

Pharmacology and Physiology in the Term Neonate

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A one-day-old male child presents for omphalocele repair. He was born to a 30-year-old G3P1 mother at 37 weeks of gestation via a planned Cesarean section for a prenatal ultrasonographic diagnosis of omphalocele. The mother was treated for gestational diabetes with daily insulin and has a history of hypothyroidism, for which she is prescribed L-thyroxin.

Pertinent findings on physical examination include midfacial hypoplasia and macroglossia. An intestinal sac is present and appears to be herniating through a defect in the umbilicus.

Vital signs: BP 60/32, P 164, T 35.8, RR 36, Sat 98% on room air. Weight: 4.4 kg, Apgar scores: 8, 8, 9.

associated with additional congenital defects. These occur in 25–50% of cases and include chromosome anomalies and cardiac defects. Omphalocele may be a component of the Beckwith–Wiedemann syndrome, which consists of hypertrophy of multiple organs. This syndrome is particularly relevant to the anesthesiologist as enlargement of the tongue may compromise the upper airway and be associated with difficult intubation. Pancreatic enlargement causes hyperinsulinism, which results in hypoglycemia and needs to be monitored intraoperatively. The key characteristic differences are summarized in Table 2.1.

Infants with gastroschisis are usually born at full term without additional isolated defects. The major pathophysiological difference between the two is that, in omphalocele, the intestinal contents remain covered with the peritoneal membrane, which protects the intestinal mucosa from the irritative effects of amniotic fluid and protects the infant from excessive evaporative fluid and temperature loss after delivery. Infants with gastroschisis lack this natural protective covering, and thus are more prone to dehydration, hypoglycemia, hypothermia, third-space fluid accumulation, electrolyte imbalance, acidosis, bleeding, and sepsis.

Management of omphalocele or gastroschisis begins immediately after birth. The extruded abdominal contents are covered with warm saline dressings and are encased in a sterile plastic bag or wrap to decrease fluid and temperature loss and discourage infection (Figure 2.2). A naso- or orogastric tube is placed for gastric decompression, normovolemia is maintained with intravenous hydration, and associated comorbidities are addressed prior to surgical repair. Antibiotics may be necessary if intestinal abnormalities are suspected.

Achieving a primary repair is the goal of surgery as failure to replace all of the intestinal contents back into the abdominal cavity increases postoperative

What Are the Differences Between Gastroschisis and Omphalocele?

Gastroschisis and omphalocele are the most common congenital abdominal wall defects with a prevalence of approximately 1:2,000–1:5,000 live births in the United States. Although each represents a distinct anatomical defect, their anesthetic considerations are the same. Each is a congenital defect that allows a portion of the intestinal viscera to extrude outside the abdominal cavity and both require surgical repair in the newborn period (Figure 2.1). Large defects are managed with a staged approach if primary closure is not possible.

An omphalocele occurs when the visceral organs fail to migrate from the yolk sac back into the abdomen early in gestation and the umbilical ring remains open; the defect is a central lesion and occurs at the insertion of the umbilicus. Gastroschisis is thought to result from an occlusion of the omphalomesenteric artery during early development. As a result, the abdominal viscera herniate through a rent in the abdominal wall, usually to the right of the umbilicus. Omphalocele is more likely than gastroschisis to be

Table 2.1 Characteristic differences between omphalocele and gastroschisis

	Omphalocele	Gastroschisis
Associated anomalies	Common	Rare
Defect location	Umbilicus	Right of umbilicus
Maternal age	Average	Young
Method of delivery	Cesarean/vaginal	Vaginal
Prognostic factors	Associated anomalies	Condition of bowel
Sac	Present	Absent
Surgical management	Not emergent	Emergent

