Neonatology

2

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DEFINITIONS

Live birth

- Live birth occurs when a fetus, whatever its gestational age, exits the maternal body and subsequently shows any signs of life, such as voluntary movement, heartbeat, or pulsation of the umbilical cord, for however brief a time and regardless of whether the umbilical cord or placenta is intact

Gestational age (GA)

- The number of weeks in a pregnancy since the 1st day of the last menstrual period or the corresponding age of gestation as estimated by a more accurate method if available. Such methods include an early obstetric ultrasonography or by adding 14 days to a known duration since fertilization (in patients who have undergone in vitro fertilization)

Small for gestational age (SGA)

- Birth weight (BW) < 10th percentile for the given GA

Large for gestational age (LGA)

- BW > 90th percentile for the given GA

Low birth weight (LBW)

- BW < 2500 g regardless of the GA

Very low birth weight (VLBW)

- BW < 1500 g

Extreme low birth weight (ELBW)

- BW of less than 1000 g (2 lb., 3 oz)

Preterm

- An infant born at < 37 weeks GA

Term

- An infant born between the 37 0/7 and 41 6/7 weeks of gestation
  - Early term: Between 37 0/7 and 38 6/7 weeks of gestation
  - Full term: Between 39 0/7 and 40 6/7 weeks of gestation
  - Late term: Between 41 0/7 and 41 6/7 weeks of gestation

Post-term

- An infant born after 42 0/7 weeks of gestation

PRENATAL CARE

Routine Prenatal Laboratory Tests

- Urine for protein, glucose, and bacteriuria
- Complete blood count (CBC)
- Blood type and Rh
- Red blood cell (RBC) antibodies
- Hepatitis B surface antigen
- Rapid plasma reagin (RPR) or venereal disease research laboratory test (VDRL)

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Table 2.1 Significant fetal ultrasonographic anatomic findings and postnatal management

Prenatal US finding	Causes	Postnatal evaluation
Dilated cerebral ventricles	Hydrocephalus, Dandy-Walker cyst, agenesis of corpus callosum	Serial head US or MRI, evaluation for other system anomalies
Choroid plexus cyst	Trisomy 18; can be a normal variant	Karyotype if indicated, Head US or MRI scan, evaluation for other system anomalies
Nuchal pad thickening	Cystic hygroma, Turner syndrome, trisomy 18 or 21	Evaluation for other system malformation, karyotype if indicated
Dilated renal pelvis	Ureteropelvic junction obstruction, vesicoureteral reflux, posterior urethral valve, ectopic ureterocele	Renal ultrasound between day 5 and 7 and at 4–6 weeks of age; voiding cystourethrogram and prophylactic antibiotic if indicated

MRI magnetic resonance imaging, *US* ultrasonography

- Human immunodeficiency virus (HIV) screening
- Rubella antibodies
- Blood work for neural tube defects and chromosomal abnormalities, if indicated
- Ultrasound at 18–20 weeks, if indicated (Table 2.1)
- Glucose challenge and/or glucose tolerance tests between 24 and 28 weeks gestation (for diagnosing gestational diabetes)
- Vaginal and rectal culture for group B streptococcus (GBS) between 35 and 37 weeks gestation, and intrapartum antibiotics if indicated
- Education about nutrition, vitamins, and pregnancy course
- Prenatal care delayed until after the first trimester is associated with higher infant mortality rate

General neonatal risks

- Delayed prenatal care
- Maternal age: Teens and > 40 years of age
- Male infants have higher mortality rates than female infants
- Multiple births
- Placental bleeding – placenta previa, placental abruption
- Uterine abnormalities
- Premature rupture of membranes
- Preterm delivery
- Chorioamnionitis
- Maternal drug abuse, e.g., cocaine
- Bacterial vaginosis

Known risk factors for prematurity

- Placental bleeding
- Uterine abnormalities
- Use of drugs such as cocaine
- Smoking
- Alcohol intake
- Maternal chronic disease
- Premature rupture of membranes
- Prior history of preterm delivery
- Chorioamnionitis
- Bacterial vaginosis
- Preeclampsia or hypertension
- Maternal age: < 18 years and > 35 years

Factors associated with high mortality rate in preterm infants

- Younger GA
- Male sex
- 5 min Apgar < 4
- Persistent bradycardia at 5 min
- Hypothermia
- Intrauterine growth restriction

Umbilical Cord

- Umbilical cord has two arteries and one vein
- Single artery umbilical cord can be associated with other organ anomalies, e.g., heart and kidneys
- Umbilical cord length is about 55 cm; umbilical cord < 40 cm is short and can be associated with fetal complications, e.g., amniotic band and arthrogryposis
- Longer cord more than 55 cm may be associated with knots, prolapse, or may entwine the fetus

Placenta

- **Placenta accreta**: Develops when the chorionic villi attaches to the myometrium of the uterine wall rather than being restricted within the decidua basalis; may occur because of previous trauma, e.g., previous cesarean section, and curettage
- **Placenta increta**: Develops when the chorionic villi invades into the myometrium
- **Placenta percreta**: Develops when the chorionic villi invades through the myometrium, sometimes extending to nearby organs such as the bladder, resulting in serious bleeding
- **Placental abruption**:
  - Develops when the placenta separates from the wall of the uterus, either partially or completely, before birth of the infant
  - Hemorrhage into the decidua basalis occurs as the placenta separates from the uterus
  - Vaginal bleeding usually follows, although a concealed retroplacental hemorrhage is possible

Cesarean Section (C-section): Indications

- Previous C-section
- Fetal distress
- Dystocia
- Fetal malpresentation
- Placenta previa
- Placenta accreta, increta, and percreta
- Other

Fetal Distress

Definitions

- **Nonstress test** is the most common noninvasive test; it monitors fetal heart rate accelerations that follow fetal movement over time
- **Early deceleration** is associated with head compression during uterine contraction, resulting in vagal stimulation and slowing of the heart rate
- **Variable deceleration** is associated with compression of the umbilical cord
- **Late deceleration** is associated with uteroplacental insufficiency. Thus, maternal hypotension, uterine hyperstimulation, preeclampsia, or any other factor that reduces uterine blood flow and limits effective oxygenations of the fetus will result in late decelerations and decreased baseline variability.
  - Persistent late decelerations associated with decreased beat-to-beat variability is an ominous pattern
  - If late deceleration is not responding to oxygen supplementation, hydration, position change, and discontinuation of labor stimulation, prompt delivery is indicated
- **Contraction stress test** is performed to determine how well a fetus will tolerate uterine contractions during delivery. It is important for testing the wellbeing of fetus, e.g., in uteroplacental insufficiency, IUGR
  - Contraction stress test measures the heart rate in relation to uterine contraction by giving oxytocin or nipple stimulation
- **Biophysical profile test** assesses fetal heart rate, movement, breathing, muscle tone, and amniotic fluid volume. It does not assess fetal growth

Causes of abnormal alpha-fetoprotein (AFP) during pregnancy

- Increased AFP
  - Neural tube defect
    - Anencephaly
    - Spina bifida
  - Abdominal wall defects
    - Gastroschisis
    - Omphalocele
  - Cystic hygroma
  - Placental abnormalities
  - Renal abnormalities, e.g.:
    - Polycystic kidney or absent kidney
    - Urinary obstruction
  - Multiple pregnancy
- Decreased AFP
  - Incorrect GA calculation
  - Trisomy 21 (Down syndrome)
  - Trisomy 18 (Edward syndrome)

DELIVERY ROOM CARE [1]

Temperature control

- To minimize heat loss, the delivered infant is first placed in a warmed towel or blanket
- Raising the environmental (room) temperature to 26 °C (78.8 °F) will also help in reducing neonatal hypothermia
- Other methods of warming infants:
  - Swaddle after drying
  - "Skin-to-skin" contact with mother
  - Polyurethane bags or wraps in infants with BWs less than 1500 g
  - Warming pads

Initial management—Once the infant is born:

- Dry the infant
- Clear the airway of secretions
- Provide warmth; place under radiant warmer
- Neonatal resuscitation if indicated

Newborn resuscitation

- Pediatrician or provider skilled in neonatal resuscitation should be present and equipment should be prepared prior to the birth of high-risk infants
- Preterm infants very likely will need at least some resuscitation, and they may develop complications from resuscitation more often than term infants

Indications for resuscitation

- Apnea or poor respiratory effort
- Cyanosis
- Bradycardia
- Poor muscle tone

Resuscitation steps

- Initial care includes providing warmth to the infant, clearing the airway, and drying and stimulating the infant
- Apneic or gasping infant with a heart rate < 100 beats/min (bpm):
  - Positive pressure ventilation (PPV) provided by bag-mask ventilation is initiated at a rate of 40–60 breaths/min
  - Chest compressions are required if the infant's heart rate remains < 60 bpm despite adequate ventilation for 30 s. Chest compressions must always be accompanied by PPV using 100% oxygen
  - Pulse oximetry is used to continuously monitor heart rate and oxygen saturation (SpO2)
  - Intubation or use of a laryngeal mask airway is needed if PPV is ineffective or prolonged, or chest compressions are being performed
- If the heart rate remains < 60 bpm despite adequate ventilation and chest compressions:
  - Intravenous administration of epinephrine is indicated (epinephrine can also be given via the endotracheal tube if vascular access is not available)
  - Cannulation of the umbilical vein is the quickest means of obtaining intravenous (IV) access in the newborn
- For infants with labored breathing or persistent cyanosis, and a heart rate ≥ 100 bpm:
  - Ensure the airway is optimally positioned and cleared of secretions; pulse oximetry is used to monitor SpO2
  - Supplemental oxygen is provided to targeted preductal SpO2
- Infants who require resuscitation are at risk of developing post-resuscitative complications
- After successful resuscitation, they require placement in a setting in which close monitoring and ongoing appropriate care can be provided

Withholding resuscitation

- Resuscitation efforts may be discontinued after 10 min of resuscitation if the neonate has demonstrated no signs of life (no heartbeat or no respiratory effort for greater than 10 min)
- Resuscitation can be withheld if it is legally acceptable and there is complete agreement among parents and care providers that the neonatal outcome is dismal

NEWBORN NURSERY CARE

Eye prophylaxis

- Ophthalmic erythromycin 0.5% ointment within 1 h after delivery
- Prevent *Neisseria gonorrhoeae* ophthalmia neonatorum

Hepatitis B prophylaxis

- Universal vaccination of newborns regardless of maternal hepatitis B virus surface antigen (HBsAg) status is recommended
- The first dose of the hepatitis B vaccine (HBV) should be given within 24 h of delivery (See Chap. 1 General Pediatrics)

Vitamin K

- Vitamin K 1 mg intramuscular (IM) injection in the first few hours after delivery prevents hemorrhagic disease of the newborn

Umbilical cord care

- In developed countries where aseptic care is routine in clamping and cutting of the umbilical cord, additional topical care beyond dry cord care is not needed to prevent omphalitis

Newborn screening

- All states in the USA require newborn screening for metabolic and genetic disorders
- Blood is collected for an initial screen between 24 and 48 h of life. Some states also require a second screen, which is usually collected between 7 and 14 days of age

Critical congenital heart defects screening

- Pulse oximetry cardiac screening for all newborns before discharge

Hearing loss

- Universal newborn hearing screening is recommended to detect infants with hearing loss

Feeding

- Breastfed infants:
  - Should be fed as soon as possible after delivery, preferably in the delivery room
  - Should receive at least 8–12 feeds per day during the newborn hospitalization
  - Rooming-in, skin-to-skin contact, frequent demand feedings in the early postpartum period, and lactation support increase the rate of successful breastfeeding
- Formula-fed infants
  - Healthy infants who are fed formula should be offered standard 19–20 kcal/oz. (20 kcal per 30 mL) iron-containing infant formula
  - Feeding on demand, but the duration between feedings should not exceed 4 h
  - The volume of feedings should be at least 0.5–1 oz. (15–30 mL) per feed during the first few days of life
- Pasteurized human donor milk may be available in some nurseries for the healthy breastfed newborn who may require supplementation
- Weight loss—term infants may lose up to 10% of their BW in the first few days of life and typically regain their BW by 10–14 days

Hypoglycemia

- Glucose screening—healthy, asymptomatic term infants born after an uncomplicated pregnancy and delivery are at low risk for significant hypoglycemia. As a result, blood glucose measurement is not routinely performed in these neonates
- Per American Academy of Pediatrics (AAP) guidelines, glucose monitoring should be performed for newborns with the following risk factors:
  - Preterm infants (infants of GA < 37 weeks)
  - Large for gestational age (LGA)
  - Small for gestational age (SGA)
  - Infants of diabetic mothers (IDM)
  - Post-term infants (GA > 42 weeks)

Hyperbilirubinemia

- Visual assessment is not accurate for estimating the degree of hyperbilirubinemia
- Use transcutaneous bilirubin or total serum bilirubin measurement
- Infants should be routinely assessed every 8–12 h and at discharge for the presence of jaundice
- Assess pre-discharge bilirubin screen and risk factors together for prediction of development or worsening of hyperbilirubinemia after discharge

24 h discharge criteria

- Full-term healthy infants between 37 and 41 weeks
- Normal spontaneous vaginal delivery
- Clinical course and physical examination at discharge have not revealed abnormalities
- Stable state at least 12 h before discharge with normal vital signs
- At least two successful consecutive feedings
- The infant has urinated regularly and passed at least one stool spontaneously
- Infant blood tests are available and have been reviewed, such as cord or infant blood type and direct Coombs test results, as clinically indicated
- Not at high risk to develop subsequent hyperbilirubinemia
- Newborn metabolic and hearing screenings have been completed

Timing of the first well-child visit after hospital discharge

- For infants with a birth hospitalization less than 48 h
  - An early follow-up visit is recommended within 48 h of discharge
- For infants with a birth hospitalization greater than 48 h
  - An initial well-child visit within 3–5 days after discharge is reasonable
  - Infants at high risk of developing worsening hyperbilirubinemia and breastfed infants should be seen by their pediatrician within 48 h of discharge

MATERNAL CONDITIONS

Premature Rupture of Membranes

Background

- Premature rupture of membranes (PROM) refers to a patient who is beyond 37 weeks gestation and has presented with rupture of membranes (ROM) prior to the onset of labor
- Preterm premature rupture of membranes (PPROM) is ROM prior to 37 weeks gestation
- Spontaneous preterm rupture of the membranes (SPROM) is ROM after or with the onset of labor occurring prior to 37 weeks gestation
- Prolonged ROM is any ROM that persists for more than 24 h and prior to the onset of labor

PROM at term (> 37 weeks gestation): Management

- Evaluate the mother by speculum examination
- Check fetal heart rate (FHR)
- Identify fetal presentation
- Most patients (90%) enter spontaneous labor within 24 h when they experience ROM at term. However, most obstetricians induce labor at this point. Evidence supports the idea that induction of labor, as opposed to expectant management, decreases the risk of chorioamnionitis without increasing the cesarean delivery rate

Preterm premature rupture of membranes (PPROM):

Risks

- Prematurity is the principal risk to the fetus
- The risk of infection increases with the duration of PPROM

