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REVIEW ARTICLE

Non-traumatic pediatric intracranial hypertension: key points for different etiologies, diagnosis, and treatment

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Abstract
Intracranial hypertension can be an acute life-threatening event or slowly deteriorating condition, leading to a gradual loss of neurological function. The diagnosis should be taken in a timely fashioned process, which mandates expedite measures to save brain function and sometimes life. An optimal management strategy is selected according to the causative etiology with a core treatment paradigm that can be utilized in various etiologies. Distinct etiologies are intracranial bleeds caused by traumatic brain injury, spontaneous intracranial hemorrhage (e.g., neonatal intraventricular hemorrhage), or the rare pediatric hemorrhagic stroke. The other primary pediatric etiologies for elevated intracranial pressure are intracranial mass (e.g., brain tumor) and hydrocephalus related. Other unique etiologies in the pediatric population are related to congenital diseases, infectious diseases, metabolic or endocrine crisis, and idiopathic intracranial pressure. One of the main goals of treatment is to alleviate the growing pressure and prevent the secondary injury to brain parenchyma due to inadequate blood perfusion and eventually inadequate parenchymal oxygenation and metabolic state. Previous literature discussed essential characteristics of the treatment paradigm derived mainly from pediatric brain traumatic injuries' treatment methodology. Yet, many of these etiologies are not related to trauma; thus, the general treatment methodology must be tailored carefully for each patient. This review focuses on the different possible non-traumatic etiologies that can lead to intracranial hypertension with the relevant modification of each etiology's treatment paradigm based on the current literature.

Keywords Intracranial pressure · Conservative · Etiology · Surgery

Introduction

Intracranial hypertension (IH) is a general term for excessive pressure within the cranial vault. It usually presents with headaches, alterations in the level of consciousness, visual disturbances, and kids' developmental or cognitive delays. The etiologies for IH vary and are usually separated into two primary groups based on the etiology of the derangement—primary intracranial hypertension (also known as idiopathic intracranial hypertension or pseudotumor cerebri) and secondary intracranial hypertension (variable etiologies—trauma, hydrocephalus, infection, tumors, acute subarachnoid hemorrhage, Chiari malformation, medication-induced, etc.). Another way to categorize increased intracranial pressure is by severity and acuity. Sustained chronic intracranial hypertension usually is better tolerated and presented with chronic headaches, visual disturbances, and even developmental and cognitive delays. On the other hand, acute IH (e.g., traumatic brain injury) is not well tolerated and can lead to acute brain herniation—this was referred to by some as "brain codes", which in analogy to cardiac codes, signify extreme cases of devastating neurological episodes that mandate immediate action to save brain tissue and prevent further injury and even death [1]. Besides specific etiologies that have a component of the mass lesion (brain tumor, intracranial bleeding, etc.) with or without secondary brain edema, most of the other etiologies pathophysiological

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mechanism leads to elevated pressure as a result of the secondary brain edema. Brain edema is traditionally classified as vasogenic or cytotoxic [1, 2]. Further understanding of the pathophysiology leads to the current paradigm stating this is a continuum process, with different stages and types of edema (usually cytotoxic edema, then ionic edema, and last vasogenic edema) [3]. Cytotoxic edema is created by progressive cell swelling mainly because of the accumulation of fluids and sodium. Vasogenic edema is primarily created by the disruption of the blood–brain barrier (BBB). This leads to the extracellular accumulation of fluid in the brain parenchyma.

The management paradigm of elevated intracranial pressure is based on pediatric traumatic brain injury research and management. Early detection of increased intracranial pressure is an essential first step to implement the right therapeutic measures [4]. In many cases, imaging and clinical evaluation is enough to diagnose elevation in intracranial pressure. In some cases, as part of diagnosis and monitoring of treatment's effectiveness, direct ICP monitoring via intraparenchymal or intraventricular catheter is considered. Direct ICP measurement is considered by many the gold standard and the most reliable technique. However, although relatively low risk, it still bears the risk for intraparenchymal or ventricular hemorrhage as well as an intracranial infection [5]. This leads to the development of a variety of non-invasive diagnostic tools to measure ICP [6]. The use of direct ICP measurement for non-traumatic etiologies is highly controversial, and its use is judged based on the case and the possible benefit of invasive monitoring [7–9].

This review thoroughly describes the different etiologies, suggested diagnosis, monitoring, and treatment for non-traumatic etiologies that lead to IH in the pediatric population.

Methodology

A thorough literature review was made using PubMed. We used general keywords for elevated intracranial pressure concerning the pediatric population (e.g., pediatric elevated intracranial hypertension, pediatric elevated intracranial pressure, elevated intracranial pressure in children). After reviewing the non-traumatic etiologies, we chose the most commonly discussed etiologies in the literature and ran another literature review for each subcategory. These etiologies are described in this review based on the different papers that were reviewed for each subcategory.

Core treatment paradigm

The treatment paradigm derived mainly from trauma studies and the development of Brain Trauma Foundation Guidelines for traumatic brain injuries [10–12]. Most clinicians agree that when the suspicion for elevated ICP is present, a stepwise tier directed paradigm should be initiated, with an elevation of the head of the bed, control blood pressure and glycemic status, and initiation of hyperosmolar treatment as needed. In the pediatric population, Yildizdas et al. [13] conducted a retrospective study of 67 children with cerebral edema caused by different etiologies. In their research, the endpoint was the duration of the comatose state and mortality for patients that were treated aggressively for elevated ICP by either mannitol, hypertonic saline, or a combination of the two. They found that those treated by mannitol did worse and deduced that hypertonic saline has some advantages over mannitol. Yet, other publications failed to achieve the same results and even found mannitol benefits like treatment choice [14, 15]. In 2016, Burgess et al. published a systematic review of RCTs comparing the two modalities in TBI treatment [16]. They stated that if taking all considerations into account and not just reducing ICP, there is no superiority of any agent over the other. They concluded that choice of therapy could be decided based on safety and that in different scenarios, different agents can be used when taking the safety profile into account [16].

The paradigm for non-traumatic elevated ICP is different in several aspects, and one of them is the possible use of high dose corticosteroids, which can be very beneficial in cases of intracranial mass effect like a new brain tumor but can be even harmful to some degree when given in the case of IH as a result of brain trauma [10, 12]. If the condition continues to evolve, most agree there is a need to control ICP and cerebral perfusion pressure (CPP) by more aggressive measures like intubation, ventilation, and possible invasive ICP monitoring. The use of induced hypothermia is still highly controversial, even for the pediatric age group. Advocates mention the good response that was observed among neonates treated with hypothermia for hypoxic-ischemic insults [17, 18]. In a multicenter phase III randomized controlled trial for severe pediatric TBI comparing induced hypothermia versus maintaining normothermia, it was found that induced hypothermia did not lead to greater mortality but also did not achieve a better neurological outcome for the patients (much more patients needed intervention in the normothermia group, but it did not reach statistical significance) [19]. The latest update for the pediatric age group from the brain trauma foundation published in 2019, still describes the controversy with a Level II evidence stating there is no benefit over normothermia for improving outcome. Yet, for overall ICP reduction, there is a level III recommendation to use moderate hypothermia [12]. For the non-traumatic etiologies of pediatric IH, there is no evidence to support either way, and we advocate using extreme caution when choosing this tool. In the case where ICP is refractory, the use of paralytic agents can be discussed (although controversial) and the consideration for barbiturate-induced coma

or decompressive craniectomy. Hemispheric decompressive craniectomy is known to increase the cranial cavity volume and thus reduce intracranial pressure, increase perfusion pressure, and preserve cerebral blood flow [20]. The use of decompressive craniectomy in non-traumatic IH settings is again highly controversial, with no evidence to support its use besides some small series and case reports.

Different etiologies for non-traumatic pediatric intracranial pressure

Pediatric hypoxic brain injury usually includes injuries with devastating results, such as near-drowning or prolonged resuscitation after cardiac arrest. The management of this kind of injury usually will consist of supportive systemic treatment with some measurement for controlling brain swelling. There is a big controversy regarding intracranial pressure monitoring, mainly because it appears not to alter the outcome [21]. Another group of pathological conditions that is atraumatic and known to be related to significant brain edema or swelling is related to metabolic disorders, such as Reye's syndrome. Past literature showed the benefit of ICP monitoring for Reye's syndrome, but like near-drowning, invasive monitoring is quite controversial regarding other anoxic encephalopathies [8]. For fulminant hepatic failure, there is controversy as well, but a growing body of literature suggests the benefit of controlling the ICP even as a bridge for transplantation. The elevated ICP in high-grade liver encephalopathy is a leading cause of mortality, and aggressive measures to control it have shown benefit [22]. In a recent review regarding different pathologies that can lead to elevated intracranial pressure, the authors describe panel recommendations for various pathologies stating the insufficient literature and evidence regarding pathologies that are not TBI related [23]. The literature focuses mainly on the major pathologies, such as TBI, stroke, sinus vein thrombosis, IIH, and infections. There is even less published data regarding the pediatric age group, and hence the treatment paradigm is deduced from the adult age group literature. The treatment paradigm in many cases will be similar, as mentioned above. Still, there is a lack of evidence in many issues regarding the different treatment aspects (e.g., invasive ICP monitoring). In this review, we will focus on the significant etiologies discussed in the literature regarding pediatric non-traumatic elevated ICP.