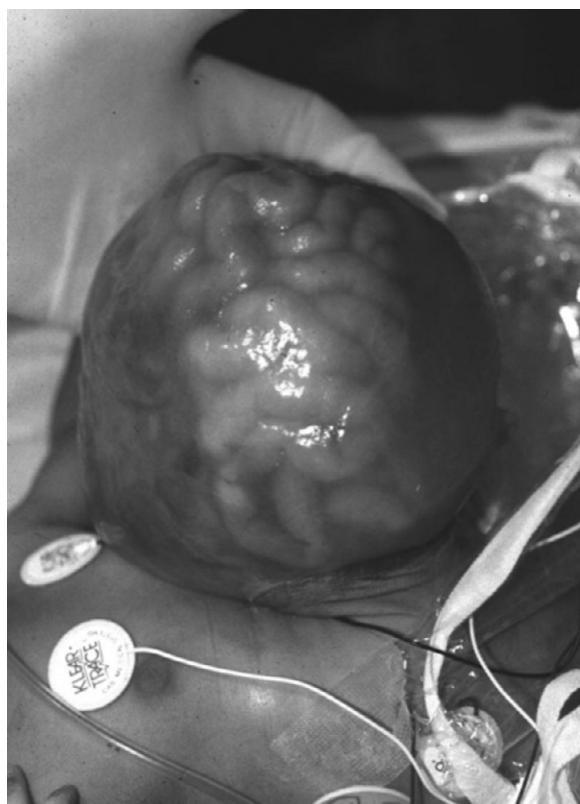


Figure 2.1 Omphalocele prior to surgery. Photograph: Ronald S. Litman, reproduced with parental permission.



Figure 2.2 Omphalocele silo. Large omphaloceles are treated with a silo and progressive constriction until primary repair. Photograph: Ronald S. Litman, reproduced with parental permission.

morbidity. However, in many cases where the abdominal cavity is too restrictive or when there is not enough skin to close the underlying defect, a partial replacement is performed, and the remaining external viscera are encased in a synthetic silo mesh allowing for complete repair to occur as a staged procedure.

In addition to its impact on intrathoracic pressure, increased intra-abdominal pressure may result in an abdominal compartment syndrome. When this occurs, venous compression leads to a decrease in preload and hypotension as well as lower limb venous congestion. High intra-abdominal pressures may lead to renal artery compression resulting in oliguria as well as decreased perfusion to the lower extremities. Bowel ischemia may also result, secondary to decreased perfusion. Adequate volume and blood replacement and full neuromuscular blockade must be maintained throughout the procedure to optimize the chances for successful primary closure.

What Are the Risks and Benefits of Staged Versus Primary Abdominal Wall Closure?

The optimal surgical management is related to the degree of bowel extrusion and the ability of the

abdominal cavity to accept bowel replacement. Infants undergoing primary closure generally require a shorter length of hospitalization and decreased utilization of parenteral nutrition.

Secondary closure techniques have evolved over the past few decades. The extruded bowel is maintained in a spring-loaded silo bag. The bag keeps the bowel intact and protected from environmental contact. This mechanism allows for daily bedside reduction of the bowel over one to two weeks providing time for the abdominal cavity to expand and accommodate without elevating abdominal pressures and interfering with ventilation.

What Are the Anesthetic Considerations for Surgical Intervention of Patients with Gastroschisis or Omphalocele?

Considerations for induction of general anesthesia are similar to those for any newborn infant with a presumed increased risk of a “full stomach” secondary to intestinal obstruction. A modified rapid sequence intubation (RSI) is performed using gentle breaths. Some pediatric anesthesiologists will prefer to temporarily remove the nasogastric tube during induction to facilitate airway management.

There are several intraoperative adverse physiologic derangements that may occur when the surgeon attempts to place a large volume of abdominal contents back into a small, restrictive abdominal cavity. Cephalad displacement of the diaphragm due to the increase in abdominal contents may significantly decrease functional residual capacity (FRC) and tidal volume, which can lead to difficult ventilation, development of atelectasis, and hypoxemia. During the repair, the anesthetist may frequently need to use manual ventilation to maintain adequate tidal volumes in response to rapid changes in lung compliance. The presence of hypoxemia despite maximal ventilation may preclude completion of a primary repair. Therefore, intraoperative management should focus on ventilatory pressures, temperature regulation, and volume status. Rapidly increasing peak pressures (when using volume-controlled ventilation) or a significant decline in tidal volume (when using pressure-controlled ventilation) should raise suspicion of abdominal pressure elevation that will compete with the ability to provide adequate minute ventilation. Fluid administration, postoperative fluid

shifts, and associated bowel edema can lead to increases in abdominal compartment pressure, low cardiac output, and renal hypoperfusion.

