Common Medical Conditions in the Neonates

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Sadiya Zinjani

4.1 Introduction

The **neonate** is the smallest of all human beings, whose arrival in this world is perhaps one of the most eagerly awaited event in the lives of the 'to be parents' and their extended families. This little bundle of joy brings not only immense happiness but sometimes also brings much anxiety and worry. This small human offspring may carry with it certain genetic disorders or may develop medical or surgical issues demanding rapid intervention. With regard to surgical issues and other invasive procedures, the necessity to administer anesthesia to these babies arises. Safe methods of anesthesia are now available for even the most premature and sickest of neonates. However, it must be remembered that neonates are not small adults, their physiology is at a complete variance with adult humans, their anatomy is still developing and their physiology is still immature.

Therefore, in the highly specialized field of neonatal anesthesia, there is a definite need to highlight various medical aspects which must be dealt with before proceeding to administer anesthetic agents and analgesic drugs to them.

In addition, before delving into the vast realm of medical problems which a newborn is either born with or may develop, it is probably appropriate to define various terminologies used for a neonate and simultaneously give a meaning to important time spans in the life of these little babies.

S. Zinjani (✉)
Department of Paediatrics, Max Smart Super Speciality Hospital, Saket, New Delhi, India

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4.2 Definitions Terminologies

A newborn may be born after completion of the normal gestational period or may be delivered earlier or later than the expected date, and the body weight (BW) may be appropriate, less or more than that expected for the gestational age (GA). Both the BW and GA have an important bearing on the survival as well as the development of the newborn. In addition, the outcome of several medical and surgical issues are weight and gestational age related, hence the significance of knowing these terminologies [1, 2].

4.2.1 As Per Gestational Age (GA)

Term babies are babies born between 37 and 42 weeks of pregnancy. They are subdivided into three categories: **early term** (37–38 weeks), **full term** (39–40 weeks), and **late term** (40–42 weeks).

Babies born before completion of 37 weeks of pregnancy are considered **preterm.** They are categorized as **extreme preterm** (GA <28 weeks), **very preterm** (GA 28–32 weeks), and **moderate-to-late preterm** (GA 32–37 weeks).

Babies born at and beyond 42 weeks of gestation or expected date of delivery (EDD) + 14 days, are considered as **post-term**.

4.2.2 As Per Birth Weight (BW)

Low birth weight (LBW) babies are those with BW less than 2500 g irrespective of GA. This may be due to prematurity or fetal growth retardation (FGR), which account for 1/3rd LBW babies, or small for gestational age (SGA) babies, which accounts for 2/3rd of LBW babies. They are further categorized as **very** LBW (VLBW) with BW less than 1500 g and **extremely** LBW (ELBW) with BW less than 1000 g.

Appropriate for gestation age (**AGA**) babies are those with BW appropriate for the GA, i.e., >2500 g or between the 10th and 90th percentile on the intrauterine growth curves. SGA babies are smaller than usual for the GA and their BW is below the 10th percentile (they are smaller than other babies of the same GA), and **large for gestational age** (**LGA**) babies have BW greater than 97th percentile for that GA and refers to babies with BW more than 4000 g. (Stanford Children's Health)

Note: LBW is a valuable public health indicator of a country's healthcare system in terms of maternal health and nutrition and in socio economic stratification. Mortality and risk of developing neurologic sequelae with impairment in cognitive skills and chronic diseases is significantly higher in LBW babies. Due to immaturity of multiple organ systems, preterm babies carry higher morbidity and mortality risks, and are the leading cause of all under-5 mortality, globally.

Intrauterine growth retardation (IUGR) is defined as fetal growth rate less than normal for the growth potential of the baby (AAP) at that gestational age. It is not defined by the subsequent BW, whereas BW is used to define SGA. It is therefore possible for a newborn to be SGA without being FGR.

Certain vital periods in the life of a baby are major determinants in the outcome of pregnancy, neonatal wellbeing, morbidity, and mortality. **Perinatal period** extends from 20 weeks (140 days) of gestation to 28 completed days (4 weeks) after birth. This is an extremely vulnerable period for the developing organs. Any misstep in this period carries with it the possibility of disastrous and serious ill effects, which may result in profound and long-lasting deficits. The **neonatal period** is the most crucial phase of life and survival during this period is of paramount importance for a baby to reach adulthood. Nearly 41% of all under-5 deaths involve neonates. Neonatal period is divided into two, **early neonatal period** (birth to 7 days of age this period accounts for 75% of neonatal deaths) and **late neonatal period** (8th day to 28 days of life). **Infancy** period includes the period from birth to 12th months (1 year) of life. The '**Golden 1000 days**' time span is a unique period during which there is the laying down of the foundation of optimum health, growth and neurodevelopment, and stretches right from the time of conception to 2 years of age.

4.3 Special Considerations [3]

4.3.1 Prematurity

Despite advances in neonatal care, preterm birth remains the leading cause of infant mortality, globally. Due to their LBW and organ immaturity, preterm babies may have various problems:

(a) Their **caloric needs** are high but due to the lack of sucking and swallowing reflexes, difficulties with oral feeding are often encountered.
(b) **Gastrointestinal** immaturity impairs digestion, absorption of carbohydrates and lipids, and increases the risk for necrotizing enterocolitis (NEC).
(c) **Pulmonary** immaturity makes them more prone to apnea and respiratory distress both of which call for very specialized care.
(d) **Neurological** immaturity contributes to the increased risk of CNS insults, which may later manifest as a poor cognitive ability, developmental delays, and other neurological sequelae.
(e) **Visual** issues such as retinopathy of prematurity (ROP) have to be guarded against.
(f) They are at increased risk for sudden infant death syndrome (SIDS).
(g) **Metabolic** immaturity, poor fat insulation, decreased glycogen stores, immature skin with increased water loss, poor vascular control, and lower maximal metabolism, narrows the range of thermal control, and makes them prone to hypothermia.

(h) Immaturity of the **immune** system places them at high risk for contracting life-threatening infections.
(i) Congenital **cardiac anomalies** such as patent ductus arteriosus (PDA) and blood pressure variations need regular monitoring and specialist referrals.

Premature newborns need continuous and prolonged specialized care and must be observed for onset of anemia and jaundice which call for prompt attention and remedial measures. Round the clock monitoring of blood sugar is essential since hypoglycemia is a potential danger that needs urgent attention.

