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Neonatology

CASE-BASED REVIEW

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Wolters Kluwer
Health

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Preface

Pediatric residents in the United States have fewer rotations in the Neonatal Intensive Care Unit (NICU) than ever before. The recent reduction in resident duty hours has also limited residents' exposure to the NICU. Nonetheless, pediatric residents are still required to have a significant understanding of neonatology. We created this resource to help residents develop this understanding through a case-based approach to neonatal diseases. We selected the topics for this book based on the most recent American Board of Pediatrics Content Specifications recommended for the Pediatrics certification examination. To make the cases realistic, we incorporated pictures and radiographs when possible. Although we originally targeted this book to pediatric residents, we think that it will also be a valuable self-learning tool for medical students and nurse practitioner students. While students can use this book on their own, they may also benefit from discussing the cases with neonatologists, neonatology fellows, and pediatricians.

DB and EGD

Contents

SECTION I

Maternal–Fetal Medicine

CASE 1

Maternal serum screening

A pregnant woman undergoes blood testing at 16 weeks' gestation.

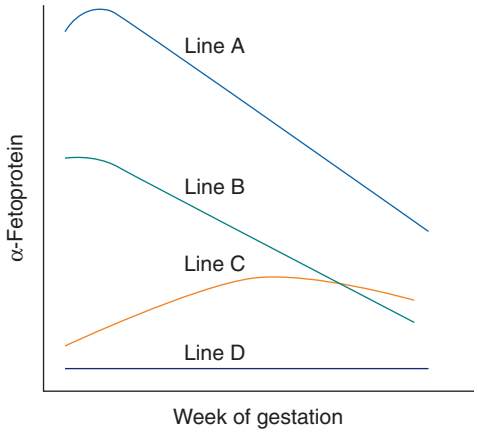

FIGURE 1.

1. Of the following, the line in Figure 1 that most likely represents the maternal serum α-fetoprotein concentration throughout pregnancy is:

   A. Line A
   B. Line B
   C. Line C
   D. Line D

The woman's test results are shown in the table below:

Test	Lab Result (Multiples of Mean, MoM)	Normal Result (MoM)
α-Fetoprotein	4.0	0.4–2.5
β-Human chorionic gonadotropin	0.8	0.4–2.5
Inhibin A	1.0	<2.5
Unconjugated estriol	0.9	>0.5

Her obstetrician meets to discuss possible reasons for these results.

2. Of the following, the diagnosis that is *not* consistent with these laboratory findings is:

   A. Gastroschisis
   B. Neural tube defect
   C. Trisomy 21
   D. Twin gestation

CASE 2

Prenatal ultrasonography

Blood screening results of a 40-year-old G3P2 pregnant woman were abnormal. Several fetal ultrasounds reveal that the fetus has multiple anomalies. The woman and her husband meet with a neurologist, a geneticist, a surgeon, and a cardiologist.

The neurologist meets with this couple to discuss the 14-week ultrasound finding shown in Figure 1. This long-axis view shows the spine (short *arrowheads*) and the head (between the two *long arrows*).

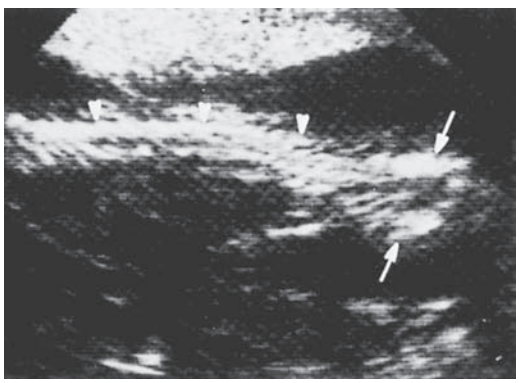

FIGURE 1. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 1.01

1. Of the following, this fetal image most likely is consistent with:

   A. Anencephaly
   B. Holoprosencephaly
   C. Hydrocephalus
   D. Meningomyelocele

The family then meets with a cardiologist to discuss the cardiac findings in the fetus. The fetal ultrasonographic findings are shown in Figure 2. The defect is confirmed by fetal echocardiography.

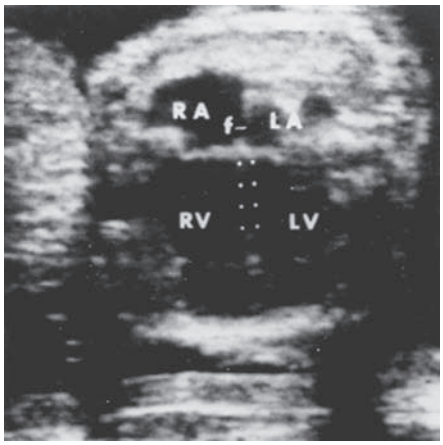

FIGURE 2. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 1.35; f=foramen

2. Of the following, the cardiac defect that is most likely in this infant is:

   A. Complete atrioventricular canal
   B. Hypoplastic left ventricle syndrome
   C. Transposition of the great arteries
   D. Large ventricular septal defect

The fetal ultrasound also demonstrates a gastrointestinal complication (Figure 3). A surgeon meets with the family to discuss the diagnosis and possible outcomes.

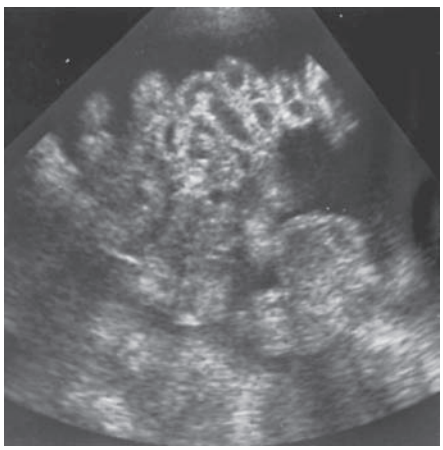

FIGURE 3. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 1.20

3. Of the following, the potential short-term complication that can occur after birth is:

   A. Dehydration
   B. Intestinal perforation
   C. Meconium plug
   D. Nonbilious emesis

The family's high-risk obstetrician is also suspicious of a genitourinary abnormality because the infant's bladder is extremely large with a thickened wall. The fetal image in Figure 4 shows the markedly dilated bladder (*B*) and dilated proximal urethra (*U*).

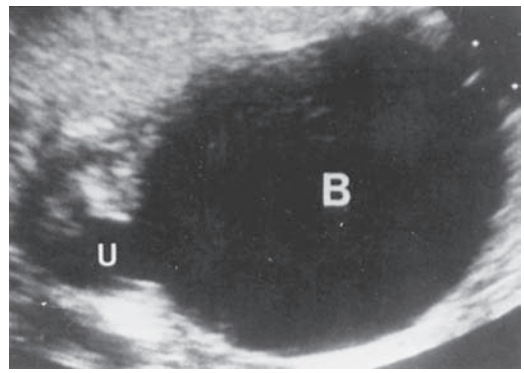

FIGURE 4. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 1.33

4. Of the following, the genitourinary abnormality that this infant is likely to have is (are):

   A. Hydronephrosis
   B. Pelviectasis
   C. Posterior urethral valves
   D. Renal agenesis

Because of the multiple anomalies in the fetus, the couple decides to terminate the pregnancy. Several years later, the woman becomes pregnant. Her blood screening results are normal. A fetal ultrasound demonstrates choroid plexus cysts. The rest of the fetal ultrasound is normal. Given her past history, the woman is extremely worried that this infant will have multiple anomalies.

5. Of the following, the diagnosis that is most likely in this fetus is:

   A. Healthy term infant
   B. Neurological issues later in life
   C. Trisomy 13
   D. Trisomy 21

CASE 3

Invasive prenatal genetic testing

A pregnant woman at 8 weeks' gestation meets with her obstetrician. She and her husband are both carriers for sickle cell disease. She asks her obstetrician if she can have prenatal testing for this disease. Her obstetrician reviews some options for prenatal DNA testing.

1. Match the figure with the prenatal invasive testing approach:

   A. Amniocentesis ____
   B. Periumbilical blood sampling ____
   C. Transabdominal chorionic villus sampling ____
   D. Transvaginal chorionic villus sampling ____

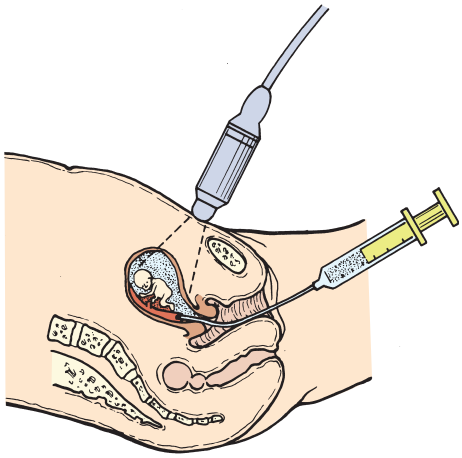

FIGURE 1. Modified from Gibbs RS, Karlan BY, Hanley AF, et al., eds. *Danforth's Obstetrics and Gynecology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. Figure 6.13