Expectant management

- The immature fetus may benefit from expectant management, even if for a short period, to allow for administration of steroids and antibiotics

Indications for delivery

- In certain circumstances (e.g., chorioamnionitis, advanced labor, fetal distress, and placental abruption with nonreassuring fetal surveillance), immediate delivery of the fetus with PPROM is indicated
- If fetal lung maturity has been documented by either amniocentesis or collection of vaginal fluid, delivery should be facilitated

Medications during expectant management

- 48 h course of IV ampicillin and erythromycin followed by 5 days of amoxicillin and erythromycin is recommended during expectant management
- In the absence of chorioamnionitis, some obstetricians give tocolysis, even with active contractions after the steroid therapy is started. The use of tocolysis should be considered only when a clear clinical benefit exists, such as in transport of the mother to a tertiary institution with a newborn intensive care unit (NICU)
- Magnesium sulfate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants

Chorioamnionitis

Background

- Inflammation of the fetal amnion and chorion membranes due to a bacterial infection

Clinical presentation

- Maternal fever (intrapartum temperature > 100.4 °F or > 37.8 °C) most frequently observed sign
- Significant maternal tachycardia (> 100 beats/min)
- Fetal tachycardia (> 160 beats/min)
- Purulent or foul-smelling amniotic fluid or vaginal discharge
- Uterine tenderness
- Maternal leukocytosis (total blood leukocyte count > 15,000 cells/μL in the absence of corticosteroid therapy)

Management

- Early delivery, supportive care, and antibiotic administration
- Pharmacotherapy for the mother includes:
  - Ampicillin and gentamicin
  - Clindamycin or metronidazole when endometritis is suspected
  - Vancomycin for penicillin-allergic patients
  - Penicillin G: Used exclusively for GBS intrapartum prophylaxis; if intraamniotic infection is suspected, antibiotic coverage should be broadened
- Pharmacotherapy for the neonate
  - Ampicillin and gentamicin
- Supportive care of the neonate with sepsis may include the following:
  - Warmth, monitoring of vital signs
  - Preparedness to perform a full resuscitation, including intubation and providing PPV
  - Treatment of hypovolemia, shock, and respiratory and/or metabolic acidosis
  - Surfactant replacement therapy
  - Glucose homeostasis
  - Assessment and treatment of thrombocytopenia and coagulopathy, if present

Preeclampsia

Defined as the presence of:

- Hypertension:
  - Systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 h apart in a previously normotensive patient, ***or***
  - SBP greater than or equal to 160 mm Hg or a DBP greater than or equal to 110 mm Hg or higher
- Proteinuria:
  - Proteinuria of ≥ 0.3 g in a 24-h urine specimen, a protein (mg/dL)/creatinine (mg/dL) ratio of ≥ 0.3, or a urine dipstick protein of 1+ (if a quantitative measurement is unavailable)

Preeclampsia with severe features is defined as the presence of one of the following symptoms or signs in the presence of preeclampsia:

- SBP of 160 mm Hg or higher or DBP of 110 mm Hg or higher, on two occasions at least 4 h apart while the patient is on bed rest (unless antihypertensive therapy has previously been initiated)
- Impaired hepatic function as indicated by abnormally elevated blood concentrations of liver enzymes (to double the normal concentration)
- Severe persistent upper quadrant or epigastric pain that does not respond to pharmacotherapy and is not accounted for by alternative diagnoses, or both
- Progressive renal insufficiency (serum creatinine concentration > 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- New onset cerebral or visual disturbances
- Pulmonary edema
- Thrombocytopenia (platelet count < 100,000/μL)

Eclampsia

- Defined as seizures that cannot be attributed to other causes in a woman with preeclampsia
- HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) may complicate severe preeclampsia

Management

- Delivery is the only cure for preeclampsia
- Patients with preeclampsia without severe features are often induced after 37 weeks gestation
- In patients with preeclampsia with severe features, induction of delivery should be considered after 34 weeks gestation. In these cases, the severity of disease must be weighed against the risks of infant prematurity. In the emergency setting, control of BP and seizures should be prioritized
- Medications used for BP control include the following:
  - Hydralazine
  - Labetalol
  - Nifedipine
  - Sodium nitroprusside (in severe hypertensive emergency refractory to other medications)
  - Magnesium sulfate is the first-line treatment for primary and recurrent eclamptic seizures

Diabetes Mellitus

Background

- Abnormal maternal glucose regulation occurs in 3–10% of pregnancies
- Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy
- GDM accounts for 90% of cases of DM in pregnancy

Risks of preexisting maternal DM on infants

- Growth restriction occurs with significant frequency in pregnancies in women with preexisting type 1 DM
- Double the risk of serious injury at birth, triple the likelihood of cesarean delivery, and quadruple the incidence of NICU admission
- Increased rate of miscarriage and birth defects in diabetic women with suboptimal glycemic control before conception
- A higher rate of congenital anomalies persists even with good glycemic control in the mother
- Anomalies involve the cardiovascular and CNS systems; abnormalities of the skeletal, genitourinary, and gastrointestinal (GI) systems are also seen

Management

- Insulin remains the standard medication for treatment of diabetes during pregnancy, but

the oral agents glyburide and metformin are increasingly being used
- Mothers should keep the fasting blood sugar value at 90–99 mg/dL, and keep 1-h, post-meal values at < 140 mg/dL
- Before diabetic women become pregnant, they should have a glycosylated hemoglobin (HbA1c) of < 6.5% and maintain the same during pregnancy
- The most common complication in a well controlled mother with DM is macrosomia

NEWBORN EXAMINATION

Apgar Score (Table 2.2)

- Dr. Virginia Apgar devised the Apgar score in 1952 as a simple and replicable method to quickly and summarily assess the health of newborn children immediately after birth
- The Apgar score alone cannot be considered to be evidence of or a consequence of asphyxia, does not predict individual neonatal mortality or neurologic outcome, and should not be used for that purpose
- Apgar score at 1 min and 5 min does not correlate well with long-term neurobehavioral sequelae

Table 2.2 Apgar score

Score	0	1	2
A—Activity	Absent	Some flexion of arms and legs	Active
P—Pulse (Heart rate)	Absent	< 100 beats/min	> 100 beats/min
G—Grimace (reflex irritability)	No response	Grimace	Cry or active withdrawal
A—Appearance (skin color)	Blue, pale	Acrocyanotic	Completely pink
R—Respiration	Absent	Slow and irregular; hypoventilation; weak cry	Good respiratory effort, crying

Apgar score is done at 1 min, 5 min routinely, and at 5-min intervals thereafter until 20 min for infants with a score less than 7

- Apgar score < 3 at 15 min has been associated with high mortality and severe neurologic sequelae

Newborn Crying

- Weak cry or high-pitched cry is abnormal
- Hoarseness can be caused by any process that affects the structure or function of the larynx
- Hoarse cry may indicate hypothyroidism or vocal cord paralysis

Temperature

- Persistent abnormal temperature in a normal temperature environment must be investigated
- Hypothermia: Look for environmental factors, sepsis, hypoglycemia, hypothyroidism, low Apgar scores (hypoxia), intracranial hemorrhage, drug withdrawal
- Hyperthermia: Look for environmental factors (overheating from incubators, radiant warmers or ambient environmental temperature; excessive bundling or swaddling), maternal fever, maternal epidural anesthesia, sepsis, adrenal hemorrhage, or CNS disorders

SKIN

- **Aplasia cutis congenita** (congenital absence of the skin):
  - Absence of a portion of skin in a localized or widespread area at birth
  - Most commonly (70%) manifests as a solitary defect on the scalp
  - Consider trisomy 13, especially if associated with midline defect
- **Acrocyanosis:** Cyanosis of hands and feet when exposed to colder temperature; this can be a normal finding
- **Generalized cyanosis:** Significant hypoxemia (e.g., cardiac or respiratory) or methemoglobinemia
- **Pallor:** Anemia or poor perfusion (e.g., placental abruption or placenta previa)

- **Cutis marmorata** (pale mottled skin): Cold environment, sepsis, or hypothermia
  - While cutis marmorata is a relatively benign disorder, persistent cutis marmorata is associated with Down (trisomy 21), Edward (trisomy 18), and Cornelia de Lange syndromes
  - Cutis marmorata may also indicate poor perfusion in infants developing sepsis. The mottled appearance of the skin in cutis marmorata usually disappears when the newborn is warmed
  - The syndrome usually resolves within weeks to months of its presentation
  - No formal treatment is necessary
- **Plethora** (very red skin): Polycythemia
- **Harlequin color change:** Cutaneous condition seen in newborn babies characterized by momentary red color changes of half the newborn, sharply demarcated at the body's midline
- **Harlequin ichthyosis:** Most severe form of autosomal recessive congenital ichthyosis that results in thickened keratin layer in fetal skin. The skin contains massive, diamond-shaped plates that are separated by deep cracks
- **Ecchymoses:** Usually due to birth trauma
- **Petechiae:** Scattered localized petechiae are common after delivery; however, extensive generalized petechiae must be investigated for thrombocytopenia, sepsis, and other causes

Subcutaneous Fat Necrosis of the Newborn (SCFN)

- Uncommon disorder characterized by firm, mobile, erythematous nodules and plaques over the trunk, arms, buttocks, thighs, and cheeks of full-term newborns
- Self-limited process that usually does not require treatment
- May be complicated by hypercalcemia and other metabolic abnormalities

Jaundice

- If present on the 1st day of life, the infant must be investigated for hemolytic anemia or sepsis

HEAD

Head Shape

- Head shape and symmetry may vary, depending on the intrauterine position, presentation at delivery, degree of molding, or the need for an instrument-assisted delivery
- Infants born by cesarean section often have a symmetrical, round head when compared to infants born vaginally whose head shape is often elongated in the occipital area with overriding sutures
- Molding is temporary overlapping of bones and must be distinguished from craniosynostosis. It typically resolves 2–3 days after birth

Fontanelles

- **Anterior fontanelle:** Diamond shaped, open, soft, and flat at birth; measures 4–6 cm at birth and usually closes at approximately 18 months of age
- **Posterior fontanelle:** Usually triangular, < 0.5 cm at birth and closes shortly after birth:
  - Hypothyroidism must be considered if posterior fontanelle is persistently opened
- **Bulging fontanelle** can be normal in a crying infant, but may be associated with hydrocephalus, birth injury, intracranial bleeding, or infection. It may be present as a late sign of increased intracranial pressure
- **Large fontanelles** may indicate hypothyroidism, hydrocephaly, in utero malnutrition, rickets, or a genetic disorder
- **Depressed anterior fontanelle** is a late sign of dehydration

Caput Succedaneum

- **Definition:** Diffuse subcutaneous edematous swelling of soft tissue of the scalp that may extend across the suture lines
- **Causes:** Secondary to the pressure of the uterus or vaginal wall
- **Outcome:** Usually resolves within 48–72 h

Cephalohematoma

Background
- Subperiosteal hemorrhage that is soft, fluctuant, cyst-like swelling with a well-defined outline
- Initially firm but becomes more fluctuant after 48 h
- Typically calcifies at the edges during resolution
- Cephalohematoma never extends across suture line

Causes
- Difficult or instrument-assisted delivery

Management
- Radiograph or computed tomography (CT) scan should be obtained if skull fracture is suspected
- Hemoglobin and bilirubin should be monitored
- Most cephalohematomas resolve within 2–3 weeks to several months

Subgaleal Hemorrhage

Background
- Serious but less common complication, usually associated with vacuum-assisted delivery
- Collection of blood between the aponeurosis and the periosteum
- Can extend to orbits and neck
- Usually secondary to rupture of emissary veins
- If massive, coagulopathy may be present

Management
- Progressive after birth but typically resolves within 2–3 weeks
- Monitor BP, hematocrit, bilirubin, and signs for hypovolemia, bleeding, and shock

Traumatic Epidural, Subdural, and Subarachnoid Hemorrhage

Risk factors
- Large head
- Prolonged labor in breech or precipitous delivery

Important
- Child abuse must be suspected in all infants with subdural hemorrhage after the immediate neonatal periods

Diagnosis
- Suspect subdural hemorrhage if megalocephaly, bulging fontanel, unexplained anemia and jaundice, or seizures
- CT scan and magnetic resonance imaging (MRI) are useful in the diagnosis

Skull Fractures

- **Linear fracture:** Linear fractures are benign and have excellent prognosis
- **Depressed fracture:** Ping-pong ball, usually not associated with loss of bone continuity; prognosis is good if neurological exam is normal
- **Basilar fracture:** Overall prognosis is guarded and there is significant risk of permanent sequelae

EYES

- **Red reflex examination:**
  - Dark spots in the red reflex, a blunted red reflex on one side, lack of a red reflex, and the presence of a white reflex are all indications for immediate ophthalmology referral
  - White pupillary reflex (leukocoria): Cataract, retinoblastoma, retinopathy of prematurity, retinal coloboma, Coats disease, persistent fetal vasculature
  - Cataract: Galactosemia, intrauterine infections (rubella); can be inherited as a dominant trait from an affected parent
- **Coloboma** (hole in the structure of the eye such as the lens, iris, retina, choroid, or optic disc)
  - CHARGE syndrome (Coloboma, Heart defect, Choanal atresia, Retarded growth and development, Genital abnormality, Ear abnormality), and trisomy 13 (Patau syndrome)
- **Brushfield spots:** Small white spots on the surface of the iris arranged in a concentric ring around the pupil; seen in healthy children but are far more common in patients with Down syndrome
- **Strabismus:** Persistent strabismus must be referred immediately; occasional eye deviation can be normal in the first 4 months of life
- **Eyelids:** Ptosis could be a sign of Horner syndrome or congenital myasthenia gravis. Check maternal history (for congenital myasthenia); check the arms and the clavicles
- **Subconjunctival hemorrhage:** Secondary to rupture of small blood vessels near the surface of the bulbar conjunctiva. Can occur normally during labor and delivery and resolves spontaneously over a period of time
- **Blue sclera:** Osteogenesis imperfecta or normal variant
- **Congenital glaucoma:** The classic triad of manifestations, any one of which should arouse suspicion of glaucoma in an infant or young child, includes epiphora, photophobia, and blepharospasm. The cornea is enlarged and becomes progressively cloudy. A corneoscleral junction more than 12 mm in diameter in the 1st year of life is highly suggestive of glaucoma

EARS

- **Malformed ears** and low set ears are associated with many syndromes, look for urogenital malformation
- **Preauricular pits and tags:** Renal ultrasound should be performed in any newborn with an ear anomaly accompanied by other dysmorphic features, family history of deafness, maternal history of gestational diabetes, or a defined syndrome

NOSE

- **Nasal stuffiness** after birth can be a sign of drug withdrawal
- **Choanal atresia** can be unilateral or bilateral (respiratory distress and cyanosis while feeding if bilateral)
- **Snuffles (rhinorrhea)** and saddle nose: Usually associated with syphilis
- **Flattened nasal bridge:** Can be a normal variant or associated with congenital syphilis, Down syndrome, or Williams syndrome