4.3.2 Fetal Growth Restriction (FGR)

This refers to a fetus smaller than it should be. FGR may be symmetrical or asymmetrical depending on the time of development of restriction in fetal growth. FGR with associated inability to handle stress puts these babies at a health risk during pregnancy, delivery and even after birth, thus increasing the probability of adverse short- and long-term outcomes. The acute neonatal consequences of FGR/IUGR are perinatal asphyxia and neonatal adaptive problems. Respiratory distress due to meconium aspiration is an adaptive issue in these neonates which may sometimes necessitate the use of mechanical ventilation. Hypoglycemia and hypocalcemia are commonly encountered metabolic imbalances. Due to a compromise in their resistance to infection, there is an increase in the incidence of sepsis. Polycythemia is another cause of high morbidity.

4.3.3 Large for Gestational Age (LGA)

As already defined includes babies with BW larger than expected for their GA or BW greater than the 90th percentile. Causes attributed are genetic, maternal, or due to a medical condition in the baby. Due to their large size, these neonates have specific problems which necessitate their inclusion in a separate group. Their delivery poses a risk for the mother with increase in operative/instrumental deliveries, more frequent genital tract lacerations, and PPH. The incidence of birth injuries (BI) (shoulder dystocia, clavicle or limb fractures, and nerve injuries) is high during normal vaginal delivery. Other common problems are perinatal asphyxia, respiratory distress, meconium aspiration, hypoglycemia, and polycythemia.

4.3.4 Hypothermia/Hyperthermia

Medical issues in neonates may be initially mild and delay in addressing them may assume serious proportions due to the inability of the ‘little one’ to compartmentalize the problem. Thus, all health issues in the neonates underscore the need for a quick assessment and rapid initiation of remedial measures. The resuscitation of the newborn may sometimes produce temperature fluctuations which may be

detrimental to life, rendering it of utmost importance to ensure that the newborn is resuscitated in a thermoneutral environment, i.e., the temperature of the resuscitation area should be maintained around 25 °C (WHO). Overexposure in a cold room will quickly result in hypothermia, which may be mild (36–36.4 °C), moderate (32–35.9 °C), and severe (<32 °C). Signs of hypothermia may be nonspecific or absent, and include pallor with bluish extremities, lethargy, and refusal of feeds. Gentle warming and adequate wrapping may ameliorate the problem. However, adoption of the preventive measures is the best policy.

Hyperthermia refers to a temperature record >37.5 °C and may be due to overwrapping or keeping the baby directly in front of a warmer or heater. This can be easily corrected by reducing the layers of clothing and removing the source of external heat.

Fever may be due to high environmental temperature or dehydration (poor oral intake). Ensuring adequate feeds at frequent intervals may help in relieving fever. Sometimes, sepsis may be the cause, and appropriate measures such as sepsis workup should be done and relevant antibiotics started.

4.3.5 Birth Injuries (BI) [4–8]

These injuries are sustained by the newborn during delivery from compression or trauma. The incidence is 3.7 per 100,000 live births. Risk factors include abnormal presentations, instrumental delivery, intra uterine versions, prolonged/precipitous labor, short maternal stature, extreme prematurity, LGA, large fetal head, and fetal anomalies, etc. BI's may be grouped as cranial, head and neck, facial (nasal, ocular, and ear), muscular, nerve, bony, soft tissue, and abdominal injuries. They may manifest as mild bruising, superficial cuts, bony fractures or bleeding into the body cavities. The most frequently encountered injuries are swelling or bruising of the head (caput succedaneum or chignon), bleeding underneath a cranial bone (cephal hematoma, subgaleal hemorrhage), subconjunctival hemorrhage, facial nerve injury, and clavicle fracture. Treatment varies from no intervention to appropriate therapy. For nerve injuries, physiotherapy is advised, and fracture clavicle requires no treatment except to pin the affected arm of the baby to the front of the clothing and reducing movement of that arm.

Note: Caput succedaneum is an extra periosteal fluid collection due to molding of the baby's head and needs no treatment. Cephal hematoma is a sub periosteal accumulation of blood following the rupture of blood vessel because of trauma during the birth. Chignon is the swelling left on an infant's head after delivery with a ventouse suction cap and usually resolves without any intervention.

4.3.6 Neonatal Asphyxia (Includes Birth Asphyxia and Perinatal Asphyxia) [9–13]

This is one of the most feared outcomes of fetal life, labor or a complicated delivery. There is lack of oxygen to the newborn during birthing leading to the inability to

establish or sustain spontaneous or adequate respiration on delivery. This produces perfusion deficit to various organs causing a hypoxic damage and can thus result in significant morbidity and mortality. If ventilation and adequate pulmonary perfusion are not established soon after birth a worsening cycle of hypoxia, hypercapnia, and metabolic acidosis sets in. The damage to the brain is of tremendous concern, since it is least likely to completely heal and may manifest in a surviving infant with either or both mental and physical deficits. **Perinatal asphyxia** is oxygen deficit from 28th week of gestation to the 7th day of life. **Neonatal asphyxia** is oxygen deficit occuring after birth. It can result in hypoxic ischemic encephalopathy (HIE) or intraventricular hemorrhage (IVH) especially in preterm newborns. A baby with severe neonatal asphyxia is cyanosed, hypotonic, has absent or poor respiratory effort and poor responses, all adding up to a low 5 min Apgar Score. Extreme asphyxia can cause cardiac arrest and death. The incidence of neonatal asphyxia has a multifactorial dependence with GA and BW being important determinants, others being maternal, fetal, placental, labor related, and cord related. Some of the maternal risk factors are age (elderly or very young mothers), lack of antenatal care, anemia, diabetes, heart disease, hypertension, and toxemia. Placental and labor related causes are placental insufficiency, placenta previa, prolonged membrane rupture, and difficult/prolonged labor. A short or a nuchal cord, a true knot, cord prolapse, and cord compression are important cord relevant risk factors. Fetal causes include both pre- and postmaturity, FGR, malpresentations, multiple pregnancies, fetal distress, and meconium aspiration.

Long-term adverse effects of birth asphyxia are cerebral palsy, motor disorders, seizure disorders and epilepsy, developmental delays, speech disorders, learning disabilities, visual and auditory impairment, respiratory problems, behavioral and emotional disorders, and feeding problems.

Prognosis: GA is an important mortality predictor in babies asphyxiated at birth. When compared to respiratory acidosis, metabolic acidosis scores far worse. A very low Apgar Score at 20 min is a reliable predictor of neurological morbidity, and a prolonged delay in the establishment of spontaneous respiration points to the development of irreversible brain damage. Babies with severe HIE have mortality rates ranging from 50–100%, and survivors may have up to 75% of residual disability rates.