These patients are at risk of hypothermia from exposed abdominal contents. Similarly, fluid evaporative losses are common, especially with gastroschisis where the surface of the intestine is uncovered and exposed to the atmosphere.

All infants, except those with the most trivial repairs, remain intubated and mechanically ventilated in the postoperative period. Abdominal compartment syndrome and respiratory compromise may continue postoperatively; therefore, paralysis and adequate sedation with an opioid infusion are essential for optimal management.

What Are the Pertinent Preoperative Diagnostic and Laboratory Evaluations Suggested for These Patients?

The diagnosis of omphalocele should alert the clinician to the possibility of numerous coexisting congenital defects. Intrapartum diagnosis should prompt fetal echocardiography and even postnatal echocardiographic evaluation, as the incidence of concomitant cardiac anomalies is as high as 25%. Pulmonary hypoplasia often necessitating ventilatory support, cloacal extrophy, and anomalies associated with VACTERL syndrome may be present. Normal karyotype patients have an incidence of other abnormalities that is as high as 80%, stressing the importance of a complete perioperative evaluation. Chromosomal abnormalities (especially trisomies 13, 18, and 21) exist in nearly 50% of patients with omphalocele. Unlike gastroschisis, the herniation in omphalocele patients is enclosed and amenable to supportive therapy while workup is obtained. Intravenous access should be obtained, and fluid resuscitation initiated. Glucose should be evaluated frequently, and if low, it should raise suspicion for Beckwith-Wiedemann syndrome. Careful cardiopulmonary workup should ensue prior to closure in a stable neonate. The bowel should be wrapped to minimize heat and evaporative loss, which, while less extreme compared with gastroschisis patients, remains greater than in patients with a closed abdomen. Naso- or orogastric tubes should be placed for decompression.

The assessment for comorbidities, while less common in patients with gastroschisis, should include

evaluation for meningocele, limb abnormalities, and intestinal atresia. Intravenous access and maintenance of fluid homeostasis is vital as well as frequent evaluation of electrolytes. In the interim, exposed bowel should be wrapped with sterile dressing and plastic to minimize infection, evaporative fluid loss, and temperature loss. The bowel should be evaluated frequently for early recognition of ischemic changes possibly due to mesenteric kinking.

What Is the Prognosis for Patients with Gastrochisis and Omphalocele?

The prognosis for omphalocele is related to the number and severity of associated congenital anomalies. The optimal mode and timing of delivery is debated although most neonates with omphalocele are delivered via cesarean section for fear of abdominal sac rupture with labor.

Prognosis for gastrochisis is generally determined by the degree of bowel injury and bowel atresia. Exposure of the bowel to amniotic fluid and degree of bowel constriction dictates the severity of injury. Gastrochisis patients have a greater incidence of developing necrotizing enterocolitis when compared with the general population. The optimal mode and timing of delivery is still debated.

What Is the Beckwith–Wiedemann Syndrome?

The incidence of Beckwith–Wiedemann is approximately 1 in 13,000–14,000 children without gender predominance.

What Is the General Phenotypic Appearance of Children with Beckwith–Wiedemann Syndrome?

Children with Beckwith–Wiedemann syndrome display signs of accelerated growth, including height and weight. Common facial abnormalities include prominent eyes, midfacial hypoplasia, macroglossia or hemihypertrophy, prominent mandible, and earlobe anomalies.

Macroglossia can lead to sleep disordered breathing and sleep apnea. In addition, hemihypertrophy can often pose difficulty with airway management.

What Are the Associated Malformations Found in Patients with Beckwith–Wiedemann Syndrome?