MOUTH

- **Epstein pearls:** Small, opaque whitish-yellow papules that are firm in consistency and are located on the mid-palatal raphe at the junction of the hard and soft palate (Fig. 2.1)
  - Represents keratin entrapment within the soft and hard palate
  - Common and benign finding

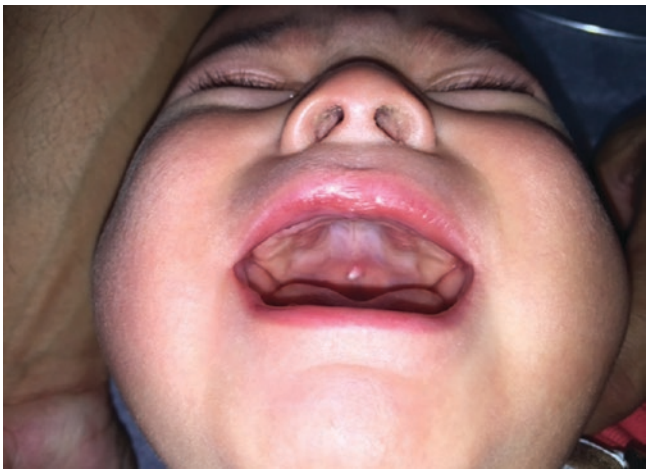

Fig. 2.1 Infant with Epstein pearl in the hard palate

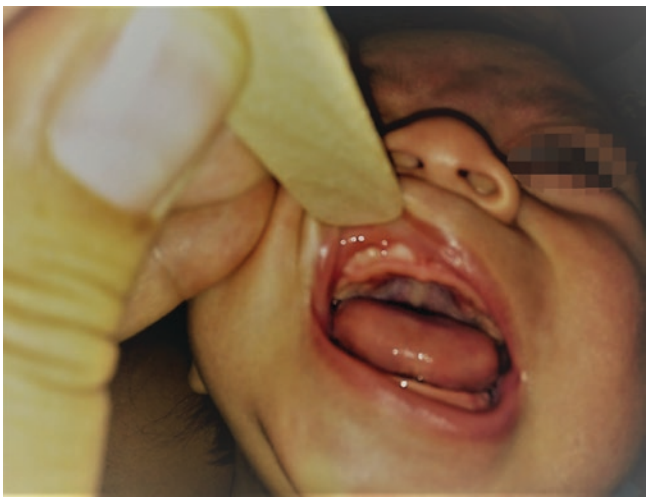

Fig. 2.2 Infant with Bohn nodules in the upper gums

- **Bohn nodules:** Grayish-white, firm nodules frequently present on the buccal or lingual aspects of the alveolar ridges (Fig. 2.2)
  - Exact etiology is unknown, but they are thought to arise from remnants of the dental lamina or from heterotopic salivary glands
  - Benign finding that will disappear with time
- **Ranula:** Translucent, firm papule or nodule found on the anterior floor of mouth, lateral to lingual frenulum
- **High arched palate:** Usually associated with syndromes
- **Pierre Robin sequence:** Triad of retrognathia or micrognathia, glossoptosis, and airway obstruction
- **Cleft lip and palate:** Can be hereditary or associated with syndromes
- **Macroglossia:** Can be congenital or acquired; associated with hypothyroidism, Beckwith-Wiedemann syndrome, Pompe disease, and Down syndrome

Natal teeth

- **Supernumerary:** Usually very loose and easy to remove with a little pinch
- **True milk teeth:** Usually hard and should not be removed (Fig. 2.3)

Ankyloglossia or tongue-tie

- Caused by a short frenulum on the underside of the tongue that prevents complete protrusion of the tongue
- Can interfere with breastfeeding and speech articulation
- Frenulotomy is recommended if interfering with feeding or speech

Fig. 2.3 Infant with two true milk lower central incisor teeth, hard to move

NECK

Brachial Plexus Injuries (BPI)

Background

- **Erb's palsy** (Duchenne-Erb palsy): Upper trunk nerve injury (C5 and C6, ±C7), due to traction on the upper trunk; most common form
- **Klumpke palsy:** Injury to the C8-T1 nerve roots; results in weakness of the hand muscles, absent grasp, and sometimes Horner syndrome
- Total brachial plexus injury involves both upper and lower roots
- Most patients have the least severe form of nerve injury (neuropraxia) and recover spontaneously or with supportive physical therapy

Classification

- Purely neurapraxic lesions
  - Stretching of nerve without disruption
  - These lesions generally are reversible and do not leave sequelae
- Axonotmetic lesions
  - Due to nerve fibers (axons) disruption with intact sheath
  - Cause degeneration of the axon distal to the injury
  - These injuries improve gradually over 4–6 months, depending on the level of the lesion
- Neurotmesis lesions
  - The most severe form
  - Involves disruption of the axon and myelin sheath (total severing, avulsion injury)
  - Muscle atrophy from a neurotmesis lesion begins 3–6 months after injury, and complete recovery is impossible (worst prognosis)

Clinical presentation

- Complete brachial plexus palsy (C5-T1)
  - Arm held limp at side
  - Deep tendon reflexes (DTRs) in the affected arm are absent
  - Moro response is asymmetrical, with no active abduction of the ipsilateral arm
  - Horner syndrome (i.e., miosis, ptosis, anhidrosis) may occur, a bad prognostic sign usually associated with avulsion injury
  - Respiratory distress and elevation of diaphragm may occur due to injury to phrenic nerve
- Erb's palsy (C5-C6, ±C7)
  - Arm adducted and internally rotated; elbow extended and the forearm pronated; wrist flexed and the hand in a fist (waiter tip position)
  - Absent Moro reflex, but grasp reflex is present on the affected side
  - In the 1st hours of life, the hand may appear flaccid, but strength soon returns
  - About 80% of patients with Erb's palsy will show complete recovery within the first 3 months, 90% recover by 12 months
- Klumpke palsy (C8-T1)
  - Rare
  - Absent grasp reflex on affected side
  - Supinated arm, elbow bent, wrist extended, and fingers flexed, "claw hand"
  - One-third of cases associated with Horner syndrome
  - Phrenic nerve injuries may be evident

Associated injuries

- The pediatrician must perform a careful examination of the infant with BPI to look for associated injuries
- The most common associated (not causative) injuries:
  - Clavicular and humeral fractures
  - Torticollis
  - Cephalohematoma
  - Facial nerve palsy
  - Diaphragmatic paralysis

Diagnosis

- Chest radiography: Look for clavicular fractures or elevation of diaphragm suggesting phrenic nerve injuries and root avulsion
- High-resolution MRI is the study of choice for evaluating brachial plexus injuries

- MRI is indicated for preoperative planning in severe cases requiring surgery

Management

- Rehabilitation must start immediately after the diagnosis. Treatment is directed towards preventing contractures:
  - Intermittent and partial immobilization: The arm can be fixed across the child's chest by pinning of his/her clothing to provide more comfort
  - Active and passive range of motion exercises
  - Dress the infant gently and avoid further traction on the arm
  - Wrist extension splint is necessary to maintain proper wrist alignment and to reduce the risk of progressive contractures
  - Assessments every 3–4 weeks are indicated
- Persistence of symptoms beyond 1 month of age suggests that the injury may require treatment
- Absence of full recovery by age of 3 months, signs of root avulsion (Horner syndrome, phrenic nerve involvement), total palsy, and Klumpke palsy are all indications for referral to orthopedics

CHEST

- Fracture of the clavicle is very common; crepitation usually found during examination
- Supernumerary nipple (polythelia) is fairly common and considered minor anomaly
- Pectus excavatum is a congenital depression of the sternum and is usually insignificant
- Widely spaced nipples are seen in Turner syndrome
- Breast hypertrophy and galactorrhea may be seen in both male and female infants (because of maternal hormones); engorgement may increase during the first few days but then usually resolves (Fig. 2.4)

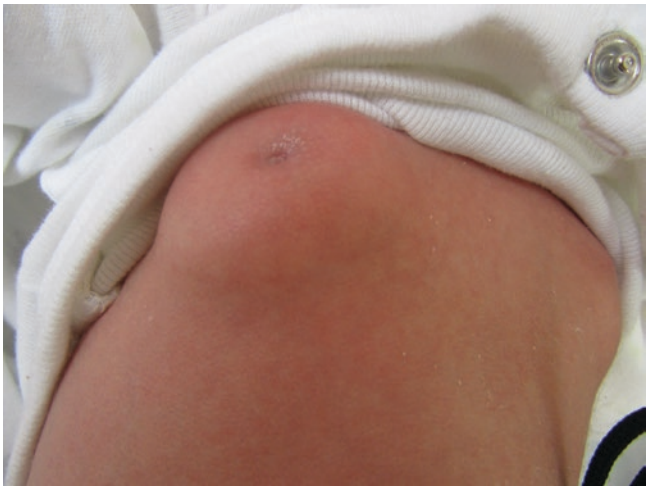

Fig. 2.4 Three-week-old infant with enlarged breast tissue, resolved spontaneously after several weeks

LUNG

Respiratory distress

- Normal respiratory rate is 40–60 breaths/min
- Respiratory rate persistently more than 60 breaths/min in the newborn period is abnormal
- Grunting, nasal flaring, retractions, and tachypnea may be transient in the first few hours after birth—transient tachypnea of the newborn (TTN). If it persists for more than 24 h, other causes must be explored

Unilateral movement of the chest

- Phrenic nerve palsy
- Diaphragmatic hernia

Cough

- Always abnormal in newborn
- Pneumonia must be considered

HEART

- **Point of maximal cardiac impulse (PMI):** Location is fourth to fifth intercostal space just medial to left mid-clavicular line
- If PMI is displaced, chest radiograph is recommended to rule out pneumothorax, dextrocardia, diaphragmatic hernia, or space-occupying lesion

- **Bradycardia:** HR < 100 bpm is abnormal. Look for sepsis, asphyxia, increased intracranial pressure, hypothyroidism, congenital heart disease, and heart block (as may be seen in infants born to mothers with systemic lupus erythematosus)
- **Tachycardia:** HR > 180 bpm. Look for fever, hypovolemia, anemia, tachyarrhythmia, hyperthyroidism, and drug withdrawal

Murmur

- Approximately 60% of infants will have a murmur auscultated in the newborn period
- Most murmurs in the neonatal period are benign. Benign murmurs are usually due to transient changes in the postnatal circulation (e.g., patent ductus arteriosus)
- 8% of murmurs at birth are associated with congenital heart disease
- Murmurs usually require workup if the following are present:
  - Persist after the first day of life
  - Presence of cyanosis
  - Evidence of poor perfusion
  - Poor feeding

Blood pressure

- SBP in term infants < 12 h usually between 60 and 90 mmHg
- BP in right arm and one leg must be determined; a pressure difference of more than 20 mmHg in favor of the arms may be considered evidence of coarctation of the aorta
- Absent/weaker pulse in the lower extremities is a red flag for coarctation of the aorta

ABDOMEN

Liver/Spleen

- Liver is normally palpated 1–2 cm below the right costal margin in the newborn
- Spleen is normally palpable not more than 1 cm below the left costal margin

Abdominal Masses

- Multicystic dysplastic kidney is the most common cause of an abdominal mass in the newborn period and is the most common cystic malformation of the kidney in infancy
- Subcapsular hematoma of the liver (traumatic delivery)

Abdominal Wall Defects

- **Umbilical hernia and diastasis recti**
  - Usually benign and self-limited conditions
  - Umbilical hernias are managed with observation, as these defects typically close by age 4 or 5 years (Fig. 2.5)
  - Any defects that persist beyond this age or the defect is larger than 2 cm should undergo surgical repair
- **Omphalocele**
  - Result of herniation of the intestine and other abdominal organs into the umbilical cord without returning into the abdominal cavity
  - The abdominal viscera are contained in a translucent sac, which is composed of amnion, Wharton jelly, and peritoneum
  - The umbilical vessels insert into the wall of the sac, and not the abdominal wall

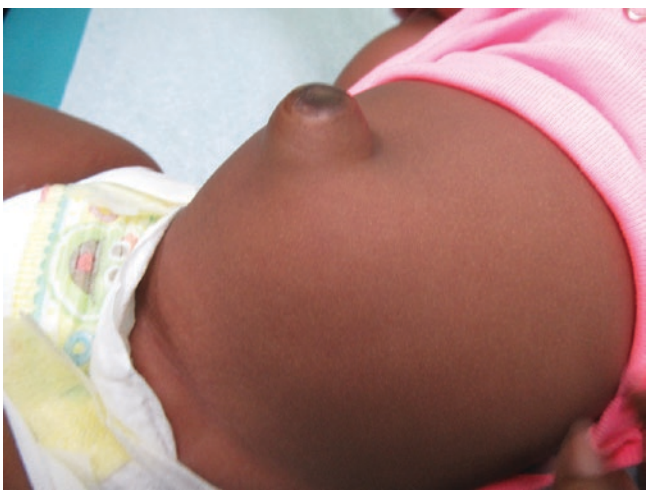

Fig. 2.5 Infant with a large umbilical hernia

  - Associated with syndromes and chromosomal abnormalities in > 50% of cases, including Beckwith-Wiedemann syndrome (omphalocele, macroglossia, organomegaly, hypoglycemia, and increased risk of childhood tumors such as Wilms tumor, neuroblastoma, and hepatoblastoma)
- **Gastroschisis**
  - Considered to be the result of a vascular accident of the omphalomesenteric artery, a failure of mesoderm formation, rupture of the amnion around the umbilical ring with herniation of the midgut, or abnormal involution of the right umbilical vein with body wall weakening
  - Full thickness defect in the abdominal wall with prolapse of the intestine through the defect
  - No covering membrane on the defect
  - Defect lies to the right of an intact umbilical cord
- **Prune belly syndrome (Eagle-Barrett syndrome)**
  - Caused by laxity of the abdominal musculature
  - Wrinkly folds of skin covering the abdomen
  - Associated with GI and genitourinary tract anomalies (obstructive uropathy) and pulmonary hypoplasia
  - Undescended testis in males
- **Urachal remnants**
  - The urachus is a structure that connects the dome of the bladder to the anterior abdominal wall at the level of the umbilicus
  - With a patent urachus, a complete communication between the bladder and umbilicus remains. Urine is noted to drain from the umbilicus
  - Remnants of this connection include a patent urachus, urachal sinus (free communication between the bladder and umbilicus), and urachal cyst
  - Umbilical polyps can be observed in association with a urachal remnant
- **Umbilical granuloma**
  - Granulation tissue may persist at the base of the umbilicus after cord separation
  - Surface of an umbilical granuloma may be smooth or irregular and is often pedunculated
  - The tissue is composed of fibroblasts and capillaries and can grow to more than 1 cm
  - Small granulomas may be treated adequately with applications of topical silver nitrate. Larger granulomas or those refractory to silver nitrate may require surgical resection
  - Umbilical granulomas must be differentiated from umbilical polyps, which do not respond to silver nitrate cauterization
- **Omphalomesenteric duct remnants**
  - Persistence of all or portions of the omphalomesenteric duct can result in fistulas, sinus tracts, cysts, congenital bands, and mucosal remnants. The most common remnant is a Meckel diverticulum
  - Patients with mucosal remnants can present with an umbilical polyp or an umbilical cyst
  - The condition should be suspected in cases of delayed separation of the cord or persistent, large, umbilical granulomas with associated drainage
- **Delayed separation of the umbilical cord**
  - The umbilical cord usually separates and sloughs by the end of the second postnatal week
  - Cord care involves keeping the area clean and dry
  - A marked delay in cord separation raises the suspicion of leukocyte adhesion deficiency (LAD), a rare disorder leading to defective neutrophil function
- **Single umbilical artery (SUA)**
  - The normal umbilical cord has one vein and two arteries
  - SUA occurs in up to 2% of all live-born infants