4.3.7 Hypoxic Ischemic Encephalopathy (HIE) [4]

Severe birth asphyxia causing injury to the brain leads to the development of HIE, which may progress to permanent brain damage, manifesting as cerebral palsy. Treatment includes (a) airway management (suction, positioning to maintain airway patency, and tracheal intubation), (b) breathing stabilization [tactile stimulation, O_2, bag mask ventilation, and positive pressure ventilation (PPV)], (c) circulation improvement (chest compressions, IV fluids, and medications), (d) drug administration (to regulate heart rate, blood pressure, renal function, and control seizures), and (e) **hypothermia induction** (to help brain cells recover, thus preventing spread and severity and permanent brain damage).

4.3.8 Birth Defects

These may be structural or metabolic defects.

(a) **Structural birth defects** [14–16], as defined by the center for disease control (CDC), are problems present in the newborn structure that can affect almost any part or parts of the body, involving either the appearance or the function of the body, or both. The incidence is 3–4%. The well-being of the baby affected with a birth defect depends on which organ or body part is involved and extent of affectation. The severity of the defect as well as the body part affected may or may not influence the expected lifespan of the afflicted baby. The most common causes of birth defects are genetic disorders, chromosomal abnormalities, and pregnancy-related issues (infections, smoking, drugs, alcohol, or substance abuse). All birth defects may not be preventable, since the cause of many may be unknown. However, adoption of a healthy lifestyle, prior and during pregnancy, will increase the chances of having a healthy baby. When planning a pregnancy, a woman should consult a health care professional, and any existing problems such as diabetes, obesity, hypertension, asthma should be addressed. Once pregnancy is confirmed, women should enroll in a prenatal care program. Major brain and spine birth defects may be prevented by ensuring an adequate intake of folic acid. Avoidance of all harmful substances in the form of drugs, cigarettes, and alcohol should be mandatory throughout pregnancy. Equally important is avoidance of all infections. All medications and vaccinations as advised by the health care provider should be taken. The most common birth defects are Cardiac, Cleft lip/palate, Down syndrome, and Spina Bifida.

The common **cardiac defects** include atrial septal defect (ASD), AV septal defect, coarctation of the aorta, transposition of the great arteries (TGA), hypoplastic left heart syndrome, Pulmonary Atresia, tetralogy of fallot (TOF), and total anomalous pulmonary venous drainage (TAPVD).

Cleft lip/palate are common birth defects and may be isolated or a part of a syndrome. Symptoms arise from the opening in the mouth as feeding difficulties during the neonatal period and infancy, and later as problems with speech. Lip repair is done at 4–6 weeks and palate repair at about 9 months to one year of age. Corrective surgery followed by speech therapy can restore normal function.

Down syndrome or Trisomy 21 is by far the most common and best-known chromosomal disorder in human with a global incidence of 1:1000–1:1100 live births (WHO). It is one of the most common cause of moderate-to-severe intellectual disability. Down syndrome is strongly associated with increasing maternal age resulting in maternal meiotic nondisjunction. Unbalanced translocation accounts for up to 4% of cases.

Spina bifida is thought to result from a combination of genetic, nutritional, and environmental factors, in which folic acid deficiency and family history of neural tube defects (NTDs) play an important role. Incidence is 1:1000 births globally, with marked geographical variations. It is a spinal disorder involving

improper closure of the neural tube. The three common types often encountered are Meningomyelocele, Meningocele, and Spina Bifida Occulta. The plethora of presentations, treatment, and time of treatment of babies with Spina Bifida is extremely variable.

Often babies with birth defects require to undergo corrective surgery during the neonatal period, which increases the risk of morbidity.

Note: Birth defects are commonly called congenital anomalies or abnormalities. A genetic disorder is a disease caused by a change in the DNA sequence, either wholly or partly. A Chromosomal disorder is a syndrome characterized by malformations or malfunctions in any of the body systems and caused by abnormalities in either the number or constitution of the chromosomes.

(b) **Metabolic birth defects: inborn errors of metabolism (IEsM)** [17–19] are disorders present from birth, affecting either the process of food breakdown or food absorption, or affecting various enzymes involved in these processes. Left untreated, some of these disorders affect the baby's development or cause organ damage and death. Neonates with IEsM may remain normal for the first few hours or days of life, and then become symptomatic with signs mimicking neonatal sepsis. Diagnosis is based on a high level of suspicion and is essential both for treatment as well as genetic counseling. The common IEsM are congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), glucose 6 phosphate dehydrogenase (G6PD) deficiency, biotindase deficiency, galactosemia (galactose-1-phosphate uridyl transferase) (GALT), phenylketonuria (PKU), and maple syrup urine disease (MSUD). Pregnancy and delivery are generally uneventful. Accompanying sepsis may mask the disorder. Babies with IEsM may present with extreme hypotonia, sluggishness, dysmorphic features, poor feeding, jaundice, hypoglycemic, altered sensorium, or seizures. Parental consanguinity with history of a similar presentation in an earlier issue is a valuable pointer towards the suspicion of IEsM. Prognosis depends on several factors such as time of diagnosis, type and severity of the disorder, availability of specific treatment options, and definitive therapeutic interventions. Some IEsM have a relatively better prognosis than others. Some children may live longer but be at risk of developing progressive neurologic deficits, learning disabilities, and mental retardation. It is, therefore, important for primary care providers to know how to recognize IEsM, manage them in the interim while awaiting definitive diagnosis, and refer them to the appropriate metabolic specialist for the collaborative management.

Note: Prompt detection requires a high index of suspicion and the early measurement of biochemical markers such as blood ammonia.

Routine antenatal and neonatal screening tests cover a wide range of IEsM [20]. A special mention is to be made of 2 IEsM: **CH** and **CAH**, where the defect lies in either the paucity of hormone produced or in the buildup of certain intermediate hormones.

(i) **Congenital Hypothyroidism (CH)** [21, 22] is a birth defect due to the absence or under development of the thyroid gland or a problem in the production of the thyroid hormone. It is one of the most common treatable

causes of intellectual disability which makes it empirical to diagnose it early and simultaneously initiate the thyroid replacement therapy. With early diagnosis and treatment, the baby is likely to have a normal, healthy life. CH is mostly sporadic, with incidence of 1: 3500 live births. Babies may be asymptomatic or present with hypotonia, hypothermia, jaundice, delayed stooling, and poor feeding. Thyroid screening is a part of routine newborn screening tests. Treatment is lifelong thyroid replacement therapy. Neonatal Hyperthyroidism is transient due to the transplacental passage of thyroid stimulating antibodies by a mother with Grave's disease.