Beckwith–Wiedemann is a disorder of increased growth (somatic overgrowth) with a predisposition to development of embryonal tumors. Malformations include abdominal wall defects and visceromegaly of one or more of the following: heart, liver, spleen, pancreas, kidneys and adrenals. Neonatal hypoglycemia occurs in up to 50% of children with Beckwith–Wiedemann syndrome due to pancreatic islet cell hyperplasia and hyperinsulinemia.

Cardiac anomalies are present in approximately 20% of patients with Beckwith–Wiedemann syndrome. Renal anomalies are common, including medullary dysplasia, nephrocalcinosis, or nephrolithiasis.

Patients with Beckwith–Wiedemann syndrome are predisposed to development of embryonal tumors especially within the first decade of life. Common tumors include Wilms, hepatoblastoma, rhabdomyosarcoma, neuroblastoma, and adrenocortical carcinoma. The risk of tumor development may be greater in children with hemihypertrophy and nephromegaly.

Discuss the Anesthetic Work-Up for a Patient with Beckwith–Wiedemann Syndrome

Patients with Beckwith–Wiedemann syndrome should undergo thorough preoperative evaluation for non-emergent cases. Examination should identify comorbidities especially cardiac anomalies and renal impairment. Complete airway examination and anticipation of potentially difficult airway. Neonatal hypoglycemia is common in this population and should be addressed. Macroglossia can predispose patients to postoperative airway obstruction.

Which Patients Are at Risk for Developing Neonatal Hypoglycemia?

This patient from this case stem has significant risk factors for being unable to maintain glucose homeostasis in the perioperative period. Being the infant of a diabetic mother places a neonate at risk for perinatal hypoglycemia. This results from fetal exposure to elevated maternal serum glucose levels. Fetal insulin secretion is increased to meet the demands of this

glucose load. After delivery, maternal glucose exposure declines precipitously while leaving the neonatal pancreas oversecreting insulin, resulting in perinatal hypoglycemia. These infants are monitored closely, often in a NICU setting, and may require maintenance infusions of glucose-containing solutions and frequent serum glucose checks. When the perinatal period and perioperative periods coincide, the anesthesia provider must remain vigilant to avoid periods of hypoglycemia, especially during general anesthesia when signs of low serum glucose are masked.

During the neonatal period, the ability for the immature liver to undergo gluconeogenesis and glycogenolysis is incomplete. After birth, the neonates' serum glucose concentration falls, rapidly stabilizing after 3 h. Plasma insulin levels fall and glucagon is mobilized. This leads to a marked decrease in neonatal hepatic glucagon stores and thus serum glucose must be carefully monitored.

During the Procedure, the Anesthesia Team Infuses D10 as Maintenance Fluid; Does This Reduce the Need for Repeated Glucose Checks?

Surgical stress response (causing catecholamine release), infusion of glucose-containing fluids, and administration of corticosteroids (during anesthesia) can lead to hyperglycemia. The sequelae of hyperglycemia in the perioperative period include: increased risk of surgical site infection, poor wound healing, and the potentially associated increased risk of intraventricular hemorrhage and retinopathy of prematurity (in preterm infants).

Elevated hematocrits, not uncommon in neonates, may result in abnormally low glucose levels, which is especially marked when the glucose levels are low. Additionally, arterial samples can have a 10–15% increase in glucose compared with venous samples.

On Postoperative Day 3, You Are Called to Evaluate the Patient for Visible Icterus: What Is the Mechanism for Jaundice in the Neonatal Period?

Neonatal jaundice with visible icterus occurs in up to 80% of healthy neonates born after 35 weeks of

gestation. The majority of neonatal jaundice resolves spontaneously with no residual effects. A small subset of patients, if left untreated, will go on to develop significant hyperbilirubinemia and encephalopathy. If jaundice is observed within the first 24 h of life, hemolytic causes must be considered.

Total bilirubin is the difference between bilirubin production and bilirubin metabolism.

Bilirubin production is the result of heme catabolism. Heme is broken down into biliverdin, and further metabolized into bilirubin. Bilirubin is conjugated in hepatocytes by the enzyme UDP-glucuronyltransferase 1A1 (UGT1A1) and excreted into the bile ducts and bowel for elimination. In neonates, bilirubin also enters the enterohepatic circulation where it is converted into the unconjugated form once again, is resorbed, and returns to the liver for re-processing.