Brain tumors

One of the significant non-traumatic etiologies of elevated ICP among the pediatric age group is mass-like lesions, such as brain tumors. The discussion of pediatric brain tumors and their treatment paradigm is lengthy and beyond this review's scope. Most cases of elevated ICP that are related to brain tumors will be treated with debulking or resection of the tumor. In other cases, when secondary hydrocephalus cannot be relieved by tumor resection, CSF diversion will be needed.

Infections

Meningitis is an infection of the brain covering mainly the dura, arachnoid, and subarachnoid space. Encephalitis and brain abscesses are infections of the brain itself, either the grey or white matter fibers. The symptoms can vary widely from mild neurological changes with or without fever to severe neurological deterioration, septic shock, and even death. The imaging modality is usually MRI, focusing on T1 with gadolinium, T2, and FLAIR sequences.

Acute severe bacterial meningitis can develop into a severe infection across the central nervous system with devastating consequences [24–27]. The high mortality and morbidity rates are mainly due to raised intracranial pressure and herniation. Although better understanding has been achieved in recent years, the mortality rate is still very high with traditional therapies for increased ICP [28]. The treatment paradigm is derived mainly from the trauma setting or acute malignant stroke syndrome. One of the possible explanations is collateral damage, such as vascular injury (that can potentially lead to areas of cerebral ischemia and stroke), cerebritis, and the evolution of brain abscess. In some cases, vascular injury leads to small punctate hemorrhagic spots that eventually can evolve into a severe infection and even significant brain infarct [29, 30]. Encephalitis is an inflammation of the brain parenchyma that can be presented as a significant neurological deficit. It primarily involves the brain yet can involve the meninges in some cases (meningoencephalitis). The impairment of viral encephalitis can result from focal or diffuse inflammation and vascular arthropathies, including pediatric stroke [26]. Among the pediatric population, the most common form of encephalitis is infection from the Herpes simplex virus. The infectious manifestations are devastating, with more than 70% mortality rate is reported in untreated cases, and almost all the patients will not return to their neurological baseline [31, 32]. Treatment success depends mainly on early anti-viral treatment. A significant reduction in mortality (in some publications to 20%) and significantly favorable results (around half of the patients will go back to baseline) can be achieved with the administration of Acyclovir [32]. The disease-associated inflammatory process is usually focal and tends to classically affect the temporal lobe. However, in some cases, parenchymal hemorrhage and areas of necrosis can be developed within the involved area, leading to mass effect and intracranial hypertension. In severe cases, even to brain herniation [33]. The peak rise in ICP varies for the individual patient but has been described in adults around

the 12th day of illness, whereas in children, the data are still lacking [34]. Barnett et al. demonstrated in their publication that within two weeks, half of the patients died due to severe mass effects causing a devastating elevation in intracranial pressure despite treatment to alleviate the pressure [34]. Hence, a better understanding of the patient's ICP is needed in the setting of acute and severe encephalitis [35]. Another important entity of encephalomyelitis is acute disseminated encephalomyelitis (ADEM). This is an inflammatory demyelinating immune-mediated disorder that usually will erupt in childhood [36]. There is a strong association between ADEM and infectious process or after vaccine administration. It is believed that the reactive immune response of the body leads to pathologic transient autoimmune response directed at myelin or other self-antigens in the CNS [36–39]. The medical treatment of ADEM is mainly high dose corticosteroids with a good prognosis as more than 50% achieve full recovery. Still, mortality is up to 12%, and refractory elevated ICP is the cause of most cases.

In cases of encephalitis or encephalomyelitis, when elevated ICP symptoms are suspected, there is a need to consider ICP monitoring and CPP management. Yet, clear management guidelines are missing, and the benefit of ICP measurement and surgical intervention is controversial when managing severe herpes encephalitis [40]. Furthermore, the management paradigm for encephalitis is related to ICP monitoring and ICP management from the traumatic brain injury (TBI) literature, which is a different etiology. As with the other entities with elevated ICP, the treatment should progress gradually with accurate monitoring of ICP in cases where there is no reliable neurological assessment. Several groups tried to describe a decision-making mechanism to identify the children with potential elevated intracranial pressure before devastating result happen. In 2020, Kostenniemi et al. published their scale of MeningiSSS (Meningitis Swedish Survival Score) trying to predict those that will benefit from strict monitoring of their ICP [41–44]. They compared the results of their scale to different known scales and were focused at the presence of altered mental status and leukopenia and circulatory distress, and found it useful in identifying children later having to undergo invasive procedures to monitor or manage their ICP as a result of bacterial meningitis [41].

Medical management of increased ICP includes different methods for relieving intracranial pressure and preserve tissue oxygenation and blood supply [35]. Treatments, such as hyperventilation, osmotherapy, corticosteroids, barbiturate coma, and induced hypothermia, were described in previous reviews, and the overall management is similar to TBI management. *Corticosteroids* are being widely used in different neurological and neurosurgical entities to reduce cerebral edema. Their use in infectious disease is questionable because of the possible increased viral or bacterial load under steroidal treatment [45]. Most authors advocate for their use in a delayed fashion after initiation of the anti-viral/bacterial treatment [45–47]. *Hyperosmolar treatment* is very widely practiced in the setting of elevated ICP in trauma as well as for elevated ICP due to infectious derived etiologies. *Barbiturate coma* is a medical therapy that is used for lowering cerebral metabolic demand, which leads to less blood influx to the brain and hence to a reduction in the intracranial pressure [35]. This therapy should be initiated after the failure of the previous tiers or the initial case was extremely severe demanding use of early radical measures. Barbiturate coma requires continuous EEG monitoring (to achieve burst suppression) as well as hemodynamic monitoring due to significant hypotensive crisis risk. In infectious diseases, several descriptions are supporting the early use of barbiturates coma in severe cases [48, 49]. The use of hypothermia has been debated for the last decade, especially in the pediatric population. Yet, as for now although the mechanism has been postulated in few publications it cannot be advocated.

Surgical treatment in elevated ICP derived from infectious disease etiology is scarce. In the pediatric population, it is mainly anecdotal and focused on previously published case reports. Yet, it has been described in the adult population [50]. Several publications advocate the use of decompressive craniectomy leading to high GOS of 4–5. Decompressive craniectomy was shown to be a significant and effective treatment methodology in patients with significant mass effect secondary to encephalitis that failed other treatments [20, 35]. Yet, cases need to be selected carefully since although functional outcome results after decompressive craniectomy look promising, there is not enough evidence to recommend the routine use of this tool in the setting of encephalitis [35]. In case the diagnosis is of a brain abscess the treatment paradigm usually involves tissue diagnosis with or without mass reduction or complete removal of the abscess followed with broad-spectrum antibiotics that will be narrowed according to microbiology answers.

Stroke—malignant MCA, others

Pediatric ischemic stroke is a devastating disease with significant mortality and morbidity. According to different publications, the mortality rate 1 month after severe pediatric stroke is around 12%, and most of the survivors will have significant neurological deficits[51–53]. The annual incidence of pediatric stroke differentiates according to etiology, with acute ischemic and hemorrhagic stroke being the most common (1–5 for hemorrhagic stroke and 2–13/100.000 children for ischemic stroke), while cerebral venous thrombosis (CVT) is the least common as possible etiology (0.5–1.0 for every 100,000 children) [54–56]. Pediatric stroke is usually ischemic rather than hemorrhagic. The treatment in pediatric stroke derived mainly from the adult

literature but had come to the establishment of the treatment paradigm that suggests the identification of the etiology, possible acute intervention, and mainly the prevention of further progression by diminution brain metabolic demands (prevention of drop in oxygen saturation, hyperthermia, hypo- or hyperglycemia, hypo- or hypertension, seizures, infections, etc.) [57]. Large ischemic stroke can lead to a significant increase in the ICP, which might lead to brain herniation, and significant morbidity, and even mortality [51]. Decompressive hemicraniectomy (DC) was shown already in several publications to be an important and significant treatment modality to achieve immediate reduction for the rapid rise in ICP and is known to reduce mortality and improving outcomes among adult patients with malignant stroke [58]. Yet, the use of this radical tool is preserved for cases in which more conservative methods, including osmolar treatment, prevention of hyperglycemia and fever, and even barbiturate coma, failed to relieve the elevated ICP. The devastating numbers of mortality and morbidity were the driving force behind the randomized controlled trials (RCTs) DECIMAL, DESTINY, and HAMLET. These trials showed that the use of DC can significantly reduce mortality (case fatality reduction closely estimated as 50–75%) without increasing the risk for severe functional outcomes. The results were for patients under the age of 60 years and that was operated on for decompressive craniectomy within 48 h from the stroke [58, 59]. Most stroke patients will not develop the devastating elevation of ICP mandate treatment. In the special setting of large MCA (Middle cerebral artery) stroke, there is the potential of developing malignant MCA syndrome, which is a life-threatening event because of acute elevation of intracranial pressure and brain herniation secondary to the development of severe brain swelling. The incidence of malignant MCA stroke in the pediatric population is much smaller in comparison to adults (2% vs. 10%) [60]. The use of ICP monitoring is less common among these patients and the treatment decision is usually derived from clinical status and imaging [61]. Yet, in cases of more aggressive treatment like barbiturate come, ICP measurement might become significant for decision-making to anticipate the need for DC. The American Heart Association guideline for the early management of adults with ischemic stroke recommends DC as a lifesaving measurement in cases of severe malignant stroke. As mentioned above, DC in the right cases within 48 h will decrease mortality and can assist in preventing further neurological deterioration [58, 62–65]. The use of DC in pediatric ischemic stroke has become more common in recent years with acknowledgment of its benefits for the adult population. There is no clear evidence regarding when DC should be done in case malignant stroke develops. Delay in utilizing DC can lead to a worse prognosis and in some cases to hemorrhagic conversion [66]. When considering all recent data, including the recent data suggesting that the use of barbiturate come is as relevant as DC for intractable elevated ICP in face of the outcome of both treatments, we can summarize that only when maximal medical management of ICP has failed, the use of DC should be considered in children suffering from a pediatric stroke [67].