(ii) **Congenital Adrenal Hyperplasia (CAH)** [23–26] is a group of autosomal recessive disorders that occur in 1:1600 live births. The most common cause is the absence of enzyme 21-hydroxylase, due to gene mutations, resulting in varying levels of the enzyme, producing a spectrum of effects. There are other rarer enzyme deficiencies which may also cause CAH. The two main forms of CAH are "**classic**" and "**non-classic."** The classic CAH is more severe, and is usually detected at birth or in infancy, and may be of the **"salt losing form"** which forms 2/3rd of this group while the remaining 1/3rd is constituted by the **"simple-virilizing form."** The nonclassic CAH is milder, more common and may not become evident until childhood or early adulthood. The sign and symptoms of classic CH include those due to cortisol deficiency (high blood sugar), life threatening adrenal crisis, atypical genetalia, high androgens (short height, early puberty, acne), altered growth, and fertility issues. Prenatal amniocentesis and Neonatal Screening tests should also include screening for CAH. An out of range result for CAH in the neonatal screening tests will necessitate further confirmation by urine and blood sampling. Treatment depends on the presenting form and includes medications (corticosteroids, mineralocorticoids, and supplements) reconstructive surgery, and psychological support [8].

(c) **Hypoglycemia:** [27, 28] Glucose is crucial for brain development as it is the main source of energy for the brain. A low blood sugar in a newborn may lead to injury and then death of the brain cells resulting in permanent damage. Neonatal hypoglycemia (NH) is one of the most common metabolic problems, and severe NH is one of the leading causes of neonatal brain injury. It is easy to recognize and treat. In the fetus, glucose diffuses across the placenta, so the fetal glucose levels are 2/3rd the maternal level. Once the umbilical cord is severed after the birth, blood glucose level may fall to dangerously low levels for the next 1–2 hrs before stabilizing by 3–4 hrs to a mean of 70 mg/dL. Monitoring of hypoglycemia in high risk neonates is of utmost importance. Babies at risk of NH are SGA, LGA, IUGR and preterm babies, those born to diabetic mothers, babies with birth asphyxia (HIE), and pregnancy with intrauterine stress and sepsis. Babies with some genetic disorders may also present with NH. Signs and symptoms include cyanosis or pallor, breathing problems (tachypnea, apnea, or grunting sounds), lethargy or irritability, muscular weakness (hypotonia), vomiting, poor feeding, weak or high pitched cry and tremors, shakiness, sweating, or seizures. Blood sugar should be tested within seconds

of appearance of symptoms. A low initial blood glucose is rechecked every 2–3 hrs for the first 24–48 hrs and close monitoring is continued until the blood sugar stabilizes. If conditions permit, then the initiation of feeding in high risk and babies with symptoms of NH should be early and repeated every 2 hrs. Babies who cannot be put on oral feeds should be treated aggressively with IV dextrose while monitoring is continued. In babies with severe hypoglycemia, glucagon may be used subcutaneously or intramuscularly.

Neonatal hyperglycemia: [9] This refers to blood sugar levels over 150 mg/dL and is very frequently iatrogenic or due to insulin resistance, glucose intolerance or inability of the neonate to control hepatic glycogenolysis. It is frequently encountered in preterm babies during parenteral glucose infusion. Other precipitating factors include infection and stress. Treatment is reduction of the dextrose infusion rate or IV Insulin infusion.

(d) **Hypocalcemia** [27, 29] is also frequently encountered metabolic disorder in the newborns. Following the transition from intrauterine to a life outside the womb, after cord clamping, there is cessation of placental transfer of calcium (Ca). Consequently, neonatal Ca levels drop to about 8–9 mg/dL (2–2.25 mmol/L), and ionized Ca falls to 4.4–5.4 mg/dL (1.1–1.35 mmol/L) by 24 hrs of birth. Serum Ca concentration subsequently rises, reaching normal levels by 2 weeks of age. Neonatal hypocalcemia may be early onset when it manifests within the first 2 days of life or late onset when symptoms appear after the 3rd postnatal day, usually by the end of the first week of life. Risk factors include prematurity, SFD, IUGR, birth asphyxia, due to immaturity of the parathyroid gland or decreased transplacental passage of calcium. Babies of diabetic mothers are also likely to manifest with signs and symptoms of hypocalcemia. The most common causes of late-onset hypocalcemia are excessive phosphate intake, hypomagnesemia, hypoparathyroidism, and vitamin D deficiency. Hypocalcemia may be asymptomatic or the baby maybe irritable, have muscle twitches, tremors, or jitteriness, lethargic with refusal of feeds, or may present with frank seizures. Treatment of early onset hypocalcemia is 10% calcium gluconate given IV slowly under heart rate monitoring. After initial acute correction of hypocalcemia, calcium gluconate is added to the IV infusion. When oral feeds are started the formula is supplemented with oral calcium gluconate. This supplementation is required usually for a few days only. Late onset hypocalcemia is treated by addition of calcitriol or calcium to infant formula until normal calcium levels are maintained. A low mineral and low phosphate formula is advised for neonates with renal impairment.

Hypercalcemia (10): neonatal hypercalcemia is said to occur when total serum calcium level is >12 mg/dL or ionized calcium level >6 mg/dL. Most common cause is iatrogenic, though hyperplasia of the parathyroid and subcutaneous fat necrosis may be sometimes implicated as causative factors. When no cause is found, it is labeled as idiopathic. Maternal hypoparathyroidism and hypocalcemia, by its stimulatory action on fetal parathyroid gland, produce hypercalcemia in the baby. It may manifest as generalized irritability, lethargy, refusal of feeds or frank seizures. Treatment is IV saline and diuretics.

4.3.9 Hematological Disorders and Bleeding

(i) **Anemia** [30–33] is defined as hematocrit (Hct) or hemoglobin (Hb) concentration >2 SD below mean for the age. Normal Hct for a term baby is around 53%, while in a 32-week baby, it is 47%. Causes of neonatal anemia are:
   (a) **Blood loss** is the most common cause. This loss may be due to obstetric causes, or feto-maternal/feto-placental transfusion. In a twin pregnancy, there may be a twin to twin transfusion in which case one twin may be anemic while other may be polycythemic. Any cause leading to internal hemorrhage in the neonate may manifest as anemia. Repeated and frequent blood sampling is another reason of anemia in the neonate.
   (b) **Hemolysis -** Increased RBC breakdown may be due to intrinsic causes (hereditary RBC disorders, RBC enzyme defects (G6PD deficiency), RBC membrane defects (hereditary spherocytosis), and hemoglobinopathies (alpha thalassemia)), or extrinsic causes (immune hemolysis Rh or ABO incompatibility acquired e.g., infection, sepsis, or drug-induced hemolysis).
   (c) **Decreased RBC production** includes anemia of prematurity seen in preterm babies due to the transient deficiency of erythropoietin, congenital hypoplastic anemia (Diamond Blackfan syndrome), and anemia due to bone marrow suppression (congenital leukemia/infections/drug induced).