  - SUA is thought to result from either aplasia or atrophy of the second umbilical artery or from persistence of the normally transient early embryonic SUA
  - Associated structural or chromosomal anomalies are seen in 27% of infants with SUA, with renal malformations being the most common finding
  - A newborn with SUA should be examined thoroughly for dysmorphic features, abdominal masses, and the presence of heart disease
  - SUA is associated with an increased risk of chromosome abnormalities such as trisomy 13, trisomy 18, and triploidy

GENITALIA

Females

- Female infants have two orifices, one for the urethra just below the clitoris and the other for the vagina. The urethral orifice must be differentiated from the vagina
- Infants can have a creamy white to slightly blood-tinged discharge 2–3 days after birth, caused by withdrawal of maternal hormones
- Imperforate hymen can result in hydrometrocolpos, which usually presents as a bulging hymen especially with crying, or an abdominal mass

Males

Penis

- Term infant's penile length is 2.5–3.5 cm
- Micropenis: Penile length < 2.5 cm is abnormal (hormonal workup is needed). Infants should be observed for evidence of metabolic derangements
- Prepuce is usually adherent and should not be forcibly retracted
- **Chordae**: The skin on the underside of the penis may be tethered to the scrotum, called chordae; this may be associated with hypospadias
- **Hypospadias:** Defect of the urethra in a male infant that involves an abnormally placed urethral meatus. Instead of opening at the tip of the glans, the urethra opens anywhere along a line running from the tip along the ventral aspect of the shaft to the junction of the penis and the perineum
  - Infants with hypospadias should not be circumcised because the foreskin is often used during surgical repair
- **Epispadias:** Meatal opening is on the dorsal surface of the penis. It is less common than hypospadias
- **Mispositioned meatus:** May be associated with urethral or kidney abnormalities and may result in poor urinary stream

Testis

- Normally in the scrotum in term infants but may be palpated in the upper scrotum or in the inguinal canal
- **Cryptorchidism** occurs in 3–5% of term male infants
  - Undescended testicles may be true undescended testicles, ectopic testicles, or retractile testicles
- **Discoloration of the scrotum** may be present in a neonate born after breech presentation or may be caused by testicular torsion or hematoma
- **Testicular torsion** can occur in infancy and presents as an enlarged testicle with overlying discoloration of the scrotum

Ambiguous Genitalia (See Also Chap. 12 Endocrinology)

- Small penis, bifid scrotum, large clitoris, and pigmented fused vulva are signs of ambiguous genitalia

- Initial screening
  - Chromosomal analysis
  - Endocrine screening
  - Serum chemistries/electrolyte tests (possible CAH)
  - Androgen-receptor levels
  - 5-Alpha reductase type II level
  - Abdominal ultrasound to evaluate for the presence of ovaries/uterus vs. testicles
  - Genetic and endocrinology consultations

Anus

- The anus should be examined carefully to confirm it is not just a fistula
- Presence of meconium does not rule out imperforate anus; meconium may pass from the fistula
- Position of the anus should be determined
- Mild mislocation of the anus may be associated with constipation later in life
- Meconium usually passes in the first 24 h of birth and 99% of term infants will pass meconium within the first 48 h
- Impaction of meconium that causes intestinal obstruction is often associated with cystic fibrosis (CF)

BACK

Sacral dimple

- A pilonidal sinus (sacral dimple) may be present at the base of the spine between the buttocks
  - Typically, benign
  - Rarely, a true sinus tract associated with a myelomeningocele may be present
  - May be associated with a tethered cord
- Abnormal pigmentation, overlying hemangioma, pigmented nevus, or a hair tuft over the lower spine may be associated with vertebral anomalies
- Indication for ultrasound or MRI
  - Multiple dimples
  - Dimple diameter more than 5 mm
  - Dimple > 2.5 cm above the anus (the higher the lesion, the higher the risk)
  - Dimple outside the sacrococcygeal region
  - Marked by a tuft of hair, skin discoloration, or skin tag
  - Base of the dimple cannot be visualized
- Indications for referral to neurosurgery
  - Abnormal ultrasound or MRI, e.g., occult spinal dysraphism; split cord malformation, dermal sinus tract, tethered spinal cord, and intraspinal lipoma
  - Other associated cutaneous findings, e.g., hypertrichosis and hemangioma
  - Abnormal neurologic examination

EXTREMITIES

Developmental dysplasia of the hip (DDH)

- Ortolani and Barlow tests (See also Chap. 13 Orthopedics) must be performed for all newborns before discharge from the newborn nursery

Hemihypertrophy

- Wilms tumor occurs in association with either isolated hemihypertrophy of the extremities or Beckwith-Wiedemann syndrome

Polydactyly

- Ulnar or postaxial polydactyly
  - The most common and usually isolated condition
  - Postaxial polydactyly more common than pre-axial polydactyly
  - Usually autosomal dominant with incomplete penetrance
- Radial or preaxial polydactyly
  - Usually syndromic and associated with other anomalies

Assessment of gestational age (Table 2.3)

Table 2.3 Gestational age ranges according to the physical characteristics of newborn and maturity

Body parts	Characteristics	Weeks of gestation range
Vernix (waxy or cheese-like white substance found coating the skin of newborn babies)	Coat the entire body	< 38 weeks
	Less coated areas	38–39 weeks
	Scant	40–41 weeks
	No vernix	> 42 weeks
Lanugo (very fine, soft, unpigmented, downy hair covers the body of a newborn)	Covers most of the body	< 32 weeks
	Disappears from face	33–37 weeks
	Present on shoulders only	38–41 weeks
	None present	≥ 42 weeks
Testes	Palpable in inguinal canal	< 36 weeks
	Palpable in upper scrotum	36–39 weeks
	Palpable in lower scrotum	≥ 40 weeks
Scrotum	Few rugae	< 36 weeks
	More rugae	36–39 weeks
	Rugae all over the scrotum	40–41 weeks
	Pendulous scrotum	≥ 42 weeks
Labia and clitoris	Prominent clitoris and labia minora	Preterm
	Labia majora is prominent	Full-term
Sole creases	No anterior sole creases	< 32 weeks
	1–2 anterior creases	32–33 weeks
	2–3 anterior creases	34–35 weeks
	2/3 of the anterior sole with creases	36–37 weeks
	Heel creases present	38–41 weeks
	Deeper creases over entire sole	≥ 42 weeks

NEONATAL CONDITIONS

Intrauterine Growth Retardation (IUGR)

Definition

- IUGR, which is defined as less than 10% of predicted fetal weight for GA, may result in significant fetal morbidity and mortality
- Second leading cause of perinatal mortality

Causes

- Fetal factors:
  - Chromosomal abnormalities (aneuploidy)
  - Multifactorial congenital malformations—cardiovascular abnormalities, renal agenesis
  - Multiple gestation
  - Infections: Congenital cytomegalovirus, toxoplasmosis, herpes simplex virus (HSV), rubella
  - Aberrant genomic imprinting—uniparental disomy
- Maternal factors
  - Chronic diseases—hypertension, chronic renal disease, systemic lupus erythematosus, DM
  - Preeclampsia early in gestation
  - Smoking, drugs, and alcohol
  - Constitutionally small mother
  - Malnutrition
- Placental factors
  - Placental infarction
  - Small placenta
  - Chronic vascular disease
  - Uteroplacental insufficiency

Symmetrical (proportional) vs. asymmetrical (relative head sparing) IUGR

- **Symmetrical IUGR** results from an early fetal insult caused by chemical exposure (e.g., nicotine from cigarette smoking), viral infection, or inherent developmental abnormalities caused by aneuploidy
- **Asymmetrical IUGR** is likely to result from uteroplacental insufficiency

Diagnosis

- Although no single biometric or Doppler measurement is completely accurate for helping make or exclude the diagnosis of growth restriction, screening for IUGR is important to identify at-risk fetuses

Multiple Births

Definition

- Multiple births occur when multiple fetuses are carried during a pregnancy with the subsequent delivery of multiple neonates

Types

- **Dizygotic twins** develop when two ova are fertilized; dizygotic twins have separate amnions, chorions, and placentas
- **Monozygotic twins** develop when a single fertilized ovum splits after conception. An early splitting (i.e., within 2–3 days after fertilization) of monozygotic twins produces separate chorions and amnions (dichorionic diamniotic). Monochorionic monoamniotic twins occur when the split takes place after the ninth day after fertilization. Cleavage of the fertilized ovum between days 4 and 8 of fertilization results in monochorionic diamniotic twins

Associated complications

- Premature delivery
- Malpresentation
- Congenital abnormalities
- Umbilical cord compression and cord entanglement
- Placental abruption
- Twin-twin transfusion syndrome
- Fetal growth restriction
- Conjoined twins
  - Occur only in monoamniotic, monochorionic twins
  - Occur in 1/50,000 births

Infant of Diabetic Mother (IDM)

Background

- About 3–10% of pregnancies are affected by abnormal glucose regulation and control. Of these cases, 80–88% are related to abnormal glucose control of pregnancy or gestational DM
- Hyperglycemia during pregnancy causes fetal hyperglycemia and fetal hyperinsulinemia
- Fetal congenital malformations are most common when maternal glucose control has been poor during the first trimester of pregnancy
- Preconceptional glycemic control in women with diabetes cannot be overstated
- Maternal hyperglycemia during late gestation is more likely to lead to fetal macrosomia, hypoxia, polycythemia, and cardiomegaly with outflow tract obstruction

Complications

- Fetal macrosomia
  - Weight > 90th percentile for GA or > 4000 g in the term infant occurs in 15–45% of diabetic pregnancies
  - Most commonly observed as a consequence of maternal hyperglycemia and fetal hyperinsulinemia
  - Infant may appear puffy, fat, ruddy, and often hypotonic
  - LGA infants should be routinely screened for hypoglycemia
- Impaired fetal growth
  - Infants whose BW is below the tenth percentile are considered SGA
  - Impaired fetal growth may occur in as many as 20% of diabetic pregnancies
  - Maternal renovascular disease is a common cause of impaired fetal growth in pregnancies complicated by maternal diabetes
  - Perinatal asphyxia is more common in infants with impaired fetal growth

- Pulmonary disease
  - IDM are at increased risk of **respiratory distress syndrome** that may present within the first few hours after birth with tachypnea, nasal flaring, intercostal retractions, and hypoxia
  - Transient tachypnea of the newborn
  - **Persistent pulmonary hypertension of newborn** secondary to polycythemia may occur
- Metabolic and electrolyte abnormalities
  - Hypoglycemia is caused by hyperinsulinemia due to hyperplasia of fetal pancreatic beta cells consequent to maternal-fetal hyperglycemia
  - Hypoglycemia may present within the first few hours of life and may persist for as long as a week
  - Infant may present with no symptoms
  - Jitteriness, irritability, apathy, poor feeding, high pitched or weak cry, hypotonia, or frank seizure activity may occur
- Hypocalcemia or hypomagnesemia
  - Symptoms may include jitteriness or seizure activity
  - Hypocalcemia (levels < 7 mg/dL) is believed to be associated with a delay in parathyroid hormone synthesis after birth
- Iron deficiency
  - 5% of all IDMs demonstrate abnormalities of iron metabolism at birth
  - Iron deficiency increases the infant's risk for neurodevelopmental abnormalities
- Polycythemia
  - Caused by increased erythropoiesis triggered by chronic fetal hypoxia
  - Clinically presents as "ruddy" appearance, sluggish capillary refill, or respiratory distress
  - Hyperviscosity due to polycythemia increases the risk for stroke, seizure, necrotizing enterocolitis, and renal vein thrombosis
- Hyperbilirubinemia
  - Common, especially in association with polycythemia
- Thrombocytopenia
- Cardiovascular anomalies
  - Cardiomyopathy with ventricular hypertrophy and outflow tract obstruction may occur in as many as 30% of IDMs
    - Cardiomyopathy may be associated with congestive failure with a weakly functioning myocardium or may be related to a hypertrophic myocardium with significant septal hypertrophy and outflow tract obstruction
  - Echocardiography is indicated if cardiomegaly or hypoperfusion are present
  - Increased risk of congenital heart defects, including (most commonly) ventricular septal defect (VSD) and transposition of the great arteries (TGA)
- Congenital malformations
  - CNS malformations are 16 times more likely in IDMs
    - Risk of anencephaly is 13 times higher
    - Risk of spina bifida is 20 times higher
  - Sacral agenesis; the risk of caudal dysplasia is up to 600 times higher in IDM
  - Increased risk of renal abnormalities—hydronephrosis, renal agenesis, and ureteral duplication
  - Increased risk of GI abnormalities—small left colon syndrome, and duodenal or anorectal atresia

Management of Hypoglycemia

- Screening policy for hypoglycemia after birth is necessary to detect hypoglycemia
- Initial feed within 1 h; screen glucose within 30 min
- Asymptomatic infant; birth—4 h of age:
  - If initial blood glucose value is < 25 mg/dL
  - Refeed and check blood glucose in 1 h
  - If blood glucose is still < 25 mg/dL, immediate IV with 2 mL/kg infusion of 10% dextrose followed by continuous infusion of dextrose at an infusion rate of 5–8 mg/kg/min

    - Failure to start maintenance dextrose infusion may result in rebound hypoglycemia as a result of heightened pancreatic insulin release triggered by the glucose infusion
    - Once the infant's glucose levels have been stable for 12 h, IV glucose may be tapered by 1–2 mg/kg/min
    - Achieve plasma glucose of 45–50 mg/dL
  - If blood glucose level is 25–40 mg/dL:
    - Refeed; provide IV dextrose as needed
- **Asymptomatic infant; 4–24 h of age:**
  - Continue feeds every 2–3 h
  - If blood glucose is < 35 mg/dL:
    - Refeed and check blood glucose in 1 h
    - If blood glucose is still < 35 mg/dL, immediate IV therapy with 2 mL/kg infusion of 10% dextrose followed by continuous infusion of dextrose at an infusion rate of 5–8 mg/kg/min
  - If blood glucose is 35–45 mg/dL, refeed; provide IV dextrose as needed
  - Provide IV dextrose if infant develops symptoms of hypoglycemia

Hyperbilirubinemia

- Jaundice occurs in approximately 60% of neonates born yearly in the USA
- Most common condition that requires medical attention and hospital readmission in newborns

