associated with graft failures in patients with liver transplantation. The management of DI includes optimal fluid management using 0.45% normal saline along with the use of vasopressin (0.5 mU/kg/h) or desmopressin (0.5 μg/h IV) infusions. Glucose-containing solutions are avoided as hyperglycemia can lead to osmotic diuresis.

40.11.7 Hypothermia

Hypothermia is one more manifestation of hypothalamic dysfunction: Profound vasodilatation and inability to compensate for heat loss results in hypothermia. Hypothermia leads to diuresis, coagulation abnormalities, myocardial dysfunction, and arrhythmias. Active and passive warming techniques can be used to avoid these complications. Also, before apnea test, the core temperature should be ensured to more than 36 °C.

40.11.8 Coagulation Abnormalities

Release of tissue thromboplastin following brain injury, infusion of excessive fluids resulting in dilution of coagulation factors, and hypothermia can contribute to the coagulopathy following brain death. Coagulopathy should be corrected using blood components before shifting the donor to the operation theater for organ retrieval.

40.11.9 Oliguria

Hypovolemia and hypotension can reduce kidney perfusion and urine output. A urine output of 1 ml/kg/h should be maintained with volume

resuscitation and inotropes for harvesting kidneys for transplantation.

40.11.10 Hormone Replacement Therapy

Although very little evidence is available for the pediatric population, hormone replacement therapy is commonly used in pediatric brain-dead organ donors. Thyroxine (T4) and triiodothyronine (T3) are the available supplements to replace depleted thyroid hormones. T4 0.8–1.4 μg/kg/h is commonly used for the replacement of thyroid hormones. The use of thyroid hormone is shown to have reduced the need for inotropic support [52]. The use of these hormones appears to be advantageous in scenarios of refractory hypotension, even with fluid and inotropic support [53]. Methylprednisolone 15 mg/kg is commonly used to replace steroids in brain-dead donors; it may have a vital role in potential patients for lung donation. In patients with established DI with hypotension, vasopressin 0.5 mU/kg/h may be used to control DI as well as to reduce the requirement of ionotropic support [54]. However, in patients with DI with hemodynamic stability, a more selective agent like desmopressin 0.5 μg/h IV is to be used for control of urine output.

40.11.11 Management of the Lung

In patients with brain death, lungs can be damaged due to blunt trauma, inhalation or thermal injury, and aspiration pneumonia. Neurogenic pulmonary edema following a neurologic injury can also lead to significant hypoxemia. Lung protective strategies can be employed during mechanical ventilation. The target partial pressure of the arterial oxygenation (PaO_2) should be more than 100 mmHg or arterial oxygen saturation (SpO_2) of more than 95% with an inspired concentration of the arterial oxygenation (FiO_2) less than or equal to 0.4. Infusion of excessive fluid can lead to increased lung water, making them non-suitable for lung transplantation. Reduced fluids can, in turn, affect kidney perfusion. In adults, it has been shown that restricted fluid infusion is associated with more availability of lungs for transplantation without affecting the quality of kidneys for transplantation [55].

40.11.12 Glucose Metabolism

Supplementation of steroids, catecholamine infusions, and no glucose usage by the brain result in hyperglycemia following brain death. This hyperglycemia can result in osmotic diuresis and exacerbation of intravascular volume depletion. Hence, dextrose-containing solutions are avoided, and insulin infusions are used to control blood sugar at a range of 120–140 mg/dl.

40.12 Conclusion

Worldwide, there is an increasing demand for organs for transplantation. The requirement can be partially fulfilled by procuring organs from brain-dead patients. Since the adult brain-dead donor recommendation cannot be applied to the pediatric age group, guidelines have been updated, which are specific for the management of potential pediatric brain-dead organ donors. Like adults, clinical criteria alone are sufficient to establish brain death in children. Ancillary tests are supplementary and do not replace neurological examination. Hemodynamic and organ-specific targets for optimization in pediatrics should be decided based on the age of organ donors. Aggressive management of brain-dead donors is associated with an increased number and better quality of organs for transplantation.

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Developing Brain and Anesthetic Neurotoxicity

41

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Key Points

- Evidence from animal studies supports a causal relationship between intravenous and inhaled anesthetic exposure and brain development, triggering increased apoptosis, with negative neurocognitive and behavioral outcomes.
- All these negative events take place during a high vulnerability period on brain development known as "brain spurt."
- Gamma-aminobutyric acid (GABA) and glutamate receptor modulation may be involved in apoptotic pathway signaling. Anesthetic drugs exert their actions through these receptors, among many others.
- Delaying non-elective surgical procedures might put children at risk of disease progression, including neurodevelopmental impairment.
- Controlled anesthetic exposure to anesthesia is difficult to accomplish.
- There is a significant genetic socioeconomic and environmental influence on neurodevelopmental outcomes.
- Short-term neurodevelopmental testing may not be relevant for diagnosis.
- Prevention, diagnosis, and prompt treatment of other perioperative complications that are closely related to worse neurological prognosis are mandatory.

41.1 Introduction

Within the last decade, animal models of anesthetic neurotoxicity and related developmental disorders have raised concerns for comparable effects in children after exposure to general anesthesia in early infancy. Millions of children undergo surgery during their first 4 years of life worldwide [1].

Almost every general anesthetic has been related to neuronal damage within the developing animal brain. This aspect is more relevant during a period of increased vulnerability within the central nervous system growth called "brain spurt" and characterized by a peak in synaptogenesis and neuronal pruning [2]. Failure to achieve significant neural connections during this period would lead to neurodegeneration of "meaningless" neurons through programmed cell death (apoptosis),

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which normally affects a significant proportion of developing neurons [3, 4].

Even if not completely elucidated yet, anesthetic drugs act either as antagonists of glutamate n-methyl-d-aspartate (NMDA) receptors or gamma-aminobutyric acid (GABA) receptor agonists [5]. Both NMDA and GABA receptors have been linked to impaired synaptogenesis and increased neuroapoptosis in alcoholic fetal syndrome [6]. Whether or not anesthetic modulation of these neurotransmitter pathways impairs synaptogenesis and/or neurodevelopment in early infancy is still a matter of debate and growing research. Translating results from animal models to clinical practice is challenging, as long as animal research procedures may not reflect the pediatric anesthetic practice [7, 8].

41.2 Human Brain Development

Human brain development is a complex and tightly regulated process that starts early in the embryonic period and extends throughout the fetal and postnatal life [9]. There is extensive genetic control over early brain development on the anatomic, cellular, and molecular levels. Recent research has improved our understanding of the different factors that influence this process. Human brain development is also dynamic and adaptive in nature, as well [10]. As a result, the brain reaches 90% of its adult size by the age of five [2, 11].

41.2.1 Embryonic Period (Conception—Week 8)

Brain development begins during the third gestational week, with neural progenitor cell (NPC) differentiation. Patterning of the neocortex into distinct functional areas starts during the embryonic period and is tightly controlled by several pathways of molecular mediators [12]. This process is subjected to refinement and modification through the influence of endogenous and exogenous stimuli later in life [13, 14].

41.2.2 Fetal Period (Week 9—Birth)

The formation of gyri and sulci starts as early as the eighth gestational week, reflecting underlying microstructural changes at the histological level [15]. The processes of neurogenesis, migration, differentiation, synaptogenesis, and myelination constitute the hallmarks of brain development in the fetal period.

- **Neurogenesis**: The adult human brain contains approximately 100 billion neurons [16]. After the 42nd embryonic day, the asymmetrical division of NPC results in one neural progenitor cell and one differentiated neuron. The differentiated neurons migrate from the ventricular zone to the neocortex [2, 17]. Neurogenesis in humans concludes around embryonic day 108 [18]. A substantial but tightly controlled loss of neuronal population occurs during this phase through apoptosis (programmed cell death). Apoptosis affects more than 50% of the developing neurons, reaching up to 70% in certain brain regions [19].
- **Migration**: Neural migration in humans peaks between 3 and 5 months of gestation and ultimately results in the formation of the six-layered neocortex [3, 20]. Post-mitotic neurons migrate through one of three possible processes: somal translocation, radial migration, and tangential migration [2, 3].
- **Differentiation**: If given the correct signals, early progenitor cells are capable of producing any neural cell type. Later types of neural stem cells exhibit "fate restriction" and lose the ability to generate different cell lines [21].
- **Synaptogenesis**: Upon reaching the cortex, migrating neurons extend axons to establish connections with other neural cells. Axonal growth and synaptogenesis are tightly molecularly controlled events. Both are essential for the development of the major neural pathways [2]. Brain spurt and pruning are followed by a systematic breakdown of up to 50% of the newly created synapsis throughout the prenatal and early postnatal life [3, 4]. This process, along with apoptosis,

ensures the normal development of the neural network.

- **Myelination**: Oligodendrocyte progenitor cells start to differentiate in the second trimester into oligodendrocytes, closely related to the neuronal axons. Myelin production from oligodendrocytes creates the myelin sheaths that increase axonal conductivity [22]. Moreover, oligodendrocytes contribute to axon integrity and neuronal survival by synthesizing neurotrophic factors [2].

41.2.3 Postnatal Life

The proliferation, migration, and apoptosis of glial progenitor cells, unlike most neurons, extend well beyond the prenatal period. In addition, glial progenitors maintain their ability to proliferate as they migrate [23]. During early postnatal life, neuronal synaptogenesis continues on a large scale until it plateaus after 2 or 3 years of age and then declines toward the adult levels during late childhood and adolescence [4].

41.3 Anesthesia-Induced Neurotoxicity in Preclinical Animal Models

41.3.1 Mechanisms of Anesthesia-Induced Neurodegeneration

Evidence of potential anesthetic neurotoxicity comes mainly from animal models, including rats, mice, guinea pigs, and non-human primates. In general, these preclinical data indicate that anesthetic agents may potentially induce neurotoxicity within the developing brain by triggering apoptosis and interfering with neurogenesis, differentiation, and synaptogenesis [8].

The apoptotic process can be activated through two different pathways. The intrinsic apoptotic pathway is triggered by internal signals that activate pro-apoptotic proteins and ultimately result in DNA cleavage and cell death. The extrinsic pathway is activated by binding of specific ligands (such as certain cytokines) to "death receptors" on the cell membranes [24]. Anesthetics may activate the extrinsic pathway, as they exert an inflammatory response in the premature brain [25]. Also, anesthetic drugs may modulate gene expression, thereby affecting cell metabolism, development, and signal transduction. This mechanism explains the potential of anesthetic drugs to trigger the intrinsic apoptotic pathway [26].

Activation of glutamatergic NMDA receptors has an excitatory effect both in the adult and premature brain. Similarly, activation of GABA receptors within the neonatal brain exhibits excitatory effects and leads to cell depolarization, despite its inhibitory effect in the adult brain [27, 28]. Additionally, both GABA and glutamate signals in the fetal brain influence neuronal proliferation and differentiation [29]. Activation of GABAA receptors also signals migrating cells to stop the process as they reach their target location [30, 31].

Anesthetic agents exert their effects by NMDA antagonism or by GABAA agonism [5]. It was shown that isoflurane and midazolam reduce inhibitory synaptic transmission and increase excitatory synaptic transmission in the thalamus of newborn rats [32]. The interference in synaptic neurotrophic signaling during this period of vulnerability induces programmed cell death by both intrinsic and extrinsic apoptotic pathways [24, 33]. Sevoflurane induces the intrinsic apoptotic pathway through long-term modulation of gene expression [26].

Neurons are not the only cell line affected by anesthesia administration. Oligodendrocytes, the myelin-generating glial cells, also go through increased apoptosis after exposure to isoflurane in primates [34].

Although apoptosis and synaptic pruning are normal processes of brain development, the increased levels of apoptotic activity and decreased synaptic density induced by anesthetic exposure may eliminate neurons that otherwise become functional components of the brain circuitry [35].

Other mechanisms involved in animal neuroanesthetic toxicity are increased neuronal progenitor cell death in rodent neonates that were

exposed to sevoflurane [36], reduced hippocampal neuronal proliferation in rats after in utero ketamine exposure [37], as well as decreased dendritic density and disrupted circuit formation through synaptogenesis following sevoflurane, isoflurane, and propofol anesthesia [38–40].

41.3.2 Risk Factors for Anesthesia-Induced Neurotoxicity

Several factors have been proposed to influence the potential of anesthetic neurotoxicities, such as the age of exposure, type of anesthetic agent, number of anesthetic exposures, duration, and the dose of anesthesia [24].