   The clinical signs and symptoms depend on the severity and the cause of anemia. The neonate besides looking pale may have both tachypnea and tachycardia, may be lethargic and feed poorly. Diagnosis is based on a detailed history (family, antenatal, obstetric, and postnatal history), and blood investigations. Radiological and imaging studies may also be required to establish a cause. Management depends on the cause and severity of the anemia. Prenatal fetal transfusion (intra uterine) may be needed in severe anemia resulting from hemolytic disease of the newborn (HDN). Postnatal anemia of prematurity may require treatment with human recombinant erythropoietin. Severe anemia may require packed RBC (PRBC) transfusion. Other causes of the anemia should be simultaneously treated.

(ii) **Neonatal polycythemia** [34] is defined as abnormally high RBC concentration with venous Hct >65%. It refers to a venous Hct greatly exceeding normal values for GA and postnatal age, and affects 0.4–5% of newborns. The effects of polycythemia are increase in the blood viscosity and reduced blood flow. With increase in blood viscosity, tissue oxygenation and perfusion are hampered and the tendency to form microthrombi sets in. The occurrence of these events in the cerebral cortex, kidneys, or adrenal glands can be disastrous, necessitating urgent management. The causes include increased erythropoiesis, as in utero hypoxia (SGA babies, postmature neonates, toxemia of pregnancy, severe maternal heart disease, maternal smoking, and other causes of placental insufficiency), maternal diabetes, neonatal hypothyroidism/hyperthyroidism, CAH, chromosomal abnormalities (trisomy 21), and transfusion related (which may occur due to delay in clamping of the cord or maternal to fetal or twin to twin transfusion). Clinical features—most polycythemic babies are asymptomatic and nonspecific symptoms

seen in many neonatal disorders, may be present, such as lethargy, hypotonia, cyanosis, and poor feeding. They may sometimes manifest with tachypnea, tachycardia, and other signs of congestive heart failure. They tend to have increased jaundice. Renal involvement may result in renal vein thrombosis, hematuria, and proteinuria. Diagnosis is established by the measurement of capillary or peripheral venous hematocrit. Management—if the venous Hct of a plethoric neonate or neonate with features suggestive of polycythemia is above 65%, a partial exchange transfusion (PET) is the treatment of choice, which involves removing some volume of blood and replacing it with saline.

(iii) **Bleeding neonate:** [35] In comparison with older children and adults the physiological immaturity in neonates results in both qualitative and quantitative differences in the various components of the hemostatic system. Most of the coagulation factors other than factors I, V, VII and platelets are reduced in term neonates. Preterms have the added disadvantage of increased vascular permeability as well as an inability to effectively utilize Vitamin K for the synthesis of coagulation factors, thus enhancing the vulnerability of these babies to bleeding, in utero or after birth. Fetal hemorrhage may be associated with twin-to-twin transfusion, APH secondary to bleeding from the fetal side of the placenta, feto-maternal transfusion, maternal anticoagulation therapy (Coumarin), and accidental injury of the placenta during caesarean section. Neonatal hemorrhage may occur due to defects in any of the steps of the hemostatic pathway, such as defects in the platelets or in the coagulatory mechanism. These defects may present in isolation or in combination. Bleeding may also result from defects in the vessel wall.

(iv) **Coagulation defects** include hemorrhagic disease of the newborn (HDN) and inherited coagulation disorders. HDN may be early, classic, or late depending on the time of presentation. Early HDN is seen in neonates born to mothers who have been on certain medications antenatally (anticonvulsants/antibiotics/antitubercular) and may manifest within the first 24 h with a large cephal hematoma, umbilical bleeding, or even with intracranial hemorrhage. Treatment is administration of Inj. Vitamin K and FFP if bleeding persists. Classic HDN manifests within 48–72 h due to lack of administration of prophylactic Vitamin K. The neonate may present with bleeding from the GIT, umbilical cord, nose, or from the circumcision site. The response to Vitamin K is dramatic. Late HDN presents after the first week of life, sometimes at 8–12 weeks, in infants on prolonged antibiotic therapy or with malabsorption (liver disease/cystic fibrosis). They may bleed from the GIT or present with mucocutaneous or intracranial bleeding. Parenteral Vitamin K therapy is the treatment of choice.

Inherited deficiency of coagulation factors rarely manifest in the neonatal period except when the deficiency is very severe. These include Hemophilia, Von Willebrand disease, and Dysfibrinogenemia. Treatment includes the administration of FFP or specific factor concentrates.

Platelet defects may be quantitative or qualitative. Neonatal thrombocytopenia has platelet count <150,000/cu mm. Most neonates with thrombocytopenia have a modest reduction in platelet count which is frequently

self-resolving. However, in the NICU, incidence of thrombocytopenia is quite significant. Quantitative platelet disorders are seen secondary to placental insufficiency, perinatal asphyxia, immune disorders, disseminated intravascular coagulation (DIC), intrauterine infections, neonatal sepsis, and NEC. Qualitative platelet disorders are uncommon and may be induced by drugs (indomethacin/antihistaminic) or may be part of a syndrome (Bernard Soulier syndrome).

Combined defects include coagulation defects as well as defects in the platelets and is classically seen in DIC. Various factors predispose to development of DIC, such as septicemia, hypothermia, asphyxia, prematurity, HMD, NEC, and severe Rh isoimmunization.

Vascular defects neonates with vascular malformations, hemangiomas, and trauma may also present with bleeding. Cavernous hemangiomas are large and deep set, and though they usually regress, they may be associated with complications which necessitate surgical removal. **C**linical features are determined by the site, severity, and cause of bleeding. A baby presenting with pallor, tachycardia, fast breathing, and falling blood pressure indicates a significant blood loss. Diagnosis in a bleeding neonate involves a battery of blood investigations. Management is by Vitamin K administration once blood has been collected for investigations. When the signs point to a significant blood loss, fresh blood transfusion will be required. In DIC and specific clotting factor deficiencies, FFP and platelets are indicated.

4.3.10 Perinatal Infections [36–41]

These include intrauterine (congenital) infections and neonatal sepsis. The fetus may get infected in utero, during the passage through the birth canal or after birth. Neonatal bacterial sepsis is one of the most common causes of neonatal mortality.