Hyperbilirubinemia results from an imbalance between bilirubin production and excretion. Neonates have only 1% of the UGT1A1 enzyme activity compared with adults. This becomes the rate-limiting step and thus makes neonates prone to hyperbilirubinemia. With most neonates, elevated serum bilirubin can be attributed to immature conjugation abilities. The minority of patients have underlying conditions such as Crigler-Najjar syndrome (abnormal UGT1A1) amongst others. Additionally, patients with G6-PD and RBC membrane deficiencies may suffer from hemolysis which can contribute to hyperbilirubinemia.

For the patient in this case, on postoperative day three, hemolysis may be a contributor. Sepsis can also lead to hyperbilirubinemia and should always be excluded especially in a postoperative patient.

What Is Kernicterus, and How Is It Prevented?

Kernicterus is a potentially devastating consequence of excessive and untreated hyperbilirubinemia. The excess bilirubin damages the basal ganglia resulting in chronic athetoid movements and cerebral palsy. The risk is exponentially related to the serum bilirubin, with levels >25 mg/dL. With improved detection and treatment strategies, kernicterus is rare in the Western world. Treatment focuses on prevention with screening tests, early intervention with

phototherapy to aid conjugation and exchange transfusion for recalcitrant patients.

Describe the Process of Protein Synthesis by the Neonatal Liver

The liver hepatocytes synthesize most plasma proteins including alpha-fetoprotein and albumin, which reach adult levels by term. All coagulation factors are produced in the liver with the exception of factor 8 which is produced in the liver and vascular endothelium. The serum concentration of coagulation factors remains low in the first few days following birth. In the United States, neonates receive an intramuscular injection of vitamin K, to increase the vitamin K dependent factors. Low factor levels may become a consideration in neonates undergoing immediate surgical procedures. This may be complicated by dilutional coagulopathy through crystalloid administration.

Identify the Differences in the Neonatal Hematologic System

Term neonates experience a physiologic anemia around 10–12 weeks of age with a decrease in hematocrit to approximately 30%. The neonate has a normal level of platelets at birth although with reduced clot strength. Early thrombocytopenia <72 h after birth is often due to maternal–fetal interaction while late thrombocytopenia >72 hrs should prompt evaluation of sepsis or necrotizing enterocolitis.

With respect to hemostasis, the neonate has reduced levels of factors 2, 7, 9, 11, and 12. However, there is a decrease in proteins C and S and an increase in vWF which partially offsets the decrease in factors. Neonates have a prolonged PT and PTT but a slightly shorter bleeding time.

How Does the Immaturity of the Fetal Liver Effect Drug Metabolism?

The liver metabolizes drugs through biotransformation followed by excretory transport. These pathways are immature in neonates.

Hepatic biotransformation is divided into phase 1 (oxidation, reduction, and hydrolysis) via the

cytochrome P450 pathway and phase 2 (conjugation/glucuronidation). The pathways mature throughout the first year of life. The concentrations of the cytochrome P450 proteins at birth are approximately 30% of adult concentrations, reaching normal levels at 1 year of age. The neonates have limited enzymatic glucuronidation and conjugation ability, which limits their metabolic capability such as the breakdown of bilirubin and morphine.

The neonates decreased ability to metabolize drugs results in increased serum levels and increased elimination half-lives. The metabolic activity is enzyme dependent and has significant inter-patient variability.

Describe the Differences in Renal Function Between the Neonatal and Adult Patient

Kidney function undergoes constant change in the neonatal period. As such, the ability of the immature kidney to deal with hypovolemia by concentrating urine is poor as is the ability to process large solute loads (Table 2.2). The differences between neonatal and adult renal function is summarized in Table 2.2.

What Are the Determinants of Neonatal Oxygenation?