- **Timing of Exposure**: The window of vulnerability to neurotoxicity reflects the period of peak synaptogenesis and is different between species. In human brain development, synaptogenesis is believed to extend between the third trimester of pregnancy and the third year of life. It peaks between the fifth and 16th postnatal day in non-human primates and between the seventh and tenth postnatal days in rodents [8, 9]. Rhesus macaque neonates exposed to ketamine on the fifth postnatal day showed increased neuronal apoptosis, but not when exposure occurred on the 35th postnatal day [41]. Exposure to inhalational and intravenous agents in young rodents induces mitochondrial injury, increases neurodegeneration, and decreases synaptogenesis in different areas of the brain in an age-dependent manner [38, 42]. On the contrary, older-aged animals exposed to anesthetics showed increased synaptic density and decreased apoptosis [39, 43].
- **Type of Anesthetic Drug**: Studies have shown significant variability in the impact of anesthetic toxicity and functional outcomes. Desflurane is responsible for increased apoptotic activity in infant mice, followed by isoflurane and sevoflurane. Even though all three agents can cause significant long-term memory deficits, only isoflurane seems to impair short-term memory [43]. Midazolam and isoflurane activate apoptosis sequentially: first in the thalamus and then in the cortex. Isoflurane alone has similar effects within multiple layers of the retina [33, 44–47]. Conversely, a single dose of etomidate has not been related to increased neuronal apoptosis or long-term behavior disorders [48]. A summary of the functional and histologic effects of commonly used anesthetics on the different stages of animal brain development has been provided in Table 41.1.
- **The Dose of the Anesthetic Agent:** The neurotoxic effect of anesthetics seems to show a dose-dependent relationship in animal models, as indicated by isoflurane administration in pregnant rats [50]. Increased apoptosis levels have been reported with higher doses of ketamine, propofol, and midazolam [45, 56, 59].
- **Frequency and Duration of Exposure:** Anesthetic neurotoxicity has also been correlated with the duration and number of anesthetic exposures [8]. Multiple exposures to ketamine and propofol significantly increase neuronal cell death and neurodegeneration and are associated with long-term memory impairment and learning disability [57, 61, 64]. Prolonged exposure to ketamine in monkeys causes a widespread increase in neocortical apoptosis and necrosis, especially within the frontal cortex [41, 65]. Similar processes are observed in the cortical and thalamic areas of rat brains and are associated with long periods of exposure to midazolam, isoflurane, propofol, and nitrous oxide [51, 60].

41.3.3 Limitations of Preclinical Studies

Translating the results of preclinical studies into human clinical settings is controversial. First, there are clear differences in structural anatomy and chronological maturation of the brain among species. As previously discussed, the period of maximum vulnerability for the human brain may extend from pregnancy to early childhood, while for other species, it peaks only postnatally and

Table 41.1 Preclinical evidence on anesthesia-related neurotoxicity

Agent	Timing of exposure	Histologic changes	Functional effects
Sevoflurane	During brain growth spurt After a brain growth spurt	↑ Neurodegeneration, neuronal progenitor cell death, apoptotic activity, and inflammatory response (IL-6) [25] ↓ Neurogenesis, dendritic density, voltage-gated CA^{+2} channel density [40] ↑ or no effect on dendritic density in prefrontal and somatosensory cortices. No significant inflammatory response or increased apoptosis [40]	Long term memory impairment, cognitive impairment, learning deficits, and ↓ social interactions [25, 36, 49]
Isoflurane	Prenatal period During a brain growth spurt After brain growth spurt	Dose-dependent ↑apoptosis [50] ↑Age- and duration-dependent apoptosis and neurodegeneration in the thalamus, substantia nigra, cingulate gyrus, and hippocampal cortex [33, 51] Apoptosis affecting both neurons and glial cells and especially myelinating oligodendrocytes [34] ↓ Synaptogenesis and density of presynaptic vesicles [38] Induced mitochondrial injury [42] No effect on apoptosis or synaptogenesis [43]	Short- and long-term learning and memory deficits [52]
Desflurane	During brain growth spurt	↑ Neurodegenerative and apoptotic activities in the thalamus, hippocampus, and dentate gyrus [53, 54]	Deficits in associative learning and long term memory [53]
Ketamine	Prenatal period During brain growth spurt	Induced neurodegeneration and decreased proliferation in the hippocampus [37] Duration-dependent ↑ apoptosis in basal ganglia [55] Dose-dependent apoptosis and neurodegeneration [56, 57]	Long-term depression- and anxiety-like behavior and impaired memory [37] Long-term memory and learning impairment [57]. Lower motivation and slow response speed [58]
Propofol	During brain growth spurt After brain growth spurt	Increased apoptosis in a linear dose-response curve [59]. Induced apoptosis and neuronal necrosis with long exposure periods or multiple exposures [60, 61] ↓ Synaptic density, synaptic transmission, and long-term potentiation in the hippocampus [39, 62] Activation of brain region-specific neuroprotective signals, ↑ synaptic density [39]	Diminished response to anxiolytics [63]. Learning and memory impairment [61, 62]
Combined midazolam, isoflurane and N2O	During brain growth spurt	Induced mitochondrial injury [42] Increased neurodegeneration and apoptosis in different areas of the thalamus and cortex depending on age, dose, or duration of exposure [33, 45, 51] ↑ Excitatory and ↓ inhibitory neural transmission in the thalamus	Short- and long-term memory and learning disability [52]

for a shorter period of time [9]. Second, animal studies report higher doses of anesthetic drugs than those used in clinical practice in humans, mostly related to a lower relative potency to achieve the desired anesthetic state in animals [8]. Third, laboratory animals often suffer from severe physiologic disturbances and increased mortality rates under anesthesia due to limitations

in airway management and monitoring [7]. Fourth, animal models are anesthetized without being subjected to surgical procedures. Liu et al. observed that surgical stress, sedatives, and anesthetic drugs might act concurrently in an intrinsic way, modulating neuroprotective and neurotoxic pathways. Noxious stimulation has been related to a decrease in the neuroapoptotic effect of ketamine [66, 67]. Finally, compared to non-research specimens, animal subjects are kept in environments that may appropriate for social enrichment and interaction, necessary for complex processes of normal behavioral and cognitive development [68].

41.4 Clinical Evidence in Pediatric Anesthetic Neurotoxicity

In contrast to the extensive preclinical evidence of an association between early anesthetic exposure, increased neuroapoptosis level, and developmental disorders, clinical evidence reported mixed results and is less compelling. Several factors may explain these discrepancies between the basic research and clinical data.

The potential impact of anesthetic exposure during the early stages of brain development is a sensitive and controversial subject for both parents and clinicians. Unfortunately, an increased number of retrospective studies discuss anesthetic neurotoxicity compared to studies with prospective designs. Multiple confounders can bias the final results of such studies and blur the relationship between variables. The prospective methodological design can control these confounders and establish a causative relationship between anesthetic exposure and negative neurodevelopmental outcomes [69, 70].

41.4.1 Surgical Condition and Preoperative Risk Factors

Several pediatric surgical conditions are related to an increased risk of developing neurobehavioral disorders [71–73]. Congenital malformations, low birth weight, severe preterm birth, perinatal infection, and hemorrhage are only some of the risk factors associated with neurodevelopmental disorders. Retrospective studies conducted on children undergoing hernia repair reported a higher incidence (77% of patients) of at least one of the aforementioned confounding conditions at birth when compared with a control group [72, 74].

Exclusive control for anesthetic exposure requires a complex protocol design that does not apply to every type of surgery [75]. Anesthetic exposure is almost always related to a surgical insult [72], and untreated pain and surgical stress per se are strongly correlated to developmental and behavioral disorders in children [76]. Significant risk of bias may be introduced in studies that do not control the type of surgery, whereas studies that focus on a single procedure have increased internal validity [72, 74, 75, 77]. Ing et al. studied several surgical procedures and reported an increased risk for language disability after anesthetic exposure. However, 24% of the procedures were myringotomies [78], possibly due to chronic otitis media. Previous research associated chronic otitis media with preoperative language impairment, supporting the fact that undiagnosed developmental disorders can be closely related to the underlying disease. A neurodevelopmental screening test was recommended as part of the perioperative assessment [79].

41.4.2 Developmental Age of Exposure and Timing of the Surgical Procedure

Surgical procedures during early infancy are rarely considered elective [69]. The potential risk imposed by the surgical procedure and anesthetic exposure must be weighed against the risk of the natural progression of the disease [69, 80]. Most studies report results for children exposed to general anesthesia before 4 years old. The vulnerability window during brain development is unknown in humans. Translation from animal studies suggests that brain development stages would correlate with a period of human

development comprised between the early third trimester of pregnancy and early childhood. This period of "brain spurt" and related increased synaptogenesis and neuronal pruning does not occur simultaneously in all brain regions, and regional vulnerability could vary throughout development [73]. Studies that include children exposed to anesthesia on a wide range of ages may dilute the effects of an under-represented age population or skew the results due to an overrepresented group.

Assessing this period of fetal brain vulnerability is challenging due to several reasons. Anesthetic procedures are commonly avoided during the last trimester of pregnancy, except for surgical emergencies, cesarean delivery, or anesthesia for labor and delivery. Moreover, regional anesthesia is preferred in these patients as long as it satisfies safety, surgical requirements, and patients' comfort. Therefore, most procedures provided under general anesthesia during the last trimester of pregnancy reveal underlying causes that could, per se, affect the long-term development of the newborn [9]. Knowledge of long-term consequences of drug exposure during the last trimester of pregnancy is mostly related to maternal alcohol consumption and antiepileptic drugs, but not anesthetics [6, 81]. When considering a brief exposure to general anesthetics, such as cesarean delivery, no increased risk of learning disabilities was reported when compared to vaginal delivery [82].

Preterm newborns that undergo surgery during their first weeks after birth may be at a greater risk for anesthesia-related neurotoxicity due to an increased vulnerability and the presence of risk factors related to the preterm birth itself or the surgical disease. However, a prospective observational study involving severe preterm babies did not support this hypothesis [83].

Benzodiazepines share GABA receptor agonist properties with barbiturates; they might also share long-term effects on cognitive development. Short-term developmental and anatomical consequences of midazolam exposure have been described on preterm babies after long-term sedation in neonatal intensive care units. However, long-term consequences of midazolam exposure have not been yet assessed [84]. Nevertheless, there is also evidence of no association between prolonged sedation/analgesia of severely preterm babies and longitudinal (5-year) neurological outcomes [85].

Short-term outcomes have been assessed after pyloric stenosis (PS), indicating slightly decreased scores in neurodevelopmental subtests at 12 months old compared to a control group. However, mean test scores were not under the average range for age [86]. The long-term impact of this procedure did not report any significant difference in educational outcomes at age 15 [73]. Studies involving hernia repair procedures before age 1 reported no differences in academic testing in children and teenagers exposed to anesthesia and surgery compared to the control group [69, 72, 87]. Yet, Block et al. [87] and Bong et al. [69] reported an increased proportion of children that scored below the fifth percentile or with diagnosed learning disorders.

A meta-analysis on retrospective studies available until 2011 showed no statistically significant increase in the odds ratio for behavioral or intellectual problems after exposure before 4 years old [88]. Retrospective studies published after 2011 [70, 71, 87, 89, 90] have shown an increase in negative neurodevelopmental outcomes after anesthesia exposure during early infancy. However, due to multiple confounding variables (study design, multiple surgeries, lack of anesthetic information, historical time of the procedures), a careful interpretation should be considered when analyzing data.

The Pediatric Anesthesia Neurodevelopment Assessment (PANDA) Study was completed in February 2016 (registered at clinicaltrials.gov NCT00881764). The authors aimed to compare neurodevelopmental results from ages 8 to 15 in a historical group of siblings with and without anesthetic exposure in their first 36 months of life with no evidence of neurotoxicity [77].

In early 2016 were published the results regarding the secondary outcome of the international multicenter, randomized controlled trial "Neurodevelopmental outcome at 2 years of age after general anesthesia and awake-regional anesthesia in infancy" (GAS). This study

provided robust evidence of no increased risk for neurodevelopmental disorder at age 2 for children undergoing hernia repair during the first year of life. The study was conducted using sevoflurane-based general anesthesia versus awake regional anesthesia alone. Results for the primary outcome (5 years old neurocognitive assessments) were published in 2019. The GAS study recruited approximately 700 children and reported that neurocognitive development was equivalent in general anesthesia and regional anesthesia study groups after 5 years of follow-up [75].

Conclusively, no prospective studies have been able to demonstrate any link between general anesthesia and impairment of neurological and cognitive development in children [91, 92].

41.4.3 Number and Duration of Exposure

Drug-associated effects usually relate to dose and duration of exposure. A potential dose-related effect has been suggested [70, 87]. Several studies have found a positive correlation between an increased number of anesthetic/surgical exposures and adverse neurodevelopmental outcomes [70, 71, 82, 84]. However, while some studies report that a single exposure may be responsible for neurodevelopmental impairment, diagnosed later on in life [69], others suggest that a single brief exposure has no impact on these outcomes [71–73, 75, 77].

41.4.4 Anesthesia-Related Confounders

Several studies attributing negative cognitive outcomes to anesthetic exposure fail to report detailed information on the anesthetic procedure. Missing data usually involves the type and dose of the drug used and intraoperative episodes of hypotension, bradycardia, hyperoxia, hypoxia, hyperglycemia/ hypoglycemia, fever, and hyponatremia [1, 79, 82, 93]. Some studies report retrospective data collected from the decade of 1970 to 1980. Negative results reported in some of these articles can be related to a lack of monitoring and identification of perioperative complications [1, 71, 73, 90, 93].

Specific anesthetic drug-related clinical evidence is inconclusive. The consequences of midazolam long-term exposure have not been yet assessed, as mentioned earlier [84]. Ketamine has also been addressed both as a neuroprotective and neurotoxic compound in different trials [94, 95].