(i) **Congenital infections** occur due to transplacental passage of the infecting agent or secondary to the infection of the placenta. Ascending infection causing amnionitis may result in in-utero bacterial infection of the fetus. The acronym TORCH is used to list infections caused by toxoplasma, other (syphilis, varicella zoster, and parvovirus) rubella, cytomegalovirus, and herpes simplex. Infections acquired in utero may cause fetal loss, FGR, premature birth and postnatal effects in the form of hepatosplenomegaly, CNS abnormalities, bleeding disorders, and features specific to the infection. Toxoplasmosis may manifest with hydrocephaly, intracranial calcifications, chorioretinitis, and convulsions. Congenital syphilis may present with interstitial keratitis, meningoencephalitis, rashes, snuffles, periostitis, and chondritis. Parvovirus B 19 infection may result in hydrops fetalis due to severe anemia. Varicella Zoster infection may result in skin lesions, microcephaly, mental retardation, cataracts, and limb hypoplasia. Congenital rubella may result in cardiac defects (PDA, PS, VSD), meningoencephalitis, and multiple ophthalmic defects (cata-

ract, micro-ophthalmia, corneal opacities, retinitis). Cytomegalovirus may produce diffuse peripheral chorioretinitis, micro-ophthalmia, microcephaly, periventricular calcifications, and psychomotor retardation. Herpes simplex infections are acquired by direct contact with an infected mother, and signs usually appear 8–10 days after exposure as cutaneous lesions or features suggestive of sepsis. HIV infection may be acquired trans placentally, during delivery due to blood exposure or post natally from breast milk. Careful perinatal management reduces the risk of transmission. In congenital intrauterine infections, much of the damage has already occurred when the baby is born, so emphasis is more on prevention rather than treatment.

(ii) **Neonatal sepsis** includes various systemic infections such as septicemia, pneumonia, meningitis, osteomyelitis, arthritis, and urinary tract infection. The incidence varies between 1 and 8 cases per 1000 live births. Approximately 1/3rd of septic newborns develop meningitis. Several maternal and neonatal predisposing factors have been identified. Depending on the onset of symptoms, it may be **early onset** (within 72 hrs) or **late onset** (after 72 hrs). Clinical features—initial signs may be nonspecific, or may manifest as hyperthermia, refusal of feeds, poor cry and decreased activity. Involvement of the various systems may produce specific features. A high index of suspicion is necessary for early diagnosis which is then confirmed by a sepsis work up. Management is supportive including care in a thermoneutral environment. Appropriate antimicrobial therapy is the mainstay of the treatment.

4.3.11 Cutaneous Manifestations [42, 43]

An important part of neonatal management is skin care. The skin is a protective organ and any break in the skin may create an opportunity for infection to set in. Common skin problems in the neonate are—traumatic injuries—these may occur during instrumental delivery or following indiscriminate chemical use. Thermal injuries may occur from the use of warming devices. Necrosis -Due to extravasation of IV solutions may cause tissue necrosis and sloughing, while prolonged use of O_2 mask or nasal tubes may result in pressure necrosis, other skin conditions - Milia are pearly white or yellow papules (sebaceous follicles) seen mainly on the nose, forehead or chin and usually disappear within few weeks of life. Neonatal acne appears as raised red or white spots on the cheeks, nose and forehead, often develop within 2–4 weeks of birth, secondary to maternal androgen stimulation. It clears up on its own. Erythema toxicum is a macular, papular or occasionally vesicular rash over the face, trunk or extremities within first 48 hrs of life and is presumed to be allergenic in nature. It is self-limiting. Abnormalities of pigmentation may present as Mongolian spots, café-au-lait spots or Naevi. The baby may have diffuse hyperpigmentation or extensive or scattered hypopigmented areas on the skin. Since some of these conditions may be syndromic, diagnosis is essential. Vascular abnormalities include various hemangiomas (port wine stain, strawberry hemangiomas) which necessitate early diagnosis as they may be suggestive of a syndrome with more

generalized effects. The presence of purpuric lesions on the skin may be a pointer to the presence of intrauterine or perinatal infections. Transient neonatal pustular melanosis is a benign idiopathic skin condition characterized by pustules, vesicles, and pigmented macules. Lesions are usually transient and resolve spontaneously. Infections may be bacterial or viral. Bacterial may manifest as impetigo which appear as pustular lesions, commonly on the face or at the skin folds, and are caused primarily by Streptococcus pyogenes or Staphylococcus aureus. These are highly contagious, and treatment should be prompt and aggressive with the use of topical antibiotic for local skin care, and systemic antibiotics for more fulminant lesions.

4.3.12 Central Nervous System

(i) **Congenital CNS malformations** are caused by either isolated or a combined array of genetic and environmental factors. Common amongst these are NTD. This is described in a separate chapter.

(ii) **Intra Ventricular Hemorrhage (IVH)** is a highly fatal condition from bleeding in the subependymal germinal matrix which may be induced by fluctuations in the cerebral blood flow, increase in cerebral venous pressure, defects in coagulation, qualitative, or quantitative defects in platelet function or due to certain vascular defects. This causes cerebral parenchymal destruction which is in turn is responsible for the associated increased mortality and in case of survivors to seizures, cerebral palsy, mental retardation, and hydrocephalus. This is more common in preterm babies (<32 weeks), but may occur in term neonates with trauma or perinatal asphyxia. Treatment is symptomatic and supportive.

(iii) **Seizures** [44, 45] is the most distinctive manifestation of an underlying cerebral or biochemical abnormality. The incidence is inversely proportional to GA and BW, being twice as common in preterms. Neonatal seizures describe the occurrence of stereotyped muscular activity or autonomic changes secondary to abnormal electric discharges in the neonatal CNS. They are classified according to their clinical presentation and may be **Subtle seizures** (commonest, mild twitching of limbs, fixation of the eyes, repeated lip movements, tachycardia or bradycardia or occasionally with apnea, which may be missed sometimes), **Clonic seizures** (may be limited to one side of the body and may present as rhythmic movements of certain muscle groups), **Tonic seizures** (generalized or focal, may involve more sustained contraction of the muscles of the limbs and autonomic changes), and **Myoclonic seizures** (worst prognosis with regard to development of neurological sequelae and seizure recurrence) manifest as quick jerky movements produced by episodic contractions of limb muscles. The causes include perinatal complications (HIE), metabolic causes (hypoglycemia, hypocalcemia, hypomagnesemia, and IEsM), infections (meningitis, TORCH), ICH, developmental defects (hydrocephalus, microcephaly, microgyria, and porencephaly), maternal drug withdrawal, accidental injection of LA into fetal scalp, drug toxicity (phenothiazine), and dys-

electrolytemia). Diagnosis is by a detailed antenatal, natal, and postnatal and family history, various laboratory investigations, imaging studies, and EEG. Treatment must be prompt. The neonate is nursed in a thermoneutral environment, airway is kept patent and necessary circulatory, and respiratory support provided. After collection of all relevant samples, the metabolic parameters are attended to, and correction of hypoglycemia, hypocalcemia and hypomagnesemia addressed. The occurrence of seizure activity makes use of antiepileptic drugs (AED) mandatory, first choice being phenobarbitone. If, however, seizures persist then midazolam or lidocaine, and second line AEDs are brought into play. In case of pyridoxine dependency, injectable pyridoxine is administered. Exchange transfusion may be resorted to in overwhelming metabolic disorders, bilirubin encephalopathy, or accidental injection of LA. Phenobarbitone and other AEDs are continued till seizures are controlled and baby appears neurologically normal. However, if abnormal neurological signs persist, AEDs are continued and the baby reassessed at monthly intervals.