Neonatal oxygen delivery depends on the amount of inspired oxygen, V/Q matching, cardiac output, and the type, concentration, and affinity of the hemoglobin. Oxygen is transported predominantly by hemoglobin with a minimal contribution of dissolved oxygen in the plasma. Dissociation of oxygen from hemoglobin is closely related to the oxygen dissociation curve and its determinants including temperature, 2,3 DPG, $[H^+]$, and hemoglobin variants. Fetal hemoglobin (HgF) has an increased O_2 affinity allowing for greater extraction of O_2 from the placenta. HgF predominates at birth and decreases to approximately 2% of total hemoglobin by 1 year. At birth, the oxygen requirement increases by >100%. To cope with these changes, the neonate has multiple adaptive mechanisms occurring at or prior to birth. Near term the fetus begins producing hemoglobin A (HgA) which, despite its lower

Table 2.2 Characteristic differences between neonatal and adult renal function

	Neonate	Adult
Renal blood flow	10% of cardiac output	25% of cardiac output
Glomerular filtration rate (mL/min/1.73 m²)	<2 Weeks – 40 >2 Weeks – 60	100–125
Concentrating ability	<6–12 Months – Low 700 mOsm	1,400 mOsm
Creatinine	Active reabsorption in first days of life Elevated serum creatinine	Not actively reabsorbed Serum levels related to renal function
Fractional excretion sodium (FENa)	<2 Weeks, Elevated	Relative to kidney function and hydration status
Extracellular fluid (ECF)	At Birth: 40% of TBW <6 Months: 30% of TBW	20% of TBW

affinity for oxygen promotes oxygen transport to tissues. The neonate has an increase in 2,3 DPG which, aside from decreasing pH also promotes transfer of oxygen to tissues.

The transitional mechanism from placental to pulmonary oxygenation at birth is discussed in the cardiovascular section.

How Do Lung Volumes in Children Compare to Those in Adults?

Pulmonary mechanics is related to the compliance of the chest wall and lung. In neonates, the chest wall, mostly composed of cartilage has the tendency to collapse outward while the lung is more prone to inward collapse. This imbalance is partially offset by the increase in laryngeal tone during exhalation and the increase in respiratory rate.

Resistance to flow is also significantly greater in neonates as a result of decreased airway diameter. In small children, minor inflammation or reduced airway diameter causes an exponential increase in resistance to gas flow. The characteristic differences between neonatal and adult pulmonary functions are highlighted in Table 2.3.

Neonatal Apnea

Neonatal apnea is defined as cessation in respiratory flow of greater than 15–20 seconds or <15 seconds if accompanied by oxygen desaturation <90% and bradycardia of <100 beats/min.

Table 2.3 Characteristic differences between neonatal and adult pulmonary function

	Neonate	Adult
Respiratory rate (breaths/min)	50	12
Tidal volume (cc/kg)	6–8	6–7
Minute ventilation (cc/kg/min)	200–250	90
Functional residual capacity (cc/kg)	25–30	30
VO ₂ oxygen consumption (cc/kg/min)	6–8	3–4
PaO ₂ (mmHg)	60–90	80–100
Dead space (cc/kg)	2	2

Central apnea is cessation of air flow in the absence of respiratory effort. In obstructive apnea, there is cessation of flow with preserved respiratory efforts. In either case, there is often a closure of the glottis with pharyngeal or laryngeal collapse.

What Are the Etiologies of Neonatal Apnea?

Neonatal apnea may have central or obstructive components or occur in combination.

The incidence of neonatal apnea is inversely related to gestational age.

Neonatal apnea is thought to result from immaturity of the central mechanism for regulation of

breathing and an immature response to hypoxia and hypercarbia and exaggerated protective response to airway stimulation.

What Are the Risk Factors for Neonatal Apnea?

Risk factors for development of neonatal apnea include: airway structural anomalies, ambient temperature fluctuation, anemia, cardiac anomalies, central nervous system (CNS) disorders, chronic lung disease, infection, metabolic derangement, necrotizing enterocolitis, prematurity, and sepsis.

Neonates are exquisitely sensitive to medication effects including general anesthetics, magnesium, prostaglandin, and opioids.