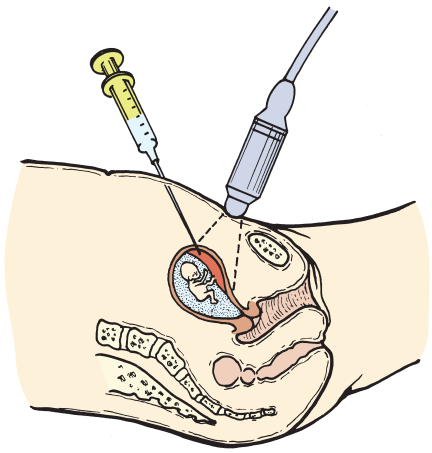

FIGURE 2. Modified from Gibbs RS, Karlan BY, Hanley AF, et al., eds. *Danforth's Obstetrics and Gynecology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. Figure 6.14

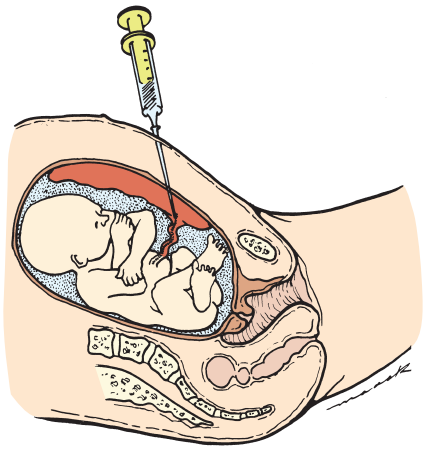

FIGURE 3. Modified from Gibbs RS, Karlan BY, Hanley AF, et al., eds. *Danforth's Obstetrics and Gynecology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. Figure 6.15

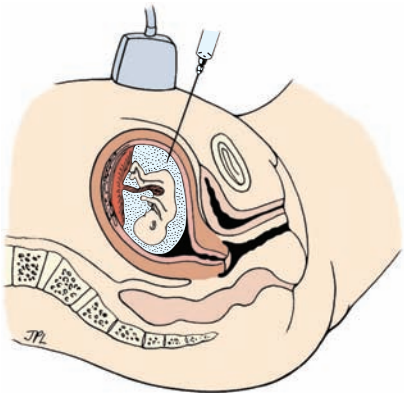

FIGURE 4. Courtesy of LifeART © 2014 Lippincott Williams & Wilkins. All rights reserved

2. Of the following, the prenatal test that is *least* helpful in the diagnosis of sickle cell disease is:

   A. Amniocentesis
   B. Fetal ultrasonography
   C. Periumbilical blood sampling
   D. Transvaginal chorionic villus sampling

Fetal DNA analysis shows that the fetus does not have sickle cell disease. The pregnancy is uncomplicated until the woman develops severe sciatica and walking becomes extremely painful. At 36 weeks' gestation, she asks her obstetrician to consider delivering the baby early because she has severe constant pain. Her obstetrician performs an amniocentesis to determine fetal lung maturity.

3. Of the following, the result that is most consistent with mature fetal lungs is a(n):

   A. Absence of phosphatidylglycerol
   B. Elevated lecithin/sphingomyelin ratio
   C. Increased amount of phosphatidylinositol
   D. Low amount of sphingomyelin

CASE 4

Fetal assessment

A pregnant woman at 39 weeks' gestation has been monitored with weekly nonstress tests. Her most recent nonstress test results are shown in Figure 1.

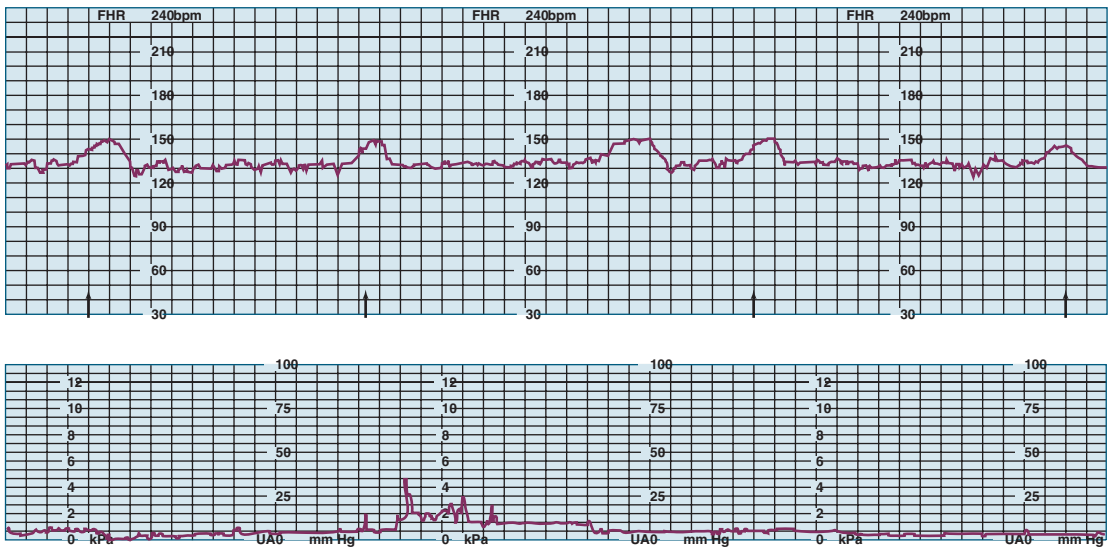

FIGURE 1. From Pillitteri A. *Maternal and Child Nursing.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 8.11

1. Of the following, the result that is most consistent with this nonstress test is:

   A. Normal amniotic fluid volume
   B. Normal fetal breathing pattern
   C. Normal fetal heart rate response to fetal movement
   D. Regular, frequent contractions

At 40 3/7 weeks' gestation, the obstetrician performs a contraction stress test, which is normal.

2. Of the following, the primary purpose of the contraction stress test is to:

   A. Assess the impact of uterine contractions on fetal tone
   B. Determine the strength of uterine contractions
   C. Evaluate for uteroplacental insufficiency
   D. Measure the impact of uterine contractions on fetal movements

Three days later, the woman contacts the obstetrician because she feels decreased fetal movements. The obstetrician performs a biophysical profile, which is normal.

3. Of the following, the measurement that is *not* part of the biophysical profile is:

   A. Amount of amniotic fluid
   B. Blood flow in the umbilical arteries
   C. Fetal breathing
   D. Fetal tone

CASE 5

Effects of maternal diabetes mellitus

A full-term male infant with macrosomia is born by cesarean delivery to a woman with insulin-dependent diabetes mellitus. The mother had extensive prenatal testing (including maternal blood testing, several fetal ultrasonographs, fetal echocardiography) to assess for anomalies in the fetus. All of these tests were normal.

1. Pregnant women with diabetes mellitus are at increased risk of having an infant with congenital anomalies. Of the following, the scenario that is associated with a *lower risk* of congenital anomalies is:

   A. Diabetes mellitus without evidence of vascular disease
   B. Good maternal glucose control before conception
   C. Good maternal glucose control during the third trimester
   D. A and B

Most congenital anomalies found in infants of diabetic women occur early in gestation. However, there is one anomaly that occurs later.

2. Of the following, the anomaly that occurs during the second half of gestation is:

   A. Caudal regression syndrome
   B. Meningomyelocele
   C. Small left colon syndrome
   D. Transposition of the great arteries

The baby's initial breastfeeding attempt was unsuccessful because he did not latch well. Because the baby's initial serum glucose is 21 mg/dL, he is brought to the Neonatal Intensive Care Unit for further care. He is given an intravenous glucose bolus and started on a continuous intravenous infusion of D10W at 60 mL/kg/day. The neonatology fellow meets with the infant's parents to discuss the reason for their baby's low serum glucose and the treatment approach.

3. Of the following, the pathogenesis of this infant's hypoglycemia is most likely:

   A. Diabetes mellitus in the infant
   B. Increased insulin production by the infant
   C. Intrauterine passage of maternal insulin to the fetus across the placenta
   D. Neonatal liver dysfunction from intrauterine exposure to maternal insulin

The infant's serum glucose then increases to 61 mg/dL. However, the infant is noted to have a right arm oxygen saturation of 84%. The rest of the infant's vital signs, including blood pressure, are normal. With a half liter per minute of 100% oxygen, the infant's oxygen saturation increases to 98%. The infant's physical examination at 3 hours of age reveals a well-appearing, ruddy infant without any respiratory distress and with a soft I/VI systolic heart murmur heard loudest at the left mid to upper sternal border. A chest radiograph is normal.

4. Of the following, the most likely cause of this infant's cyanosis is:

   A. Cyanotic heart disease
   B. Polycythemia
   C. Respiratory distress syndrome
   D. Transient tachypnea of the newborn

The baby has the following laboratory findings:

- Na = 131 mEq/L
- K = 3.1 mEq/L
- Cl = 95 mEq/L
- HCO_3 = 16 mEq/L
- Ionized calcium = 0.88 mmol/L

5. Of the following, the electrolyte abnormality that is often found in infants born to women with diabetes mellitus is:

   A. Hypocalcemia
   B. Hypochloremia
   C. Hypokalemia
   D. Hyponatremia

CASE 6

Effects of maternal lupus

A full-term, well-appearing female neonate is noted to have a low resting heart rate. The infant's mother is in excellent health without any medical problems. The infant's electrocardiogram is shown in Figure 1.