4.3.13 Cardiovascular System

Many neonatal CVS issues have been dealt with in other chapters in this book, so we shall focus on those CVS problems which have remained untouched so far (**shock**, **hypertension**).

(i) **Shock** [46–48] is an acute state of pathophysiological dysfunction due to inadequate and ineffective tissue perfusion. Though initially reversible, persistent tissue hypoperfusion may progress to a state of decompensation which is ultimately fatal. Shock may manifest with signs of tissue hypoperfusion (cold extremities, cyanosis, and prolonged CRT), hypotension, initial tachycardia progressing to end stage bradycardia, tachypnea, apnea, oliguria, hypotonia, and gradually increasing poor responsiveness.

Note: The recognition of hypotension in the neonate is important to prevent the secondary effects of cerebral ischemia or IVH. Treatment besides being prompt must be aggressive. In neonates, the BP varies according to the BW, GA and postnatal age. An arbitrary range of the normal systolic BP in preterm ranges between 50 and 62 mmHg and diastolic between 26–36 mmHg. In term babies, a systolic BP of 70 mmHg with a diastolic of 44 mmHg is considered normal. Shocks are classified into five types—(a) hypovolemic, (b) cardiogenic, (c) obstructive, (d) septic, and (e) distributive (*secondary to impairment of the vascular tone as is seen in sepsis and anaphylaxis)*. Various causes attributed are blood loss (IVH, abruptio placenta), congenital cardiac defects, birth asphyxia, pneumothorax, severe anemia, hypoxic ischemic cardiac/pulmonary injury, fulminant sepsis, and DIC. Treatment is preventive. Once the signs of shock appear, management should be aggressive since reversal of secondary complications is extremely difficult. Establishment of ade-

quate tissue perfusion and oxygenation is the goal of therapy with administration of fluids, appropriate blood products, and vasopressor infusion.

(ii) **Hypertension** [49–51] is seen in 3% of NICU admissions, and is usually secondary to cardiac or renal cause. In a term neonate a systolic of >90 mmHg with diastolic >60 mmHg, while in a preterm, a systolic >80 mmHg with diastolic >50 mmHg, is labeled as hypertension. Clinical features may be nonspecific, such as feeding difficulties, tachycardia, tachypnea, apnea, hematuria, lethargy, skin mottling, and rarely seizures. Causes of neonatal hypertension are listed as renal (renal artery stenosis, acute tubular necrosis, polycystic kidney disease, hydronephrosis, renal artery thromboembolism secondary to umbilical catheterization, renal cortical necrosis secondary to asphyxia or polycythemia, obstructive uropathy and renal tumors), CVS (coarctation of aorta, abdominal aortic atresia), endocrinal (CAH, hyperaldosteronism, hyperthyroidism, hypercalcemia and SIADH (syndrome of inappropriate secretion of ADH), and drug induced (aminophylline). Investigations include assessment of renal functions, TFT (thyroid function test), plasma rennin activity, cortisol, 17-OHP (hydroxy progesterone), aldosterone levels, Xray chest, renal USG and Echocardiography.

Treatment depends on the severity and cause of hypertension. Medications include Beta blockers, ACE inhibitors, diuretics, and calcium channel blockers.

Note: Coarctation of aorta is suspected when femoral pulses cannot be palpated, and arm BP is higher than in the legs. While treating hypertension it is important to avoid drastic falls in the BP during drug therapy.

4.3.14 Respiratory System

(i) **RDS** [52, 53] is one of the more common causes of NICU admission, with an incidence as high as 30% in preterm, 21% in post-term and 4% in term neonates. The National Neonatal Perinatal Database of India (NNPD) defines respiratory distress as the presence of any two of the three features—RR >60/min, subcostal/intercostals recession, and expiratory grunt/groaning. Additional features are nasal flaring and suprasternal retraction. RDS occurrence is largely dependent on the gestational age, surfactant deficiency (in preterm), and Transient Tachypnea of Newborn (TTN) (in post-term and term neonates). *RDS is discussed in another chapter of this book.*

(ii) **Apnea** is defined as cessation of breathing associated with bradycardia (HR<80 bpm) and changes in skin color (pallor/cyanosis). This pause in breathing may extend to 20 sec or more. Apnea may be a manifestation of immaturity of the respiratory system as seen in preterms or it may be a feature of other neonatal problems. Occurrence of apnea prompts immediate intervention in the form of ensuring airway patency, O_2 administration, treatment of the underlying cause, and other supportive measures.

(iii) **Bronchopulmonary dysplasia (BPD)** [54, 55] is a chronic lung disease of neonates predominantly preterms who require assisted ventilation and or O_2

therapy. BPD may develop due to several causes, prematurity being most important, others being mechanical ventilation, O_2 therapy, infections, cardiac defects (PDA), and genetic factors. Positive pressure ventilation (PPV) with high FiO_2 predisposes the immature lung to oxidative stress and barotrauma followed by defective lung repair. The presence of inflammation due to underlying infections worsens lung injury. Neonate may present with rapid shallow respiration, which may be paradoxical, and coarse crepitations and rhonchi on auscultation. Diagnosis is confirmed by radiological evidence of generalized haziness with occasional areas of pneumonic infiltrates or segmental atelectasis. Prevention forms an important part of **management**, with antenatal steroids to mothers at risk for premature labor. In the labor room, delayed cord clamping, early use of CPAP and selective use of surfactant, plays an important role in the reducing the severity and incidence of BPD. Time targeted O_2 use for resuscitation is also beneficial. Early initiation of parenteral feeding with rapid switch to enteral feeds also has a protective effect. Newer ventilation strategies are being adopted in the management of BPD. Surfactant, Vitamin A, methylxanthine, and steroids are the mainstay of preventional pharmacological strategies. Treatment is aimed at maintaining sufficient ventilation with minimal support, in which early CPAP plays an important role. When mechanical ventilation becomes imminent, regular titrating of the settings to minimize lung trauma is important. Pharmacological therapy forms a part of the treatment of established BPD. Significant morbidity with the development of asthma like symptoms and other compromised lung functions are the long-term sequelae in babies who recover from BPD.