What Are the Treatments for Neonatal Apnea?

Treatment should start with a focus on identifying patients at risk for apnea, avoidance of inciting factors and adjustment of anesthetic technique when appropriate. Regional anesthetics provide a lower incidence of postoperative neonatal apnea compared with general anesthesia. Continuous positive pressure, including nasal CPAP (for obstructive apnea) and caffeine supplementation are commonly used to decrease the incidence of neonatal apnea. Gentle tactile stimulation will often break the apneic cycle.

Suctioning the airway prior to extubation may help to reveal an exaggerated response to stimulation leading to breath holding. Postoperative neonatal apnea is discussed in greater detail in Chapter 18.

The preanesthesia evaluation should include:

1. Identification of neonates having received treatment for apnea.
2. Consideration of the safest anesthetic and avoidance of inciting agents.
3. Postoperative discharge planning in cases of post gestational age <60 weeks.
4. Identification and avoidance of apnea risk factors.

Review the Differences Related to Spinal Anesthetics Between Neonates and Adults

There are numerous physiologic differences that must be considered when performing a spinal anesthetic on a neonate.

At birth, the spinal cord terminates around L3 to L4 and at L1 at approximately 1 year of age. Thus, spinals in neonates should be placed at L4–5 or L5–S1 to avoid injury. The volume of local anesthetic required is greater in the neonate owing to a greater cerebrospinal fluid (CSF) volume of 4 cc/kg compared with 2 cc/kg in adults. Additionally, 50% of the neonate's CSF remains in the spinal canal compared with 25% in adults leading to dilution of local anesthetics. The neonate's spinal cord has increased blood supply compared with adults and results in increased uptake of local anesthetic and a shorter duration of action. Spinal anesthetics are discussed in greater detail in Chapter 7.

Identify the Differences in Metabolism of Fentanyl and Morphine in the Neonate Compared to the Adult

Neonates require significantly less morphine than adults or older children, as their ability to metabolize morphine is not fully complete. Following administration, a neonate will display a greater serum concentration of morphine, and its active metabolites, morphine-3 and morphine-6 glucuronide, compared with an adult. Clearance of fentanyl is also reduced in the neonatal period to 70–80% of adult clearance and normalizes at about two weeks.

How Does Minimum Alveolar Concentration Relate to Age?

The minimum alveolar concentration (MAC) for inhaled anesthetic agents is directly related to age. For isoflurane and desflurane, MAC is high in neonates, peaks during infancy, and steadily declines throughout life. The MAC for sevoflurane peaks in the neonatal period and steadily declines throughout life.

What Is the Incidence of Congenital Hypothyroidism (CH)?

The incidence of CH is approximately 1 in 2,000–4,000 live births.

What Are the Clinical Characteristics of CH?

Newborn screening programs remain one of the greatest advances in medicine aimed at reducing preventable morbidity and mortality. Children with CH are generally normal at birth, emphasizing the

importance of screening. Less than half of children with CH show signs by three months and only 70% will show signs by twelve months. The incidence of CH is greatest in premature infants with nearly 50% showing signs of CH when born at <30 weeks of gestation. Low or absent thyroid hormone, if untreated leads to mental retardation, severe growth restriction and brain developmental restriction. These children often have deficits in attention, arithmetic, memory and verbal skills in addition to abnormal muscle tone, ataxia, poor coordination, and strabismus. Congenital hypothyroidism is the leading cause of preventable mental retardation.

What Risks Are Associated with Maternal Hypothyroidism?

Maternal thyroid hormone is critical to fetal neurodevelopment in early pregnancy. Infants born to

mothers with untreated hypothyroidism are at risk for mental retardation, hearing loss, and a variety of motor delays. Mothers should be screened for hypothyroidism in early pregnancy. Mothers with known hypothyroidism often require increased supplementation to account for the needs of the developing fetus.

What Are the Main Disorders Screened for by the Neonatal Screening Programs?

Neonatal screening programs vary by state. These screening tests generally focus on disorders of fatty acids, amino acids, organic acids, hemoglobinopathies, hypothyroidism, adrenal hyperplasia, biotinidase deficiency, galactosemia, and cystic fibrosis.