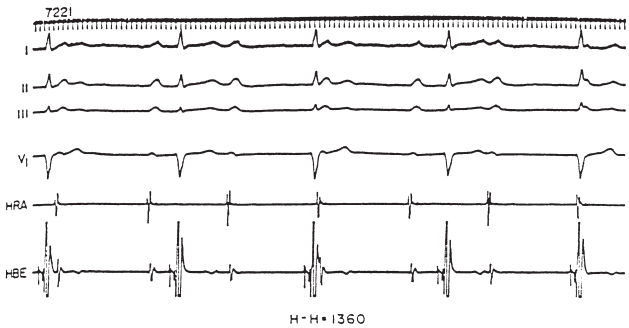

FIGURE 1. From Miles MM, Klein LS. Sinus nodal dysfunction and atrioventricular conduction disturbances. In: Naccarelli GV, ed. *Cardiac Arrhythmias: A Practical Approach*. Mount Kisco, NY: Futura; 1991:269

1. Of the following, the electrocardiographic diagnosis of this infant is:

   A. Complete heart block
   B. First-degree heart block
   C. Sinus bradycardia
   D. Wenckebach second-degree heart block

Soon after birth, the infant is noted to have a rash involving the face and trunk.

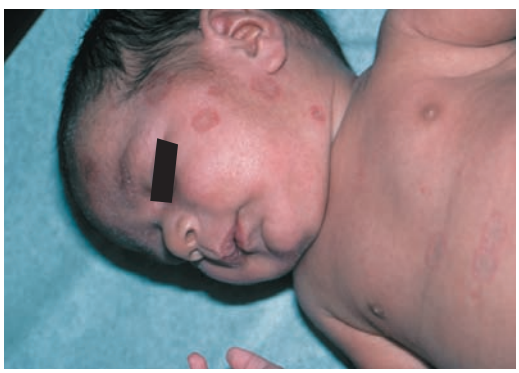

FIGURE 2. From Goodheart HP. *Goodheart's Photoguide of Common Skin Disorders*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 25.33

Additional tests are performed on the mother to help identify the cause of this infant's medical issues.

2. Of the following, the maternal antibodies that are most likely associated with this infant's clinical findings are:

   A. Anti-acetylcholine receptor (AChR) antibodies
   B. Antiphospholipid antibodies
   C. Anti-Ro/SSA and anti-La/SSB antibodies
   D. Thyroid-stimulating hormone receptor–blocking antibodies

Testing of the infant's mother confirms that she has these serum antibodies.

3. Of the following, the percentage of affected infants with this disease who are born to an undiagnosed, healthy woman is:

   A. <2%
   B. 25%
   C. 50%
   D. 90%

The infant in this vignette has additional testing.

4. Of the following, the laboratory finding that is most likely to be found in this infant is:

   A. Hypocalcemia
   B. Indirect hyperbilirubinemia
   C. Polycythemia
   D. Thrombocytopenia

CASE 7

Maternal medications

A 39-year-old woman with a seizure disorder and a clotting abnormality finds out that she is 13 weeks' pregnant. Although she had not been taking any anticoagulant medication, she has been taking her antiseizure medication regularly. Her obstetrician discusses the potential impact of anticonvulsant use during pregnancy.

1. Of the following, the statement that is most accurate is:

   A. All anticonvulsants marketed prior to 1976 have been shown to have teratogenic effects.
   B. Although intrauterine anticonvulsant exposure can lead to dysmorphic features, neurological outcomes are not altered in exposed children.
   C. Fetal risk of anticonvulsant exposure is greatest if the exposure occurs during the third trimester.
   D. Major malformations associated with intrauterine anticonvulsant exposure occur in more than 50% of exposed fetuses.

Ultrasonography at 14 weeks' gestation reveals that the fetus has a cleft palate.

2. Match the morphogenesis problem with the resulting fetal abnormality:

A. Deformation	1. Amniotic bands
B. Disruption	2. Arthrogryposis caused by intrauterine constraints
C. Dysplasia	3. Cleft palate
D. Malformation	4. Hemangioma

Delivery is induced at 34 weeks' gestation because of concerns about significant intrauterine growth restriction. A neonatologist examines the infant after birth and observes that the infant also has digit and nail hypoplasia in addition to a cleft palate.

Postdelivery, the woman develops a deep vein thrombosis and is placed on warfarin.

A few years later, the woman meets with her obstetrician in anticipation of expanding her family. Her obstetrician changes her anticoagulant therapy from warfarin to heparin and, in consultation with a neurologist, discontinues her antiseizure medication.

3. Of the following, potential effects of warfarin exposure during the first trimester are:

   A. Ebstein anomaly
   B. Microtia, cerebellar hypoplasia, and transposition of the great arteries
   C. Nasal hypoplasia and stippled bone epiphyses
   D. Yellow-brown discoloration of deciduous teeth

During this pregnancy, the fetal imaging is normal and there are no medical concerns in either the woman or the fetus. However, at 30 weeks' gestation, the woman is admitted to the hospital in preterm labor. Because of the teratogenic effects of her antiseizure medications in her first child, she is extremely concerned about potential effects of tocolytic medications. Her obstetrician discusses the risks and benefits of several possible tocolytic agents.

4. Of the following, the tocolytic medication that has been associated with pulmonary hypertension in the newborn is:

   A. Indomethacin
   B. Magnesium sulfate
   C. Nifedipine
   D. Terbutaline

CASE 8

Maternal substance use

A woman and her husband have tried for several years to have a baby. Because they have been unsuccessful, they meet with an adoption agency. The agency offers them an option to adopt a 6-month-old boy. The couple then meets with a pediatrician to review the infant's medical history. Upon review of the medical records, the pediatrician notes that the baby was born by emergent cesarean section because of placental abruption.

1. Of the following, the maternal drug that has been associated with placental abruption is:

   A. Cocaine
   B. Heroin
   C. Methadone
   D. Morphine

During the newborn period, the infant had the following symptoms after birth:

- Irritability
- Shrill, high-pitched cry
- Tremors
- Hyperreflexia
- Hypertonia
- Nasal stuffiness
- Tachypnea
- Frequent sneezing
- Poor feeding
- Loose, watery stools
- Vomiting

2. Of the following, the maternal drug that is *least* likely to lead to neonatal withdrawal symptoms is:

   A. Codeine
   B. Heroin
   C. Methamphetamine
   D. Methadone

These withdrawal symptoms resolved with treatment, and by a few weeks of age, the infant was symptom-free and not receiving any medications.

3. Of the following, potential drugs that can be used to treat neonatal withdrawal are:

   A. Methadone
   B. Morphine sulfate
   C. Phenobarbital
   D. All of the above

The pediatrician then looks at a picture of the infant and tells the couple that the infant likely has fetal alcohol syndrome.

4. Of the following, a common physical finding in infants with fetal alcohol syndrome is (a):

   A. Long nose
   B. Long palpebral fissures
   C. Macrocephaly
   D. Thin upper lip

The parents are not concerned about the infant's physical features but want to know about the baby's long-term neurological prognosis.

5. Of the following, the *least* likely neurological outcome in this infant is:

   A. Behavioral issues
   B. Cognitive deficits
   C. Macrocephaly
   D. Structural brain abnormalities

Given the potential of significant medical issues in this baby, the family decides not to pursue the adoption. A few weeks later, the adoption agency contacts the couple again about a 7-month-old infant girl. The infant's medical records reveal that the mother smoked one pack per day throughout the pregnancy. She had monthly drug testing that was negative except for one positive test for marijuana. The infant was born at term gestation with a normal birth weight and did not have any medical problems after birth. She has been developing appropriately without any medical concerns. The couple again meets with the pediatrician to discuss the potential effects of smoking on the baby.

6. Of the following, a potential effect of prenatal exposure to tobacco is:

   A. Intestinal atresia
   B. Macrosomia
   C. Postterm delivery
   D. Sudden infant death syndrome

CASE 9

Delivery room assessment

Fetal heart rate monitoring of a fetus at 40 weeks' gestation reveals decreased fetal heart rate variability and a prolonged late deceleration. The obstetrician asks the neonatology team to be present for an emergent cesarean delivery.

After delivery, the infant is brought over to a radiant warmer. The neonatology team, consisting of a neonatologist, neonatology fellow, pediatric resident, and neonatal nurse, evaluates the infant. The team begins to dry the baby and provide stimulation. Because the infant does not have any respiratory effort, the pediatric resident provides bag-mask ventilation and the nurse places a pulse oximeter on the infant's right wrist. The nurse reports that the infant's heart rate

is 80 beats per minute. The resident continues to provide positive-pressure ventilation. At 1 minute of age, the team notes that the infant has:

- A heart rate of 78 beats per minute
- An oxygen saturation of 65%
- No respiratory effort
- No spontaneous movements
- No tone
- Poor perfusion

1. Of the following, the clinical finding that is *not* used when calculating an infant's Apgar score is:

   A. Activity
   B. Color
   C. Perfusion
   D. Respiratory rate

2. Of the following, the number that corresponds to this infant's Apgar score at 1 minute is:

   A. 0
   B. 1
   C. 2
   D. 3

The team continues to provide positive-pressure ventilation and the infant's heart rate increases to 150 by 2 minutes of age. The infant starts to breathe spontaneously and becomes active. The Apgar score at 5 minutes of age is 8. The father asks the neonatologist about the significance of his infant's low Apgar score at 1 minute of age.

3. Of the following, the statement that the neonatologist is most likely to say to the father is:

   A. An amplitude electroencephalogram can help assess if the infant's status at 1 minute of age has impacted the infant's brain activity.
   B. The infant's Apgar score < 3 at 1 minute of age correlates with a 1% risk of cerebral palsy.
   C. The infant's Apgar score is a poor indicator of neurological outcome.
   D. The infant is at increased risk for seizure activity in the first 24 hours of age.