The GAS study proposed a unique methodological design that allowed for specific control of sevoflurane administration, as the sole general anesthetic used during this study. Two groups of patients were randomized to awake regional anesthesia or general anesthesia plus regional analgesia for inguinal hernia repair. No sedation was used in the awake group, except for oral dextrose. Early detection and treatment of perioperative complications were accomplished per study protocol [75]. Accurate study designs, such as GAS, are able to control perioperative variables (i.e., type of anesthesia) when investigating developmental disorders; however, few pediatric surgeries can be performed safely under regional anesthesia alone.

41.4.5 Demographics

There is a difference between male and female gender performances on neurodevelopmental tests, and preclinical evidence also suggests gender-specific vulnerability to neurotoxicity [52]. Further, PS and hernia repair are more prevalent in males [72, 73]. Neurodevelopment relies on multi-dimensional influences, such as biological factors, psychological factors, and social conditions. Confounding variables, such as a history of parental drug abuse or low educational level, among others, can have a negative impact on a child's development. Such variables should be taken into consideration if the study subjects belong to a socially disadvantaged population [70, 74]. For instance, Medicaid patients have reported a greater incidence of behavioral or developmental disorders than the general population [70].

Environmental and social confounders can be partially controlled when the compared groups belong to a cohort of siblings. Furthermore, monozygotic twin studies also control for genetic variability. The genetic vulnerability can be related to an increased risk for surgical disease [70, 79].

41.4.6 Migration and Loss to Follow-up

Migration, and subsequent loss to follow-up, imposes challenges on outcome variable analysis. Healthier children tend to migrate more than unhealthy subjects skewing the follow-up results. Additionally, loss to follow-up can be attributed to a non-traditional education, difficult to match with standard school test level imposed by the study design. Finally, parental perception of learning disorders can increase these patients' participation and skew the measured outcome [69].

41.4.7 Outcome Variable Selection

Several outcome variables have been reported as a result of different published studies, such as specific neurodevelopmental tests, academic achievement and assessments, and neurodevelopmental disorders according to the International Classification of Diseases (ICD-9) codes. Diverse sources were accessed to collect data, including medical reports, medical databases, educational reports, parental and teacher interviews, and prospective testing [69, 74, 79].

Anesthetic exposure has been associated with a 4.5-fold increase in the risk of future learning disorders. However, academic differences have not been consistent [69, 72, 73]. ICD-9 has been used to detect learning disorders after anesthetic exposure [74]. However, no strong correlation exists between the ICD diagnosis, academic achievement, and neurodevelopmental test results [89]. The Medicaid database diagnoses are also considered to be a blunt tool for neurodevelopmental diagnosis [70]. Neurodevelopmental disorder assessment should be conducted considering age-specific and test-specific sensitivity [75, 78, 80].

Studies based on academic results might be more relevant for concerned parents who are more interested in academic achievement rather than in intelligence quotient results (IQ) [72, 73, 79]. Most studies have been inconclusive and do not show a statistically significant difference in academic performance (assessed by diverse methods) after results are corrected by potential confounders [87].

Attention-deficit/hyperactivity disorder (ADHD) and autism have also been suggested to be a consequence of early anesthetic exposure [90]. However, ADHD studies based on functional magnetic resonance imaging did not show differences on the activation of ADHD "response inhibition" pathways in children not diagnosed with ADHD and exposed to general anesthesia before 2 years old compared to non-exposed control groups [96].

Lately, it has been suggested that visually evoked potentials (VEPs) may be used to evaluate anesthetic neurotoxicity. Oba et al. [97] conducted a single-blind prospective trial that compared the VEPs of a group of children who had over 15 anesthetic exposures due to corrosive esophagitis versus a healthy population of children. VEPs were significantly altered in the treatment group.

41.4.8 Timing of Assessment

The available published studies usually have predetermined follow-up time points, when either the neurodevelopmental assessments are conducted or previous diagnoses or reports are collected. Obviously, this study design has serious limitations. Children with developmental disorders can sometimes overcome their counterparts and "catch up" later in life [98]. Some studies report early neurodevelopmental assessments [74, 75, 84]. These results should not be underestimated, but they may be less relevant than long-term evaluations due to decreased sensitivity or potential neuroplasticity effect.

Table 41.2 Potential neuroprotective drugs

Preclinical studies	Human studies
• Human recombinant erythropoietin • Xenon • Dexmedetomidine • Clonidine • Lithium • Melatonin • Xestospognin C	• Magnesium sulfate • Calcium channel blocker • Allopurinol

41.5 Pharmacological Neuroprotection Strategies

Several drugs have been proposed as neuroprotective in animal models, only a few of them being tested in humans (Table 41.2) [99–111]. No recommendations can be made regarding this subject in pediatrics [95].

41.6 Future Prospects

Future research should provide further insight into the higher number and longer exposures to general anesthetics (longer than 1 h). It is possible, the relationship with potential neurotoxicity and neurological development alteration at young ages as well as studies that address the implications of anesthetic exposure on patients that are already at risk for neurological impairment.

41.7 Conclusion

Addressing the problems of anesthesia-related neurotoxicity and adverse effects on the developing brain remains a challenging task given the limitations of in vivo models and difficulties in designing prospective well-controlled trials in humans.

From our perspective, the neurotoxicity of general anesthetics in children still remains a potential/non-confirmed risk. Therefore, we must not "miss the forest for the tree." In clinical practice, the risk of surgical delay must be weighed against the potential, uncertain anesthetic neurotoxicity risks. Morbidity and mortality may result from the natural progression of the disease, including developmental impairment. Moreover, the human brain neurodevelopment period is extended over several years. This might make the impact of anesthetic exposure less significant than its effect on the faster-developing animal brain. In general, entirely elective surgical procedures before the age of 4 should not be conducted. It is also arguable whether the potential and still unproven risks of anesthesia effects on development have to be mentioned during the anesthesia informed consent process on the preoperative visit. Some institutions mention it as a standard procedure, whereas some physicians discuss it with parents if asked specifically [112].

Perioperative anesthesia care should promptly provide high-quality care, prevent, detect, and treat complications to minimize the risk for neurodevelopmental consequences. Regional anesthesia/analgesia should be considered whenever possible. Training in pediatric anesthesia is essential to ensure adequate anesthetic care for these patients. Further clinical and translational research is justified to understand better neurocognitive development processes and the role of anesthesia and surgical stress on the developing brain.

Conflict of Interest Nil.

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Anesthesia for Radiation Therapy in Children

42

Sachidanand Jee Bharati, Wasimul Hoda, and Brajesh Kumar Ratre

Key Points

- Radiotherapy (RT) is one of the effective treatment modalities in pediatric malignancies of the central nervous system (CNS).
- Anesthesiologists play a vital role in the provision of radiotherapy, which is directly linked to the successful treatment of pediatric cancers.
- Pediatric radiation therapy for intracranial malignancies begins with computed tomography-based planning and simulation, followed by definitive radiotherapy.
- Repeated RT sessions requiring anesthesia has its own complications, and anesthesiologists have to work outside their comfort zone in a remote location.
- The real challenge is to create a similar condition each time in a successive RT session by providing a motionless child with limited anesthesia resources.
- Apart from the toxicities of radiation, an anesthesiologist has to consider the psychosocial, emotional, and cognitive aspects of RT on the child and the family.

42.1 Introduction

The solid tumors of the central nervous system (CNS) are the most common cancers in the pediatric population. It accounts for about 25% of tumors seen in children [1]. Due to advancements in treatment modalities, the prognosis and 5-year survival rate have improved steadily [1]. Along with surgery and chemotherapy, radiation oncology forms the cornerstone in the treatment and outcome of CNS tumors. Radiation therapy (RT) is used for both curative as well as palliative intent. It is one of the primary management modalities for primary CNS lymphoma, glioma, and brain metastasis [2].

The procedure is usually brief, where a motionless patient is needed to be on radiotherapy bed. Mostly, the supine or, sometimes, the prone position is needed [3]. Further, the anesthesia provider needs to work outside their comfort zone of the operating room. Patient vitals need to be monitored continuously from a remote location with limited resources. Hence, it is a challenge to provide safe and effective anesthesia in pediatric patients receiving radiotherapy. An anesthesiologist must have a clear understanding of the disease, its loco-regional effects, toxicities of cancer therapy, and psychosocial vulnerabili-

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ties of the children and their families. Therefore, the anesthesiologist must formulate an appropriate anesthetic plan which is safe for a child even if used repeatedly [4].

42.2 Pediatric Neurological Tumors and Indications for Radiotherapy

Pediatric brain tumors need a multimodal approach for its comprehensive management (Table 42.1). In the majority of such tumors, neurosurgery is the treatment of choice, followed by radiotherapy. The duration of radiotherapy varies depending on the type and location of the tumor [5]. In the pediatric age group, medulloblastoma is one of the most common malignant brain tumors. In up to one-third of cases, it involves meningeal lining and spinal cord at the time of diagnosis. Such children usually receive radiation to the cranium and spine after surgery [6]. Children who are less than 3 years of age may also require chemotherapy. The primary treatment for astrocytoma and ependymoma is neurosurgery; for low-grade astrocytoma, radiotherapy may be recommended. For high grades, a combination of surgery, radiotherapy, and chemotherapy is often necessary. Radiotherapy in ependymoma is usually recommended after surgery in older children.

42.3 Technology and Types of Radiotherapy

Radiotherapy uses ionizing radiations, but the exact mechanism of action on cancer cells is still unexplored [7]. However, the breaking of nucleic double-stranded deoxyribonucleic acid (DNA) is the most important cellular effect of radiation. It leads to irreversible loss of cellular reproducibility and, eventually, cellular death. However, in clinical therapy, indirect ionizing of cells via free-radical intermediaries formed from the radiolysis of cellular water is most seen. The ionizing radiation also disrupts the normal cell cycle necessary for cell growth, cell senescence, and apoptosis [8, 9]. These changes eventually result in cell death.

The changes at the cellular level after therapeutic dose conventional multifraction radiotherapy regimen can be summarized as 4Rs of radiobiology [7]: (a) repair of sublethal damage, (b) repopulation, (c) redistribution, and (d) reoxygenation.

Table 42.1 List of pediatric neurological tumors and their treatment modalities [5]

S. no.	Type of malignancy	Relative incidence	Treatment
1.	Medulloblastoma/PNET/ pinealoblastoma	16–20%	Complete surgical resection Cranial/spinal radiotherapy (RT) and chemotherapy
2.1.	Astrocytoma (gliomas)	35–50%	Low grade: Surgical resection, radiotherapy, and chemotherapy may be given.
		10%	High grade: Radiotherapy and chemotherapy are combined with surgery.
3.	Brain stem glioma	10–20%	Surgery or radiotherapy + chemotherapy
4.	Ependymoma	8–10%	Radiotherapy after surgery
5.1.1.	Germ cell tumors	4–7%	Mature teratoma: Surgery
			Pure germinoma: Surgery + radiotherapy
			Non-germinomas: Surgical resection + chemotherapy + radiotherapy
6.	Aggressive infantile embryonal tumors (i.e., atypical teratoid rhabdoid tumor)	3%	Complete surgical resection Radiotherapy and chemotherapy
7.	Craniopharyngiomas	3%	Surgery For recurrence: Surgery + radiotherapy
8.	Acute leukemia		Chemotherapy and radiotherapy

Conventional multifraction radiotherapy enables normal tissue to recover between two fractions. This also reduces damage to normal tissues. Redistribution of proliferating cell populations from radioresistant to radiosensitive phase throughout the cell cycle increases cell damage in fractionated treatment as compared to single-session treatment. Repopulation is seen if the interval is of more than 6 h. The cells repopulate and result in an increase of surviving fraction. The hypoxic cells at the center of the tumor are resistant to radiation. These hypoxic cells get reoxygenated during the fractionated course of therapy. Now these reoxygenated cells are more radiosensitive to further radiation therapy [9].

Commonly used radiotherapy is external beam RT (EBRT) and internal RT. EBRT or teletherapy is the most frequently used form of radiotherapy in children. The patient lies on a radiotherapy bed, and an external source of radiation is projected at a particular predefined part of the body [7], whereas in internal RT, radiation sources are placed as close as possible to the tumor. Depending upon the way of radiation placement inside the body, the internal radiation therapies can be categorized as interstitial, intracavitary, intraluminal, and intravenous. Brachytherapy is placing a radioactive substance directly inside or close to the tumor [10]. It allows delivering a higher total dose of radiation to treat a smaller area and in a shorter time taking an edge over EBRT.

3-D conformal radiotherapy (3-DCRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), stereotactic radiosurgery, or Gamma Knife is other newer modalities for RT [11–14].

42.4 Preparation for Radiotherapy

When a child is planned for EBRT, he or she must undergo the process of simulation and planning, followed by radiotherapy. For immobilization, either a customized aquaplast mold or blue bag is used (Fig. 42.1a, b). Simulation, as well as RT, needs equal preparedness and monitoring (Fig. 42.2a, b).

Simulation allows the radiation oncologist to locate the exact anatomical landmark for delivery of external beam radiation, dose, position, and number of sessions. The simulation process may last from few minutes to hours depending upon the cooperation of children and the technologists who perform the simulation [15].