Sinus venous thrombus—spontaneous, trauma-related

Cerebral sinus vein thrombosis (CSVT) is a known phenomenon that can happen in a variety of clinical statuses. The brain vasculature system allows the blood to be drained through the different venous sinuses. In case one of the major sinuses is occluded, there is a steep rise in ICP due to lack of blood drainage from the brain. CSVT and arterial stroke differ for both the clinical evolution as well as the natural history [68]. CSVT accounts for 0.5% of all stroke cases [69]. The respective incidence in children and neonates is higher than in adults [70–72]. Most of the cases will involve either the superior sagittal sinus (SSS) or transverse sinus (TS). Etiologies may vary widely. The most common causes are prothrombotic states, either genetically imposed or acquired. Other pathologies include malignancy, hematological pathologies, inflammatory systemic disorders, postoperative related, infections (i.e. mastoiditis), trauma, jugular vein catheterization, and more [73–76]. Recent publication focused on the risk factors for CSVT among pediatric patients found that in a multivariant analysis head/neck infection, head/neck trauma, and mechanical ventilation are independent risk factors for the development of pediatric CSVT [72].

The management paradigm includes diagnosis by imaging, usually either MRI with a specific focus on venous system (MRV), CTV, or even venography (Fig. 1). The treatment goal is to stop the progression of the thrombotic event as well as understanding the causative etiology. In cases where there is altered mental status and suspected elevated ICP, urgent steps are taken to control ICP, measure it, and actively lowering it [77]. In 2008 and later in 2011, several important manuscripts were published with the recommended use of anticoagulation for children [78–81].

ICP management in the setting of sinus vein thrombosis includes several treatment options, such as acetazolamide administration, external ventricular drainage (that allows ICP monitoring as well as an effective treatment to lower excessive pressure), CSF shunt insertion, or even DC [68]. Decompressive craniectomy was found to be effective for CSVT when there is large parenchymal hemorrhage, or an acute mass effect secondary to cerebral swelling and failure of conservative treatment for decreasing intracranial pressure [82]. The use of thrombectomy either endovascular or surgical has been an issue for debate in recent years. Some centers advocate the use of endovascular treatment first when the patient starts to have neurological deterioration or

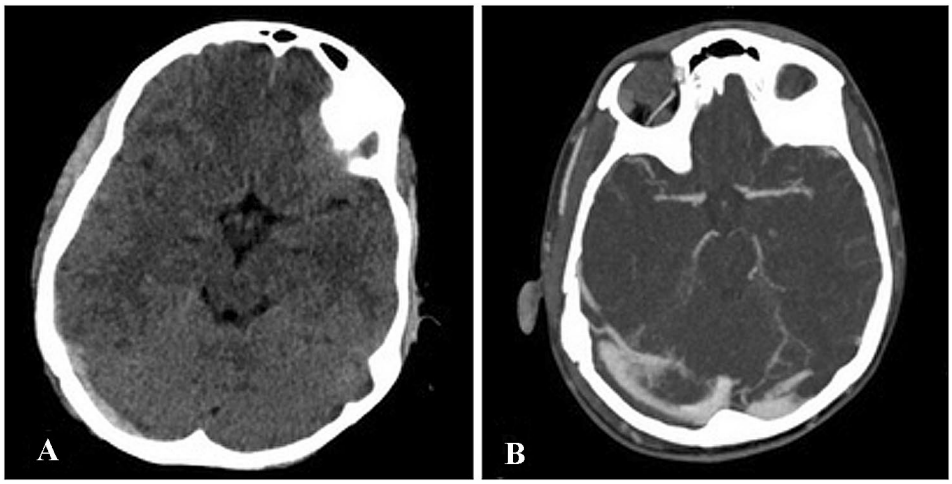

Fig. 1 Transverse sinus thrombosis. Sinus vein thrombosis can be seen in regular CT scan as hyper density (**a**) around the sinus (as a result of blood stasis), and as a filling defect in CT venogram (**b**)

have significant findings in imaging and conservative treatment failed [83]. Yet, when taking the published data that we have today, in cases where the pressure is building up within the brain in a more diffuse pattern, a better treatment paradigm will be measuring neurological status and ICP when needed, use of mannitol or hypertonic saline, and even barbiturate coma. DC in these cases should be the last result [84, 85].

Idiopathic primary increased ICP

Idiopathic intracranial hypertension (IIH) is diagnosed in patients with elevated intracranial pressure with normal brain parenchyma and small ventricles that lack an identifiable cause for elevated pressure. IIH is seen predominantly in young women of childbearing age and among obese girls, however, it can be seen across all ages, genders, a wide range of body mass indices (BMI), ethnicities, and socioeconomic statuses. The pathophysiology of IIH remains uncertain.

Incidence of IIH in pediatrics has been difficult to estimate given the paucity of appropriate studies in this population. It has been reported that 37% of all cases of IIH are children, and 90% of these are between the ages of 5–15 years old [86]. Previous studies found the incidence of primary intracranial hypertension (PIH) to be 0.47–1.2 per 100,000 children, higher than that of secondary intracranial hypertension (SIH), which was 0.32 per 100,000 children [87–89].

The presentation of patients with PIH varies with age. It is harder to diagnose in younger children due to more subtle symptoms and the ability to communicate their symptoms [90]. The most common presenting symptom and the most consistent symptom is headaches, which is present in 30–96.5% of patients [91–93]. Headaches are described as worse in the morning and can be exacerbated by straining, coughing, Valsalva, and bending down. Visual changes are the second most common symptom and are present in > 70% of patients [91]. Yet, bilateral papilledema or optic disc swelling is the most common finding on an exam with a frequency of 87% in children [94]. In pre-pubertal children, incidentally found bilateral papilledema is common and it has been reported in as high as 33% of the cases in the literature. However, papilledema is not identified in every patient and although it is often found bilaterally, it can also be seen unilaterally. If papilledema is left untreated, it can lead to sudden or gradual blindness as the increased pressure causes circumferential compression of the retinal ganglion cells in the optic nerve [86]. Visual field cuts are seen in 74–85% of patients on presentation and the most common defect is an enlarged blind spot [92, 95, 96]. Transient visual obscurations (TVO) described as blacking out of the vision for approximately one second are also widely reported and tend to be exacerbated by either straining, Valsalva, bending, etc. Blurry vision is a very common, however, nonspecific complaint. Diplopia has been reported in 16–42.3% of patients [90, 93, 97]. Unilateral abducens palsy can present as esotropia and diplopia when looking towards the side of the affected eye. In the literature, cranial nerve VI palsies have been reported as low as 12% of patients and as high as 60% of cases [91, 93, 98, 99]. Tinnitus is also a common symptom seen in 40–50% of patients and is often pulsatile and unilateral [90, 91]. Other symptoms of increased intracranial pressure are also seen, and in rare cases, even spontaneous CSF leak can be the presenting symptom [92, 96, 98]. It is important to note that the symptoms can be similar to those caused by posterior fossa lesions including but not limited to cranial nerve VII palsy, ataxia, nuchal rigidity, Babinski sign [100].

The latest criteria include (1) signs and symptoms of elevated intracranial pressure as discussed above, (2) lack of focal neurologic deficits (excluding cranial nerve IV and VI palsies), (3) normal CSF studies, (4) CSF opening pressure of > 18 cm H20 in children < 8 years old or > 25 cm H20 in

children > 8 years old or < 8 years old without optic nerve edema, and (5) normal or small ventricles [89].