Pathophysiology

- Hemolysis of RBCs→hemoglobin is released
- Biliverdin is formed from heme through the action of heme oxygenase
- Biliverdin reductase reduces biliverdin to unconjugated (indirect) bilirubin
- **Unconjugated bilirubin** binds to albumin and is transported to the liver
- **Unconjugated bilirubin** can become unbound if albumin is saturated or if bilirubin is displaced from albumin by medications (e.g., sulfisoxazole, streptomycin, chloramphenicol, ceftriaxone, ibuprofen, salicylates)
- **Unbound unconjugated bilirubin** can cross the blood-brain barrier and is toxic to the CNS
- Once unconjugated bilirubin reaches the liver, it is conjugated by uridine diphosphate glucuronosyl transferase (**UGT1A1**)
- **Hepatic UGT1A1** increases dramatically in the first few weeks after birth
- At 30–40 weeks gestation, UGT1A1 values are approximately 1% of adult values, rising to adult concentrations by **14 weeks of age**
- Conjugated (direct) bilirubin is excreted into the intestine via the gallbladder and bile duct
- Bacteria in the intestine can deconjugate bilirubin, allowing it to be reabsorbed into the blood. The rest of the bilirubin is excreted with the stool

Physiologic Jaundice

Background

- Unconjugated hyperbilirubinemia that occurs after the first postnatal day
  - Jaundice that is visible during the first day of life is pathologic
  - Infants who present with jaundice after 3–4 days of life may also require closer scrutiny and monitoring
  - In infants with severe jaundice or jaundice that continues beyond the first 1–2 weeks of life:
    - Check for galactosemia and congenital hypothyroidism in newborn metabolic screen results
    - Explore family history
    - Evaluate infant's weight curve
    - Elicit mother's impressions of the adequacy of breastfeeding
    - Assess stool color
- It can last up to 1 week
- **Total serum bilirubin (TSB)** concentration peaks in the first 3–5 postnatal days in term infants
- A decline to adult values over the next several weeks

- TSB concentrations vary greatly in infants, depending on race, type of feeding, and genetic factors

Physiologic jaundice occurs in infants for a number of reasons:

- Increased breakdown of fetal erythrocytes due to:
  - Shortened lifespan of fetal erythrocytes (70–90 days)
  - Higher erythrocyte mass in neonates
- Hepatic excretory capacity is low because of:
  - Low concentrations of the binding protein ligandin in the hepatocytes
  - Low activity of glucuronyl transferase, the enzyme responsible for binding bilirubin to glucuronic acid, thus making bilirubin water soluble (conjugation)
  - Thus, neonates have a high rate of bilirubin production and an impaired ability to extract bilirubin from the body

Clinical presentation

- Jaundice
- The TSB concentration peaks at approximately 5.5 mg/dL (94.1 μmol/L) by the third postnatal day in white and African American infants
- By 96 h of age, 95% of infants have TSB concentrations of < 17 mg/dL
- Bilirubinemia > 17 mg/dL is not physiologic

Risk factors for development of severe hyperbilirubinemia in newborns > 35 weeks GA

- Jaundice observed in the first 24 h of age
- Predischarge TSB or transcutaneous bilirubin in the high-risk zone
- Blood group incompatibility (ABO or Rh) with positive direct antiglobulin test; other known hemolytic disease such as glucose-6-phosphate dehydrogenase deficiency
- GA of 35–36 weeks
- Previous sibling requiring phototherapy
- Cephalohematoma or significant bruising
- Poor feeding
- Exclusive breastfeeding
- East Asian race (defined by mother's description) or Mediterranean descent
- Jaundice observed before discharge
- Macrosomic infant of a diabetic mother
- Male gender

Early Onset Breastfeeding Jaundice

Background

- Early onset breastfeeding jaundice (manifests in the first 3 days of life) is the most common cause of unconjugated hyperbilirubinemia

Causes

- Breastfeeding exaggerates physiologic jaundice in the first postnatal week because of caloric deprivation, leading to an increase in enterohepatic circulation
- Mild dehydration and delayed passage of meconium also plays roles

Prevention

- Successful breastfeeding decreases the risk of hyperbilirubinemia
- Infants need to be fed at least 8–12 times in the first few days after birth to help improve the mother's milk supply
- The best way to judge successful breastfeeding is to monitor infant urine output, stool output, and weight
- Newborns should have four to six wet diapers and three to four yellow, seedy stools per day by the fourth day after birth
- Breastfed infants should lose no more than 10% of their body weight by the third or fourth postnatal day
- Formula supplementation may be necessary if the infant has significant weight loss, poor urine output, poor caloric intake, or delayed stooling

- Water and dextrose solutions should not be used to supplement breastfeeding because they do not prevent hyperbilirubinemia and may lead to hyponatremia

Late Onset Breast Milk Jaundice

Background

- Thought to be a normal exaggeration of physiologic jaundice in human milk fed infants
- Indirect hyperbilirubinemia that develops in an otherwise healthy breastfed newborns after the first 4–7 days of life and may persist for 6–12 weeks
- Exact mechanism is not entirely clear
- It is suggested that beta-glucuronidases and non-esterified fatty acids in the human milk inhibit enzymes that conjugate bilirubin in the liver

Management

- Breastfeeding should be continued and parents reassured
- Ensure there are no other causes of prolonged hyperbilirubinemia (e.g., galactosemia, hypothyroidism, urinary tract infection (UTI), hereditary spherocytosis)
- If serum bilirubin levels continue to rise or > 20 mg/dL, breastfeeding can be discontinued for 48 h to observe whether a decrease in TSB concentration occurs. Phototherapy may be considered:
  - During this time, the mother should continue to express milk to maintain her supply and supplement the infant with formula
  - TSB concentrations usually peak between 12 and 20 mg/dL (205.2 and 342.1 μmol/L) and should decrease by 3 mg/dL (51.3 μmol/L) per day. If this decrease occurs, breastfeeding should be restarted
  - Phototherapy, if needed, can be administered with standard phototherapy units and biliblankets

Jaundice in Premature Infants

- Hyperbilirubinemia is more common and more severe in preterm infants and lasts longer
- Sick preterm newborns are more likely to have a delay in initiating enteral nutrition, resulting in an increase in enterohepatic circulation
- Kernicterus is extremely uncommon; however, kernicterus does occur at lower TSB concentrations, even without acute neurologic signs
- TSB values as low as 10–14 mg/dL (171.0–239.5 μmol/L) have resulted in milder forms of bilirubin-induced neurologic dysfunction in preterm infants
- Initiation of phototherapy according to the weight of infants and associated complications is paramount (Table 2.4) [2]

Table 2.4 Suggested use of phototherapy and exchange transfusion in preterm infants < 35 weeks gestational age[b]

	Phototherapy	Exchange transfusion
Gestational age (wk)	Initiate phototherapy total serum bilirubin[a] (mg dl^{-1})	Total serum bilirubin (mg dl^{-1})
< 28 0/7	5–6	11–14
28 0/7–29 6/7	6–8	12–14
30 0/7–31 6/7	8–10	13–16
32 0/7–33 6/7	10–12	15–18
34 0/7–34 6/7	12–14	17–19

[a]Use the lower range of the listed total serum bilirubin (TSB) levels for infants at greater risk for bilirubin toxicity (e.g., lower gestational age, serum albumin levels < 2.5 g/dL, clinically unstable infants). Recommendations for exchange transfusion apply to infants who are receiving intensive phototherapy but whose TSB levels continue to increase to the levels listed. For all infants, an exchange transfusion is recommended if the infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonus, high-pitched cry)

[b]From Maisels et al. [2], with permission

Unconjugated Hyperbilirubinemia

Causes

- Increased bilirubin production
- Deficiency of hepatic uptake
- Increased enterohepatic circulation
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency; more common in African American
- Blood group incompatibility
- Structural defects in erythrocytes
- Impaired conjugation of bilirubin

Gilbert syndrome

- Autosomal recessive condition in which UGT1A1 activity decreases mildly in hepatocytes, typically resulting in a benign unconjugated hyperbilirubinemia
- The likelihood of severe hyperbilirubinemia is increased if the infant also has G6PD deficiency

Crigler-Najjar syndrome type 1

- Autosomal recessive
- Severe deficiency of UGT1A1 results in intense jaundice in the first days of life and persists thereafter. Bilirubin encephalopathy develops in the first few days or month after birth

Crigler-Najjar syndrome type 2

- Autosomal dominant
- Bilirubin levels are generally < 20 mg/dL
- The incidence of bilirubin encephalopathy is low.

Conjugated Hyperbilirubinemia (See Also Chap. 22 Gastroenterology)

Background

- Conjugated bilirubin concentration greater than 1 mg/dL when the TSB concentration is < 5 mg/dL (85.6 μmol/L) ***or***
- Conjugated bilirubin level > 20% of the TSB if the total is > 5 mg/dL

Causes

- Biliary atresia
- Thyroid abnormalities
- Galactosemia
- Alagille syndrome
- Choledochal cyst
- Viral infections, e.g., cytomegalovirus (CMV), human immunodeficiency virus (HIV)
- Bacterial infections (UTI, syphilis); sepsis
- Idiopathic neonatal hepatitis
- Prolonged parenteral nutrition

Kernicterus

Background

- Kernicterus is brain injury caused by unconjugated bilirubin deposition in basal ganglia and brain stem nuclei
- Bilirubin can cross the blood-brain barrier and enter the brain tissue if it is unconjugated and unbound to albumin, or if there is damage to the blood-brain barrier
- Acute bilirubin toxicity may occur in a term infant if there are no signs of hemolysis and the TSB concentration is greater than 25 mg/dL
- Physicians should be concerned if the TSB concentration is above 20 mg/dL in a term infant who has hemolysis

Clinical presentation

- Bilirubin-induced neurologic dysfunction (BIND) is the term applied to the spectrum of neurologic abnormalities associated with hyperbilirubinemia, approximately 15% of babies with BIND have no neurologic signs
- Clinical features have been well described and can be divided into 3 stages:
- **Phase 1** (first few days of life):
  - Decreased alertness
  - Hypotonia
  - Poor feeding, poor suck

- A high index of suspicion of possible BIND at this stage that leads to prompt intervention can halt the progression of the illness, significantly minimizing long-term sequelae
  - Of note, seizure is not typically associated with acute bilirubin encephalopathy
- **Phase 2** (variable onset and duration):
  - Hypertonia of the extensor muscles is a typical sign. Patients present clinically with retrocollis (backward arching of the neck), opisthotonus (backward arching of the back), or both. Infants who progress to this phase develop long-term neurologic deficits
- **Phase 3** (infants aged > 1 wk): Hypotonia is a typical sign

Chronic Bilirubin Encephalopathy

- Clinical features evolve slowly over the first several years of life in the affected infant
- The clinical features can be divided into phases:
  - First phase occurs in the first year of life: Hypotonia, hyperreflexia, and delayed acquisition of motor milestones
  - Tonic neck reflex can be observed
- Extrapyramidal abnormalities: Athetosis is the most common movement disorder, although chorea can also occur
  - Upper extremities are usually more affected than the lower ones; bulbar functions can also be impacted
- Visual abnormalities:
  - Ocular movements are affected, most commonly resulting in upward gaze
  - Horizontal gaze abnormalities
  - Gaze palsies
- Auditory abnormalities:
  - High frequency hearing loss
  - Delayed language acquisition
- Abnormalities of dentition: Dental enamel hypoplasia
- Cognitive function is relatively spared, but minor intellectual deficits can also occur

ABO and Rh Incompatibility (See Chap. 10 Hematology/Oncology)

- ABO incompatibility may occur if the mother's blood type is O and the infant's blood type is A or B
- Infants should be assessed for jaundice at a minimum of every 8–12 h after birth; earlier assessment is indicated if cord bilirubin is > 1.5 mg/dL

Transcutaneous Bilirubin Devices

- Newer devices used to detect transcutaneous bilirubin (TcB) have been shown to correlate well with TSB
  - Important to note that TcB assessments and clinical examination are unreliable after phototherapy
- Once TcB or TSB has been measured, the result should be interpreted based on the nomogram
  - The value should be plotted on the nomogram to assess the risk level and whether or not treatment is indicated
- AAP Subcommittee on Hyperbilirubinemia has recommended assessing TSB or TcB on all newborns before discharge [3]

Management of Hyperbilirubinemia

Feeding

- More frequent feeding (breastfeeding or bottle feed) every 2–3 h

Phototherapy

- Phototherapy works by converting bilirubin into a water-soluble compound, lumirubin, which is excreted in the urine or bile
- When bilirubin decreases to 13–14 mg/dL, discontinue phototherapy
- Consider exchange transfusion if the TSB is not decreasing or is moving closer to the level for exchange transfusion

- Depending on the cause of hyperbilirubinemia, measuring TSB 24 h after discharge to check for rebound is an option

Complications of phototherapy

- Insensible water loss (increase fluid intake or the volume and frequency of feeding)
- Phototherapy may be associated with loose stool
- Retinal damage (covering the eye is routine during phototherapy)

Treatment of hyperbilirubinemia if bilirubin level is not decreasing

- Intravenous immunoglobulin
- Exchange transfusion

Hemorrhagic Disease of the Newborn

Background

- Also referred to as vitamin K deficiency bleeding
  - Transient deficiency in vitamin K-dependent factors
- Presents in three forms:
  - **Early** (first 24 h): Associated with maternal use of drugs such as anticoagulants, barbiturates, carbamazepine, phenytoin, some cephalosporins, rifampin
  - **Classic** (2–7 days of life): Associated with no vitamin K prophylaxis at birth
  - **Late** (after 1 week of age): Occurs in exclusively breastfed infants who have not received adequate vitamin K prophylaxis, and with vitamin K malabsorption, e.g., neonatal hepatitis, biliary atresia

Clinical presentation

- Bleeding can occur anywhere, e.g., GI, nasal, subgaleal, intracranial, circumcision bleeding, following cord separation, after phlebotomy

Diagnosis

- Elevated PT due to low vitamin K

Treatment

- Treat with 1 mg IV vitamin K ± fresh frozen plaza (FFP)

Prevention

- 1 mg vitamin K IM administration after birth

Respiratory Distress Syndrome (RDS) (aka Hyaline Membrane Disease)

Background

- The most common cause of respiratory failure in the newborn
- Occurs almost exclusively in premature infants
- The incidence and severity of RDS are related inversely to the GA of the newborn infant
- RDS develops in premature infants because of impaired surfactant synthesis and secretion leading to lung atelectasis
- RDS does not occur in all preterm babies
- Surfactant protein (SP) deficiency occurs in a small group of term infants with severe respiratory distress that leads to intractable respiratory failure and death
  - SP-B deficiency is the most common form and occurs as an autosomal recessive trait

Surfactant is stored in type II alveolar cells and composed of

- Dipalmitoyl phosphatidylcholine
- Phosphatidylglycerol
- Apoproteins (SP-A, B, C, and D)
- Cholesterol

Risk factors

- Prematurity
- Maternal DM
- C-section
- Asphyxia
- Male gender
- Hypothermia
- Multiple gestations
- Family history of a sibling who developed RDS

Factors that decrease the risk of RDS

- Premature rupture of membranes
- Maternal hypertension
- Sub-acute placental rupture
- Maternal use of narcotics