The next morning, the pediatrician and a third-year medical student examine the full-term infant in the newborn nursery. The pediatrician discusses the physical examination findings in a full-term infant compared with those of a preterm and postterm infant.

4. Of the following, the physical finding often found in a preterm infant is (are):

   A. Cracked, wrinkled skin
   B. Excessive plantar creases
   C. Instant recoil of ear pinna
   D. Minimal flexion of arms and legs at rest

CASE 10

Delivery room resuscitation

A group of medical students attend a simulation course about neonatal resuscitation. The instructor begins the class by showing a video of a resuscitation using a high-fidelity newborn simulator. The instructor asks the students to identify the resuscitative actions that were appropriate.

1. Of the following, the action that is most appropriate in the resuscitation of a newborn is:

   A. Continued stimulation of a newborn with a slow heart rate and apnea
   B. Establishment of a patent airway before applying positive-pressure ventilation
   C. Placement of a pulse oximeter probe on the newborn's right wrist after 5 minutes of positive-pressure ventilation
   D. Technique of applying low peak inspiratory pressure by bag-mask ventilation for the first few assisted breaths

Using a newborn mannequin, the instructor then demonstrates appropriate bag-mask ventilation and chest compressions. The students review the details of these techniques and then practice on the mannequin.

2. Of the following, the most appropriate technique to provide effective chest compressions in a newborn is:

   A. Apply compressions over the upper third of the newborn's sternum
   B. Compress to a depth one-third the anterior–posterior diameter of the chest
   C. Provide chest compressions and bag-mask breaths in a ratio of 2:1
   D. Use the two-finger technique instead of the two-thumb-encircling-hands approach

3. Of the following, an indication for beginning chest compressions in a newborn is:

   A. If the heart rate does not increase above 60 beats per minute despite effective ventilation with oxygen for 30 seconds
   B. If the heart rate is less than 30 beats per minute immediately after birth
   C. If the newborn remains cyanotic despite appropriate bag-mask ventilation
   D. If the newborn's perfusion is extremely poor after 30 seconds of bag-mask ventilation

The instructor then shows the students a chest radiograph (Figure 1) of a 30-minute-old newborn born at 36 weeks' gestation with severe respiratory distress. Thin meconium was noted when the membranes ruptured prior to delivery and there were no sepsis risk factors.

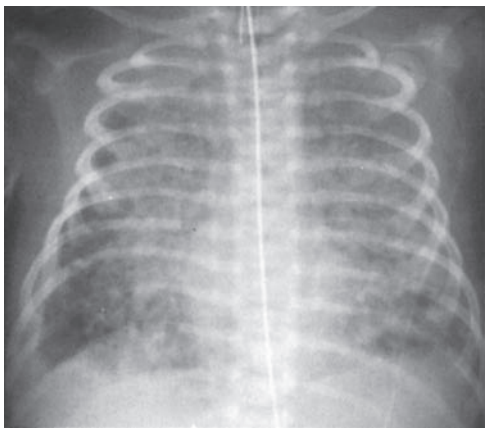

FIGURE 1. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 29.9

4. Of the following, the approach that might have decreased the severity of this newborn's respiratory disease is:

   A. Administration of maternal steroids prior to delivery
   B. Initiation of continuous positive airway pressure soon after birth
   C. Intubation and suctioning the infant's trachea if the infant was not vigorous immediately after birth
   D. Minimal use of oxygen supplementation in the delivery room

CASE 11

Small-for-gestational-age infant

Figure 1 shows three fetal growth curves.

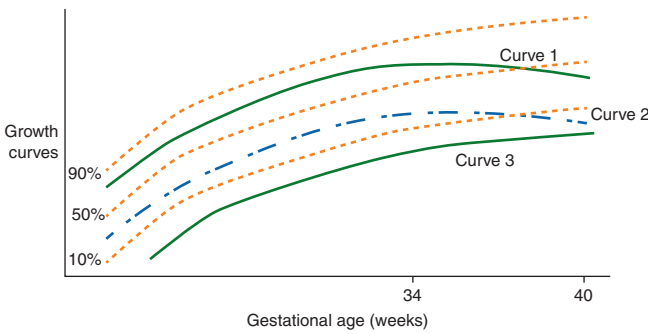

FIGURE 1.

1. Of the following, the graph(s) **(Figure 1)** that represents a fetus with intrauterine growth restriction (IUGR) is (are):

   A. Curve 1
   B. Curve 2
   C. Curve 3
   D. Curves 1 and 2

2. Of the following, the most likely cause of the fetal growth pattern in Curve 3 is:

   A. Familial short stature
   B. Maternal gestational diabetes
   C. Pregnancy-induced hypertension
   D. Twin gestation

A high-risk obstetrician is closely monitoring a pregnant woman with pregnancy-induced hypertension because of fetal growth restriction. After a poor fetal biophysical profile at 36 weeks' gestation, the obstetrician decides to induce labor. Because the fetal heart rate patterns show late decelerations with each contraction, the obstetrician delivers the baby by cesarean.

The neonatal team attends the delivery and needs to administer bag-mask ventilation because the infant emerges apneic. After 1 minute of assisted ventilation, the infant is breathing spontaneously and well-appearing. The baby's birth weight is 2,000 g, which is 6th percentile for a baby born at 36 weeks' gestation.

3. Of the following, the morbidity that is most likely in this infant is:

   A. Anemia
   B. Hypercalcemia
   C. Hyperthermia
   D. Hypoglycemia

CASE 12

Initial care of the premature infant

A pregnant woman presents to the hospital with spontaneous rupture of membranes and contractions. Her obstetrician orders antenatal steroids and antibiotics. Although tocolysis is attempted, her labor progresses and she delivers a preterm infant at 28 weeks' gestation with a birth weight of 1,200 g (70%).

1. Of the following, the term that best describes this infant is:

   A. Low-birth-weight (LBW) infant
   B. Very low-birth-weight (VLBW) infant
   C. Extremely low-birth-weight (ELBW) infant
   D. Micropremie

The neonatology team cares for the infant immediately after delivery. At 5 minutes of age, the infant is receiving facial continuous positive airway pressure because of respiratory distress and appears hypotonic with decreased reflex irritability. The infant's Apgar score is 5 and 6 at 1 and 5 minutes, respectively.

The neonatology fellow updates the parents in the delivery room. The parents express concern that the baby's Apgar score is lower than their older child's score; the parents relate that the infant's sibling was born at 39 weeks' gestation and had an Apgar score of 8 at 1 minute of age and 9 at 5 minutes of age. The fellow is reassures the parents and discusses that a premature infant often cannot achieve as high an Apgar score as does a full-term infant.

2. Of the following, the physiologic reason why premature infants often cannot achieve an Apgar score above 6 is:

   A. A low resting heart rate
   B. Neurologic immaturity
   C. Persistence of fetal circulation
   D. Poor perfusion

The baby is then brought to the Neonatal Intensive Care Unit for further care. The neonatal nurse places the infant on a radiant warmer and assesses the infant's vital signs. The pediatric resident orders laboratory studies, a chest radiograph, and an intravenous solution containing total parenteral nutrition. The pediatric resident meets with the family to discuss the results of these studies and the management plan.

3. Of the following, the current issue that is *least* likely to be present in this 1-hour-old infant is:

   A. Anemia of prematurity
   B. Hypoglycemia
   C. Hypothermia
   D. Hypoxemia

4. Of the following, the laboratory studies that were most likely sent on this infant are:

   A. Blood urea nitrogen and serum creatinine
   B. Complete blood cell count and blood culture
   C. Serum electrolytes
   D. Serum transaminases

SECTION I

Answers

CASE 1 ANSWERS

1. C. Line C

α-Fetoprotein is a protein that is produced by the fetal yolk sac during early gestation. After peak production by the fetus at ~13 weeks' gestation, the fetal α-fetoprotein concentrations decrease. The fetal serum α-fetoprotein is then excreted into fetal urine and enters the amniotic fluid. Thus, the amniotic fluid α-fetoprotein curve corresponds directly with the fetal serum α-fetoprotein curve. α-Fetoprotein can diffuse across the placenta into the maternal circulation. The peak maternal α-fetoprotein concentration typically occurs at approximately 32 weeks' gestation. These three α-fetoprotein curves are represented in Figure 2.

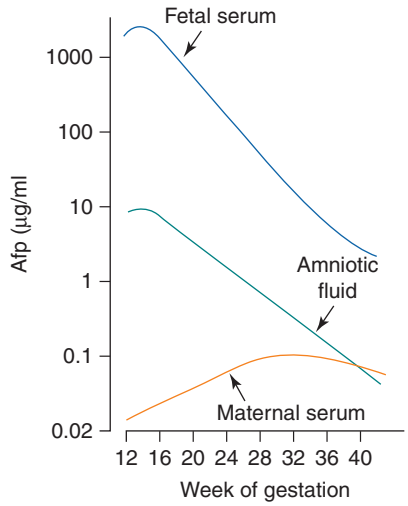

FIGURE 2. From Seppala M, ed. *Amniotic Fluid.* 2nd ed. New York, NY: Excerpta Medica; 1978, with permission

2. C. Trisomy 21

The combination of maternal serum α-fetoprotein, unconjugated estriol, β-human chorionic gonadotropin, and inhibin A testing is known as a quadruple screen. It is typically measured between 14 and 20 weeks' gestation, with 16 weeks' gestation being the optimal time. Assessment of these results can help determine the risk of fetal chromosomal anomalies, particularly trisomy 21 and trisomy 18. If this second trimester testing is combined with first trimester maternal pregnancy-associated plasma protein A (PAPP-A) levels and first trimester nuchal translucency measurements, the detection rate of trisomy 21 approaches 90% to 95%.