Diagnostic studies consist of MRI to rule out a mass lesion and a lumbar puncture for opening pressure (OP) and CSF studies. This is important to note in infants that have open sutures, as the increased ICP may lead to an increasing head circumference and a bulging fontanelle, but not papilledema [100]. Magnetic resonance venography (MRV) is the test of choice to rule out venous sinus thrombosis and is especially necessary for atypical patients, atypical presentations, patients with recent infections in sinuses or ears, patients refractory to routine medical treatment, and patients with a more sudden presentation. MRV has also been recommended in children as these are considered atypical patients and data shows 11% of cases are positive for venous sinus thrombosis [100, 101].

Imaging studies should reveal normal brain parenchyma and normal to small ventricles. Findings that are common in patients with intracranial hypertension include slit-like ventricles, empty sella, protrusion of the optic nerve head anteriorly, flattening of the posterior globe, dilatation of the optic nerve sheath, abnormal appearance of the optic nerve through its orbital portion, enhancement of the posterior sclera (Fig. 2) [95, 102, 103]. Presence of these findings assists in diagnosis, but their absence does not rule out IIH.

A lumbar puncture (LP) serves as a diagnostic test, may provide patients with temporary relief of symptoms caused by elevated ICP, and it also assists in treatment decisions as by removing some CSF it demonstrates whether CSF diversion would be effective. However, it is important to note that the patient's response to the LP is not diagnostic of IIH. The pressure would return to what it was prior to LP within 1–2 h [104, 105]. In equivocal cases, the intracranial pressure can be monitored for an extended period via lumbar drain or intracranial pressure monitor.

Treatment for IIH should be designed by a multidisciplinary team involving a primary care doctor, a neurologist, a dietitian, an ophthalmologist, and if there is an ultimate need for surgical intervention, neurosurgery. The main reason to treat IIH is to prevent blindness and to provide pain relief. The first line of treatment is medical management. In patients who are overweight, this consists of first and foremost a weight loss plan. It has been shown that weight loss of as little as 6% body weight can result in resolution of papilledema [106]. Alternatives for weight loss include diet, exercise, and in adults, it may include surgical interventions like laparoscopic banding and gastric bypass.

Acetazolamide is the first-line medication for IIH in both adults and children. Acetazolamide is a carbonic anhydrase inhibitor that leads to decreased CSF production [107]. If acetazolamide is not effective, other possible medications are furosemide and methazolamide. Furosemide can be used alone or with acetazolamide as a synergistic effect has been reported. It is important to note the possible side effects of these medications. Acetazolamide can lead to a metallic taste and furosemide to hypokalemia. Given the need to monitor potassium levels and replace potassium accordingly, furosemide is considered a second-line medication when treating children [108]. Topiramate and methazolamide are both weak carbonic anhydrase inhibitors used as well. Octreotide can be used in adults, however, in children, it is not recommended given that it inhibits growth hormone and IGF-1 [109]. Lastly, corticosteroids can be used in combination with acetazolamide in cases of sudden rapid visual decline [90].

Surgical interventions are indicated if medical management fails if a patient does not tolerate medical management, if papilledema is severe, or if vision loss is rapidly progressing as weight loss and medications take some time to work [90]. Options for surgical interventions include (1)

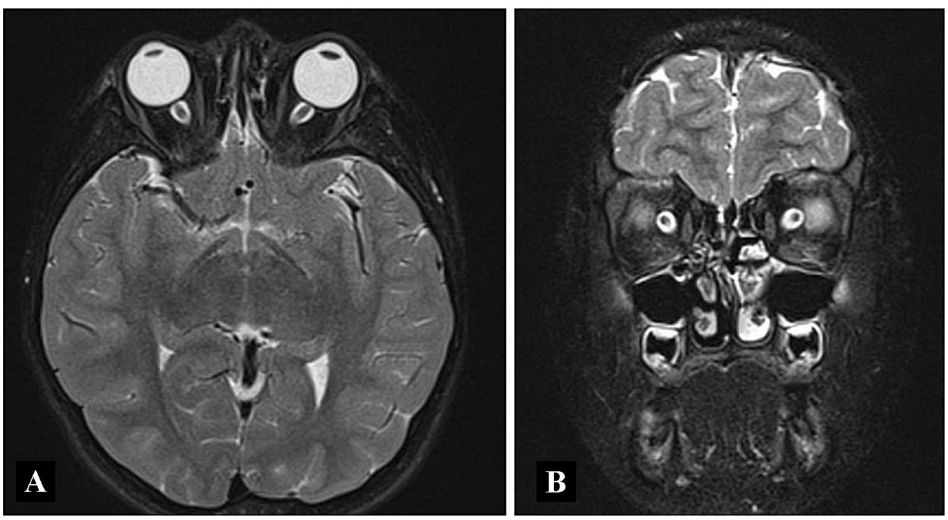

Fig. 2 Idiopathic intracranial pressure. Previously known as pseudotumor cerebri, this entity by definition should be without any intracranial etiology that can result in mass effect. One of the signs being used in recent years is the T2 changes in the optic nerve sheath (**a**—axial, **b**—coronal), as a sign for intracranial pressure and builds up of papillary edema

CSF diversion via ventriculoperitoneal shunt (VPS) or lumbar-peritoneal shunt (LPS) placement and (2) optic nerve sheath fenestration (ONSF). Serial lumbar punctures are advocate by some as spontaneous remissions are common within months to a year of onset. Surgeries like subtemporal or suboccipital decompressions are not in the frontline of the surgical armamentarium and are used rarely.

CSF diversion is ideal for patients that complain of headaches as their primary symptom. Shunting decreases intracranial pressure and helps relieve both headaches and papilledema. Debate still exists regarding what type of shunt is better for patients with IIH. Abubaker et al. compared VPS and LPS. The study determined that VPS has a failure rate of 14% and a revision rate of 30% whereas LPS has a failure rate of 11% and a revision rate of 60% [110].

Patients should be followed for at least 2 years with serial imaging to rule out any obscure, developing, or difficult to diagnose the secondary cause of intracranial hypertension [86]. Outcome data are scarce for the pediatric population. 43–68% of adult patients describe a persistent, yet different headache after treatment [100]. Papilledema does not resolve in about 15% of patients [86]. Permanent visual loss is reported in 2–24% of patients in the literature [86]. Estimates for recurrence are around 18–20%, but a relationship between BMI and risk of recurrence has not been identified [111].

Craniosynostosis

Craniosynostosis is a condition that is diagnosed whenever there is premature closure of one or more of the skull sutures. Incidence has been reported as 1 in 2000–2500 live births [112]. Craniosynostosis is classified by the specific suture or sutures involved, and it can be syndromic or nonsyndromic, with 80–90% of hospitalized children having the nonsyndromic subtype [112, 113]. Craniosynostosis can lead to increased ICP, especially in syndromic craniosynostosis cases. In this subgroup, increased ICP has been reported in 30–50% of cases [114]. Elevated ICP is more common in patients with multiple sutures that are prematurely fused than in patients with single fused sutures [115]. However, elevated ICP has been reported in 11–14% of cases with a single fused suture [114]. Craniofacial dysmorphic syndromes are typically associated with the fusion of multiple sutures and special care has to be taken when evaluating these patients for interventions as their risk for increased ICP is higher than single suture craniosynostosis (i.e. Crouzon, Apert, Pfeiffer, Kleeblattschädel syndromes, amongst others).

Increases in ICP can lead to abnormal development of the brain with significant consequences for these children [116]. An older study identified that for the first 6 years of life, ICP increased with age [115, 116]. ICP monitoring has been studied in patients with craniosynostosis and it can be used to diagnose elevated ICP and make treatment decisions regarding surgical intervention and timing of surgery if determined necessary. The threshold for elevated ICP differs across the literature and across age groups, which limits the generalization of study results for guidelines and the application of these results in general practice. The most common parameters in the literature are as follows: ICP is normal if it is < 10 mmHg, ICP is borderline if it measures 10–15 mmHg, and ICP is considered elevated if > 15 mmHg [115, 117–119]. Yet others suggested that a more sensitive way of diagnosing patients with elevated ICP is to calculate the frequency of ICP elevations > 20 mmHg, rather than making the diagnosis based on the calculated mean ICP [120].

The expected findings of increased ICP and imaging reflective of increased ICP are not common in patients with craniosynostosis [114, 118]. Possible symptoms of increased ICP in these patients are persistent headaches, sleep disturbance, irritability, nausea, deteriorating attention span or academic performance, mental delay [120]; however, these cognitive declines and mental delay findings are wildly debated in the literature as to their association with increased ICP and the long-term effects of ICP elevations on function and development in the presence of other factors that can lead to these same developmental issues [116]. Papilledema is not commonly identified in young children with non-syndromic craniosynostosis and raised ICP [118, 121]. On imaging, one can see decreased subarachnoid spaces, sulcal effacement, beaten copper appearance of the calvarium with a sensitivity of 82% and specificity of 27% [118]. Tuite et al. studied 123 patients with craniosynostosis focusing on imaging findings and ICP [119]. Certain imaging patterns were found to be normal in different age groups and not others. They identified that in children < 18 months old diffuse beaten copper patterns, effacement of the basal cisterns or the sulci were strong predicting factors for the presence of elevated ICP [122]. It is crucial to note that those findings did not predict elevated ICP in older children, as they are seen in these patients even in the presence of normal ICP. Hydrocephalus was the most sensitive indicator of elevated ICP when accounting for all patients; however, they found that hydrocephalus only detected 40% of patients with elevated ICP. They noted that suture diastasis and dorsum sella erosion had a specificity of at least 90% for elevated ICP [119]. When analyzing imaging findings for patients with craniosynostosis, age is a very important factor that assists in determining the relevance of any findings and whether it will change the treatment plan.