Clinical presentation

- Same as that seen in other conditions that cause respiratory distress
- Tachypnea usually > 60 breaths/min
- Expiratory grunting (from partial closure of glottis)
- Subcostal and intercostal retractions
- Cyanosis
- Nasal flaring
- Extremely premature neonates may develop apnea and/or hypothermia

Diagnosis

- Chest radiograph (Fig. 2.6)
  - Bilateral, diffuse, reticular granular, or ground glass appearance
  - Diffuse atelectasis and air bronchograms (prominent air bronchograms represent aerated bronchioles superimposed on a background of collapsed alveoli)

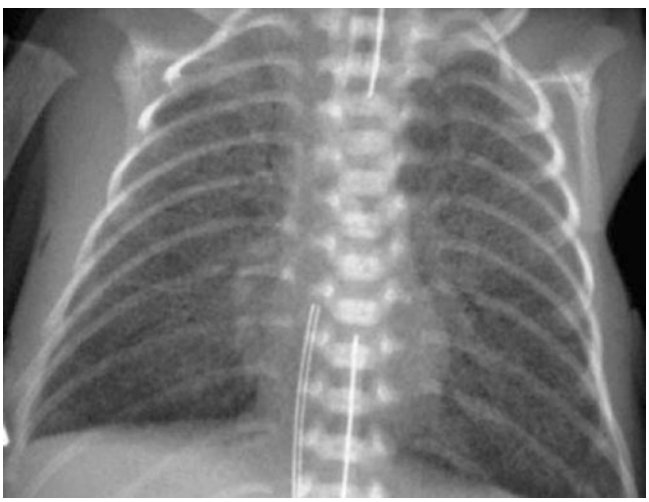

Fig. 2.6 Chest radiograph of premature newborn shows a bilateral and symmetrical diffuse ground glass lung appearance with a hyperinflated thorax (due to intubation). Without intubation, the thorax typically has a low volume. In some patients, air-bronchograms can be seen. The patient has venous and arterial umbilical catheters

  - Poor lung expansion
  - The appearance of GBS pneumonia on chest radiograph can be identical to that of RDS
- Blood gas
  - Hypoxia
  - Metabolic acidosis
  - Hypercarbia
- Fetal lung test for maturity prediction
  - Lecithin-to-sphingomyelin ratio ***and/or***
  - Testing for the presence of phosphatidylglycerol in amniotic fluid obtained by amniocentesis

Management

- Prenatal administration of steroids (betamethasone)
- Maintain core temperature
- Nasal continuous positive airway pressure (CPAP) is often used for initial stabilization in spontaneously breathing premature infants immediately after birth
- Intubation and mechanical ventilation (MV) in infants who do not respond to noninvasive ventilation strategies and surfactant therapy
- Surfactant prophylaxis may be considered in infants < 27 weeks gestation
- Prophylactic surfactant may be considered for neonates > 26 weeks but < 30 weeks gestation if intubation is required or if the mother has not received any prenatal steroids
- Many institutions practice only rescue surfactant
- When possible, duration of MV should be shortened by early extubation to CPAP after surfactant administration, provided the newborn is otherwise stable
- IV fluids if respiratory status is not stable: 10% glucose in the first 24 h
- Parenteral nutrition should be provided to very preterm infants
- Treat with antibiotics until sepsis is ruled out
- Cardiac causes should be considered in worsening cases despite appropriate therapy

Prenatal steroids

- Decreases the incidence and severity of RDS
- Usually given to women at 24–34 weeks gestation with high risk for preterm birth, e.g., premature rupture of membrane

Transient Tachypnea of the Newborn (TTN)

Background

- TTN is a common, relatively benign self-limited disease in newborns
- Infants with TTN present within the first few hours of life with tachypnea, increased oxygen requirement, and arterial blood gases (ABGs) that do not reflect carbon dioxide retention
- TTN is the result of a delay in clearance of fetal lung fluid by the lymphatics and pulmonary circulation, with resultant transient pulmonary edema
- Most common in infants delivered between 37 and 42 weeks gestation
- Common with C-section delivery in the absence of labor
- Other risk factors are male sex; perinatal asphyxia; umbilical cord prolapse; and maternal complications such as asthma, diabetes, and anesthesia and analgesia during labor

Clinical presentation

- Signs of respiratory distress (e.g., tachypnea, nasal flaring, grunting, retractions, cyanosis in extreme cases) become evident shortly after birth
- The disorder is transient with resolution usually occurring within 72 h after birth
- Extreme cases may exhibit cyanosis
- Prolonged course > 72 h or clinical deterioration may suggest other diagnosis

Diagnosis

- Chest radiograph:
  - Hyperinflation
  - Prominent perihilar vascular markings, which correlates with the engorgement of the lymphatic system with retained lung fluid
  - Fluid in the fissures
  - Small pleural effusions may also be present

Treatment

- Supportive care
- Supplemental oxygen may be required
- Antibiotics may be considered until sepsis has been ruled out
- Provide IV hydration and nutrition

Persistent Pulmonary Hypertension of the Newborn (PPHN)

Background

- PPHN is defined as the failure of the normal circulatory transition that occurs after birth
  - Syndrome characterized by marked pulmonary hypertension that causes hypoxemia secondary to right-to-left shunting of blood at the foramen ovale and ductus arteriosus
- Most often recognized in term or near-term neonates but can also occur in preterm infants
- Selective serotonin reuptake inhibitors (SSRIs), commonly prescribed antidepressants, have been reported to be associated with PPHN, especially during the third trimester of pregnancy
- Genetic factors may increase susceptibility to pulmonary hypertension, e.g., polymorphisms of the carbamoyl phosphate synthase gene and urea cycle enzyme genes
- Higher frequency in babies with Down syndrome

Etiology and common associated conditions

- Idiopathic
- RDS
- Polycythemia
- Hypoglycemia

- Meconium aspiration
- GBS pneumonia
- Sepsis
- Diaphragmatic hernia
- Pulmonary hypoplasia
- IDM
- Down syndrome

Clinical presentation

- Usually symptoms appear in the first 24 h
- Tachypnea
- Cyanosis
- Respiratory distress (grunting, flaring, retraction, tachycardia)
- Profound and often labile hypoxemia
- Preductal and postductal oxygen saturation gradient difference of at least 10% (with preductal saturations being higher)
- Loud, single second heart sound (S2)
- A harsh systolic murmur secondary to tricuspid regurgitation may be heard
- Systemic hypotension, shock, and evidence of poor perfusion may occur

Diagnosis

- Hypoxemia is universal and poorly responsive to 100% oxygen
- Differential cyanosis: Higher oxygen saturation in preductal blood (right radial artery) than that obtained from tibial arteries (postductal)
- Echocardiography is essential for distinguishing congenital heart disease from PPHN, which is a diagnosis of exclusion
  - Right ventricular hypertrophy
  - Bowing of the interventricular septum into the left ventricle
  - Tricuspid regurgitation
  - Right-to-left or bidirectional shunting at the patent foramen ovale and/or patent ductus arteriosus

Management

- Treatment of the underlying cause is the most important step
- Minimize stimulation
- Maintain a normal body temperature and correct electrolytes, glucose abnormalities and metabolic acidosis
- Maintain adequate systemic BP
- MV; avoid hyperventilation
- Inhaled nitric oxide
- Extracorporeal membrane oxygenation (ECMO)

Meconium Aspiration Syndrome (MAS)

Background

- Meconium aspiration is one of the most common etiologies of respiratory failure in newborns
- Because meconium is rarely found in the amniotic fluid prior to 34 weeks gestation, meconium aspiration primarily affects infants born at term and post-term

Factors that increase the risk of meconium aspiration

- Placental insufficiency
- Maternal hypertension
- Preeclampsia
- Oligohydramnios
- Maternal drug abuse, especially of tobacco and cocaine
- Maternal infection/chorioamnionitis
- Fetal hypoxia and acidosis

Clinical presentation

- Cyanosis
- Nasal flaring
- End-expiratory grunting
- Intercostal retractions
- Tachypnea
- Barrel chest in the presence of air trapping
- Auscultated rales and rhonchi (in some cases)
- Yellow-green staining of fingernails, umbilical cord, and skin may be observed

Diagnosis

- Chest radiograph
  - Air trapping and hyperexpansion from airway obstruction
  - Diffuse chemical pneumonitis (streaky, linear, or patchy infiltrates)
  - Acute atelectasis
  - Pneumomediastinum and other air leak syndromes

Prevention of MAS

- AAP recommendations
  - If the infant is not vigorous (defined as depressed respiratory effort, poor muscle tone, and/or heart rate < 100 beats/min): Place the infant on a radiant warmer, clear the secretions with a bulb syringe, and proceed with the normal steps of newborn resuscitation (i.e., warming, repositioning the head, drying, and stimulating). If after these initial steps the infant is still apneic or the heart rate is < 100 beats bpm, administer PPV to minimize the delay in initiating ventilation
  - If the infant is vigorous (defined as normal respiratory effort, normal muscle tone, and heart rate > 100 beats/min): Do not electively intubate. Clear secretions and meconium from the mouth and nose with a bulb syringe and proceed with the normal steps of neonatal resuscitation
  - Resuscitation should follow the same principles as for infants born through clear amniotic fluid

Management

- Oxygen therapy
- Surfactant therapy commonly used
- Noninvasive or invasive MV
- Supportive care—Maintain fluid and electrolyte balance; maintain normal BP
- Inhaled nitric oxide
- ECMO if infant unresponsive to medical management

Pneumothorax and Pneumomediastinum

Background

- Pneumothorax refers to the presence of air or gas in the pleural cavity between the visceral and parietal pleura
- Pneumomediastinum is air in the mediastinum that may be confused with pneumothorax
- Pneumothorax may be iatrogenic or spontaneous
- Factors associated with pneumothorax:
  - Overly vigorous resuscitation at birth
  - RDS
  - MAS
  - Pneumonia
  - Pulmonary hypoplasia
  - Assisted ventilation

Clinical presentation

- Depends on the severity and size of the pneumothorax
- Tension pneumothorax:
  - Cyanosis
  - Hypoxemia
  - Tachypnea
  - Sudden decrease in heart rate
  - Hypotension
  - Narrowed pulse pressure
  - Decreased breath sounds on the affected side
  - Shift of the maximal cardiac impulse away from the affected side

Chest radiograph

- Shift of mediastinum away from the side of pneumothorax
- Depressed diaphragm
- Displacement of the lung to the opposite side

Management

- Symptomatic tension pneumothorax is an emergency

  - Transillumination of the chest is useful for immediate diagnosis
  - Limited time for chest radiograph confirmation
- If the patient is deteriorating rapidly:
  - A 22–24-gauge needle or angiocath can be inserted for aspiration (thoracentesis). The site of puncture should be at the second or third intercostal space along the midclavicular line
  - Thoracostomy or chest tube placement may be needed
- Asymptomatic pneumothorax: 100% oxygen administration for 8–12 h may be considered. The rate of resolution of spontaneous pneumothoraces is not improved with oxygen supplementation. Because of concerns regarding the risks of hyperoxia, we do not routinely administer supplemental oxygen above the concentration needed to maintain adequate saturation.

Neonatal Sepsis

Background

- Neonatal sepsis may be categorized as early onset or late onset
- Newborns with **early onset sepsis** (< 72 h): 85% present within 24 h, 5% present at 24–48 h, and a smaller percentage present within 48–72 h. Onset is most rapid in premature neonates
- **Late onset sepsis** occurs at > 72 h–28 days of life and is acquired from the caregiving environment
- The microorganisms most commonly associated with early onset infection include the following:
  - GBS
  - *Escherichia coli*
  - Coagulase-negative *Staphylococcus*
  - *Staphylococcus aureus*
  - *Haemophilus influenzae*
  - *Listeria monocytogenes*
  - Enterococci
  - *Haemophili* and other Gram-negatives (*Klebsiella, Enterobacter, Citrobacter, Acinetobacter, Pseudomonas*)
- The microorganisms most commonly associated with late onset infection include the following:
  - Coagulase-negative *Staphylococcus*
  - *S. aureus*
  - *E. coli, Klebsiella,* enterococci, *Pseudomonas, Serratia*
  - *Candida*
  - GBS

Risk factors

- Maternal GBS status
- Premature ROM
- Prolonged ROM
- Maternal fever
- Maternal UTI
- Prematurity
- Chorioamnionitis
- Low BW
- Male gender
- Intrapartum or postpartum instrumentation

Initial clinical presentations of infection

- In newborns, signs of infection are nonspecific and can be subtle or dramatic (Table 2.5)

Common clinical manifestation of bacterial sepsis

- Pneumonia
- Meningitis
- Bacteremia
- Osteomyelitis
- UTIs

Investigations

- Cultures (blood, urine, cerebrospinal fluid)
- CBC and differential (normal count does not rule out sepsis)
  - Neutropenia, especially an absolute neutrophil count < 1800 cells/mcL
  - Immature-to-total (I/T) neutrophil ratio > 0.15 in the first 24 h of life is suggestive of sepsis
  - Thrombocytopenia
- C-reactive protein (CRP)
- Procalcitonin
- Coagulation studies

Table 2.5 Initial clinical presentations of infection in newborn infants

System	Possible clinical presentation of neonatal sepsis
General	Temperature instability
	Hypoglycemia
	Poor feeding
Respiratory	Apnea
	Tachypnea, nasal flaring, grunting, retractions
	Cyanosis
Cardiovascular	Pallor, mottling, cold, clammy skin
	Tachycardia, bradycardia, hypotension
	Delayed capillary refill
Gastrointestinal	Vomiting (bilious or nonbilious)
	Abdominal distension
Central nervous system	Seizures
	Tremor
	Abnormal reflexes
	Irregular respiration
	Full fontanel
	High-pitched cry
Hematologic system	Pallor, jaundice
	Thrombocytopenia, bleeding, petechiae, purpura
Renal	Oliguria
Others	Leukocytosis or leukopenia
	Elevated immature WBCs, e.g., bands
	Elevated C-reactive protein
	DIC
	Lactic acidosis
	Hypoxemia

WBCs white blood cells, *DIC* disseminated intravascular coagulation

- Lumbar puncture is warranted for early- and late onset sepsis
- HSV PCR testing in suspected cases
- Chest radiograph
- MRI may be needed late in the course of complex neonatal meningitis to document obstructive hydrocephalus
- Head ultrasonography in neonates with meningitis may reveal evidence of ventriculitis, abnormal parenchymal echogenicity, extracellular fluid, and chronic changes
- Serially, head ultrasonography can reveal the progression of complications

Management

- When neonatal sepsis is suspected, treatment should be initiated immediately because of the neonate's relative immunosuppression
- Begin antibiotics as soon as diagnostic tests are performed
  - Early onset sepsis: Ampicillin and gentamicin
- An infant with temperature instability needs thermoregulatory support with a radiant warmer or incubator