In this vignette, the pregnant woman's quadruple screen is normal except for an elevated α-fetoprotein. An isolated maternal serum α-fetoprotein elevation can result from the following:

- Neural tube defect
- Omphalocele or gastroschisis
- Sacrococcygeal teratoma
- Cloacal exstrophy
- Multiple gestation
- Underestimation of gestational age (i.e., pregnancy is further along than previously thought)

A low maternal serum α-fetoprotein concentration may be found in infants with trisomy 21 or trisomy 18.

Because maternal serum α-fetoprotein test results have a high false-positive rate, further testing, such as fetal ultrasonography and amniocentesis, is necessary to determine if there is any significance to an abnormal value.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the significance of abnormal maternal serum α-fetoprotein concentrations
- Know that the measurement of maternal serum α-fetoprotein concentration is a useful screening test for the diagnosis of open neural tube defects in a fetus

SUGGESTED READINGS

Blumenfeld Y. First trimester screening for fetal aneuploidy. *NeoReviews*. 2012;13:e4–e8.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York, NY: McGraw-Hill; 2009.

CASE 2 ANSWERS

1. A. Anencephaly

This ultrasonographic image demonstrates a poorly developed, small head that is most consistent with anencephaly. Anencephaly is caused by a failure of the anterior tube to close, leading to degeneration of the forebrain within the first month of gestation. This results in absence of most of the brain tissue, skull, and scalp; an affected fetus may have sparing of the brainstem and cerebellum. The maternal serum α-fetoprotein is often elevated. Ultrasonographic findings are typically apparent by 15

weeks' gestation. This abnormality needs to be distinguished from a ruptured encephalocele or amniotic bands involving the scalp. Although holoprosencephaly, hydrocephalus, and meningomyelocele can all be diagnosed by fetal ultrasonography, these findings are not apparent on this radiographic image.

2. D. Large Ventricular septal defect

The fetal ultrasound imaging shows two ventricular chambers that are not separated by a septum (*white dots*). Thus, the fetus in this vignette also has a large ventricular septal defect. Transabdominal echocardiography can be helpful to further delineate cardiac defects. The optimal timing of performing transabdominal echocardiography is between 18 and 32 weeks' gestation; however, this procedure can be performed as early as 14 weeks' gestation. A transvaginal approach can be performed as early as 10 weeks' gestation, but the quality of the images are dependent on the position and activity of the fetus.

Most cardiac defects are apparent by routine fetal ultrasonography between 18 and 22 weeks' gestation. If a defect is observed, it can be further delineated by fetal echocardiography. The following cardiac defects may not always be identified by fetal echocardiography:

- Small ventricular or atrial septal defect,
- Coarctation of the aorta, and
- Minor valve abnormalities.

3. A. Dehydration

This fetal ultrasound demonstrates loops of bowel without a covering sac outside the abdominal cavity; this abnormality is consistent with a gastroschisis. In this lesion, the abdominal wall defect is located to the right of an intact umbilical cord. The diagnosis is typically made in the second trimester. An infant with gastroschisis has a 10% to 20% risk of additional anomalies. Because bowel is exposed, infants with gastroschisis are at increased risk for dehydration and infection after birth. If an intestinal atresia is present (~16% of affected infants), infants may have bilious emesis.

In contrast to gastroschisis, an omphalocele is an abdominal wall defect that has a covering membrane (*large white arrow* in Figure 5) with an umbilical vein (*uv* in image) that is part of the herniated mass. The liver is often within the covered sac (designated as *L* in Figure 5). An infant with an omphalocele has a much higher risk of additional anomalies (45%–80%) compared with an infant who has a gastroschisis.

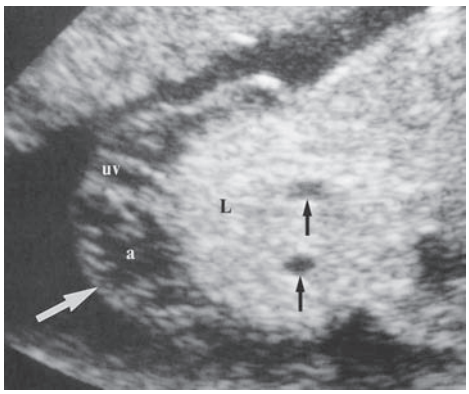

FIGURE 5. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 1.21

4. C. Posterior urethral valves

The image shown in this vignette is most consistent with posterior urethral valves. This diagnosis is suggested by fetal ultrasonography if there is bilateral hydronephrosis, a hydroureter, a thick-walled large bladder, and dilation of the proximal urethra. The diagnosis can be confirmed postnatally by a voiding cystourethrogram that demonstrates the valve leaflets.

5. A. Healthy term infant

Choroid plexus cysts are thought to be caused by fluid- and debris-filled neuroepithelial folds. This finding is usually isolated and seen in ~0.5% of normal fetuses. If the fetus has other anomalies, the finding of these cysts raises the possibility that the fetus has trisomy 18.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that prenatal ultrasonography can detect major fetal anomalies (e.g., hydrocephalus or anencephaly, myelomeningocele, congenital heart defects, gastrointestinal or genitourinary abnormalities) as early as 16 weeks' gestation

SUGGESTED READINGS

Bianchi D, Crombleholme T, D'Alton M, et al. *Fetology: Diagnosis and Management of the Fetal Patient*. 2nd ed. New York, NY: McGraw-Hill; 2010.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 3 ANSWERS

1. A = 4, amniocentesis; B = 3, periumbilical blood sampling; C = 2, transabdominal chorionic villus sampling; D = 1, transvaginal chorionic villus sampling

There are several prenatal methods for fetal DNA analysis. An amniocentesis is performed by placing a needle into the amniotic cavity with guidance from real-time ultrasonography. Possible indications for performing an amniocentesis include:

- Increased risk for fetal chromosomal abnormalities
- Increased risk for genetic or biochemical abnormalities
- Increased risk for open neural tube defects
- Assessment of fetal lung maturity

In periumbilical blood sampling, also known as cordocentesis, a needle is placed through the pregnant woman's abdomen

into the umbilical cord using real-time ultrasonography. The most common indications for performing this procedure include:

- Need for rapid chromosomal analysis
- Assessment for fetal anemia in red cell isoimmunization
- Evaluation for fetal infection
- Evaluation of nonimmune hydrops
- Assessment for fetal thrombocytopenia in alloimmune thrombocytopenia

Chorionic villus sampling allows for reliable testing for DNA analysis, karyotype, and biochemical abnormalities early in pregnancy. In the transvaginal (also known as transcervical) approach, a catheter is placed through the cervix into the placental tissue using real-time ultrasonography. A syringe containing nutrient medium is then attached to the catheter and pulled back until villi are visible in the syringe. In the transabdominal approach, a needle is placed across the pregnant woman's abdomen into the placenta using real-time ultrasonography and villi are aspirated into the syringe. Chorionic villus sampling is usually performed by a transvaginal approach; however, a transabdominal approach can be used if karyotype analysis is needed late in pregnancy.

2. B. Fetal ultrasonography

DNA testing can be performed using amniotic fluid obtained by an amniocentesis, fetal blood obtained by periumbilical blood sampling, and placental cells obtained from chorionic villus sampling. If a specific DNA abnormality is of concern, chorionic villus sampling is the preferred method because this procedure obtains the largest amount of tissue for testing. At present, some of the most common diseases that can be prenatally diagnosed using DNA analysis include:

- α_1-Antitrypsin deficiency
- Congenital adrenal hyperplasia
- Cystic fibrosis
- DiGeorge syndrome
- Fragile X syndrome
- Muscular and myotonic dystrophy
- Ornithine transcarbamylase deficiency
- Phenylketonuria
- Retinoblastoma
- Sickle cell disease
- Spinal muscular atrophy
- Thalassemia
- Tay–Sachs disease
- Wiskott–Aldrich syndrome

Cell-free DNA obtained from the maternal circulation is an exciting new method of fetal genetic testing. Currently, maternal blood can be analyzed to determine fetal gender, fetal Rh (D) genotype, some aneuploidies, and some single gene disorders.

3. B. Elevated lecithin/sphingomyelin ratio

During the end of the third trimester, the fetal lung begins to mature. An amniocentesis can measure specific surfactant components to assess for fetal lung maturity. Phosphatidylglycerol typically increases after 34 weeks' gestation and correlates with lung maturation. Similarly, lecithin content increases with advancing gestational age and increasing lung maturity. Because sphingomyelin is a lipid within amniotic fluid that is not related to fetal lung maturation, it can be used to standardize amniotic fluid volume changes. Thus, the ratio of lecithin to sphingomyelin correlates with lung maturation and normalizes amniotic fluid volume. Phosphatidylinositol is present in fetal lung fluid in the beginning of the third trimester, and its levels decrease as the lung matures. Thus, the following are consistent with mature fetal lungs:

- Presence of phosphatidylglycerol (10%)
- Elevated lecithin/sphingomyelin ratio (ideal if >2)
- Low amounts of phosphatidylinositol ($\leq 2\%$)

This diagnostic approach to fetal lung maturity assessment is no longer commonly performed. This is partly because obstetricians are performing elective preterm deliveries only for significant maternal or fetal indications and the fetal lung maturity results would not impact their decision to deliver an infant.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Chorionic villus sampling

- Know that sickle cell disease can be diagnosed prenatally (e.g., chorionic villus sampling, amniocentesis, fetal erythrocytes)

Amniocentesis

- Know the appropriate tests for predicting the absence of neonatal respiratory distress syndrome

SUGGESTED READINGS

Bianchi D, Crombleholme T, D'Alton M, et al. *Fetology: Diagnosis and Management of the Fetal Patient*. 2nd ed. New York, NY: McGraw-Hill; 2010.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Martin RJ, Fanaroff AA, Walsh MC. *Fanaroff and Martin's Neonatal–Perinatal Medicine: Diseases of the Fetus and Infant*. 9th ed. Philadelphia, PA: Mosby; 2010.