The gold standard to diagnose elevated ICP is invasive monitor placement. ICP monitoring is indicated for children who present with persistent symptoms of increased

ICP in the absence of any objective symptoms on imaging or ophthalmologic evaluation [117].

Surgery for correction of craniosynostosis is only necessary in about 20% of cases [86]. Most children with mild craniosynostosis do not show significant symptoms, even in the presence of elevated ICP. In the presence of elevated ICP, early surgery is indicated for cranial vault expansion (for kids with fused sutures). Cranial vault expansion has been shown to relieve symptoms of increased ICP [123].

Chiari malformation

A Chiari malformation is characterized typically by a hindbrain abnormality and CSF flow disturbance. There are several types, from Chiari 0–Chiari IV; however, they do not relate to each other embryologically [124]. Treatment via posterior fossa decompression relieves symptoms and reduction in the size of the syrinx [125]. A Chiari I malformation, or simply a Chiari malformation, is the most common type and it is defined by elongated "pegged" cerebellar tonsils with > 5 mm of tonsillar herniation through the foramen magnum in a way that creates compaction of the foramen magnum. It presents later in life than the other types, typically in adulthood during the second or third decade of life [124, 126]. The most common presenting symptoms are pain, most commonly suboccipital pressure-like headaches (81% of cases) exacerbated by straining, physical activity, Valsalva, and bending down [126]. Chiari, I malformation is associated with syringomyelia in 20–85% of cases [124, 127, 128]. The alterations of CSF flow in these patients are believed to cause the syrinx.

The surgical intervention in Chiari malformation is intended to decompress the posterior fossa and brainstem and reestablish CSF flow. Surgery includes a suboccipital decompression and depending on the case, a cervical laminectomy, duraplasty, and tonsillar shrinking. Asymptomatic patients do not require treatment.

The need for CSF diversion in those patients that underwent decompression surgery is not clear. The previous publication found a significant abnormal pulsatile pressure gradient between the intracranial and lumbar compartments, which is even worse in patients with a syrinx [129]. Yet, the second intervention for CSF diversion after decompression surgery is rare [130].

Acquired Chiari, I malformations can occur when there is a significant gradient between the intracranial and cervical compartments. This can occur in the setting of over drainage from a lumboperitoneal shunt or in patients with CSF leaks. Patients with hydrocephalus or idiopathic intracranial hypertension can also develop downward herniation of tonsils and an acquired Chiari I malformation [128].

Hydrocephalus

Hydrocephalus is a well-known pathology in the pediatric population. Many etiologies can lead to hydrocephalus among the pediatric population. A full discussion of this topic is beyond the scope of this review.

Conclusion

Increased intracranial pressure is a potentially devastating process, especially in the young population. Different etiologies can lead to increased pressure due to brain edema, mass effect, or obstructive hydrocephalus. When clinical signs and symptoms suggesting the rise of intracranial pressure are present, urgent measures need to be taken to preserve cerebral tissue perfusion, oxygenation, and hence brain function.

Summary

- The gold standard to diagnose elevated ICP is invasive monitor placement
- The treatment is a tier-based treatment similar to the traumatic brain injury guidelines
- For Herpes simplex encephalitis, acyclovir therapy dramatically reduces mortality, and around half of the patients return to normal function.
- Some studies are supporting the utility of decompressive craniotomy in severe encephalitis, but true evidence is lacking.
- For adults with malignant stroke, decompressive hemicraniectomy is an effective and recommended treatment for elevated ICP that failed conservative treatment, which can reduce mortality and improve functional outcome. It is recommended to consider the same treatment methodology in the pediatric population, although the lack of age-specific data.
- For patients with CSVT, decompressive craniectomy should be considered in the presence of large mass effect (e.g., intracerebral hemorrhage or malignant cerebral edema) with signs for decompensation (pending herniation).
- For idiopathic intracranial hypertension, surgical interventions are only indicated if medical management fails, if a patient does not tolerate medical management, if papilledema is severe, or if vision loss is rapidly progressing as weight loss and medications take some time to work.

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References

1. Cadena R, Shoykhet M, Ratcliff JJ (2017) Emergency neurological life support: intracranial hypertension and herniation. Neurocrit Care. https://doi.org/10.1007/s12028-017-0454-z
2. Klatzo I (1967) Presidental address. Neuropathological aspects of brain edema. J Neuropathol Exp Neurol. 26(1):1–14
3. Simard JM, Kent TA, Chen M, Tarasov KV, Gerzanich V (2007) Brain oedema in focal ischaemia: molecular pathophysiology and theoretical implications. Lancet Neurol 6(3):258–268. https://doi.org/10.1016/S1474-4422(07)70055-8
4. Steinborn M, Friedmann M, Makowski C, Hahn H, Hapfelmeier A, Juenger H (2016) High resolution transbulbar sonography in children with suspicion of increased intracranial pressure. Childs Nerv Syst 32(4):655–660. https://doi.org/10.1007/s00381-015-3001-2
5. Luerssen TG (1997) Intracranial pressure: current status in monitoring and management. Semin Pediatr Neurol 4(3):146–155
6. Wiegand C, Richards P (2007) Measurement of intracranial pressure in children: a critical review of current methods. Dev Med Child Neurol 49(12):935–941. https://doi.org/10.1111/j.1469-8749.2007.00935.x
7. Sala F, Abbruzzese C, Galli D, Grimaldi M, Abate MG, Sganzerla EP et al (2009) Intracranial pressure monitoring in pediatric bacterial meningitis: a fancy or useful tool? A case report. Minerva Anestesiol 75(12):746–749
8. Le Roux PD, Jardine DS, Kanev PM, Loeser JD (1991) Pediatric intracranial pressure monitoring in hypoxic and nonhypoxic brain injury. Childs Nerv Syst 7(1):34–39. https://doi.org/10.1007/BF00263831
9. Odetola FO, Bratton SL (2005) Characteristics and immediate outcome of childhood meningitis treated in the pediatric intensive care unit. Intensive Care Med 31(1):92–97. https://doi.org/10.1007/s00134-004-2501-4
10. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ et al (2017) Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery 80(1):6–15. https://doi.org/10.1227/NEU.0000000000001432
11. Kochanek PM, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S et al (2012) Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. Pediatr Crit Care Med 13(Suppl 1):S1-82. https://doi.org/10.1097/PCC.0b013e31823f435c
12. Kochanek PM, Tasker RC, Carney N, Totten AM, Adelson PD, Selden NR et al (2019) Guidelines for the management of pediatric severe traumatic brain injury, third edition: update of the brain trauma foundation guidelines, executive summary. Neurosurgery. https://doi.org/10.1093/neuros/nyz051
13. Yildizdas D, Altunbasak S, Celik U, Herguner O (2006) Hypertonic saline treatment in children with cerebral edema. Indian Pediatr 43(9):771–779
14. Marcin JP, Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J et al (2002) Factors associated with adverse outcomes in children with diabetic ketoacidosis-related cerebral edema. J Pediatr 141(6):793–797
15. Sherry NA, Levitsky LL (2008) Management of diabetic ketoacidosis in children and adolescents. Paediatr Drugs 10(4):209–215
16. Burgess S, Abu-Laban RB, Slavik RS, Vu EN, Zed PJ (2016) A systematic review of randomized controlled trials comparing hypertonic sodium solutions and mannitol for traumatic brain injury: implications for emergency department management. Ann Pharmacother 50(4):291–300. https://doi.org/10.1177/1060028016628893
17. Gunn AJ (2000) Cerebral hypothermia for prevention of brain injury following perinatal asphyxia. Curr Opin Pediatr 12(2):111–115
18. Gunn AJ, Gluckman PD, Gunn TR (1998) Selective head cooling in newborn infants after perinatal asphyxia: a safety study. Pediatrics 102(4 Pt 1):885–892
19. Adelson PD, Wisniewski SR, Beca J, Brown SD, Bell M, Muizelaar JP et al (2013) Comparison of hypothermia and normothermia after severe traumatic brain injury in children (Cool Kids): a phase 3, randomised controlled trial. Lancet Neurol 12(6):546–553. https://doi.org/10.1016/S1474-4422(13)70077-2
20. Pérez-Bovet J, Garcia-Armengol R, Buxó-Pujolràs M, Lorite-Díaz N, Narváez-Martínez Y, Caro-Cardera JL et al (2012) Decompressive craniectomy for encephalitis with brain herniation: case report and review of the literature. Acta Neurochir (Wien) 154(9):1717–1724. https://doi.org/10.1007/s00701-012-1323-3
21. Bohn DJ, Biggar WD, Smith CR, Conn AW, Barker GA (1986) Influence of hypothermia, barbiturate therapy, and intracranial pressure monitoring on morbidity and mortality after near-drowning. Crit Care Med 14(6):529–534. https://doi.org/10.1097/00003246-198606000-00002
22. Paschoal FM, Nogueira RC, Ronconi KA, de Lima OM, Teixeira MJ, Bor-Seng-Shu E (2016) Multimodal brain monitoring in fulminant hepatic failure. World J Hepatol. 8(22):915–923. https://doi.org/10.4254/wjh.v8.i22.915
23. Cook AM, Morgan Jones G, Hawryluk GWJ, Mailloux P, McLaughlin D, Papangelou A et al (2020) Guidelines for the acute treatment of cerebral edema in neurocritical care patients. Neurocrit Care 32(3):647–666. https://doi.org/10.1007/s12028-020-00959-7
24. Flores-Cordero JM, Amaya-Villar R, Rincón-Ferrari MD, Leal-Noval SR, Garnacho-Montero J, Llanos-Rodríguez AC et al (2003) Acute community-acquired bacterial meningitis in adults admitted to the intensive care unit: clinical manifestations, management and prognostic factors. Intensive Care Med 29(11):1967–1973. https://doi.org/10.1007/s00134-003-1935-4
25. Hsu CL, Chang CH, Wong KN, Chen KY, Yu CJ, Yang PC (2009) Management of severe community-acquired septic meningitis in adults: from emergency department to intensive care unit. J Formos Med Assoc 108(2):112–118. https://doi.org/10.1016/S0929-6646(09)60041-3
26. Abulhasan YB, Al-Jehani H, Valiquette MA, McManus A, Dolan-Cake M, Ayoub O et al (2013) Lumbar drainage for the treatment of severe bacterial meningitis. Neurocrit Care 19(2):199–205. https://doi.org/10.1007/s12028-013-9853-y