An anesthesiologist's backup is required for younger children, and before going through sim-

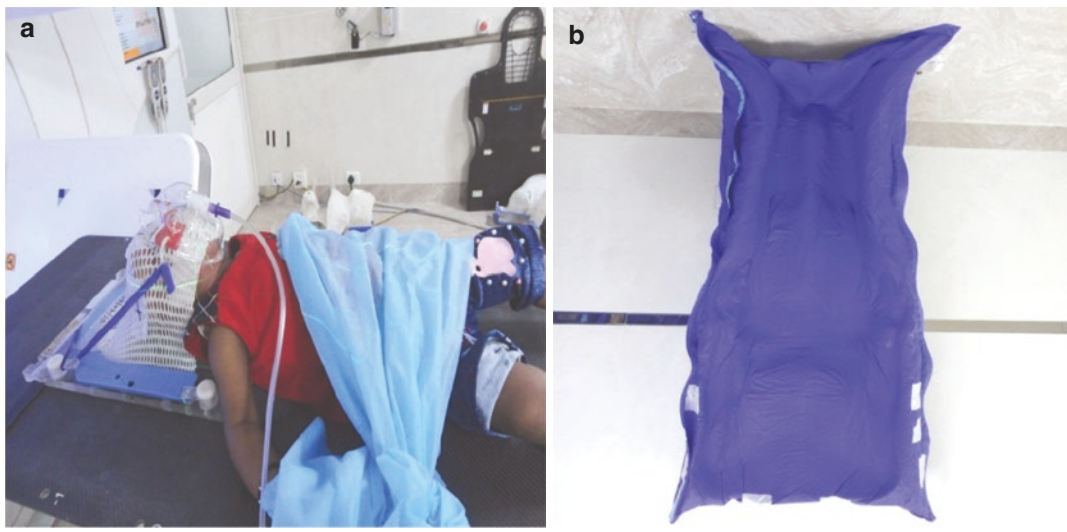

Fig. 42.1 (**a**) Child with aquaplast face mask. (**b**) Blue bag for immobilization

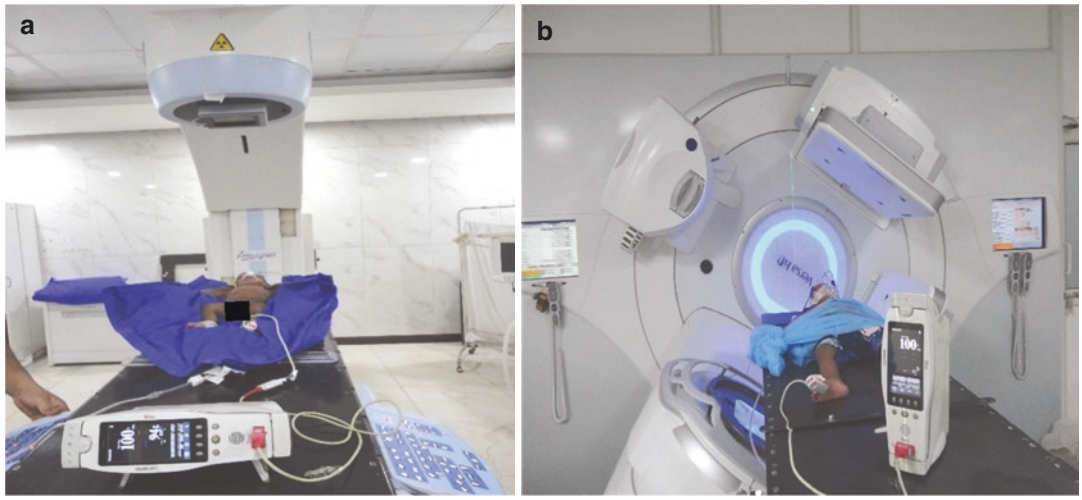

Fig. 42.2 (**a**) Child in simulation suite; (**b**) child in radiotherapy suite

ulation process, the child should undergo a detailed evaluation by the anesthesiologist. The challenges of anesthesia for RT may be related to the patient or the location as below [16].

- **Patient related:** Children presenting for radiotherapy should not be graded as ASA 1 patients. In addition to the local and systemic effects of tumor, children may receive concurrent chemotherapy. They may have associated toxicities of chemotherapy. The child may have delayed gastric emptying due to chemotherapy, opioids, stress, comorbidity, and an increased risk of aspiration. Children may have upper airway infections or other illnesses that may complicate general anesthesia. Difficult cannulation is also one of the major challenges for the anesthesiologist, especially when receiving chemotherapy.
- **Location related:** In remote site anesthesia with restricted access to the patient, especially during simulation and radiation delivery, staff and parents should leave the room, and child is monitored using video cameras and slave monitor. For providing anesthesia in a radiation suite, a complete setup should be arranged, including anesthesia workstation, emergency drug cart, difficult intubation kit, and all pediatric airway and other airway securing devices should be handy. Most of the patients who require anesthesia for simulation and radiotherapy do well with monitored anesthesia care (MAC) (Fig. 42.3). During simulation and radiotherapy, patients can be monitored from an adjacent room through radioprotective glass windows or by closed-circuit television (CCTV) cameras. Circuit hose extension can be needed to place the machine at an appropriate distance so that it cannot obstruct the lateral movement of the linear accelerator.

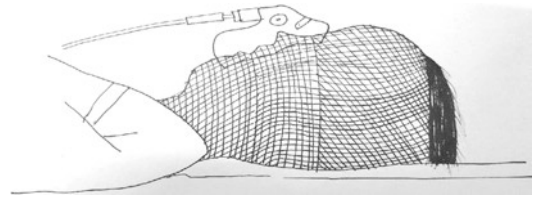

Fig. 42.3 Anesthesia for simulation and radiation therapy with molded face mask under monitored anesthesia care (MAC)

42.5 Role of Anesthesiologist

The radiotherapy in children becomes challenging to anesthesiologists as they have to work in remote locations as any other nonoperating room

anesthesia (NORA) procedure. The radiation treatment involves initial planning and sessions of multiple EBRT. The planning is called as simulation, where the radiation oncologist marks the exact anatomical location to be included in the radiation field. A child needs anesthesia during both procedures. Therefore, an anesthesiologist needs to have adequate preparation in the procedure room, preprocedural clinical assessment, following fasting guidelines, and planning for the right sedation plan [17].

The important responsibilities of an anesthesiologist during simulation and ERBT sessions can be the selection of an ideal "sedation plan" with goals such as reducing apprehension, fear, and anxiety in child and parent, obtaining child cooperation, immobilization on the couch while on therapy, adequate amnesia, reducing discomfort and having adequate analgesia, and preventing fall and ensuring child safety. Adequate preparation and arrangement of necessary equipment and lifesaving drugs with a recommended checklist with the acronym of SOAPME (suction, oxygen, airway, pharmacy, monitors, equipment) should be ensured in case of an emergency (Table 42.2) [18]. The preparation should be as such that the child could easily undergo general endotracheal anesthesia at the procedure room in case of an emergency. It is always prudent to check all the equipment before each sedation procedure.

Table 42.2 SOAPME checklist

S (suction)	Appropriate size catheters and functioning suction apparatus
O (oxygen)	Adequate supply with functioning flowmeters
A (airway)	Appropriate size airway devices such as nasopharyngeal and oropharyngeal, laryngoscopes (both Miller and Macintosh), endotracheal tubes, supraglottic airway, face mask, and resuscitation bag
P (pharmacy)	Basic drugs for life support and resuscitation, hypnotics-sedatives, and their antagonists
M (monitors)	Standard monitors for SpO_2, HR, end-tidal CO_2 ($EtCO_2$), and RR
E (equipment)	Ancillary like defibrillator

The preprocedural clinical assessment of the child should include a record of medical history, physical examination, and risk assessment in special cases. The medical history should include the history of any illness related to the respiratory, cardiovascular, renal, or hepatic systems; previous sedations, anesthesia, surgeries, hospital admission, and complications if any; allergies; current medications; recent episodes of upper respiratory infection, fever, snoring, sleep apnea, or hypoventilation syndrome; and effect of tumor and side effects of previous surgery or chemotherapy. During physical examination, baseline vitals such as heart rate, respiratory rate, oxygen saturation (SpO_2), blood pressure (BP), body temperature, weight of child, auscultation of the chest, and airways examinations should be done. Congenital abnormalities such as tetralogy of Fallot have been associated with Wilms' tumor [19].

Proper risk assessment and management are needed in a few special cases associated with increased sedation-related adverse effects. Prior craniotomies or tumors involving the brain stem are associated with lower cranial nerve involvement. In such patients at higher risk for regurgitation and aspiration, adequate fasting must be ensured. Similarly, ketamine is contraindicated in patients with supratentorial tumors having features of increased intracranial pressure. Children undergoing radiotherapy for brain metastasis in cases of Wilms' tumor may present with a large abdominal mass which may impair normal respiration in supine position. Children with associated anterior mediastinal mass may cause respiratory distress in the supine position. Cardiovascular (acute or chronic) toxicity can be seen in children receiving anthracyclines. Rhythm and conduction disturbances are features of acute toxicity in such cases. A child with a history of bleomycin therapy can present with pulmonary toxicity. It may present as new episodes of cough and respiratory difficulty with or without respiratory failure.

American Society of Anaesthesiologists (ASA) fasting guidelines should be followed in these children with 2 h for clear liquids, 4 h for breast milk, and 6 h for formula feed and light

meal [20]. After discussing the various aspects of anesthesia with parents, informed consent should be obtained and attached to the patient's record. As the process is painful, sedation is needed in most cases. No fixed guidelines are available for monitoring during RT. Continuous monitoring is needed as the child remains inside the radiotherapy suite, and direct physical observation may not be possible. Therefore, two monitors are required in the radiotherapy suite [21–23]; one is attached to the child while the other is connected to the anesthesia machine. For real-time monitoring, a slave monitor is attached, or CCTV can be installed in the room to visualize the child fully. One camera may be focused on the monitor if the slave monitor is not available [21–23] (Fig. 42.4).

Arrangements are made so that the sounds of pulse oximetry and ECG are heard clearly outside the suite. It can be done if a mic is connected to the loudspeaker placed outside. Therefore, a child may be observed from outside while ongoing therapy. Observation of chest wall movement and plethysmograph on the monitor allows the rapid detection of sedation-related adverse effects [22–25]. Vital signs should be recorded before and after the procedure, after every 5 mins if the procedure is prolonged in a time-based chart. Level of consciousness, HR, BP, respiratory rate, $EtCO_2$ with nasal prongs, and SpO_2 is monitored and documented [22–25]. Noninvasive BP monitoring can interfere with optimal sedation and causes pain; therefore, it should be avoided

Fig. 42.4 Child being monitored from outside the radiation suite while undergoing radiation therapy

[22–25]. Supplemental oxygen is given in all cases to delay the onset of desaturation [22–24]. The cables and tubing should be of longer length than usual to avoid disconnection during radiotherapy sessions. The bispectral index (BIS) monitoring is not commonly used as the procedure is of short duration, and studies have shown to be useful in children of more than 1 year [25].

Benzodiazepine, especially midazolam, has gained popularity for short-term sedative procedures because of its short half-life, anxiolytic, and amnestic property. Since external beam RT is a painless procedure, midazolam alone is tolerated well and does not require any narcotics. A 50–100 mg/kg intravenous dose provides adequate sedation to allow for the placement monitors and aquaplast face mask [26]. Flumazenil must be available in an emergency drug cart when benzodiazepines are used for sedation.

If the child is more agitated and midazolam is insufficient, most anesthesiologists choose propofol. When a child received a pretreatment of midazolam, a bolus of 0.5–1 mg/kg is sufficient to complete radiation therapy [27]. This dose can be used for simulation process along with maintenance dose of 7–10 mg/kg/h. Propofol is a stand-alone drug; it can be given without pretreatment of benzodiazepines [28]. The only problem with propofol is injection site pain. FDA has recently approved fospropofol, a prodrug of propofol for day-care sedation procedure. Fospropofol is converted to propofol in the liver by alkaline phosphatase. Compared to propofol, fospropofol does not cause a burning sensation during the intravenous injection, but the patient may have a tingling and burning sensation in the genitals and perianal region; it takes a longer time for peak effect and has prolonged action time. Thus, patients may have smoother hemodynamic and less respiratory depression compared to propofol. Studies suggest that a dose of 6.5 mg/kg is sufficient for the procedure, and if required, maintenance doses of 1.5–2 mg/kg are given [29].

In a study by Evans et al. [30], the researchers used both propofol and sevoflurane for radiation therapy; propofol is given for induction of anesthesia and then sevoflurane for maintenance.

When radiation therapy was completed, then sevoflurane was stopped. Patients have a shorter recovery time of 5–10 min and have no side effects.

Ketamine, an NMDA receptor antagonist, is another drug that can be used with or without benzodiazepine pretreatment. If the child is pretreated with midazolam, the incidence of post-procedure delirium is decreased. A dose of 0.5 to 1 mg/kg is sufficient for the completion of radiation therapy. Ketamine can be combined with propofol for the simulation process. Tachyphylaxis is common with a repeated dose of ketamine, but the literature suggests that the recovery time is not prolonged, and drug metabolism increases. Previously, it was hypothesized that daily use of propofol may develop tolerance, but recent literature is against this [31–33].