Medications

- The antibiotics commonly used to treat neonatal sepsis include:
  - Ampicillin and gentamicin for early onset sepsis
  - Nafcillin/vancomycin and gentamicin/cephalosporins for late onset sepsis (antibiotic coverage should be directed at organisms implicated in hospital-acquired infections)
- The choice of antibiotic agents should be based on the specific organisms associated with sepsis

Group B Streptococcal Infection in Neonates

Background

- GBS, also known as *Streptococcus agalactiae*, is best known as a cause of postpartum infection and as the most common cause of neonatal sepsis
- Neonates can acquire the organism vertically in utero or from the maternal genital tract during delivery
  - Although the transmission rate from mothers colonized with *S. agalactiae* to neonates delivered vaginally is approximately 50%, only 1–2% of colonized neonates go on to develop invasive GBS disease
- Preterm neonates have higher rates of GBS late onset disease
- Early onset GBS sepsis often presents within 24 h of delivery but can become apparent up to 7 days postpartum
- Late onset GBS sepsis is defined as infection that presents between 1 week postpartum and age 3 months

- Optimal timing of maternal GBS screening is between 35 and 37 weeks gestation
- Adequate treatment of maternal GBS infection does not rule out GBS infection in infants

Indication of intrapartum GBS prophylaxis

- Previous infant with invasive GBS disease
- GBS bacteriuria during any trimester of the current pregnancy
- Positive GBS vaginal-rectal screening culture in late gestation during current pregnancy
  - Intrapartum antibiotic prophylaxis is not indicated in the two above circumstances if a cesarean delivery is performed before onset of labor on a woman with intact amniotic membranes
- Unknown GBS status at the onset of labor (culture is not done, incomplete, or results unknown) and any of the following:
  - Delivery at < 37 weeks gestation
  - Amniotic membrane rupture ≥ 18 h
  - Intrapartum temperature ≥ 100.4 °F (≥ 38.0 °C)
  - Intrapartum nucleic acid amplification test (NAAT) positive for GBS

Secondary prevention of early onset GBS disease among newborns

- If no GBS prophylaxis was needed, the infant should be managed with routine newborn care
- Full diagnostic evaluation and antibiotic therapy if any signs of neonatal sepsis at any time
- Blood culture, CBC with differential at birth (limited evaluation), and antibiotic therapy if chorioamnionitis
- If intrapartum antibiotic prophylaxis (IAP) was not given ≥ 4 h before delivery and infant < 37 weeks gestation, or duration of rupture of membrane is ≥ 18 h, do a limited evaluation and observe for at least 48 h or more in the hospital
- If IAP was not given ≥ 4 h before delivery, infant > 37 weeks gestation and duration of rupture of membrane < 18 h, observe for at least 48 h or more in the hospital
- If the mother received IAP > 4 h before delivery and the infant is > 37 weeks and asymptomatic, provide routine clinical care

Clinical presentation

- Early onset GBS infection manifests with bacteremia, sepsis, pneumonia, and meningitis
  - Most infants present early in the first 8–12 h
  - Respiratory distress (tachypnea, grunting, and retractions)
  - Cyanosis, apnea, poor perfusion, hypotension, and signs of sepsis can rapidly develop
  - Shock
  - Death can occur
- Late onset GBS infection presents as:
  - Meningitis
  - Occult bacteremia
  - Focal infections such as osteomyelitis or arthritis, facial cellulitis, submandibular cellulitis, or cellulitis-adenitis in other regions

Diagnosis

- Leukopenia or leukocytosis
- Bandemia
- Thrombocytopenia
- Abnormal PT and PTT
- Chest radiograph may show signs of pneumonia
- Abnormal CSF studies in cases of meningitis (See also Chap. 9 Infectious Diseases)

Treatment

- Ampicillin and gentamicin are used empirically for treatment of GBS disease and substituted with penicillin once the organism is cultured from a sterile site
- Pneumonia and septicemia usually require treatment for 10–14 days
- Meningitis usually treated for 14–21 days

Prevention guidelines

- The drug of choice for intrapartum prophylaxis remains intravenous penicillin, with ampicillin as an acceptable alternative.

- Both agents are given every 4 h until delivery, with at least one dose administered 4 h before birth.
- Well-appearing infants whose mothers received adequate intrapartum prophylaxis should be observed for at least 48 h. No diagnostic testing required.
- Well-appearing infants > 37 weeks gestation and none/inadequate maternal prophylaxis with rupture of membranes < 18 h before delivery should be observed for 48 h. No diagnostic testing required.
- Well-appearing infants with none/inadequate maternal prophylaxis and either < 37 weeks gestation or rupture of membranes > 18 h before delivery should have limited evaluation (blood culture, CBC with diff and platelets at birth or 6–12 h) and be observed for 48 h.

Congenital Toxoplasmosis

Background

- Risk of transmission exists with primary infection but not if the infection is acquired before conception
- Infection in the first trimester is less frequent but results in more severe disease, including fetal death in utero or severe CNS involvement, such as cerebral calcifications and hydrocephalus
- Infection in the third trimester is more frequent, and the infant appears normal at birth, but the symptoms may appear later in life, e.g., chorioretinitis
- Treatment during pregnancy has been shown to reduce the rate of transmission and seems to reduce serious neurological sequelae

Clinical presentation

- Classic triad
  - Chorioretinitis (Fig. 2.7)
  - Hydrocephalus
  - Intracranial calcifications
- Hydrops fetalis and death
- IUGR

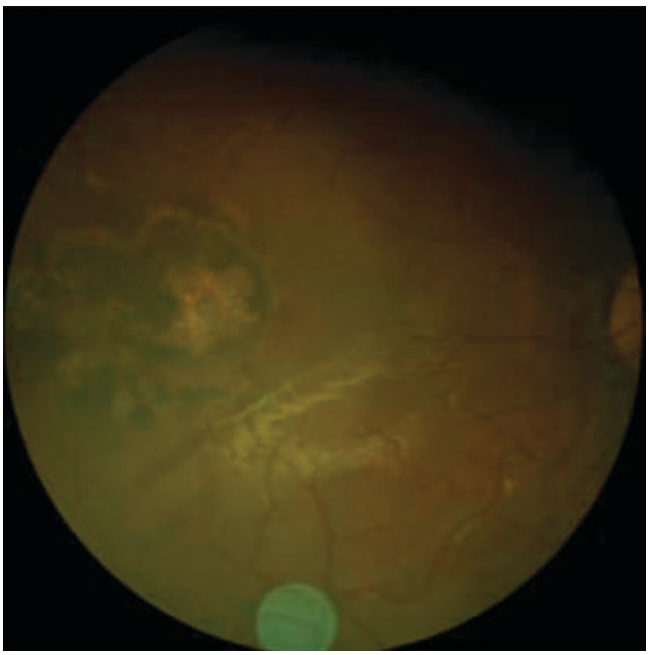

Fig. 2.7 Chorioretinal scar of the right eye, due to toxoplasmosis. (Courtesy of Violeta Radenovich MD MPH, Children's Eye Center, Department of Ophthalmology, Texas Tech University, El Paso, Texas)

- Thrombocytopenia
- Prematurity
- Cytopenias
- Jaundice
- Maculopapular rash
- Visual and learning disabilities

Important

- Approximately, 75% of congenitally infected infants are asymptomatic at birth, but up to 85% of children will develop visual and learning disabilities later in life if they are not treated in infancy

Treatment

- Pyrimethamine and sulfadiazine for 1 year

Congenital Syphilis

Background

- Congenital syphilis is more likely to occur with maternal primary or secondary syphilis, if maternal disease is of unknown duration or

untreated, if < 4 weeks have elapsed between treatment and delivery, or if maternal plasma nontreponemal titer (VDRL or RPR) is > 1:16 after therapy or delivery
  - The transmission rate approaches 90% if the mother has untreated primary or secondary syphilis
- Fetal infection can develop at any time during gestation

Clinical presentation
- Asymptomatic: 60% of infants born with congenital syphilis are asymptomatic at birth
- Hepatomegaly: The most common physical finding, reported in almost 100%, usually with abnormal liver function
- Signs of congenital syphilis are nonspecific and include:
  - Prematurity and low BW
  - Hepatomegaly with or without splenomegaly
  - Hutchinson teeth, skeletal abnormalities, e.g., periostitis or osteitis
  - Generalized lymphadenopathy
  - Maculopapular rash—also vesicular rash and bullae—may develop. These lesions are highly contagious
  - Rhinitis ("snuffles"). Nasal secretions are highly contagious
  - Thrombocytopenia
  - Coombs negative hemolytic anemia with hydrops
- Abnormal CSF examination is seen in half of symptomatic infants but can also be found in 10% of those who are asymptomatic

Diagnosis
- Nontreponemal serology screening tests: RPR and VDRL are the best screening tools
- A fourfold or greater rise in titer in the infant compared to the mother signifies probable active disease
- Fourfold increase in titer following therapy suggests reinfection or relapse and necessitates reevaluation

Treponema-specific tests
- *Treponema pallidum* immobilization, fluorescent treponemal antibody absorption (FTA-ABS), and *T. pallidum* particle agglutination (TPPA) are used to confirm a positive nontreponemal serology screening test
- These test findings become positive soon after infection and typically remain positive for life, despite adequate treatment
- These test results do not correlate with disease activity and are not quantified

Management
- Treat congenital infection, either proven or presumed, with 10–14 days of aqueous crystalline penicillin G or penicillin G procaine
- Aqueous crystalline penicillin G is recommended if congenital syphilis is proved or is highly suspected
- Base dosage on chronological, not gestational, age
- The recommended dosage of aqueous crystalline penicillin G is 50,000 U/kg IV every 12 h (1 week or younger), then every 8 h for infants older than 1 week for a total of 10 days of therapy
- The dose for penicillin G procaine is 50,000 U/kg IM as a single daily dose for 10 days

Infection is suspected with the following:
- Physical or radiographic evidence of active disease
- Serum quantitative nontreponemal titer at least four times greater than the maternal titer
- Reactive CSF VDRL test result or abnormal CSF cell count and/or protein levels
- Positive IgM FTA-ABS test findings
- Positive dark-field microscopy findings or positive findings when staining for treponemes in placenta or umbilical cord

Failure to Pass Meconium in the First 48 h of Life

Background

- 97% of term infants and 76% of premature infants pass a stool in the first 24 h of life
- Almost every infant will have passed meconium by 36 h (99.8%) of age. 99% of premature infants pass a stool by 48 h

Differential diagnosis

- Constipation
- Anorectal anomalies (imperforate anus)
- Meconium plug
- Meconium ileus
- Hirschsprung disease
- Ileal atresia
- Incarcerated hernia
- Malrotation

Meconium Plug Syndrome

Background

- A transient form of distal colonic or rectal obstruction suspected to be related to transient decrease in intestinal motility
- Meconium plug syndrome is the most common form of functional distal obstruction in newborns
- More common in infants of diabetic mothers
- Usually occurs in the lower colon or anorectal region

Common associated conditions

- Small left colon syndrome
- Magnesium sulfate therapy for preeclampsia
- Maternal drug abuse
- CF
- Hypothyroidism
- Hirschsprung disease

Clinical presentation

- Failure to pass meconium in the first 24–48 h
- Relieved by passage of meconium plugs

Management

- Plain radiograph for any newborn who did not pass stool within the first 48 h of life
- Hyperosmolar Gastrografin enemas are considered the initial diagnostic procedure and are often therapeutic in patients with meconium plug syndrome
- Rectal biopsy should be considered in all these infants because of the high risk of Hirschsprung disease (up to 38%)

Meconium Ileus

Background

- Meconium ileus represents obstruction of the small bowel caused by accumulation of sticky and inspissated intraluminal meconium
- The third most common cause of neonatal small bowel obstruction
- Accounts for about 30% of cases of intestinal obstruction in newborns
- Meconium ileus occurs in 10–20% of patients with CF
  - In most cases, this results from intestinal and pancreatic dysfunction associated with CF
  - However, not all patients with meconium ileus have CF

Clinical presentation

- Abdominal distention, delayed passage of meconium, and bilious emesis
- Sometimes the impacted meconium can be palpated
- Massive distention, abdominal tenderness, or abdominal erythema indicates the presence of complications such as volvulus, intestinal necrosis, perforation, and meconium peritonitis

Diagnosis

- Abdominal radiographs: May reveal signs of either small or large bowel obstruction (distended bowel, few air-fluid levels, and in the

right lower abdomen), meconium mixed with air "soap bubble," which has a ground-glass appearance on plain film
- The presence of calcifications, free air, or very large air-fluid levels suggests complications
- The small bowel is of narrow caliber below the plug and dilated above the plug
- Sweat test or genetic testing for all infants with meconium ileus because of high risk of CF

Management
- Simple meconium ileus may be successfully treated by administration of a diatrizoate meglumine (Gastrografin) enema and IV fluids; the success rate is 16–50%
- If the Gastrografin enema is unsuccessful, operative evacuation of the obstructing meconium by irrigation will be necessary
- Complications such as atresia, perforation, and meconium peritonitis always require immediate surgery, including resection, intestinal anastomosis, and ileostomy

Necrotizing Enterocolitis (NEC)

Background
- NEC is the most common GI medical/surgical emergency occurring in preterm neonates
- Acute inflammatory disease with variable damage to the intestinal tract, ranging from mucosal injury to full-thickness necrosis and perforation
- NEC affects close to 10% of infants who weigh less than 1500 g, with mortality rates of 50% or more, depending on severity
- It can also be observed in term and near-term babies
- The main cause of NEC is still unclear, but the risk is higher in premature infants

Clinical presentation
- Feeding intolerance
- Delayed gastric emptying, high gastric residuals
- Abdominal distention, abdominal tenderness, or both
- Ileus/decreased bowel sounds
- Abdominal wall erythema (advanced stages)
- Hematochezia
- Apnea, bradycardia
- Labile body temperature
- Lethargy
- Decreased peripheral perfusion
- Shock (in advanced stages)
- Cardiovascular collapse
- Bleeding diathesis (consumption coagulopathy)

Diagnosis
- Abdominal radiograph
  - The mainstay of diagnostic imaging is abdominal radiography; radiographic appearance of NEC depends on severity
  - Abnormal gas pattern
  - Dilated loops
  - Thickened bowel walls (suggesting edema/inflammation)
  - Pneumatosis intestinalis (intramural air bubbles) is a radiologic sign pathognomonic of NEC
  - Abdominal free air is ominous and usually requires emergency surgical intervention
  - Portal gas represents air present in the portal venous system. Its presence is considered to be a poor prognostic sign

Laboratory studies
- Hyponatremia
- Metabolic acidosis
- Thrombocytopenia
- Leukopenia or leukocytosis with left shift
- Neutropenia
- Prolonged PT and activated PTT (aPTT), decreasing fibrinogen, rising fibrin split products (in cases of consumption coagulopathy)

Management
- Nothing by mouth and IV fluids
- Rapid nasogastric decompression
- Start IV antibiotics after cultures are taken:

  - Frequently used regimen is ampicillin, aminoglycoside (e.g., gentamicin) or third-generation cephalosporin (cefotaxime), piperacillin and tazobactam, and clindamycin or metronidazole
  - Vancomycin should be included if *Staphylococcus* coverage is deemed appropriate
  - Medical management usually continues for 10–14 days with parenteral nutrition provided during that time
- Consult with a pediatric surgeon at the earliest suspicion of developing NEC

Indication for surgery
- Intestinal perforation with free air in the peritoneal space
- Peritoneal tap showing feces or pus
- Deteriorating clinical condition despite medical treatment
- Compartment syndrome

Note: Patients who are extremely small and ill may not have the stability to tolerate laparotomy. If free air develops in such a patient, one may consider inserting a peritoneal drain under local anesthesia in the NICU.