27. Franco-Paredes C, Lammoglia L, Hernández I, Santos-Preciado JI (2008) Epidemiology and outcomes of bacterial meningitis in Mexican children: 10-year experience (1993–2003). Int J Infect Dis 12(4):380–386. https://doi.org/10.1016/j.ijid.2007.09.012
28. Lindvall P, Ahlm C, Ericsson M, Gothefors L, Naredi S, Koskinen LO (2004) Reducing intracranial pressure may increase survival among patients with bacterial meningitis. Clin Infect Dis 38(3):384–390. https://doi.org/10.1086/380970
29. Kim YS, Sheldon RA, Elliott BR, Liu Q, Ferriero DM, Täuber MG (1995) Brain injury in experimental neonatal meningitis due to group B streptococci. J Neuropathol Exp Neurol 54(4):531–539
30. Breeze RE, McComb JG, Hyman S, Gilles FH (1989) CSF production in acute ventriculitis. J Neurosurg 70(4):619–622. https://doi.org/10.3171/jns.1989.70.4.0619
31. Whitley RJ, Kimberlin DW (2005) Herpes simplex encephalitis: children and adolescents. Semin Pediatr Infect Dis 16(1):17–23. https://doi.org/10.1053/j.spid.2004.09.007
32. Steiner I, Budka H, Chaudhuri A, Koskiniemi M, Sainio K, Salonen O et al (2010) Viral meningoencephalitis: a review of diagnostic methods and guidelines for management. Eur J Neurol 17(8):999-e57. https://doi.org/10.1111/j.1468-1331.2010.02970.x
33. Singhi P, Saini AG, Sahu JK, Kumar N, Vyas S, Vasishta RK et al (2015) Unusual clinical presentation and role of decompressive craniectomy in herpes simplex encephalitis. J Child Neurol 30(9):1204–7. https://doi.org/10.1177/0883073814546688
34. Barnett GH, Ropper AH, Romeo J (1988) Intracranial pressure and outcome in adult encephalitis. J Neurosurg 68(4):585–8. https://doi.org/10.3171/jns.1988.68.4.0585
35. Safain MG, Roguski M, Kryzanski JT, Weller SJ (2015) A review of the combined medical and surgical management in patients with herpes simplex encephalitis. Clin Neurol Neurosurg 128:10–6. https://doi.org/10.1016/j.clineuro.2014.10.015
36. Granget E, Milh M, Pech-Gourg G, Paut O, Girard N, Lena G et al (2012) Life-saving decompressive craniectomy for acute disseminated encephalomyelitis in a child: a case report. Childs Nerv Syst 28(7):1121–4. https://doi.org/10.1007/s00381-012-1733-9
37. Alexander M, Murthy JM (2011) Acute disseminated encephalomyelitis: treatment guidelines. Ann Indian Acad Neurol 14(Suppl 1):S60-4. https://doi.org/10.4103/0972-2327.83095
38. Borras-Novell C, García Rey E, Perez Baena LF, Jordan Garcia I, Catella Cahiz D, Cambra F (2015) Therapeutic plasma exchange in acute disseminated encephalomyelitis in children. J Clin Apher 30(6):335–9. https://doi.org/10.1002/jca.21388
39. Koelman DL, Chahin S, Mar SS, Venkatesan A, Hoganson GM, Yeshokumar AK et al (2016) Acute disseminated encephalomyelitis in 228 patients: a retrospective, multicenter US study. Neurology 86(22):2085–93. https://doi.org/10.1212/WNL.0000000000002723
40. Kumar G, Kalita J, Misra UK (2009) Raised intracranial pressure in acute viral encephalitis. Clin Neurol Neurosurg 111(5):399–406. https://doi.org/10.1016/j.clineuro.2009.03.004
41. Johansson Kostenniemi U, Karlsson L, Silfverdal SA, Mehle C (2020) MeningiSSS: a new predictive score to support decision on invasive procedures to monitor or manage the intracerebral pressure in children with bacterial meningitis. Neurocrit Care 32(2):586–95. https://doi.org/10.1007/s12028-019-00792-7
42. Bijlsma MW, Brouwer MC, Bossuyt PM, Heymans MW, van der Ende A, Tanck MW et al (2016) Risk scores for outcome in bacterial meningitis: systematic review and external validation study. J Infect 73(5):393–401. https://doi.org/10.1016/j.jinf.2016.08.003
43. Olson D, Lamb MM, Gaensbauer JT, Todd JK, Halsey NA, Asturias EJ et al (2015) Risk factors for death and major morbidity in guatemalan children with acute bacterial meningitis. Pediatr Infect Dis J 34(7):724–8. https://doi.org/10.1097/INF.0000000000000720
44. Pelkonen T, Roine I, Monteiro L, Cruzeiro ML, Pitkäranta A, Kataja M et al (2012) Prognostic accuracy of five simple scales in childhood bacterial meningitis. Scand J Infect Dis 44(8):557–65. https://doi.org/10.3109/00365548.2011.652666
45. Ramos-Estebanez C, Lizarraga KJ, Merenda A (2014) A systematic review on the role of adjunctive corticosteroids in herpes simplex virus encephalitis: is timing critical for safety and efficacy? Antivir Ther 19(2):133–9. https://doi.org/10.3851/IMP2683
46. Kamei S, Sekizawa T, Shiota H, Mizutani T, Itoyama Y, Takasu T et al (2005) Evaluation of combination therapy using aciclovir and corticosteroid in adult patients with herpes simplex virus encephalitis. J Neurol Neurosurg Psychiatry 76(11):1544–9. https://doi.org/10.1136/jnnp.2004.049676
47. Fitch MT, van de Beek D (2008) Drug Insight: steroids in CNS infectious diseases—new indications for an old therapy. Nat Clin Pract Neurol 4(2):97–104. https://doi.org/10.1038/ncpneuro0713
48. Tiroumourougane SV, Raghava P, Srinivasana S, Badrinath (2003) Management parameters affecting the outcome of Japanese encephalitis. J Trop Pediatr 49(3):153–6
49. Solomon T, Dung NM, Kneen R, Thao T, Gainsborough M, Nisalak A et al (2002) Seizures and raised intracranial pressure in Vietnamese patients with Japanese encephalitis. Brain 125(Pt 5):1084–93
50. Schwab S, Jünger E, Spranger M, Dörfler A, Albert F, Steiner HH et al (1997) Craniectomy: an aggressive treatment approach in severe encephalitis. Neurology 48(2):412–7
51. Shah S, Murthy SB, Whitehead WE, Jea A, Nassif LM (2013) Decompressive hemicraniectomy in pediatric patients with malignant middle cerebral artery infarction: case series and review of the literature. World Neurosurg 80(1–2):126–33. https://doi.org/10.1016/j.wneu.2013.06.001
52. Farooq MU, Abbed KM, Fletcher JJ (2009) Decompressive hemicraniectomy in a 19-month-old female after malignant cerebral infarction. Pediatr Neurosurg 45(2):146–50. https://doi.org/10.1159/000209654
53. Gandhi SK, McKinney JS, Sedjro JE, Cosgrove NM, Cabrera J, Kostis JB et al (2012) Temporal trends in incidence and long-term case fatality of stroke among children from 1994 to 2007. Neurology 78(24):1923–9. https://doi.org/10.1212/WNL.0b013e318259e25c
54. Simma B, Höliner I, Luetschg J (2013) Therapy in pediatric stroke. Eur J Pediatr 172(7):867–75. https://doi.org/10.1007/s00431-012-1863-9
55. Agrawal N, Johnston SC, Wu YW, Sidney S, Fullerton HJ (2009) Imaging data reveal a higher pediatric stroke incidence than prior US estimates. Stroke 40(11):3415–21. https://doi.org/10.1161/STROKEAHA.109.564633
56. Steinlin M, Pfister I, Pavlovic J, Everts R, Boltshauser E, Capone Mori A et al (2005) The first three years of the Swiss Neuropaediatric Stroke Registry (SNPSR): a population-based study of incidence, symptoms and risk factors. Neuropediatrics 36(2):90–7. https://doi.org/10.1055/s-2005-837658
57. Lanthier S, Armstrong D, Domi T, deVeber G (2005) Post-varicella arteriopathy of childhood: natural history of vascular stenosis. Neurology 64(4):660–3. https://doi.org/10.1212/01.WNL.0000151851.66154.27
58. Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A et al (2007) Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol 6(3):215–22. https://doi.org/10.1016/S1474-4422(07)70036-4