Newer agents like alpha-2 agonist dexmedetomidine have also been tried through intravenous and intranasal routes. Many literatures suggest that for short-term procedural sedation, dexmedetomidine is a good option [34, 35]. The major disadvantages of dexmedetomidine are the prolonged time needed for the initial loading dose of drug and side effects like bradycardia and hypotension. In one study, researchers compare nasal dexmedetomidine with nasal ketamine, and they found that the supplement requirement of propofol is reduced in the dexmedetomidine group [36]. A recent meta-analysis suggests that intranasal dexmedetomidine is a new, effective, and safe drug for day-care procedural pediatric sedation [35]. The route and dosage of various drugs used in present-day practice are listed in Table 42.3.

After sedation, a child is adequately wrapped to radiotherapy couch to prevent movement and accidental falls. If a child is awakened, starts moving, or is about to fall, the therapy is interrupted. The child is sedated again, and the target site is assured to be appropriate.

Documentation is essential to record general condition and consciousness level, the SpO_2, HR, $EtCO_2$, and RR before and after the procedure. It is also recommended to document vitals at 5 min interval if the procedure is prolonged. Drugs administered, doses, routes, and any unwanted event should be documented for future assessment and planning [21–23, 37]; any complication like nausea and vomiting or difficulty during the procedure should be managed [38]. The recovery room should be well staffed (one nurse for four patients) and equipped (with a pediatric pulse oximeter, oxygen supply, and a standby ventilator). Children post sedation should be observed

Table 42.3 Common drugs used in present-day practice for pediatric sedation

Drug	Route	Dosage	Side effects
Midazolam	Oral Intranasal Rectal Intravenous	0.5 mg/kg (max 20 mg, 30 min beforehand) 0.2 mg/kg 0.4 mg/kg 0.3–1.0 mg/kg 0.05–0.2 mg/kg (sedation), >0.5 mg/kg (deep sleep)	Headache Nausea Vomiting Cough Drowsiness Hiccups
Ketamine	Intranasal Intramuscular Intravenous	3–9 mg/kg 2–5 mg/kg 0.5–2.0 mg/kg	Nausea Vomiting Dizziness Diplopia Drowsiness Dysphoria Confusion
Dexmedetomidine	Intranasal Intravenous	1.5–3.0 μg/kg 0.5–1.0 μg/kg bolus over 10 min followed by 0.2–0.5 μg/kg infusion	Hypotension Hypertension Nausea Vomiting Dry mouth Bradycardia
Propofol	Intravenous	An initial bolus of 2.0 mg/kg and repeated boluses titrating to immobility	Injection site pain Hypotension Myoclonus

in the recovery area until they gain consciousness fully and fulfill all the criteria for discharge (Fig. 42.5) such as easily arousable with preprocedural mental status, stable cardiorespiratory status with protective reflexes and patent airway, actively moving limbs, responsible attending adult, and write clear instructions and emergency number if needed.

Adverse outcomes such as hypoxia due to airway obstruction or airway collapse, respiratory depression due to oversedation or aspiration of oral secretions, or gastric contents/vomitus are the most common reported complication; actual incidence is unknown. Undetected or untreated bradycardia secondary to hypoxia can result in cardiac arrest and even death. Multiple medications, inadequate pre-procedure assessment of risk factors, poor monitoring, medication errors, and improper care in recovery increase the risk of complication. However, most of these complications are preventable if the anesthesiologist is vigilant [15, 39].

Fig. 42.5 Playful child in mother's lap with oxygen support after recovery

42.6 Anesthesia Technique

Children under the age of 3 years do not understand the requirement of lying still for treatment, and the use of sedation or general anesthesia is often required. There is currently no guideline available to define when to give general anesthesia to children; it should depend upon the local practice of the institution. During the simulation, children who require general anesthesia or sedation can tolerate monitored anesthesia care (MAC) during EBRT because the procedure is very brief and lasts for minutes only. As defined by the ASA task force, moderate sedation is sufficient for the procedure (Table 42.4) [22].

Historically, older hypnotic and sedative drugs like chloral hydrate or paraldehyde were used for sedation in children, but these drugs have been associated with several issues like the bitter taste, unreliable and unpredictable effects, and wearing off. The child may become excessively drowsy and sedated [16]. NICE guideline recommends

Table 42.4 ASA task force definition of stages of sedation [40]

Sedation level	Response	Airway	Respiratory system	Cardiovascular system
Mild sedation	Normal	Patent	Spontaneous respiration	Normal
Moderate sedation	Response to verbal/ tactile stimulation	Patent	Spontaneous respiration	Normal
Deep sedation	Response to painful stimuli	Assistance require	Inadequate	Usually normal
General anesthesia	Loss of consciousness	Intervention requires for patency of airway.	Positive pressure ventilation may be required.	May be affected

the use of general anesthesia and some mental health professional who provides a comfortable atmosphere for the child to become calmer and more cooperative during anesthesia and radiotherapy [39]. Play area preparation has been used in many pediatric hospitals setting to facilitate the treatment [16].

For an agitated and young child, the simulation process should be done under general anesthesia or deep sedation. Securing airway supraglottic devices such as laryngeal mask airway (LMA) may be utilized, and intubation should be avoided. Muscle relaxation is generally not required for the procedure except in retinoblastoma cases where paralysis of extraocular muscle is needed [15]. After completing the simulation, the child should be shifted to the postanesthesia care unit, and RT will be planned for the next day. In most of the centers, pediatric RT is scheduled in the morning session to be done on a day-care basis. Intravenous (IV) route is preferred for drug administration as many children might have recently completed their chemotherapy or receiving concomitant chemotherapy with a cannula in situ. Children may be neutropenic due to chemotherapy and radiotherapy and are more prone to bacterial infection, so aseptic measures should be taken to place IV cannula. EMLA cream can be used to decrease the pain of needle prick. Radiotherapy is planned for 5 days in a week for 4–6 weeks; hence, it should be preferred to secure a fresh IV cannula every Monday and should be.

Airway Management During the Procedure: Preoxygenation should be done before giving drugs, and supplemental oxygen should be provided over the aquaplast mask using a face mask or nasal cannula with $EtCO_2$ attachment. Airway position can be manipulated by chin lift and jaw thrust, and it may require placement of neck or chest roll. Airway management is challenging when an immobilization device or aquaplast face mask was placed. When airway obstruction cannot be controlled by manipulation, oral airway or supraglottic device placement is required. For general anesthesia, supraglottic airway devices should be used.

42.7 Radiation-Induced Toxicity and Complications

Radiation toxicity can be divided into three subgroups [41]: (a) acute toxicities, within 6 weeks of treatment; (b) early delayed toxicities, within 4 months of irradiation, and (c) late delayed toxicities, beyond 4 months to several years later postirradiation.

42.7.1 Mechanism of Toxicity

CNS toxicity can be better understood by understanding the toxicities on the cellular level. Radiation injury to brain parenchyma includes and initiates pathological changes in neuronal and glial cells and surrounding vascular structures [41]. Four important factors that lead to the development of CNS toxicity are (1) injury to vasculatures, (2) deletions of O-2A (oligodendrocyte-2 astrocyte progenitors) and mature oligodendrocytes, (3) deletion of neural stem cells in the hippocampus, cerebellum, and cortex, and (4) altered cytokine expression [40].

42.7.2 Acute and Early Delayed Toxicities of Cranial Irradiation

Side effects manifesting within 6 weeks of completion of radiation therapy are considered to be early side effects. Due to transient demyelination, the effects are transient and self-limiting in nature [42]. Children may present with fatigue, nausea, vomiting, headache, and focal neurological deficits. These side effects were commonly encountered when patients used to receive doses greater than 2 Gy per fraction. Therefore, according to current NCCN guidelines, it is advised not to deliver conventional doses greater than 2 Gy in one fraction to avoid these acute side effects. Side effects manifesting within 4 months of radiation treatment are early delayed effects. It manifests as transient demyelination and somnolence. Early to late side

effects are usually mild and reversible and resolve spontaneously as in cases of early toxicities.

42.7.3 Fatigue

Fatigue and lethargy are the most common side effects when a child undergoes radiotherapy for CNS. Fatiguability is usually experienced around 2 weeks of radiation exposure. The child is lethargic and slow in activity with less interest in playing. The symptoms are maximum around the completion of therapy and get resolves within a few months [43, 44]. Somnolence syndrome is a severe form of fatigue associated with profound lethargy and lack of concentration. It is typically seen as early delayed toxicity approximately 5–6 weeks after RT [45].

42.7.4 Alopecia and Radiation Dermatitis

Hair loss or alopecia is also considered to be a common side effect. The hair follicles exposed during radiation are prone to fall, and alopecia is seen in that area. It may be localized, sparse, or patchy depending on scalp exposure. Repeated higher doses can cause permanent damage to hair follicles leading to permanent alopecia [46].

Radiation dermatitis is a common finding of the scalp in children undergoing RT. It is a desquamating rash, mild in nature, and is treated with moisturizing ointments. In severe rare cases of moist desquamation, topical antibiotic ointment is being useful.

42.7.5 Late Delayed Toxicities of Cranial Irradiation

Late delayed side effects are mostly irreversible and progressive in nature. Therefore, it becomes prudent when discussing the various radiation toxicities. These toxicities may manifest as late as 4 months of treatment up to decades later. The patient may present with significant cognitive deterioration [40–42]. It has a devastating impact on patients' quality of life. A decline in neurocognitive function post radiation for a brain tumor is important delayed toxicity. Etiology is a multifactorial phenomenon as other factors may have cumulative effects that contribute to cognitive decline. The relationship between radiation toxicity and cognitive decline has been well observed, studied, and documented [40–42]. The concurrent use of chemotherapy, along with radiation, can add up the cognitive deterioration. It is important to recognize toxicity caused in either combination or individually. Recent advances in imaging technology help in a more accurate assessment of radiation-induced brain injury. It may further expand our comprehensive knowledge and understanding of critical brain structures that are very sensitive to the harmful effects of ionizing radiation [40–42].

42.8 Effects of Repetitive Anesthesia and Radiotherapy on Neurologic System

Over the years, many studies in various animal models demonstrated a link between anesthetic agents and neurodegenerative changes [47–49]. Nearly all commonly used anesthetic agents, including benzodiazepines, propofol, ketamine, volatile aesthetics, and nitrous oxide, have some neurogenerative properties [50, 51]. Literature reveals that for different effects like sedation, amnesia, and analgesia, anesthetic agents act on various receptors and modulate neuronal activities [52, 53].

Anesthetic agents block normal neurotransmission in GABAergic and glutamate systems after binding with GABA and NMDA receptors, respectively, thereby causing synaptic deprivation and activation of intrinsic neuroapoptotic cascade and mitochondrial disruption [51, 52]. Decrease dendritic and spine formation also plays a role in neurodegeneration. Literature also supports that single or multiple exposures with anesthetic agents in young children less than 4 years of age have a learning problem during

childhood and adolescence [54–56]. Stratmann et al. assessed the outcome in children who received general anesthesia at age less than 1 year, and a unique recognition memory test was done between the ages of 6–11 years. The children who received general anesthesia had a significantly lower recollection score than control [57]. However, the PANDA trial, which had a superior study design (the Pediatric Anesthesia Neurodevelopment Assessment) [58], did not find any significant cognitive, behavioral, and memory function changes in children exposed to general anesthesia in comparison to control.

A meta-analysis suggests neurodevelopmental deficits, especially cognitive and behavioral, after general anesthesia and surgery. The number of exposures is more important than exposure time before 4 years of age [59]. Researchers also found that repeated exposure to ketamine negatively impacts the developing brain [60]. The US Food and Drug Administration (FDA) has advised that repeated and prolonged exposures of anesthetic and sedative drugs before the age of 3 years can potentially harm the development of children's brains. O'Leary JD et al. comprehensively reviewed five pre- and paraclinical trials [61–64] and concluded that anesthetic and sedative drugs transiently disrupt normal neural activity [65].

Dexmedetomidine is a newer sedative and hypnotic agent that gives conscious sedation; it is a highly selective αλπηα-2 adrenergic receptor agonist. Dexmedetomidine binds with the presynaptic-2 receptor at locus ceruleus to produce hypnosis and anxiolysis and binds to α-2 receptor in the spinal cord to produce analgesia [66]. US FDA approved it for procedural sedation in spontaneously ventilated adults [67]. There is no interaction of dexmedetomidine with either GABA or NMDA receptors, so it is a new drug for study related to anesthesia neurotoxicity. Many preclinical animal trials suggest that dexmedetomidine does not cause neurodegenerative changes caused by some common anesthetics like isoflurane, ketamine, and propofol, and even it ameliorates these changes caused by common agents [68–73].

Children who survive after brain irradiation exhibits decrease white matter volume as compare to other children. Imaging studies show that demyelination and necrosis radiation therapy cause neurotoxicity and neurocognitive deficits mainly by microvascular damage and decreasing white matter volume [74–76]. White matter is myelinated axons responsible for neuronal synapses. White matter myelination occurs in the first few years of life [76]. During these early years of myelination and synaptogenesis, RT causes apoptosis of neuronal and endothelial cells. Damage to these cells causes further secondary ischemic axonal and oligodendrocytic death that may be responsible for long-term neurocognitive impairment. Radiation also causes the breakdown of blood-brain barrier leading to inflammation and edema [77, 78]. Reddick et al. in a multicentric prospective study of 383 childhood brain tumor survivors found a strong correlation between cerebral irradiation and decrease in white matter mass and decline in neurocognitive function, and it is a progression with time [79]. Fractional anisotropy is a quantitative index assessed in diffuse tensor imaging that reflects axonal degeneration or decrease myelination. Fractional anisotropy is decreased in patients with cancer survivors who receive cranial irradiation [80].