CASE 4 ANSWERS

1. C. Normal fetal heart rate response to fetal movement

The nonstress test assesses the fetal heart rate in response to fetal movements. The upper strip of the nonstress test, shown in the question, represents the fetal heart rate pattern and the lower strip corresponds with uterine activity. *Arrows on the bottom of the upper strip* indicate fetal movement.

If a fetus has two accelerations in heart rate that are associated with fetal movements within a 20-minute period, the nonstress test is reactive. A nonreactive nonstress test result occurs if there are fewer than two accelerations in heart rate during a period of 20 minutes. In this scenario, the test is then repeated ~20 minutes later. While a reactive nonstress result *is* predictive of intrauterine survival for 7 days, a nonreactive nonstress test *may* suggest a compromised fetus. Because a nonreactive result is not specific for poor fetal well-being, further testing (e.g., biophysical profile) is required.

This fetal strip demonstrates a reactive nonstress test because the fetus has four accelerations following four fetal movements. The strip also shows that the fetus has good heart rate variability throughout the monitored period. While a nonstress test also demonstrates uterine activity, regular and frequent contractions are not seen on this fetal strip. A nonstress test does *not* measure the fetal breathing pattern or amniotic fluid volume.

An example of a nonreactive nonstress test is shown in Figure 2B. While the upper panel **(A)** shows that the fetal heart rate increases in response to two fetal movements, the lower panel **(B)** shows that the fetal heart rate does not change after a fetal movement.

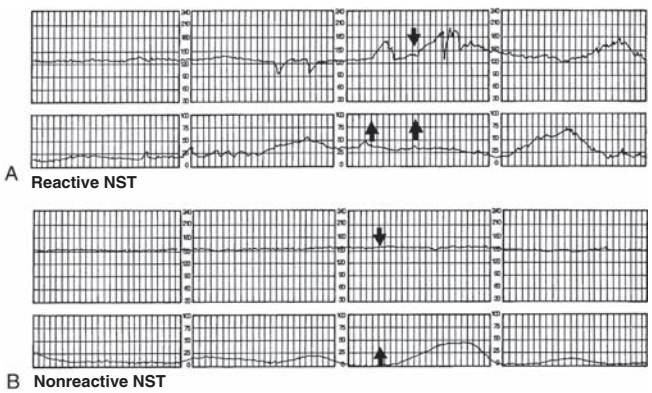

FIGURE 2. From Beckmann CRB, Ling FW, et al. *Obstetrics and Gynecology*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. Figure 5.02

2. C. Evaluate for uteroplacental insufficiency

A contraction stress test assesses the fetal heart rate in response to contractions. If the fetus has a late deceleration (decrease in fetal heart rate 10–30 seconds after the beginning of a contraction) associated with half of the contractions, prompt intervention is required. A positive (i.e., abnormal) test result suggests uteroplacental insufficiency that may be associated with an increased risk for intrauterine fetal demise, intolerance of labor, and perinatal depression.

3. B. Blood flow in the umbilical arteries

The biophysical profile assesses fetal well-being by combining the results of a fetal ultrasound and a nonstress test. It measures five discrete variables:

- Nonstress test
- Fetal body movement
- Fetal breathing
- Fetal muscle tone
- Amniotic fluid volume

Each of these parameters receives a score of 2 if normal or 0 if abnormal. The highest score is 10, suggesting a well fetus who does not require any intervention. If the biophysical score is 0 or 2, the obstetrician is likely to deliver the fetus because of the possibility of fetal asphyxia.

Blood flow within the umbilical arteries moves from the fetal to placental circulation. Doppler studies can assess the blood flow in the umbilical arteries during diastole to evaluate placental insufficiency. If the placenta is not functioning well, the placental vascular resistance will increase. If this happens, the flow through the umbilical arteries will be decreased or, if the placental vascular resistance is extremely high, the flow in the umbilical arteries will be reversed. Possible umbilical artery Doppler study results are:

- Normal umbilical artery blood velocity
- Increased resistance but blood flow is still present during diastole
- Absence of umbilical arterial blood flow during diastole (leads to decreased blood flow from the fetus to the placenta)
- Reversal of umbilical arterial blood flow during diastole

Doppler flow studies of the umbilical arteries are not part of the biophysical profile fetal assessment.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Nonstress test: Know that the nonstress test monitors fetal heart rate reactivity in response to fetal activity
- Stress test: Recognize that the stress test is used to evaluate uteroplacental insufficiency
- Biophysical profile: Know the factors used by obstetricians in evaluating fetal well-being

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York, NY: McGraw-Hill; 2009.

CASE 5 ANSWERS

1. D. Diabetes mellitus without evidence of vascular disease and good maternal glucose control before conception

Congenital anomalies are more frequent among infants of diabetic mothers than among healthy control infants. This risk of anomalies is greatest in women who have severe diabetes mellitus. For example, a woman with insulin-dependent diabetes

who does not have any vascular disease has an ~9% risk of having an infant with congenital anomalies. In contrast, if the woman has nephropathy or retinopathy, this risk increases to ~22%. Recent studies have found that the risk of congenital anomalies correlates with the degree of uncontrolled diabetes prior to conception. If a woman achieves glycemic control prior to conception, the risk of congenital anomalies is ~2.5% compared with ~7.8% in women who attain glycemic control after becoming pregnant. Glycemic control in pregnant women can be assessed by measuring the hemoglobin A1C values, with lower hemoglobin A1C values correlating with better glucose control.

2. C. Small left colon syndrome

The fetal structural anomalies associated with women with diabetes mellitus typically occur prior to 2 months' gestation, at the time of organogenesis. Most of these anomalies involve the cardiac and neurological systems and include:

- Cardiac: transposition of the great arteries, ventricular septal defect, atrial septal defect, hypoplastic left heart syndrome, aortic stenosis, coarctation of the aorta
- Neurologic: meningomyelocele, encephalocele, anencephaly

Infants are also at risk for caudal regression syndrome, which consists of spinal abnormalities and syringomyelia. Renal anomalies (hydronephrosis, renal agenesis, cystic kidneys) and intestinal atresias can also occur.

Small left colon syndrome usually occurs during the second half of gestation, after organogenesis is complete. In this syndrome, the diameter of the descending colon, sigmoid colon, and rectum are smaller than normal. The cause is thought to be related to large changes in maternal and fetal serum glucose concentrations. Affected infants often present with signs of intestinal obstruction, such as bilious emesis and abdominal distention.

3. B. Increased insulin production by the infant

If pregnant women with insulin-dependent diabetes mellitus have increased serum glucose concentrations, then glucose will cross the placenta into the fetal circulation. The fetus responds appropriately to this increased glucose by increasing pancreatic insulin production. After birth, the infant continues to produce insulin even though the glucose supply from the mother has now stopped. As a result, hypoglycemia can occur soon after birth. Over time, the infant's pancreatic production of insulin decreases and the infant can be weaned from supplemental glucose. Thus, the cause of the hypoglycemia in the infant in this case is most likely from increased insulin production by the infant.

4. B. Polycythemia

Infants born to women with insulin-dependent diabetes are at increased risk of having polycythemia. This association is likely a result from increased oxygen consumption in utero, prompting the fetal bone marrow to produce more red blood cells to increase oxygen-carrying capacity. After birth, cyanosis may then occur because of an increase in blood viscosity, which results in poor blood flow and decreased tissue oxygenation. Similar to the infant in this case, babies with polycythemia often appear ruddy and have an oxygen requirement.

The infant in this vignette is unlikely to have cyanotic heart disease because his oxygen saturation increased to normal with supplemental oxygen. While the infant is likely to have a patent ductus arteriosus at 3 hours of age, it is unlikely to be causing the cyanosis. If the cause of this infant's cyanosis is from significant right-to-left shunting across a patent ductus arteriosus, one would expect the infant to have radiographic evidence of decreased pulmonary blood flow and the cyanosis should be more significant. If the infant had significant left-to-right shunting across a patent ductus arteriosus, one would expect the infant to have radiographic evidence of increased pulmonary blood flow. An infant with retained fetal lung fluid leading to transient tachypnea of the newborn may have a small oxygen requirement but also should have an increased respiratory rate and radiographic evidence of increased fetal lung fluid. Infants of diabetic women are at increased risk for surfactant deficiency even if they are born at term gestational age; however, this is unlikely in this case because the infant does not have any respiratory distress.