Congenital Diaphragmatic Hernia (CDH)

Background
- Herniation of abdominal viscera into the thoracic cavity through a defect in the diaphragm
- There is a variable degree of pulmonary hypoplasia associated with a decrease in cross-sectional area of the pulmonary vasculature and alterations of the surfactant system
- Approximately 85% are left-sided
- Approximately 50–60% are diagnosed antenatally

Clinical presentation
- Respiratory distress, tachypnea, grunting, retraction, and cyanosis
  - Respiratory distress and cyanosis in the first minutes or hours of life, although a later presentation is possible
  - The respiratory distress can be severe and may be associated with circulatory insufficiency, requiring aggressive resuscitative measures
- Scaphoid abdomen
- Increased chest wall diameter
- Heart sounds may be shifted to the right in patients with left-sided CDH
- Bowel sounds may be heard in the chest with a decrease in breath sounds bilaterally
- Associated anomalies: Dysmorphisms such as craniofacial abnormalities, extremity abnormalities, or spinal dysraphism may suggest syndromic congenital diaphragmatic hernia

Laboratory tests
- ABG measurements to assess for pH, PCO2, and PaO2
- Chromosome studies, including microarray analysis, if associated anomalies
- Levels of serum electrolytes, ionized calcium, and glucose
- Continuous pulse oximetry is valuable in the diagnosis and management of PPHN

Imaging studies
- Chest radiography to confirm diagnosis of CDH and to rule out pneumothorax
- Cardiac and renal ultrasonography to rule out associated anomalies
- Cranial sonography when an infant is considered for ECMO
  - Prognosis is worse if ECMO is required

Delivery room management
- Avoiding mask ventilation and immediately intubating the trachea

- Endotracheal intubation and MV: Required in infants with severe CDH who present in the first hours of life

Management

- Placement of a sump/Replogle tube and connecting it to continuous suction to prevent bowel distention and further lung compression
- Avoiding high peak inspiratory pressures with MV; synchronizing ventilation with the infant's respiratory effort
- Continuous monitoring of oxygenation, BP, and perfusion
- Maintaining glucose and ionized calcium concentrations within reference range
- Vasoactive agents (e.g., dopamine, dobutamine, milrinone) as needed
- Echocardiogram is a critically important imaging study, and it guides therapeutic decision by measuring pulmonary and systemic artery pressure
- Surgical correction

Hypoxic Ischemic Encephalopathy (HIE)

Background

- Perinatal asphyxia, more appropriately known as hypoxic-ischemic encephalopathy (HIE), is characterized by clinical and laboratory evidence of acute or subacute brain injury due to asphyxia
- Birth asphyxia causes 23% of all neonatal deaths worldwide

Pathogenesis

- Brain hypoxia and ischemia due to systemic hypoxemia, reduced cerebral blood flow, or both are the primary physiological processes that lead to hypoxic-ischemic encephalopathy
- Excitatory amino acid (EAA) receptor overactivation plays a critical role in the pathogenesis of neonatal hypoxia-ischemia
- During cerebral hypoxia-ischemia, the uptake of glutamate, which is the major excitatory neurotransmitter of the mammalian brain is impaired
- Accumulation of Na^+ coupled with the failure of energy-dependent enzymes such as Na^+/K^+-ATPase leads to rapid cytotoxic edema and necrotic cell death

Diagnosis

- Profound metabolic or mixed acidemia (pH < 7) in an umbilical artery blood sample, if it was obtained
- Persistence of an Apgar score of 0–3 for longer than 5 min
- Neonatal neurologic sequelae (e.g., seizures, coma, hypotonia)
- Multiple organ involvement (e.g., kidney, lungs, liver, heart, intestines)

Clinical presentation

- Mild hypoxic-ischemic encephalopathy
  - Muscle tone may be slightly increased, and deep tendon reflexes may be brisk during the first few days
  - Poor feeding, irritability, excessive crying or sleepiness may be observed
  - The neurologic examination findings normalize by 3–4 days of life
- Moderately severe hypoxic-ischemic encephalopathy
  - The infant is lethargic, with significant hypotonia and diminished deep tendon reflexes
  - The grasp, Moro, and suck reflexes may be sluggish or absent
  - The infant may experience occasional periods of apnea
  - Seizures may occur within the first 24 h of life
  - Full recovery within 1–2 weeks is possible and is associated with a better long-term outcome
- Severe hypoxic-ischemic encephalopathy
  - Stupor or coma is typical. The infant may not respond to any physical stimulus

  - Breathing may be irregular, and the infant often requires ventilatory support
  - Generalized hypotonia and depressed deep tendon reflexes are common
  - Neonatal reflexes (e.g., sucking, swallowing, grasping, Moro) are absent
  - Skewed deviation of the eyes, nystagmus, bobbing, and loss of "doll's eye" (i.e., conjugate) movements
  - Pupils may be dilated, fixed, or poorly reactive to light
  - Seizures
  - Irregularities of heart rate and BP are common during the period of reperfusion injury
  - Death from cardiorespiratory failure

Laboratory studies

- Serum electrolyte levels, renal, liver, and cardiac function study
- Coagulation system—includes PT, PTT, and fibrinogen levels
- ABG—Blood gas monitoring is used to assess acid base status and to avoid hyperoxia and hypoxia, as well as hypercapnia and hypocapnia

Imaging studies

- Head imaging study, e.g., MRI of the brain or cranial ultrasonography
- Electrocardiogram (ECG)
- Electroencephalogram (EEG)
- Hearing test
- Retinal and ophthalmic examination

Management

- Fluid and ventilation management
- Treatment of seizures
- Hypothermia therapy (selective brain cooling or total body hypothermia)
  - Extensive experimental data suggest that mild hypothermia (3°–4°C below baseline temperature) applied no later than 6 h following injury is neuroprotective

Intraventricular Hemorrhage (IVH) and Leukomalacia

Background

- A predominant disorder of preterm infants
- Originates in the periventricular subependymal germinal matrix with subsequent entrance of blood into the ventricular system

Risk factors

- Extreme prematurity
- Hypoxic-ischemic insult
- Coagulopathy
- Respiratory disturbances—hypercarbia, hypocarbia, pneumothorax, hypoxemia, rapid alterations in blood gases
- Rapid volume expansion
- Sudden elevation of arterial BP

Classification of IVH

- Grade I: Hemorrhage is confined to the germinal matrix
- Grade II: IVH without ventricular dilatation
- Grade III: IVH with ventricular dilatation
- Grade IV: Intraparenchymal hemorrhage

Clinical presentation

- Sudden drop in hematocrit level
- Apnea
- Bradycardia
- Acidosis
- Seizures
- Change in muscle tone
- Catastrophic syndrome (rapid onset stupor, coma, respiratory abnormalities, seizures, decerebrate posturing, fixed pupil to light, flaccid quadriparesis)

Diagnosis

- Ultrasonography is the study of choice
- All infants younger than 30 weeks gestation should be screened by cranial ultrasonography at 7–14 days postnatal life and at 36–40 weeks postmenstrual age. Instead of a

cranial ultrasound, some institutions prefer to obtain a brain MRI at term corrected age
- Serial ultrasonography is indicated weekly to follow for progression of hemorrhage and the development of post-hemorrhagic hydrocephalus

Complication
- Obstructive hydrocephalus
- Nonobstructive hydrocephalus
- Developmental impairment
- Cerebral palsy
- Seizures

Prognosis
- Grade I and grade II hemorrhage: Neurodevelopmental prognosis is excellent
- Grade IV (severe with either periventricular hemorrhagic (PVH) infarction and/or periventricular leukomalacia): Mortality approaches 80%. A 90% incidence of severe neurological sequelae including cognitive and motor disturbances

Prevention
- Use of antenatal steroids
- Avoid hypoxia-ischemia
- Avoid large and rapid fluctuation of BP
- Avoid rapid infusion of volume expanders
- Correct acid base abnormalities
- Correct coagulation abnormalities
- Gentle handling of preterm babies

Teratogens (Table 2.6)

Table 2.6 Teratogens

Drug name	Effect on fetus
Phenytoin	Broad, low nasal bridge
	Midface hypoplasia and epicanthal fold
	Distal digital or nail hypoplasia
	Wide spaced eyes (hypertelorism)
	Intellectual disability
	IUGR
	Cardiovascular abnormalities
	Bleeding (vitamin K deficiency)
Valproic acid	Neural tube defect (spina bifida)
	Cardiac, renal, and limb anomalies
Carbamazepine (CBZ)	Orofacial clefts
Warfarin	Bone stippling
	Facial anomalies
	Fetal bleeding and death
Lithium	Ebstein anomalies
	Hypothyroidism
	Nephrogenic diabetes insipidus
	Macrosomia
Cocaine	Limb defect or reduction
	Intracranial hemorrhage
	Leukomalacia
	Nonduodenal intestinal atresia
	Gastroschisis (most likely due to disruption of omphalomesenteric artery)
Marijuana	No specific feature to identify because of possible poly-drug abuse
	Irritability
	Tremulousness
	Abnormal response to visual stimuli
Cigarette smoking	Low birth weight for gestational age
Danazol	Virilization
Tetracycline	Retarded skeletal growth, pigmentation of teeth, hypoplasia of enamel, cataract, limb malformations

Fetal Alcohol Syndrome

Background
- Adverse fetal, neonatal, and pediatric effects occur with maternal alcohol consumption during pregnancy
- The greater the intake of alcohol, the more severe the signs
- No safe amount of alcohol during pregnancy has yet been determined

Clinical presentation
- Small for GA
- Short palpebral fissures (< 10% for age)
- Epicanthal folds
- Micrognathia
- Midface hypoplasia
- Microphthalmia
- Smooth philtrum
- Thin upper lip
- Microcephaly
- Irritability in infancy
- Intellectual impairment (mild to moderate intellectual disability)

- Cognitive impairment
- Hyperactivity in childhood or attention-deficit/hyperactivity disorder (ADHD)
- Skeletal abnormalities, e.g., radioulnar synostosis
- Hearing and visual abnormalities, e.g., deafness and strabismus

PEARLS AND PITFALLS

- It is important to recognize that visual estimation of the degree of jaundice can lead to errors, particularly in darkly pigmented infants.
- Infants < 38 weeks gestation, particularly those who are breastfed, are at higher risk of developing hyperbilirubinemia and require closer surveillance and monitoring.
- All bilirubin levels should be interpreted according to the infant's age in hours. A systematic assessment for the risk of severe hyperbilirubinemia should be performed on all infants before discharge.
- The most common bacterial pathogen for early onset sepsis is GBS, followed by *E. coli.*
- HSV PCR testing in the asymptomatic newborn should be delayed for 24–48 h after birth in order to differentiate viral replication in the newborn from transient colonization of the newborn at birth.
- The congenital infection most commonly associated with hydrops fetalis is parvovirus B19.
- The most common cause of respiratory distress in the term newborn is transient tachypnea of the newborn (TTN). This is a self-limited disorder and usually resolves within 48 h.
- Nonvigorous newborns with meconium-stained amniotic fluid *do not* require routine intubation and tracheal suctioning. However, meconium-stained amniotic fluid is a perinatal risk factor that requires the presence of one resuscitation team member with full resuscitation skills, including endotracheal intubation.
- The most common form of esophageal atresia and tracheo-esophageal fistula is esophageal atresia with a distal fistula (88% of cases), where the upper esophagus ends in a blind pouch and the trachea is connected by a fistula to the distal esophagus.
- Approximately 85% of congenital diaphragmatic hernias (CDH) are left sided; in these patients, there can be herniation of the small or large bowel and other solid intra-abdominal organs. Patients with CDH who require ECMO have worse prognosis than those who do not require ECMO.
- In newborns who present with bilious vomiting, one of the most important diagnoses to exclude is malrotation with or without volvulus.
- Infants with volvulus constitute a surgical emergency and require prompt medical and surgical intervention. Up to 80% of affected patients receive a diagnosis during the neonatal period, with 50% presenting in the first week after birth. If not recognized in a timely fashion, volvulus can lead to catastrophic loss of bowel with resultant lifelong disability and even death.
- Gastroschisis presents as a full thickness defect in the abdominal wall with prolapse of the intestine through the defect. There is no covering membrane, and the defect lies to the right side of an intact umbilical cord.
- In omphalocele, the defect is midline and the prolapsed organs are always covered with a protective membrane consisting of amnion on the outer surface, peritoneum on the inner surface, and Wharton jelly in between.
- Omphaloceles contain a variable amount of intestine, often parts of the liver, and occasionally other organs.
- There is no evident genetic cause for gastroschisis; associated intestinal atresias may be present. In contrast, omphaloceles are associated with syndromes and chromosomal

abnormalities in over 50% of cases, including Beckwith-Wiedemann syndrome (omphalocele, macroglossia, organomegaly, hypoglycemia, and increased risk for childhood tumors such as Wilms tumor, neuroblastoma, and hepatoblastoma).

References

1. Fernandes CJ. Neonatal resuscitation in the delivery room. In: Post TW, editor. UpToDate. Waltham: UpToDate. http://www.uptodate.com. Accessed 13 Jan 2019.
2. Maisels MJ, Watchko JF, Bhutani VK, Stevenson DK. An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation. J Perinatol. 2012;32:660–4.
3. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114:297–316.

Suggested Reading

Barnes-Powell LL. Infants of diabetic mothers: the effects of hyperglycemia on the fetus and neonate. Neonatal Netw. 2007;26:283–90.

Campbel DE. Neonatology for primary care. Elk Grove Village: American Academy of Pediatrics; 2015.

Gornall AS, Kurinczuk JJ, Konje JC. Antenatal detection of a single umbilical artery: does it matter? Prenat Diagn. 2003;23:117–23.

Hibbs AM, Black D, Palermo L, Cnaan A, Luan X, Truog WE, et al. Accounting for multiple births in neonatal and perinatal trials: systematic review and case study. J Pediatr. 2010;156:202–8.

Laptook A, Tyson J, Shankaran S, McDonald S, Ehrenkranz R, Fanaroff A, National Institute of Child Health and Human Development Neonatal Research Network, et al. Elevated temperature after hypoxic-ischemic encephalopathy: risk factor for adverse outcomes. Pediatrics. 2008;122:491–9.

Ment LR, Bada HS, Barnes P, Grant PE, Hirtz D, Papile LA, et al. Practice parameter: neuroimaging of the neonate: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2002;58:1726–38.

Norton ME, Scoutt LM, Feldstein VA, editors. Callen's ultrasonography in obstetrics and gynecology. 6th ed. Philadelphia: Elsevier; 2017.

Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S543–60.