4.3.15 Liver and GIT

(i) **Neonatal jaundice or hyperbilirubinemia** [56, 57] is the most common morbidity in the neonates in the 1st week of life, occurring in 60% of term and 80% of preterm babies. It is visible as a yellow staining of the skin and eyes resulting from an increase in the total bilirubin beyond 5 mg/dL. Detection and monitoring of jaundice are important since hyperbilirubinemia can have adverse effects and induce bilirubin encephalopathy. Pathogenesis of neonatal jaundice is explained by three main factors—increased bilirubin production due to larger volume and shorter life span of fetal RBCs, immature hepatic functions which is responsible for reduced hepatic uptake, conjugation and bilirubin clearance, and bilirubin reabsorption by the enterohepatic circulation.

Physiological jaundice is a normal occurrence in the nearly 60% term and 70% preterm neonates and is due to the physiological immaturity of the newborn to handle high bilirubin load. Detectable jaundice appears by 30–72 hrs, peaks by days 3–4 to a maximum of 12 mg/dL and then starts declining. In preterm babies the onset is similar, the peak is higher (15 mg/dL), appears slightly later (days 5–7), and decline is more gradual. Diagnosis is based on the time of appearance of jaundice, peak level, time of decline, and absence of pathological factors. **Pathological Jaundice** is defined as total bili-

rubin level more than 5 mg/dL in 24 hrs (beyond physiological limits). The distinction between physiological and pathological jaundice is arbitrary and the two conditions frequently overlap. Causes attributed are—blood-related (Feto maternal blood incompatibility, hereditary spherocytosis/ elliptosis, non-spherocytic hemolytic anemias, G6PD/pyruvate kinase deficiency, alpha thalassemia, drug-induced hemolysis, hematomas, cerebral or pulmonary hemorrhage, and polycythemia, metabolic and endocrine (galactosemia, familial nonhemolytic jaundice types 1and 2, Gilbert's disease, hypothyroidism, tyrosinosis, infants of diabetic mothers, hypermethioninemia, and hypopituitarism), Obstructive (biliary atresia, dubin johnson/rotor's syndrome, choledochal cyst, pyloric stenosis, intestinal atresia/stenosis, meconium plug syndrome, and Hirschsprung's disease), and Others (sepsis, intrauterine infections, RDS, HIE, and breast milk jaundice). Clinical assessment should be done 12 hrly intervals in hospital admitted babies and reassessed within 48 h postdischarge. Any doubt in the clinical assessment should be confirmed by a laboratory measurement of the total serum bilirubin. At risk neonates, should be kept under enhanced surveillance, such as preterm/SGA/IDM neonates, babies with a large cephalhematoma or significant bruising, newborn's with ABO/Rh incompatibility or G6PD deficiency, babies with siblings with history of significant jaundice, and a rate of rise of total bilirubin >5 mg/dL per day. Clinical tests are done in both the mother and the baby and depending on the level of the unconjugated bilirubin fraction further treatment suggested. Hospitalization and double surface phototherapy are offered to babies with the bilirubin level above the age specific cutoff. If however, the unconjugated bilirubin fraction is in the critical range or the neonate shows signs of bilirubin encephalopathy then a double volume exchange transfusion is done. In all cases, other supportive and specific treatment is continued.

Note: *AAP (American Academy of Pediatrics) has laid down age specific nomograms for phototherapy and exchange transfusion which are referred to for deciding the treatment to be followed in jaundiced neonates*.

Direct or unconjugated hyperbilirubinemia occurs due to ineffective or failed excretion of conjugated bilirubin into the duodenum. The level of conjugated bilirubin is >2 mg/dL. It may develop due to damage to the liver cells by infective/toxic or metabolic factors or due to obstruction in the bile flow, due to **extra or intrahepatic biliary atresia (EHBA).** EHBA results from obstruction or stenosis of the extrahepatic biliary tree and accounts for 25–30% cases of neonatal cholestasis. In the absence of medical or surgical intervention, the disease progresses rapidly to liver failure and death within 2–3 years. Primary treatment of EHBA is surgical and if applied early may effectively restore bile flow from the liver to the intestines. Liver transplant may be lifesaving in infants in whom this surgery fails.

Kernicterus or bilirubin encephalopathy occurs when unconjugated bilirubin crosses the blood brain barrier and gains access into the neonates' brain leading to varying degrees of neuronal injury. The unconjugated bilirubin level at which kernicterus occurs varies. However, the presence of Rh/ABO incompatibility along with family history of RBC abnormalities add to the

increased risk of development of pathological hyperbilirubinemia. Clinical features include lethargy, refusal of feeds, a shrill cry, opisthotonus, rigidity, sensory–neural deafness, visual abnormalities, and convulsions.

Prevention of neurotoxicity is the bottom line in the management of hyperbilirubinemia. Exchange transfusion remains the undisputed definitive mode of clearing blood of bilirubin.

(ii) **Necrotizing Enteroclitis (NEC)** [58–60] is one of the common GIT emergencies seen in the NICU. It generally occurs in premature formula fed neonates, by about 2–3 weeks age. It has also been seen in term and border line term babies. It results from damage to the intestinal tract, ranging from mucosal injury to full thickness necrosis and perforation. Depending on the severity of the intestinal damage, mortality rate may even go up to 50%. Clinical features include abdominal distension, erythema of abdominal wall, increased gastric aspirate, signs of peritonitis, and bloody diarrhea. There may be respiratory distress with frequent episodes of apnea/bradycardia, temperature fluctuations, pallor, hypo/hyperglycemia, and bleeding from various sites. Along with biochemical investigations, abdominal radiography helps in confirming the diagnosis with demonstration of Pneumatosis Intestinalis. Treatment is initially medical with the stoppage of oral feeds, gastric decompression, aggressive antibiotic therapy, and CVS and respiratory support. Development of pneumoperitoneum (indicative of intestinal perforation) makes surgical treatment mandatory.

(iii) **Intestinal obstruction** is one of the most frequent neonatal emergencies with an incidence of 1:2000 live births, and includes gastric outlet obstruction, duodenal obstruction, intestinal malrotation and atresia, Hirschsprung's disease, and anorectal malformations.

These are dealt with in detail in a separate chapter.

4.4 Conclusion

The immaturity of many organ systems and metabolic processes together with the "circulation in transition" in the neonate, more particularly the preterm neonate make the administering of anesthesia in these small human beings a more than usual risky proposition. The commonly encountered medical issues which need to be carefully looked into while planning any invasive/surgical procedure have been enumerated in the earlier pages. This discussion on anesthesia relevant medical issues in the neonate will help in guiding upcoming neonatal anesthetists in ensuring the administration of "safe" and effective anesthesia to these precious little souls.

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