5. A. Hypocalcemia

Infants born to women with diabetes mellitus are at increased risk for hypocalcemia. This most likely results from a delay in the appropriate parathyroid hormone response after birth. Infants born to women with diabetes are also at risk for hypomagnesemia as a result of the decreased postnatal parathyroid hormone response and maternal hypomagnesemia from renal losses leading to decreased placental transfer of magnesium during gestation. Hypocalcemia and hypomagnesemia usually occur within the first few days of life, especially if the infant has respiratory distress.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that congenital anomalies are more frequent among infants of diabetic mothers than among normal control infants
- Understand the pathogenesis of hypoglycemia in an infant of a diabetic mother
- Recognize that an infant of a diabetic mother is at risk for hypoglycemia, hypocalcemia, polycythemia, and small left colon syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Nold JL, Georgieff MK. Infants of diabetic mothers. *Pediatr Clin N Am*. 2004;619–637.
White BA and Porterfield SP. *Endocrine and Reproductive Physiology*. 4th ed. St Louis, MO: Mosby; 2012.

CASE 6 ANSWERS

1. A. Complete heart block

This infant's electrocardiogram shows complete heart block because there is no association between the depolarization of the atria and the ventricles. In first-degree heart block, the PR interval is consistently prolonged but is followed by a QRS complex. Infants with sinus bradycardia will have a slow heart rate with a normal sinus rhythm evident by a QRS complex appropriately following every P wave. In a Wenckebach pattern of second-degree atrioventricular heart block (also known as Mobitz type I), electrocardiographic findings will demonstrate increasing PR intervals followed by QRS complexes until the PR interval becomes so prolonged that an atrial impulse is not conducted and the QRS complex is absent.

2. C. Anti-Ro/SSA and anti-La/SSB antibodies

The infant described in this vignette has complete heart block and annular erythematous plaques on the face and trunk. These two findings are found in infants with neonatal lupus erythematosus. Neonatal lupus is a rare autoimmune disease that is usually benign and self-limited. It is caused by maternal anti-Ro/SSA and/or anti-La/SSB antibodies that cross the placenta.

A rash is the most common clinical manifestation of neonates with lupus. This rash usually appears during the first weeks of life and is characterized by round or elliptical erythematous lesions with a central clearing (i.e., annular erythema). These findings are typically found on the face and scalp but can also be observed on an infant's neck, trunk, and extremities. The classic malar rash found in adults with lupus is uncommon in infants with lupus. The rash typically resolves spontaneously by 8 months of age when the maternal autoantibodies have been completely cleared from the infant's body. Sometimes, residual skin abnormalities such as dyspigmentation, telangiectasias, or skin atrophy may occur.

Infants with neonatal lupus can have first-, second-, or third-degree (i.e., complete) heart block caused by antibody-mediated injury to the fetal and neonatal cardiac conduction tissues. Neonatal lupus is responsible for ~85% of cases of complete heart block. However, the incidence of complete heart block in infants born to mothers with anti-Ro/SSA or anti-La/SSB antibodies is low, only 1% to 2%. If a woman with lupus has a child with neonatal lupus and heart block, the risk of heart block increases dramatically to ~16% to 18% in subsequent pregnancies. Complete heart block can be associated with significant morbidity and mortality.

3. C. 50%

Approximately half of the infants affected with lupus are born to undiagnosed, healthy mothers. These asymptomatic women are often diagnosed after delivery, when their infant presents with symptoms of neonatal lupus.

4. D. Thrombocytopenia

Infants with neonatal lupus are at risk of the following clinical manifestations:

- Cutaneous (~70%)
- Cardiac (~65%)
- Hematologic (35%)
- Hepatobiliary (9%–25%)

Hematologic complications include anemia, thrombocytopenia, and neutropenia. These manifestations typically occur during the second week of life and resolve by 3 months of age. If hematologic manifestations are severe and persistent, treatment with intravenous immunoglobulin and/or corticosteroids may be indicated. Hepatobiliary findings typically include transiently elevated transaminases and conjugated hyperbilirubinemia, first occurring at a few weeks of age. In addition to these complications, recent data suggest that affected infants are also at risk for central nervous system injury. Thus, affected neonates require close neurological follow-up.

Based on these clinical manifestations, if an infant is diagnosed with neonatal lupus, the following tests are recommended:

- Electrocardiogram
- Complete blood count
- Transaminases
- Direct bilirubin

In addition, head imaging should be considered, particularly if an infant has neurological symptoms. If an affected infant has hematuria or proteinuria, an evaluation for nephritis should be considered.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Identify the clinical picture of neonatal lupus, including heart block
- Know which tests are useful in evaluating neonatal lupus

SUGGESTED READINGS

Frankovich J, Sandborg C, Barnes P, et al. Neonatal lupus and related autoimmune disorders of infants. *NeoReviews*. 2008;9:e206–e217.
White BA and Porterfield SP. *Endocrine and Reproductive Physiology*. 4th ed. St Louis, MO: Mosby; 2012.

CASE 7 ANSWERS

1. A. All anticonvulsants marketed prior to 1976 have been shown to have teratogenic effects

All antiseizure medications marketed prior to 1976, including carbamazepine, hydantoin, phenobarbital, and valproate, have been shown to have teratogenic effects when exposure occurs during the *first* trimester. These effects have varying clinical manifestations and degrees of severity. The most common manifestations observed in infants are:

- Digit hypoplasia,
- Growth restriction,
- Midface hypoplasia, and
- Microcephaly.

Intrauterine exposure to carbamazepine and valproate also increases the risk for meningomyelocele. Fortunately, the associated major malformations are relatively uncommon. Indeed, most of the major malformations found in infants exposed to intrauterine anticonvulsants are also common in unexposed children. Older children exposed to anticonvulsants in utero are at increased risk for cognitive disabilities.

The infant described in this vignette has some clinical features that are consistent with intrauterine hydantoin exposure. The fetal hydantoin syndrome consists of:

- Digit and nail hypoplasia
- Craniofacial features, such as wide anterior fontanel; metopic ridging; ocular hypertelorism; broad, depressed nasal bridge; short nose; cleft lip and palate
- Growth deficiency, usually of prenatal onset
- Mental deficiency, usually mild

2.

A. Deformation	2. Arthrogryposis caused by intrauterine constraints
B. Disruption	1. Amniotic bands
C. Dysplasia	4. Hemangioma
D. Malformation	3. Cleft palate

There are four types of problems in morphogenesis: malformation, deformation, disruption, and dysplasia. A malformation is caused by an abnormality in tissue formation associated with an environmental exposure, a genetic abnormality, or an unknown cause. These problems typically impact the fetus during the first trimester and can lead to minor or major malformations. Some examples of malformations are:

- Anencephaly
- Bladder exstrophy
- Branchial sinus or cyst
- Cleft lip or palate
- Diaphragmatic hernia
- Hypospadius
- Intestinal atresias
- Meningomyelocele
- Omphalocele
- Transposition of the great arteries

The recurrence risk typically ranges between 1% and 5%. A syndrome occurs when a fetus has many primary malformations caused by one etiology.

A deformation occurs when there are mechanical forces that alter normal tissue formation. Some examples of deformations are arthrogryposis caused by intrauterine constraints and breech deformation sequence. Most deformations have a good prognosis and the risk for recurrence is very low, unless there is a persistent issue, such as a bicornate uterus.

A disruption occurs when there is a breakdown of normal tissue. Some examples of disruptions are:

- Amniotic bands
- Limb reduction defects as a result of vascular anomalies
- Porencephaly

A dysplasia is an abnormal organization of cells within tissues caused by a deregulation. A hemangioma and ectodermal dysplasia are examples of dysplasias.

3. C. Nasal hypoplasia and stippled bone epiphyses

First-trimester exposure to warfarin can lead to a syndrome of nasal hypoplasia and stippled epiphyses. Approximately one-third of exposed fetuses have these findings. Affected infants often present with upper airway obstruction that is improved with an oral airway. Because heparin does not cross the placenta, heparin has not been associated with teratogenic effects and is often used as a substitute for warfarin.

Previous data has identified an association between intrauterine exposure to lithium and Ebstein anomaly. However, recent studies question this association.

First-trimester exposure to retinoic acid can lead to abnormal findings, such as central nervous system abnormalities, microtia, and cardiac defects. The possible central nervous system findings include hydrocephalus, microcephaly, abnormalities in neuronal migration, and posterior fossa structural abnormalities.

Maternal tetracycline intake during pregnancy has been associated with a yellow-brown discoloration of deciduous teeth and impaired bone growth in the exposed child.

4. A. Indomethacin

Prolonged use of indomethacin, a prostaglandin synthase inhibitor, is associated with risks, including oligohydramnios, premature closure of the ductus arteriosus, renal insufficiency, pulmonary hypertension, ileal perforation, and necrotizing enterocolitis.

Magnesium sulfate decreases uterine contractility by inhibiting acetylcholine release from the neuromuscular junction and functioning as a calcium antagonist. Postnatal effects of intrauterine exposure to magnesium sulfate include decreased peristalsis, hypotension, hypotonia, and apnea.

Nifedipine is a calcium-channel blocking agent that decreases uterine contractility. Prolonged use of nifedipine during pregnancy can lead to uteroplacental insufficiency.

Terbutaline is a β2-agonist that leads to decreased intracellular calcium, inhibiting uterine contractility. Use of terbutaline during pregnancy can lead to fetal tachycardia.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that the use of some anticonvulsants during pregnancy is associated with an increased risk of fetal anomalies
- Know the effect on a fetus of lithium use during pregnancy
- Know that isotretinoin is a potent teratogen
- Know the effect on a fetus of warfarin use during pregnancy
- Understand the effects of drugs given to the mother during labor (e.g., opiates, β-adrenergic tocolytic agents) on the fetus/neonate

SUGGESTED READINGS

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Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York, NY: McGraw-Hill; 2009.
Jones KL. *Smith's Recognizable Patterns of Human Malformations*. 6th ed. Philadelphia, PA: WB Saunders; 2005.
Holmes LB. The teratogenicity of anticonvulsant drugs: a progress report. *J Med Genet*. 2002;39:245–247.