The hippocampus is also an important site in CNS, where neurogenesis occurs throughout life. It involves memory formation and consolidation and is the most radiosensitive zone with associated neurocognitive changes. Damage or structural changes in the hippocampus area, like decreased volume after irradiation, are strongly associated with poor IQ, decreased learning, and retaining ability [77–79].

Liu et al. reported that children who survive after cranial irradiation after medulloblastoma have a significant thinner cerebral cortex than controls [81]. This will also suggest the correlation between cranial irradiation, gray matter volume, and neurocognitive changes. Some researchers also reported that cranial irradiation causes frontoparietal cortical changes associated with impaired memory [82].

42.9 Special Concerns: Pain, Psychological Impact on Child and Parents

As the child has to undergo invasive and painful procedures (surgery, chemotherapy, and radiation therapy), childhood cancer negatively impacts the child and their family. Even though the radiotherapy is painless, children may experience psychological distress. They are scared of new hospital members, unfamiliar hospital surroundings, equipment, and procedure. Separation from parents brings anxiety, making a child uncomfortable [83, 84]; children with brain tumors undergoing radiotherapy experience boredom. A school-going child misses his classroom activities and their close friends.

Multiple sessions of radiotherapy bring stress for the child and the whole family. Family experience physical, psychological, emotional, and social struggles. The overall situation is described as unstable, where the family's prime focus is toward protecting their child during the various therapies.

The parents are concerned about the side effects and its outcome in terms of child survival, physical and mental health, and future neurocognitive functions. Family is disrupted as they have to stay for a long period of time in the hospital. Multiple sessions, repeated IV cannulations, and pre-procedure fasting make the situation overwhelming, bringing enormous emotional instability in parents. After the end of treatment, they experience challenges as child life is no more the same. The child has to make various adjustments called "new normal." Even after the treatment, family has to deal with their emotional scars and fears related to the cancer recurrence. It indicates the utmost need for psychological support among parents of children undergoing radiotherapy. A psychoeducational intervention both for the child and parent is found to be beneficial. It includes a play program and interactive support to get familiar with the hospital staff members; equipment, surroundings, and radiotherapy procedures are found to be useful [85]. It helps in reducing pediatric distress, parental anxiety, and apprehensions. Play therapy sessions combined with audiovisual aids, for example, cartoons for younger children of less than 7 years before the start of treatment with EBRT, have been reported to be beneficial [80, 86, 87]. Distraction techniques have also been found to be effective and are found to decrease the need for sedation.

42.10 Conclusion

Pediatric radiotherapy needs an interdisciplinary approach for safe and effective execution. In pediatric malignancies, radiotherapy has a curative role apart from palliation. The success of radiotherapy depends on the accuracy of radiotherapy in terms of dose and site where it has to be given. The critical steps in pediatric radiotherapy are planning and simulation, successive radiotherapy without interruptions, and uncomplicated recovery after each radiotherapy session. Anesthesia is required at each step as during each radiotherapy session, the exactness of dose and site should be maintained. Anesthesiologist plays a vital role in completing radiotherapy, which is directly linked to the cure for pediatric cancer. The real challenge for anesthesiologist is to create a similar condition at each time in successive radiotherapy sessions by providing a motionless child with limited anesthesia resources.

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43 Neurological Perspectives in Pediatric Cardiac Surgery

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Key Points

- Various neurological manifestations may complicate cardiac surgery in pediatric patients in the perioperative period, ranging from subtle symptoms to long-term neurological impairments.
- Children with congenital heart disease (CHD) have a greater incidence of associated congenital malformations of the central nervous system (CNS).
- Improved perioperative neuromonitoring using electroencephalography (EEG), near-infrared spectroscopy (NIRS), transcranial Doppler TCD), and evoked potentials may help to improve surgical outcomes in these children.
- Few children may be complicated with intracranial bleed due to frequent anticoagulation and may require urgent neurosurgical intervention.
- Management of such children requires careful anesthetic planning and meticulous management strategies to avoid secondary brain ischemia culminating in further neurological complications.

43.1 Introduction

Brain injury remains a major source of morbidity associated with congenital heart surgery. In pediatric patients, neurological injury after cardiac surgery may manifest as stroke, postoperative cognitive dysfunction, delirium, or more subtle signs leading to a long-term sequel and neurodevelopmental impairments [1]. These complications may eventually compromise the quality of life and even lead to increased mortality [2]. Hence, advanced neurological monitoring during pediatric cardiac surgery may help in improving outcomes in these patients. A subset of postoperative patients may require urgent neurosurgical interventions and need optimization before emergency surgery to prevent disastrous results.

43.2 Pediatric Cardiac Surgery and Neurologic Involvement

Congenital heart disease (CHD) is considered the most common birth defect globally. Approximately 25% of children born with CHD require intensive surgical intervention within the first year of life. Children with CHD also have a higher incidence of associated congenital malformation of the cen-

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Table 43.1 Important pediatric cardiac pathologies associated with neurological sequel

- Endocardial cushion defects, ventricular septal defect (Down's syndrome)
- Patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrial septal defect (ASD) (trisomies 13 and 18)
- DiGeorge and velocardiofacial syndromes (CATCH 22)
- Interrupted aortic arch (type B)
- Truncus arteriosus
- Tetralogy of Fallot (TOF)
- Hypoplastic left heart syndrome
- Transposition of great arteries

tral nervous system (CNS). Literature suggests a greater prevalence of neurological abnormalities before cardiac surgery in infants; some studies mentioned it even more than 50% [2, 3]. These abnormalities include microcephaly, behavioral dysregulation, feeding difficulties, and hypotonia, accompanied by abnormal electrophysiologic studies [4]. Any child with a severe CHD is at risk of neurological injury with altered blood flow characteristics and metabolic demands. Table 43.1 listed a few important cardiac pathologies where children undergoing surgeries for these lesions are more prone to develop neurological complications. It is generally agreed that children undergoing relatively complicated surgeries are more predisposed to develop postoperative neurological complications. Also, there are specific patient populations at higher risk of neurologic dysfunction. Congenital and acquired lesions in the brain are relatively common preoperatively in the hypoplastic left heart syndrome [4, 5]. Periventricular leukomalacia (PVL) is also commonly noted in term infants with CHD [6]. Also, pediatric cardiac surgery is said to contribute to the development of PVL, and hence, better intraoperative management in these patients would contribute to acceptable outcomes [7]. Children who recently had congenital heart surgery may appear normal at the outset; however, their neurodevelopmental outcomes may not be normal. Long-term and even short-term patient survival with complex CHD has improved significantly over the past several decades [8, 9]. This led to a paradigm shift from mortality reduction to morbidity prevention.

43.3 Neurodevelopmental Abnormalities After Cardiac Surgery

Approximately 40–70% of children who survive post-cardiac surgery experience cognitive, motor, neurodevelopmental, psychological, emotional, and behavioral difficulties during childhood and adolescence, as confirmed by the Boston Circulatory Arrest Study [10–13]. The abnormalities include mild impairment in cognition, reduced academic performance in learning, and impairments in social cognition and core communication skills (e.g., the higher incidence is seen in autism). There may be neuropsychological issues in visual construction, working memory, and executive functioning and perception. Behavioral difficulties such as inattention, increased aggressive nature, and delayed fine and gross motor skill development may also be observed.

43.4 Mechanisms of Neurological Injury After Cardiac Surgery

Neurological injuries during cardiac surgical procedures are mainly due to perioperative hypoxic-ischemic or reperfusion injury because laminar cortical necrosis and periventricular white matter lesions are commonly seen at autopsy [14]. Hypoxic-ischemic injury is the result of a mismatch between the energy requirement and availability in the brain. The studies on neuropathological aspects of infants after cardiac surgery in deep hypothermia highlight that white matter lesions in the cerebral cortex appear to be more severe and more prevalent than cortical gray matter lesions [15]. Any change in perfusion and metabolism of cerebral tissue during heart surgery is extreme, complex, and often interrelated. When these changes are more than the brain's capacity to maintain a supply-demand balance of oxygen, a hypoxic-ischemic/reperfusion insult gets triggered. Certain factors which determine oxygen availability in the brain during the intraoperative period may be divided as:

- Extrinsic (those of which are associated with the extracorporeal circulation, e.g., pulsatility loss, no pump flow or low-flow states, hypothermia, and embolism).
- Intrinsic (such as autoregulation derangement of cerebral blood flow).

During surgeries involving circulatory arrest with deep hypothermia, oxygen delivery to the brain may also be deranged by multifocal vaso-occlusive phenomena created by the bypass circuit or global hypoperfusion due to the excessive attenuation of the flow rate of the bypass circuit [16]. Cardiopulmonary bypass (CPB) is employed in many pediatric cardiac surgeries and increases the risk of brain injury. Particularly vulnerable to ischemic insult are the basal ganglia during CPB [15]. Cerebral autoregulation is to be maintained during the bypass period, which is crucial in preventing brain injury during cardiac surgery as pediatric autoregulatory limits are not clearly known.

Various biomarkers have been investigated for their role in detecting the severity of neurological injury in pediatric patients undergoing cardiac surgery [16]. Neuron-specific enolase, a dimeric isoenzyme of the glycolytic enzyme enolase, is found in the neuronal cytoplasm. The S100 protein is a dimeric acidic and calcium-binding protein and has also been used as a biomarker of neurological injury. Glial fibrillary acidic protein (GFAP) is a cytoskeletal protein found in the CNS astroglia. However, the use of these biomarkers remains uncommon, and there is not much evidence supporting their role and usefulness [16].

43.4.1 Focal or Multifocal Hypoxic-Ischemic Injury

Pediatric patients have smaller absolute blood volume, and hence, there are greater chances of embolic and inflammatory disturbances occurring while priming the CPB circuit. The bubble oxygenators replaced with membrane devices have reduced but not completely removed the embolic "load" of bypass circuits. Both particulate and gaseous emboli may enter into the bypass circuit directly from the surgical field. The circulating emboli bypass the normal pulmonary filtration bed and enter the systemic circulation and thence cerebral arterial circulation due to the circuit delivering oxygenated blood to the aorta directly. Also, inflammatory cascades get activated during CPB, which leads to a diffuse injury to the cardiovascular system that results in a postperfusion syndrome associated with multi-organ failure in severe cases. Multiple pathways get triggered, including those involving complement, eicosanoids, and kallikrein. They activate the generation of free radicals, cause depletion of antioxidants, and upregulation of adhesion molecules on endothelial cells and neutrophils. These highly activated neutrophils prove to be the potent mediators of reperfusion injury to the brain. Although hypothermia tends to delay and modify the effect of such processes, however, it does not eliminate them.

43.4.2 Global Hypoxic-Ischemic Injury

Deep hypothermia is the most accepted way of suppressing the consumption of oxygen during surgery. During deep hypothermic cardiac arrest (DHCA), the blood supply to the brain is impaired. The oxygen availability to the brain may be limited by hypothermia-induced increase in cerebral vascular resistance, impairment of pressure-flow autoregulation in the brain, and increased affinity of oxygen with hemoglobin. During periods of decreased perfusion pressure, the normal response involving oxygen delivery to the brain is maintained initially by vasodilatory response followed by an increase in oxygen extraction. However, they are compromised during hypothermia. The duration of DHCA, which is safe for a particular patient, cannot be assessed. It has been proved that prolonged uninterrupted DHCA may have poor neurologic effects, and brief periods of

DHCA have not been associated consistently with adverse outcomes [17]. Available literature suggests that the relationship between DHCA duration and the neurodevelopmental sequel is not linear, with the brain injury risk increasing significantly after 40 min or so [17, 18].

43.4.3 Pulsatile vs. Nonpulsatile Flow

Most institutes in the United States use nonpulsatile bypass devices and hemodilution to reduce the magnitude of red blood cell trauma. Apart from its advantages, all these techniques, including deep hypothermia, have serious adverse effects on cerebral oxygen delivery. During CPB, the nonpulsatile perfusion, most often at low-flow rates, may fail to maintain adequate perfusion in the distal capillary beds and may lead to deranged autoregulation.

43.4.4 Regional Cerebral Perfusion (RCP) vs. Deep Hypothermic Circulatory Arrest (DHCA)

When a surgical field free from blood is required, particularly during aortic arch reconstruction, the target of cerebral blood flow (CBF) maintenance with traditional CPB is impossible. Most of the protocols involve either selective cerebral perfusion (SCP) or deep hypothermic circulatory arrest (DHCA) for these scenarios. The perfusion strategy that provides cerebral blood flow while providing a bloodless surgical field for aortic arch reconstruction is RCP. Andropoulos et al. demonstrated better 1-year neurodevelopmental outcomes for aortic arch reconstruction surgeries using RCP compared to DHCA [19]. It is important to keep the duration of DHCA to a minimum. RCP is almost always used in combination with DHCA and is often used in infants and children. The only exception to this is in neonates, where RCP may be difficult to establish.