59. Marklund N (2017) Decompressive craniectomy, ICP monitoring and secondary necrosectomy as treatment options in patients presenting with malignant ischemic infarctions extending beyond the middle cerebral artery territory. Acta Neurochir (Wien). https://doi.org/10.1007/s00701-017-3331-9
60. Smith SE, Kirkham FJ, Deveber G, Millman G, Dirks PB, Wirrell E et al (2011) Outcome following decompressive craniectomy for malignant middle cerebral artery infarction in children. Dev Med Child Neurol 53(1):29–33. https://doi.org/10.1111/j.1469-8749.2010.03775.x
61. Schwab S, Aschoff A, Spranger M, Albert F, Hacke W (1996) The value of intracranial pressure monitoring in acute hemispheric stroke. Neurology 47(2):393–8
62. Vahedi K, Vicaut E, Mateo J, Kurtz A, Orabi M, Guichard JP et al (2007) Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). Stroke 38(9):2506–17. https://doi.org/10.1161/STROKEAHA.107.485235
63. Hofmeijer J, Kappelle LJ, Algra A, Amelink GJ, van Gijn J, van der Worp HB et al (2009) Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. Lancet Neurol 8(4):326–33. https://doi.org/10.1016/S1474-4422(09)70047-X
64. Jüttler E, Bösel J, Amiri H, Schiller P, Limprecht R, Hacke W et al (2011) DESTINY II: DEcompressive Surgery for the Treatment of malignant INfarction of the middle cerebral arterY II. Int J Stroke 6(1):79–86. https://doi.org/10.1111/j.1747-4949.2010.00544.x
65. Jüttler E, Unterberg A, Woitzik J, Bösel J, Amiri H, Sakowitz OW et al (2014) Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke. N Engl J Med 370(12):1091–100. https://doi.org/10.1056/NEJMoa1311367
66. Grant GA (2015) Is there a role for decompressive craniectomy in children after stroke? World Neurosurg 83(1):44–5. https://doi.org/10.1016/j.wneu.2013.08.049
67. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J et al (2016) Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med 375(12):1119–30. https://doi.org/10.1056/NEJMoa1605215
68. Filippidis A, Kapsalaki E, Patramani G, Fountas KN (2009) Cerebral venous sinus thrombosis: review of the demographics, pathophysiology, current diagnosis, and treatment. Neurosurg Focus 27(5):E3. https://doi.org/10.3171/2009.8.FOCUS09167
69. Bousser MG, Ferro JM (2007) Cerebral venous thrombosis: an update. Lancet Neurol 6(2):162–70. https://doi.org/10.1016/S1474-4422(07)70029-7
70. Agnelli G, Verso M (2008) Epidemiology of cerebral vein and sinus thrombosis. Front Neurol Neurosci 23:16–22. https://doi.org/10.1159/000111258
71. deVeber G, Andrew M, Adams C, Bjornson B, Booth F, Buckley DJ et al (2001) Cerebral sinovenous thrombosis in children. N Engl J Med 345(6):417–23. https://doi.org/10.1056/NEJM2001080934506 04
72. Sellers A, Meoded A, Quintana J, Jallo G, Amankwah E, Nguyen ATH et al (2020) Risk factors for pediatric cerebral sinovenous thrombosis: A case–control study with case validation. Thromb Res 194:8–15. https://doi.org/10.1016/j.thromres.2020.06.013
73. Canhão P, Ferro JM, Lindgren AG, Bousser MG, Stam J, Barinagarrementeria F et al (2005) Causes and predictors of death in cerebral venous thrombosis. Stroke 36(8):1720–5. https://doi.org/10.1161/01.STR.0000173152.84438.1c
74. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, Investigators I (2004) Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke 35(3):664–70. https://doi.org/10.1161/01.STR.0000117571.76197.26
75. Ferro JM (2006) Causes, predictors of death, and antithrombotic treatment in cerebral venous thrombosis. Clin Adv Hematol Oncol 4(10):732–3
76. Stam J (2005) Thrombosis of the cerebral veins and sinuses. N Engl J Med 352(17):1791–8. https://doi.org/10.1056/NEJMra042354
77. Lebas A, Chabrier S, Fluss J, Gordon K, Kossorotoff M, Nowak-Göttl U et al (2012) EPNS/SFNP guideline on the anticoagulant treatment of cerebral sinovenous thrombosis in children and neonates. Eur J Paediatr Neurol 16(3):219–28. https://doi.org/10.1016/j.ejpn.2012.02.005
78. Monagle P, Chalmers E, Chan A, deVeber G, Kirkham F, Massicotte P et al (2008) Antithrombotic therapy in neonates and children: American college of chest physicians evidence-based clinical practice guidelines. Chest 133(6 Suppl):887S-968S. https://doi.org/10.1378/chest.08-0762
79. Roach ES, Golomb MR, Adams R, Biller J, Daniels S, Deveber G et al (2008) Management of stroke in infants and children: a scientific statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. Stroke 39(9):2644–91. https://doi.org/10.1161/STROKEAHA.108.189696
80. Saposnik G, Barinagarrementeria F, Brown RD, Bushnell CD, Cucchiara B, Cushman M et al (2011) Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 42(4):1158–92. https://doi.org/10.1161/STR.0b013e31820a8364
81. Chalmers E, Ganesen V, Liesner R, Maroo S, Nokes T, Saunders D et al (2011) Guideline on the investigation, management and prevention of venous thrombosis in children. Br J Haematol 154(2):196–207. https://doi.org/10.1111/j.1365-2141.2010.08543.x
82. Einhäupl K, Bousser MG, de Bruijn SF, Ferro JM, Martinelli I, Masuhr F et al (2006) EFNS guideline on the treatment of cerebral venous and sinus thrombosis. Eur J Neurol 13(6):553–9. https://doi.org/10.1111/j.1468-1331.2006.01398.x
83. Nyberg EM, Case D, Nagae LM, Honce JM, Reyenga W, Seinfeld J et al (2017) The addition of endovascular intervention for dural venous sinus thrombosis: single-center experience and review of literature. J Stroke Cerebrovasc Dis 26(10):2240–7. https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.05.006
84. Ferro JM, Crassard I, Coutinho JM, Canhão P, Barinagarrementeria F, Cucchiara B et al (2011) Decompressive surgery in cerebrovenous thrombosis: a multicenter registry and a systematic review of individual patient data. Stroke 42(10):2825–31. https://doi.org/10.1161/STROKEAHA.111.615393
85. Ferro JM, Bousser MG, Canhão P, Coutinho JM, Crassard I, Dentali F et al (2017) European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis—endorsed by the European Academy of Neurology. Eur J Neurol 24(10):1203–13. https://doi.org/10.1111/ene.13381
86. Greenberg MS (2016) Handbook of neurosurgery.
87. Gordon K (1997) Pediatric pseudotumor cerebri: descriptive epidemiology. Can J Neurol Sci 24(3):219–21
88. Bursztyn LL, Sharan S, Walsh L, LaRoche GR, Robitaille J, De Becker I (2014) Has rising pediatric obesity increased the incidence of idiopathic intracranial hypertension in children? Can J Ophthalmol 49(1):87–91. https://doi.org/10.1016/j.jcjo.2013.09.015
89. Gillson N, Jones C, Reem RE, Rogers DL, Zumberge N, Aylward SC (2017) Incidence and demographics of pediatric intracranial