Suggested Reading

- Beardsall K. Measurement of glucose levels in the newborn. *Early Hum Dev.* 2010;86(5):263–7. PMID: 20542649.
- Blazer S, Zimmer EZ, Gover A, Bronshtein M. Fetal omphalocele detected early in pregnancy: associated anomalies and outcomes. *Radiology.* 2004;232:191–5. PMID: 15220502.
- Brantberg A, Blaas HG, Haugen SE, Eik-Nes SH. Characteristics and outcome of 90 cases of fetal omphalocele. *Ultrasound Obstet Gynecol.* 2005;26:527–37. PMID: 16184512.
- Büyükgebiz A. Newborn screening for congenital hypothyroidism. *J Clin Res Pediatr Endocrinol.* 2013;5S1:8–12. PMID: 23154158.
- Christison-Lagay ER, Kelleher CM, Langer JC. Neonatal abdominal wall defects. *Semin Fetal Neonatal Med.* 2011;16:164–72. PMID: 21474399.
- Coté CJ, Zaslavsky A, Downes JJ, et al. Postoperative apnea in former preterm infants after inguinal herniorrhaphy. A combined analysis. *Anesthesiology.* 1995;82:809–22. PMID: 7717551.
- Davis RP, Mychaliska GB. Neonatal pulmonary physiology. *Semin Pediatr Surg.* 2013;22:179–84. PMID: 24331091.
- Diaz-Miron J, Miller J, Vogel AM. Neonatal hematology. *Semin Pediatr Surg.* 2013;22:199–204. PMID: 24331095.
- Grijalva J, Vakili K. Neonatal liver physiology. *Semin Pediatr Surg.* 2013;22:185–9. PMID: 24331092.
- Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. *J Pediatr.* 2012;161:787–91. PMID: 22727868.
- Hiraki S, Green NS. Newborn screening for treatable genetic conditions: past, present and future. *Obstet Gynecol Clin North Am.* 2010;37:11–21. PMID: 22727868.
- Kaplan M, Bromiker R, Hammerman C. Hyperbilirubinemia, hemolysis, and increased bilirubin neurotoxicity. *Semin Perinatol.* 2014;38:429–37. PMID: 25284470.
- Lerman J, Robinson S, Willis MM, Gregory GA. Anesthetic requirements for halothane in young children 0–1 month and 1–6 months of age. *Anesthesiology.* 1983;59:421–4. PMID: 6638549.
- López T, Sánchez FJ, Garzón JC, Muriel C. Spinal anesthesia in pediatric patients. *Minerva Anestesiol.* 2012;78:78–87. PMID: 22211775.
- Maitra S, Baidya DK, Khanna P, et al. Acute perioperative pain in neonates: An evidence-based review of neurophysiology and management. *Acta Anaesthesiol Taiwan.* 2014;52:30–7. PMID: 24999216.
- Nandi-Munshi D, Taplin CE. Thyroid-related neurological disorders and complications in children. *Pediatr Neurol.* 2015;52(4):373–82. PMID: 25661286.
- Nargoian C, Ririe DG, Bennun RD, et al. Hemifacial microsomia: anatomical prediction of difficult intubation. *Paediatr Anaesth.* 1999;9:393–8. PMID: 10447900.
- Sale SM. Neonatal apnoea. *Best Pract Res Clin Anaesthesiol.* 2010;24:323–36. PMID: 21033010.

- Sulemanji M, Vakili K. Neonatal renal physiology. *Semin Pediatr Surg.* 2013;22:195–8. PMID: 24331094.
- Weksberg R, Shuman C, Beckwith JB. Beckwith-Wiedemann syndrome. *Eur J Hum Genet.* 2010;18:8–14. PMID: 19550435.
- Yaster M, Scherer TL, Stone MM, et al. Prediction of successful primary closure of congenital abdominal wall defects using intraoperative measurements. *J Pediatr Surg.* 1989;24:1217–20. PMID: 2531789.