43.4.5 CPB-Related Inflammatory Response

During CPB, various factors such as nonphysiological perfusion, local oxygen supply, and insufficient blood supply can lead to the release of many pro-inflammatory cytokines like IL-6, TNF-α, and S-100β from lymphocytes resulting in systemic inflammation, which causes greater damage to the brain. Despite improved CPB circuits, these inflammatory cytokines are generated due to foreign body contact activation, endothelial damage, and surgical trauma stimulation leading to noninfectious systemic inflammatory response syndrome.

43.4.6 pH Stat vs. Alpha Stat

These are two acid-based management protocols used during CPB. In the alpha-stat strategy, the pH and $PaCO_2$ of the arterial blood are measured at 37 °C and maintained at 7.40 and 40 mmHg, respectively, regardless of the patient's actual temperature. In pH-stat management, the in vivo pH of the arterial blood is maintained at 7.40 by adjusting the $PaCO_2$ to 40 mmHg at the actual hypothermic temperature. The arterial blood gases are always assessed at 37 °C; however, pH values are corrected for patients' actual body temperature in pH stat while it is assumed the same for any actual body temperature in alpha stat. It has important implications for blood gas management as CO_2 has to be added for pH-stat corrections, which increases CBF by vasodilation. This improves oxygenation on the one hand; however, it may lead to an embolic load to the brain. Unlike in adults, where alpha stat is suggested to lead to a better neurological outcome, the pH-stat strategy has resulted in better neurological outcomes in children [20, 21].

43.4.7 Hematocrit and Transfusion Management

Anemia is deleterious for patients undergoing cardiac surgery [22]. Severe anemia affects oxy-

gen supply to the brain and must be corrected. At the same time, blood transfusions may also exert an undesirable effect on the outcome of these patients. The transfusion target in cardiac surgery is a hematocrit value of 20–24% or less [23]. However, the target is usually higher, up to 30%, especially in neonates and infants when DHCA is planned as it acts as an oxygen reserve during DHCA.

43.5 Neurological Monitoring During Pediatric Cardiac Surgery

- **Near-Infrared Spectroscopy (NIRS)**

  This device enables real-time measurement of cerebral oxygenation. Many devices working on the principle of NIRS are available in the market, but the working principle of all devices remains the same, i.e., optical spectrophotometry. An absolute decrease in NIRS values less than 50 or a drop of more than 20% from baseline becomes significant and needs corrective interventions [24]. The advantages of NIRS as a monitoring device include its noninvasiveness, ability to continuously monitor cerebral oxygenation, and being nonoperator dependent. NIRS has been widely utilized during pediatric cardiac procedures. Hoffman et al. explored the neurodevelopmental outcomes in children with CHD. They observed various associations with several procedures, feeding status, hospitalization duration, oxygen saturation, and somatic and cerebral oximetry [24]. They observed that higher arterial oxygen saturation and narrower arterial-cerebral NIRS differences were attributed to better or improved motor performance. In contrast, the total duration of surgical procedures, ECMO, and birth weight were not the risk factors associated with worse outcomes. The use of bilateral NIRS has been documented to detect aortic cannula malposition during pediatric congenital heart surgery [25]. The decrease in the saturation on one side compared to the other led to the detection of reduced blood flow due to aortic cannula malposition, and timely correction led to the prevention of major catastrophe.
- **Transcranial Doppler (TCD)**

  Also known as the "stethoscope of the brain," TCD is based on the Doppler principle. TCD technology provides the clinicians with a real-time CBF evaluation. By insonating the middle, anterior, and posterior cerebral arteries, the flow velocities in these vessels can be determined, which shows a good correlation with the CBF [26]. TCD can be very useful during periods of deep hypothermic cardiac arrest (DHCA) as well as during rewarming to ensure appropriate cerebral perfusion [27]. In addition, TCD can detect presence of emboli, which appear as high-intensity transient signals (HITS) [28].

  The use of TCD also with other treatment modalities has been shown to reduce worse postoperative neurological outcomes [28]. However, there are pitfalls in TCD use as a monitoring device during pediatric cardiac surgeries as it is technically challenging to measure a specific artery of the brain when pulsatile perfusion is lost during CPB, and it measures only regional cerebral blood flow as it cannot measure CBF volume if cerebral vascular resistance and perfusion pressure are changing.
- **EEG**

  Perioperative EEG can be used to diagnose intraoperative seizures in pediatric patients undergoing cardiac procedures. Intraoperative seizures in these patients are quite common though the effect of perioperative seizures on overall outcome has been debated [29]. Also, EEG monitoring identifies burst suppression or electric silence during cooling. A problem with unprocessed EEG is difficulty in the interpretation of signals. Processed EEG and EEG-based depth of anesthesia monitors like BIS, entropy, and cerebral state index (CSI) monitor allows ease in interpretation [30].

  BIS uses the algorithm-based analysis of multiple EEG parameters and integrates them into a single, dimensionless number. It is quite reliable in infants and young children and has been used quite often worldwide. During car-

diac surgery, BIS monitoring has been reported to detect brain ischemia in real time. The BIS monitoring has been used to identify burst suppression or electric silence to help determine when the brain is adequately cooled, and cerebral metabolism is sufficiently slowed before initiating DHCA [30].

The CSI is a portable handheld device that captures EEG from electrodes on the forehead and the mastoid. A complex algorithm is then used to calculate CSI, using a fuzzy logic combination of four sub-parameters of EEG signal represented as a dimensionless number between 0 and 100. It requires a larger area for sensor placement on the front of the forehead compared to BIS. It is less useful than other EEG-based monitors, and presently, there is a paucity of literature and thus difficult to recommend any of the EEG-based monitoring for routine use in infants and children who are undergoing CPB.

- **Evoked Potential Monitoring**

  Evoked potential monitoring is more common in adult patients. In pediatric patients, incomplete maturation of conduction pathways in the nervous system makes these less useful. Somatosensory-evoked potentials (SSEPs) have been used in children more than 2 years of age [29].

43.6 Neurological Abnormalities Before Cardiac Surgery

There is a high prevalence of neurological abnormalities to the tune of 50% before cardiac surgeries. These can be categorized into preoperative neurologic disorders of fetal onset, including cerebral dysgenesis and chromosomal disorders and neurological injury of postnatal onset. The risk of cerebral dysgenesis is associated with specific cardiac lesions like hypoplastic left heart syndrome, where the brain may be abnormally developed like agenesis of the corpus callosum, microdysgenesis, holoprosencephaly, and immature cortical mantle. These may present clinically as seizures, altered consciousness, and abnormal motor tone in infants. Later presentations include developmental delay, epilepsy, and cerebral palsy. Certain chromosomal disorders like trisomies 11, 18, and 21 include both cardiac and neurological malformations. Trisomy 21 (Down's syndrome) presents as cognitive impairment, epilepsy, narrow superior temporal gyrus, and disproportionately small cerebellum and brain stem. Associated heart defects include endocardial cushion defects, VSD, and PDA. Chromosomal 22q11 defects present as cardiac defects, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia. The two most common, DiGeorge and velocardiofacial syndrome, have neurological and cognitive manifestations associated with structural cardiac defects. There is an abnormal development of the third and fourth pharyngeal pouches manifesting as conotruncal cardiac malformations, including interrupted aortic arch (type B), truncus arteriosus, and tetralogy of Fallot. Microcephaly and hypocalcemic seizures occur very often in these children. A high rate of autism and attention deficit hyperkinetic disorder has also been reported in such children [31].

43.7 Neurological Complications After Pediatric Cardiac Surgery

- **Delayed Recovery**

  Prolonged impairment of mentation after cardiac surgery and anesthesia is of prime concern. A thorough neurological evaluation should follow the usual approach for assessment of any impaired consciousness patient. Common etiologies which need to be excluded are hypothermia and postoperative hepatic or renal impairment, which directly alters mentation or does so in the setting of altered metabolism or excretion of anesthetic drugs. Prolonged action of neuromuscular blockers in the postoperative phase delays the recovery of motor function and, if severe, may mimic impaired consciousness, which may be excluded at the bedside with a peripheral nerve stimulator. Fast-tracking anesthetic regimens including low-dose fentanyl and ketamine have been attempted to prevent delayed

recovery and facilitate early discharge after pediatric cardiac surgery [32].

Postoperative seizures are prevalent after cardiac surgery, and a prolonged postictal state should be thought of early in the evaluation of a depressed mental status [33]. A definitive cause is usually not established early in most cases, and many of these children demonstrate hypoxic-ischemic/reperfusion injury.

- **Postoperative Seizures**

  Postoperative seizures occur in up to 50% of neonates who have undergone open-heart surgery. Clinically evident seizures have been reported in 5–20% of neonates during the postoperative period [33]. Some seizures have a definitive cause, such as hypocalcemia, hypoglycemia, and cerebral dysgenesis. They may also result from hypoxic-ischemic or reperfusion injury due to generalized brain hypoperfusion (e.g., cardiac arrest) or focal vaso-occlusive insults in the brain. The exact etiology remains unknown in most cases but is likely to be due to many factors with risk associations that include younger onset at surgery, the use and duration of DHCA, the type of heart defect (e.g., aortic arch obstruction), and genetic susceptibility [34].

  Post-pump seizures are different in several aspects from other post-hypoxic seizure subtypes. They typically develop later than those occurring after perinatal asphyxia. Children with post-pump seizures may have a better prognosis than that of asphyxia-related seizures, where up to 50% of survivors are permanently disabled neurologically [35]. Subclinical postoperative seizures (without any clinical correlate) are said to be very common after neonatal surgery, and continuous EEG monitoring is recommended for them [35]. The treatment of seizures should first involve excluding reversible causes such as glucose and electrolyte imbalances. Repetitive seizures and status epilepticus should be treated effectively by the rapid achievement of therapeutic anticonvulsant levels through IV antiepileptic drugs.

  Most of the post-pump seizures are treated by lorazepam, which is followed by phenytoin or phenobarbital. Potential signs and symptoms of cardiac toxicity because these agents in children recovering from cardiac surgery should be carefully monitored, particularly when treatment is initiated. The short range of susceptibility to post-pump seizures allows early withdrawal of anticonvulsants in most cases.

- **Periventricular White Matter Injury**

  Periventricular white matter injury is believed to occur perioperatively and is transient in most cases; the onset of these lesions is unclear. The risk factors include prolonged duration of exposure to CPB with or without DHCA, inflammatory mediators activated by CPB, early diastolic hypotension, and hypoxemia. The prolonged duration of CPB predisposes to the development of periventricular white matter injury [36]. MR spectroscopy may reveal decreased N-acetyl-aspartate and, of late, abnormalities in the postoperative oxidative mechanisms in the brain as observed in lactate-to-choline ratios [36]. Clinically, it may manifest as seizures, lower brain maturation score, neurodevelopmental delay, and long-term cognitive dysfunction.

- **Stroke**

  The incidence of stroke after cardiac surgery in children ranges from 2.5 to 8 per 100,000 population [37]. There are several mechanisms involved in stroke associated with heart disease, which include [1] cardioembolic (cardiac source of emboli); [2] paradoxical, i.e., cardiac anatomy that permits an embolus of systemic venous origin access to the cerebral circulation; or [3] venous, e.g., cerebral vein thrombosis due to central venous hypotension and stasis of venous blood. The risk factors for the stroke of cardiogenic origin include stasis, altered vascular endothelium, and hypercoagulability along with the presence of paradoxical embolic pathways.

  CPB leads to an increased risk of cerebral vascular occlusion since particulate or gaseous matter generated during bypass avoids any sort of filtration by the pulmonary circulation and gains direct access to the systemic arterial circulation.

In the postoperative period, factors that make the stroke more vulnerable include stasis of blood (intracardiac or extracardiac), altered vascular endothelial surfaces (native or prosthetic), and, in some cases, a procoagulant shift in humoral clotting systems [38]. Intracardiac stasis results from global ventricular dysfunction or low-flow stasis. A transient or prolonged increase in central venous pressures leads to local thrombosis in the right atrium and large veins. Any prosthetic material in such areas of low flow increases the chance of thrombus formation, and the presence of a native or iatrogenic right-to-left shunt can lead to paradoxical embolization. Increased right atrial pressures transmitted to the venous circulation of the brain also make it more susceptible to venous thrombosis, particularly in the dural venous sinuses. Increased systemic venous pressures lead to protein-losing enteropathy, liver function impairment, and pleural effusions, which lead to disturbance in the humoral coagulant systems [38].

In infants, stroke often leads to focal seizures or altered mentation, with focal motor deficits being subtle. In the later infancy or early childhood, stroke usually presents as acute focal motor deficits, visual dysfunction, or language disturbances. Important decisions like secondary stroke prophylaxis with anticoagulants should be administered to balance the risk of repeated embolization to the brain and secondary hemorrhage into an area of already established cerebral infarct. The recurrent risks of cardioembolic stroke are presently unknown in children.

- **Spinal Cord Injury**

  It is a rare complication following pediatric cardiac surgery and usually occurs after repairing aortic coarctation (0.4–1.5%) [39]. Spinal cord injury in the intraoperative period is mediated by hypoxia and ischemic/reperfusion injury due to the involvement of watershed territories, especially in the lower thoracic cord, where transverse infarction may lead to postoperative paraplegia. One more watershed zone lies between the anterior and posterior spinal circulation territories, and perioperative hypoxia in this zone culminates in anterior spinal involvement predominantly.