hypertension. Pediatr Neurol 73:42–7. https://doi.org/10.1016/j.pediatrneurol.2017.04.021
90. Aylward SC, Reem RE (2017) Pediatric intracranial hypertension. Pediatr Neurol 66:32–43. https://doi.org/10.1016/j.pediatrneurol.2016.08.010
91. Sivaswamy L (2016) Pediatric intracranial hypertension . Pediatr Neurol Briefs 30(10):39. https://doi.org/10.15844/pedneurbriefs-30-10-2
92. Dessardo NS, Dessardo S, Sasso A, Sarunić AV, Dezulović MS (2010) Pediatric idiopathic intracranial hypertension: clinical and demographic features. Coll Antropol 34(Suppl 2):217–21
93. Aylward SC, Aronowitz C, Roach ES (2016) Intracranial hypertension without papilledema in children. J Child Neurol 31(2):177–83. https://doi.org/10.1177/0883073815587029
94. Mallery RM, Friedman DI, Liu GT (2014) Headache and the pseudotumor cerebri syndrome. Curr Pain Headache Rep 18(9):446. https://doi.org/10.1007/s11916-014-0446-z
95. Friedman DI, Liu GT, Digre KB (2013) Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 81(13):1159–65. https://doi.org/10.1212/WNL.0b013e3182a55f17
96. Babikian P, Corbett J, Bell W (1994) Idiopathic intracranial hypertension in children: the Iowa experience. J Child Neurol 9(2):144–9. https://doi.org/10.1177/088307389400900208
97. Aylward SC, Waslo CS, Au JN, Tanne E (2016) Manifestations of pediatric intracranial hypertension from the intracranial hypertension registry. Pediatr Neurol 61:76–82. https://doi.org/10.1016/j.pediatrneurol.2016.04.007
98. Cinciripini GS, Donahue S, Borchert MS (1999) Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. Am J Ophthalmol 127(2):178–82
99. Kesler A, Fattal-Valevski A (2002) Idiopathic intracranial hypertension in the pediatric population. J Child Neurol 17(10):745–8. https://doi.org/10.1177/088307380201701014
100. Friedman DI, Jacobson DM (2002) Diagnostic criteria for idiopathic intracranial hypertension. Neurology 59(10):1492–5
101. Standridge SM, O'Brien SH (2008) Idiopathic intracranial hypertension in a pediatric population: a retrospective analysis of the initial imaging evaluation. J Child Neurol 23(11):1308–11. https://doi.org/10.1177/0883073808318056
102. Maralani PJ, Hassanlou M, Torres C, Chakraborty S, Kingstone M, Patel V et al (2012) Accuracy of brain imaging in the diagnosis of idiopathic intracranial hypertension. Clin Radiol 67(7):656–63. https://doi.org/10.1016/j.crad.2011.12.002
103. Fraser JA, Leung AE (2014) Reversibility of MRI features of pseudotumor cerebri syndrome. Can J Neurol Sci 41(4):530–2
104. Dandy WE (1937) Intracranial pressure without brain tumor: diagnosis and treatment. Ann Surg 106(4):492–513
105. Johnston I, Paterson A (1974) Benign intracranial hypertension. I. Diagnosis and prognosis. Brain 97(2):289–300
106. Johnson LN, Krohel GB, Madsen RW, March GA (1998) The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). Ophthalmology 105(12):2313–7. https://doi.org/10.1016/S0161-6420(98)91234-9
107. McCarthy KD, Reed DJ (1974) The effect of acetazolamide and furosemide on cerebrospinal fluid production and choroid plexus carbonic anhydrase activity. J Pharmacol Exp Ther 189(1):194–201
108. Schoeman JF (1994) Childhood pseudotumor cerebri: clinical and intracranial pressure response to acetazolamide and furosemide treatment in a case series. J Child Neurol 9(2):130–4. https://doi.org/10.1177/088307389400900205
109. Deftereos SN, Panagopoulos G, Georgonikou D, Karageorgiou CE, Karageorgiou E, Piadites G (2011) Treatment of idiopathic intracranial hypertension: is there a place for octreotide? Cephalalgia 31(16):1679–80. https://doi.org/10.1177/0333102411424211
110. Abubaker K, Ali Z, Raza K, Bolger C, Rawluk D, O'Brien D (2011) Idiopathic intracranial hypertension: lumboperitoneal shunts versus ventriculoperitoneal shunts–case series and literature review. Br J Neurosurg 25(1):94–9. https://doi.org/10.3109/02688697.2010.544781
111. Ravid S, Shahar E, Schif A, Yehudian S (2015) Visual outcome and recurrence rate in children with idiopathic intracranial hypertension. J Child Neurol 30(11):1448–52. https://doi.org/10.1177/0883073815569306
112. Di Rocco F, Arnaud E, Renier D (2009) Evolution in the frequency of nonsyndromic craniosynostosis. J Neurosurg Pediatr 4(1):21–5. https://doi.org/10.3171/2009.3.PEDS08355
113. LoPresti M, Buchanan EP, Shah V, Hadley CM, Monson LA, Lam S (2017) Complete resolution of papilledema in syndromic craniosynostosis with posterior cranial vault distraction. J Pediatr Neurosci 12(2):199–202. https://doi.org/10.4103/jpn.JPN_15_17
114. Gault DT, Renier D, Marchac D, Jones BM (1992) Intracranial pressure and intracranial volume in children with craniosynostosis. Plast Reconstr Surg 90(3):377–81
115. Renier D, Sainte-Rose C, Marchac D, Hirsch JF (1982) Intracranial pressure in craniostenosis. J Neurosurg 57(3):370–7. https://doi.org/10.3171/jns.1982.57.3.0370
116. Takahashi Y, Hori M, Shimoji K, Miyajima M, Akiyama O, Arai H et al (2017) Changes in delta ADC reflect intracranial pressure changes in craniosynostosis. Acta Radiol Open 6(9):2058460117728535. https://doi.org/10.1177/2058460117728535
117. Baird LC, Gonda D, Cohen SR, Evers LH, LeFloch N, Levy ML et al (2012) Craniofacial reconstruction as a treatment for elevated intracranial pressure. Childs Nerv Syst 28(3):411–8. https://doi.org/10.1007/s00381-011-1615-6
118. Wall SA, Thomas GP, Johnson D, Byren JC, Jayamohan J, Magdum SA et al (2014) The preoperative incidence of raised intracranial pressure in nonsyndromic sagittal craniosynostosis is underestimated in the literature. J Neurosurg Pediatr 14(6):674–81. https://doi.org/10.3171/2014.8.PEDS1425
119. Tuite GF, Evanson J, Chong WK, Thompson DN, Harkness WF, Jones BM et al (1996) The beaten copper cranium: a correlation between intracranial pressure, cranial radiographs, and computed tomographic scans in children with craniosynostosis. Neurosurgery 39(4):691–9
120. Eide PK, Helseth E, Due-Tønnessen B, Lundar T (2002) Assessment of continuous intracranial pressure recordings in childhood craniosynostosis. Pediatr Neurosurg 37(6):310–20. https://doi.org/10.1159/000066311
121. Bannink N, Joosten KF, van Veelen ML, Bartels MC, Tasker RC, van Adrichem LN et al (2008) Papilledema in patients with Apert, Crouzon, and Pfeiffer syndrome: prevalence, efficacy of treatment, and risk factors. J Craniofac Surg 19(1):121–7. https://doi.org/10.1097/SCS.0b013e31815f4015
122. Rosenberg JB, Shiloh AL, Savel RH, Eisen LA (2011) Noninvasive methods of estimating intracranial pressure. Neurocrit Care 15(3):599–608. https://doi.org/10.1007/s12028-011-9545-4
123. Cohen SR, Dauser RC, Newman MH, Muraszko K (1993) Surgical techniques of cranial vault expansion for increases in intracranial pressure in older children. J Craniofac Surg. 4(3):167–76 (**discussion 74–6**)
124. Strayer A (2001) Chiari I malformation: clinical presentation and management. J Neurosci Nurs 33(2):90–6
125. Iskandar BJ, Hedlund GL, Grabb PA, Oakes WJ (1998) The resolution of syringohydromyelia without hindbrain herniation after posterior fossa decompression. J Neurosurg 89(2):212–6. https://doi.org/10.3171/jns.1998.89.2.0212

126. Milhorat TH, Chou MW, Trinidad EM, Kula RW, Mandell M, Wolpert C et al (1999) Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery 44(5):1005–17
127. Attenello FJ, McGirt MJ, Gathinji M, Datoo G, Atiba A, Weingart J et al (2008) Outcome of Chiari-associated syringomyelia after hindbrain decompression in children: analysis of 49 consecutive cases. Neurosurgery 62(6):1307–13. https://doi.org/10.1227/01.neu.0000333302.72307.3b
128. Doberstein CA, Torabi R, Klinge PM (2017) Current concepts in the pathogenesis, diagnosis, and management of type I Chiari malformations. Rhode Island Med J 100(6):47–9
129. Frič R, Eide PK (2015) Comparison of pulsatile and static pressures within the intracranial and lumbar compartments in patients with Chiari malformation type 1: a prospective observational study. Acta Neurochir (Wien). 157(8):1411–23. https://doi.org/10.1007/s00701-015-2465-x (**discussion 23**)
130. Frič R, Eide PK (2016) Perioperative monitoring of pulsatile and static intracranial pressure in patients with Chiari malformation type 1 undergoing foramen magnum decompression. Acta Neurochir (Wien) 158(2):341–7. https://doi.org/10.1007/s00701-015-2669-0 (**discussion 6–7**)