- **Brachial Plexus and Peripheral Nerve Injury**

  Prolonged immobility, arm abduction, and abnormal positioning predispose to brachial plexus injury [40]. Excessive abduction intraoperatively can also lead to peripheral nerve injuries. Postoperatively, bilateral foot drop has been documented in a child who had undergone corrective surgery for double outlet right ventricle (DORV) and associated transposition of great arteries [41]. Most of the cases are transient and tend to improve with time.

  Brachial plexus injuries are also quite common after cardiac catheterization [40]. Symptoms often resolve completely and gradually on their own. The insertion of central venous catheters via internal jugular vein during a cardiac catheterization may lead to upper brachial plexus injury by direct physical trauma or due to extravasation of blood into the plexus.

  Phrenic nerve injury can occur due to hypothermia due to ice packs around the heart or direct intraoperative transection. Malposition of chest tubes may also lead to such types of injuries [42]. The diagnosis can be confirmed by electromyography (EMG) and nerve conduction studies (NCS). Most of the injuries to the phrenic nerve resolve spontaneously on their own. Sometimes, diaphragmatic plication (more likely in infants than children) or, in rare instances, diaphragmatic pacing is required.

- **Behavioral Problems**

  These children are predisposed to develop behavioral problems in the form of irritability and organic mental changes [43]. Delirium and dementia after adult cardiac surgery has been a topic of research; however, it received less attention in the pediatric population. It has been suggested that the incidence of delirium after cardiac bypass surgery is 49%, and delirium is an independent predictor of prolonged ICU length of stay [44]. Delirium occurs within the first 1–3 days after cardiac

Table 43.2 Long-term neurological sequel

• Mental retardation
• Cerebral palsy
• Seizure disorder
• Motor deficits and paraplegia
• Learning disorders and behavioral abnormalities
• Communication difficulties related to language and speech
• Communicating hydrocephalus

surgery and usually lasts for short periods of time. In a multivariate pediatric model, the development of postoperative delirium has been observed to be associated with an age less than 2 years, developmental delays, higher RACHS-1 (Risk Adjustment for Congenital Heart Surgery) score, cyanotic heart disease, and albumin less than 3 gm/dl.

- **Long-Term Neurological Sequelae**

  These children remain at risk of neurodevelopmental impairment in the later stages (Table 43.2) in the domains of intelligence, motor behavior, academics, speech, attention, and language [45]. The patients with higher socioeconomic status has been found to correlate with better language and speech outcomes [46].

  TOF or VSD corrections in infancy with combined low-flow bypass and circulatory arrest are linked to reduced neurodevelopmental outcomes regarding formal intelligence, motor behavior, and academic achievement [47].

43.8 Neurosurgical Procedures After Pediatric Cardiac Surgery

The use of anticoagulation in pediatric cardiac patients predisposes to the development of spontaneous intracranial bleed. There is paucity in the literature concerning the incidence of intracranial hemorrhagic complications with anticoagulation, which has been reported to be ranging from 0.6 to 1.4% per year in a few studies [48]. All intracranial bleed leads to a mass effect and raised intracranial pressure (ICP) and needs immediate neurosurgical decompression.

43.8.1 Preparation of a Pediatric Patient for Neurosurgery After Cardiac Surgery

The child's neurological status must be documented; any child with decreased consciousness and inability to maintain the airway should be intubated and put on mechanical ventilation. Those with raised ICP would be lethargic, with decreased consciousness, failure to feed, repeated vomiting, Cushing's triad, etc. Repeated vomiting predisposes to dehydration, electrolyte abnormalities, and gastric aspiration. Minimum investigations are to be advised before neurosurgery, including hemoglobin and serum electrolytes. Additional studies include electrocardiography (ECG), coagulation profile, renal and hepatic functions, as well as a recent 2D echocardiography to understand the functional status of the heart and the status of repair/prosthesis. Adequate blood must be arranged if significant blood loss is anticipated. Reversal of anticoagulation will be required, and adequate blood products, including fresh frozen plasma (FFP), cryoprecipitates, four-factor prothrombin complex concentrate (PCC), and reversal agents, may need to be arranged. Any sedative premedication is contraindicated in these children with raised ICP due to the worsening effects of hypercarbia on cerebral dynamics. Electrolyte correction must be initiated at the earliest. Children with seizures must be administered the loading dose of antiepileptics before taking them for surgery.

43.8.2 Reversal of Anticoagulation

There is no consensus guideline on the reversal of anticoagulation in this patient population. For children on warfarin treatment, vitamin K must be administered (0.5–2 mg) in three sequential doses, and four-factor PCC must be given for reversal in the dose of 50 U/kg. INR should be rechecked 30 min after the administration of PCC. FFP can be employed if PCC is not available; however, it is generally not suited as the volume required is

higher for reversing warfarin effects, especially if INR >2. Protamine is used to normalize the activated partial thromboplastin time (aPTT), for the children, heparinized earlier.

43.8.3 Measures to Reduce ICP

While preparing the patient for neurosurgery, controlling measures should be taken up to maintain ICP within normal values. Mannitol is an osmotic diuretic used in doses of 0.25–1 gm/kg to reduce brain edema. However, prolonged use of mannitol is associated with electrolyte abnormalities, renal failure, and rebound cerebral edema. Diuretics like furosemide have also been used as adjuncts to mannitol [49]. Hypertonic saline (3%) in doses of 2–4 ml/kg can also be used to manage cerebral edema (maximally tolerated osmolality up to 360 mOsm/kg). However, rapid plasma expansion, pulmonary edema, hypernatremia, and renal parameters are monitored in these children. These patients should be nursed in a 30° head-up position without any head rotation. If the child is intubated, adequate sedation to prevent irritability, coughing, and bucking on the endotracheal tube should be prevented by administering fentanyl 0.5–1 μg/kg/h and/or midazolam 0.1–0.2 mg/kg/h.

Transient hyperventilation may be employed to reduce ICP for some time before other measures take effect. However, in situations like Fontan physiology, uncorrected TOF, or DORV, hyperventilation and dehydration should not be the primary strategies to control ICP. Hyperventilation in such scenarios would lead to hemodynamic collapse and CO_2 washout in the presence of limited pulmonary blood flow and may worsen neurological outcome. It is pertinent to maintain adequate cerebral perfusion and early decompressive craniectomy to control the ICP rapidly.

43.8.4 Optimization of the Child

Target hemoglobin of 9–10 gm/dl should be aimed for before being taken up for urgent neurosurgical intervention [50]. Reversal of anticoagulation should be ensured before initiation of surgery. Any episode of hypotension or hypertension in neurologically impaired patients will affect the outcome and must be prevented. Fever increases the cerebral metabolic rate and is deleterious for these children; hence, normothermia must be ensured. Operation theater should be warmed before shifting the child to prevent the occurrence of hypothermia. Preoperative euvolemia should be maintained. Any episode of hypo- or hyperglycemia may contribute to poor outcomes in these children; hence, glucose levels of 120–180 mg/dl may be targeted. The avoidance of secondary markers of brain injury (Table 43.3) is of utmost importance for achieving a good neurological recovery.

Table 43.3 Causes of secondary brain insults

Systemic insults	Intracranial insults
Hypoxemia/hypercarbia	Raised ICP
Hypotension/hypertension	Midline shift/herniation
Hypo−/hyperosmolality	Epilepsy
Hypo−/hyperglycemia	Vasospasm
Low cardiac output	Hydrocephalus
Hyperthermia	Intracranial bleed

43.8.5 Intraoperative Management

The conduct of neurosurgery after a cardiac intervention becomes very challenging for a neuroanesthesiologist. The anesthesia goal is to avoid any further increase in ICP during induction and prevent and treat secondary brain injuries. Most commonly used induction agents (propofol 0.5–2 mg/kg and thiopental 3–5 mg/kg) reduce ICP; however, it may lead to significant hypotension in these children with already compromised conditions. Hemodynamic support such as an intra-aortic balloon pump or a high dose of inotropes may be required in some cases. A high-dose opioid induction with fentanyl 2–5 μg/kg or morphine 0.15–0.2 mg/kg achieves good hemodynamic stability. Induction agents like etomidate 0.2–0.5 mg/kg or ketamine 1–2 mg/kg may be used along with opioids or benzodiazepines (midazolam 0.15 mg/kg) to achieve a deep anesthetic plane without compromising hemodynamics. When the ventilation is controlled and

normocapnia is ensured, ketamine does not lead to a rise in ICP. The concurrent administration of opioids may control tachycardia, short-acting beta-blockers (esmolol 0.5 mg/kg), or dexmedetomidine. A non-depolarizing muscle relaxant is usually used to facilitate intubation. A large-bore IV access suitable for age must be ensured along with central venous cannulation to administer vasoactive agents if required depending on the type of surgery. Minimum monitoring includes ECG, SpO_2, noninvasive blood pressure monitoring, as well as an invasive arterial line for beat-to-beat monitoring. Children with uncorrected cardiac defects and the potential for right-to-left shunting, such as patent foramen ovale and patent ductus arteriosus, are at risk for paradoxical air embolism caused by cerebral infarction. Hence, specialized neurophysiologic and cardiac monitoring should be ensured in these children, such as transcranial Doppler, NIRS, and transesophageal echocardiography (TEE). Monitoring of the cardiac output (FloTrac), jugular venous oximetry ($SjVO_2$), and evoked potentials may also be used depending on the type and duration of surgical procedure. TIVA is preferred for the maintenance of anesthesia although low concentrations of inhalational agents can also be used. However, nitrous oxide should be avoided as it causes an increase in ICP and cerebral metabolism. Fentanyl is the most commonly used opioid for intraoperative analgesia; the sedative and respiratory depressive effects of fentanyl may be prolonged in children. Frequent glucose measurements are recommended intraoperatively to detect any inadvertent hypoglycemia or hyperglycemia. Immature renal function may lead to an inability to handle excessive fluid and solute load readily. Immature cardiorespiratory physiology associated with infants and small children makes fluid management even more challenging. Holliday-Segar formula is commonly used to calculate the maintenance fluid requirement during the intraoperative period.

The presence of pacemakers complicates anesthetic management though they are mostly placed for temporary conditions such as third-degree AV block, complete AV dissociation, and bradycardia. Magnet placement and resetting of pacemakers to asynchronous mode are done before anesthesia induction to avoid electrocautery interference. A telemetric programmer and an experienced operator should be present during surgery. Careful monitoring of the arterial pressure is essential during electrocautery as ECG monitoring is also affected by the interference [51]. Monopolar cautery should be avoided in such circumstances.

43.9 Complications During Surgery

Pediatric patients undergoing neurosurgery are at a higher risk of developing hemodynamic instability during neurosurgical procedures. This is because a higher cardiac output is diverted to the brain in children than in adults. The head of infants and children amounts to a relatively larger percentage of the body surface area and blood volume. Also, they are more prone to develop cardiac arrhythmias due to recent surgical intervention on the heart. They may already be receiving anti-arrhythmic drugs, and their interactions with anesthetic agents must be kept in mind.

Due to the use of anticoagulants, these children are more prone to bleeding [48]. Adequate reversal must be ensured, and coagulation parameters should be restored before taking up these children for neurosurgery. Perioperative point-of-care testing such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM) and Sonoclot may be used to identify coagulation abnormalities and treated accordingly by administering blood and blood products [48]. The use of tranexamic acid bolus 10 mg/kg followed by 1–2 mg/kg/h infusion may reduce the generalized oozing from the surgical field. Good hemostasis must be ensured before the dural closure to facilitate early anticoagulation in the immediate postoperative period.

Neonates and small children are especially at risk for hypothermia. Hypothermia can cause cardiac arrhythmias, increased bleeding, and surgical site infections. Hence, hypothermia should be prevented, and the child's temperature should be monitored intraoperatively.

43.10 Postoperative Management

Postoperative management should be a continuation of intraoperative maneuvers. After undergoing neurosurgery, pediatric patients should be admitted into an intensive care unit under constant monitoring of cardiac functions. Clear communication regarding history, medications, operative events, and anticipated course of the child is essential. A repeated neurological examination and a CT scan of the head are imperative to diagnose any deterioration in clinical status at the earliest. Postoperatively, short-acting sedative agents may be used on a case-to-case basis to allow a prompt neurological assessment. In addition to this, adequate respiratory and hemodynamic management are necessary. Maintenance IV fluids titrated to dynamic indices of fluid responsiveness should be continued in the postoperative period. The decision to initiate anticoagulation following surgery should be based on discussion among intensivist, neurosurgeon, and a cardiologist. Prophylactic anticoagulation may be initiated after 48–72 h of achieving adequate hemostasis; however, the therapeutic levels need to be individualized.

43.11 Conclusion

Neurological complications remain very common after cardiac surgery in pediatric patients. Adequate monitoring during the cardiac procedures helps us diagnose these problems early and prevent a permanent sequel. In children posted for neurosurgery following cardiac surgery, the reversal of anticoagulation, optimization of cardiac condition, and continued attempts to ICP reducing measures should be ensured before the proposed neurosurgery.

Conflict of Interest None.

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