CASE 8 ANSWERS

1. A. Cocaine

Cocaine use during pregnancy is associated with spontaneous abortions, preterm delivery, stillbirth, and placental abruption. Exposed infants are at increased risk for skull abnormalities, cutis aplasia, porencephaly, ileal atresia, cardiac abnormalities, intestinal ischemia, and urinary tract abnormalities. Intrauterine exposure also increases the risk for long-term neurodevelopment impairments, although it is uncertain if these effects are related to pregnancy exposure or postnatal environment.

Heroin use during pregnancy is not associated with teratogenic effects but has been linked to intrauterine growth restriction, preterm delivery, and stillbirth.

Use of morphine and methadone during pregnancy has minimal teratogenic effects.

2. C. Methamphetamine

Signs of neonatal withdrawal are nonspecific, as evident in the infant described in this vignette. If a pregnant woman takes the stimulant methamphetamine, withdrawal signs are observed in only a small number of exposed infants (~4%). These signs are usually less severe than with methadone or heroin exposure and often demonstrate the impact of the amphetamine rather than withdrawal from its effects.

Narcotics, such as buprenorphine, codeine, heroin, methadone, morphine, and oxycodone, are the most common causes of neonatal withdrawal syndrome.

Infants exposed to intrauterine alcohol can also have ethanol withdrawal, although the symptoms are less severe than in infants withdrawing from opiates.

3. D. All of the above

Nonpharmacologic approaches to infants with neonatal abstinence syndrome include:

- Demand feeding
- Gentle handling
- Minimize noise
- Swaddling

Pharmacologic treatment is determined by the specific clinical symptoms in the infant and the type of exposed drug. Hospitals use an abstinence scoring system that helps determine the severity of symptoms. If the score reaches a certain level, the infant is started on medications to minimize excessive excitation and decrease the risk for seizures. Medications include:

- Buprenorphine
- Methadone
- Morphine sulfate
- Phenobarbital

Once an infant has low scores, the medication is slowly decreased. The length of treatment can vary from weeks to months.

4. D. Thin upper lip

First-trimester alcohol exposure can lead to teratogenic effects in the fetus. Infants with fetal alcohol syndrome have distinctive facial features. The three most common facial findings in this syndrome are:

- A smooth philtrum
- Thin upper lip
- Short palpebral fissures

Additional facial findings include a flat midface, micrognathia, minor ear anomalies, low nasal bridge, and epicanthal folds (Figure 1). Fetal alcohol syndrome is also associated with other abnormalities, including intrauterine growth restriction, cardiac defects, and neurological effects.

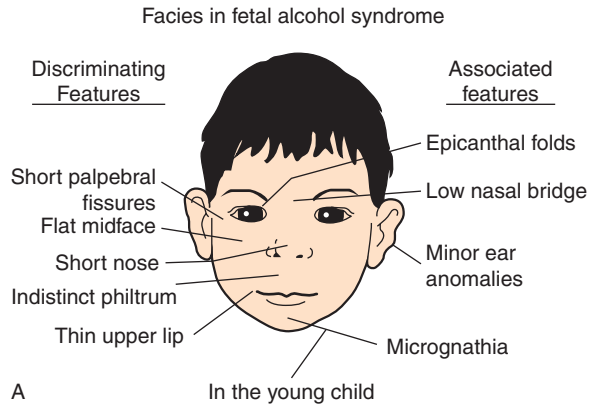

FIGURE 1. Characteristic features of a child with *fetal alcohol* syndrome. Modified from Sadler T. *Langman's Medical Embryology*. 9th ed. Image Bank. Baltimore, MD: Lippincott Williams & Wilkins; 2003

5. C. Macrocephaly

Fetal alcohol syndrome is the most common cause of mental retardation in developed countries. In the United States, this syndrome is estimated to occur in 1 to 3 per 1,000 live births, with a higher occurrence in certain populations, such as Native Americans. Infants with prenatal exposure to alcohol are at risk for neurobehavioral issues, such as attention deficit/hyperactivity disorder, poor impulse control, problems with memory or attention, problems in social perception, and autism.

Affected infants may also have structural central nervous system abnormalities such as:

- Decreased size of cerebrum, cerebellum, basal ganglia
- Dandy–Walker malformation
- Heterotopia
- Holoprosencephaly
- Microcephaly (small head size)

- Microencephaly (small brain size)
- Partial or complete agenesis of the corpus callosum
- Ventricular enlargement

The adverse effects on brain development caused by intrauterine alcohol exposure are believed to be most impacted by peak blood-alcohol concentration. Structural central nervous system abnormalities and craniofacial abnormalities are strongly associated with heavy alcohol consumption during the first trimester. In contrast, the development of microcephaly is thought to correspond to the amount of alcohol exposure during late gestation.

6. D. Sudden infant death syndrome

Intrauterine tobacco exposure has been associated with the following:

- Placental abruption
- Placenta previa
- Premature rupture of membranes
- Premature delivery
- Low-birth-weight infant
- Neurobehavioral issues

Prenatal exposure to smoke places infants at increased risk for sudden infant death syndrome.

The effects of marijuana use during pregnancy are not clear. Some studies have demonstrated long-term cognitive deficits and neurobehavioral concerns, but this has not been consistently found.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Neonatal abstinence syndrome

- Know the association between the maternal use of cocaine and neonatal withdrawal syndrome
- Know the association between the maternal use of barbiturates and neonatal withdrawal syndrome
- Know the association between the maternal use of opiates and neonatal withdrawal syndrome
- Know the association between the maternal use of amphetamines and neonatal withdrawal syndrome
- Know the management of neonatal abstinence syndrome

Fetal alcohol exposure

- Recognize the physical features of fetal alcohol syndrome
- Know that fetal alcohol syndrome is a frequently documented cause of mental retardation
- Know the association between the maternal use of alcohol and neonatal withdrawal syndrome

Maternal marijuana and smoking

- Know the association between the maternal use of marijuana and any fetal abnormalities
- Know the association between the maternal use of tobacco and any fetal abnormalities

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Burgos AE, Burke Bl. Neonatal abstinence syndrome. *NeoReviews*. 2009;10:e222–e229.

Gleason CA. Fetal alcohol exposure: effects on the developing brain. *NeoReviews*. 2001;2:e231–e236.

CASE 9 ANSWERS

1. C. Perfusion

In 1953, Virginia Apgar published a method to evaluate the physical condition of a newborn soon after birth. This assessment evaluates five clinical signs:

- Appearance (i.e., color)
- Pulse (i.e., heart rate)
- Grimace (i.e., reflex irritability)
- Activity (i.e., muscle tone)
- Respirations (i.e., respiratory effort)

To recall the specific components of the Apgar score, it may be helpful to remember that the first letter of each sign spells the word "Apgar." The perfusion of an infant is not part of the Apgar score.

2. B. 1

After birth, the medical team reports an infant's Apgar score by assessing the infant's color, heart rate, reflex irritability, tone, and respiratory effort. This assessment occurs at 1 and 5 minutes of age; if the Apgar score is less than 7 at 5 minutes of age, the scoring is continued every 5 minutes until the score is 7 or greater for up to 20 minutes. The team provides a score of 0, 1, or 2 for each of the five clinical signs, as shown in Figure 1.

Apgar Scoring Chart

		Score	
Sign	0	1	2
Heart rate	Absent	Slow (<100)	>100
Respiratory effort	Absent	Slow, irregular; weak cry	Good; strong cry
Muscle tone	Flaccid	Some flexion of extremities	Well flexed
Reflex irritability			
Response to catheter in nostril	No response	Grimace	Cough or sneeze
or slap of sole of foot	No response	Grimace	Cry and withdrawal of foot
Color	Blue, pale	Body pink, extremities blue	Completely pink

FIGURE 1. Courtesy of Artesia Assets © 2014 Lippincott Williams & Wilkins. All rights reserved

The infant in this vignette has a heart rate, but it is less than 100 beats per minute. This corresponds to a score of 1. Because the infant is cyanotic without any respiratory effort, tone, or reflex irritability, the other signs have a score of 0 and the infant's total score is 1.

3. C. The infant's Apgar score is a poor indicator of neurological outcome

The Apgar score was created to describe an infant's clinical condition after birth and was not intended to predict neurological outcome. While a low Apgar score at 1 minute of age shows that an infant needs medical assistance, it does not indicate long-term problems, especially if the 5-minute score is high. Thus, the neonatologist is most likely to tell the infant's father that the Apgar score is a poor indicator of neurological outcome.

An amplitude electroencephalogram is used to assess an infant's cerebral activity to determine whether a newborn meets criteria for therapeutic hypothermia. Eligible neonates have evidence of fetal distress, neonatal distress, physical examination findings consistent with neonatal encephalopathy, and an abnormal cerebral function monitor recording.

The majority of full-term infants who develop cerebral palsy have a normal Apgar score. However, if an infant's Apgar score is extremely low (<3) at 10 or 20 minutes of age, there is a small but increased risk of cerebral palsy.

Infants with hypoxic-ischemic encephalopathy are at increased risk for seizure activity after birth. Infants with an abnormal neurological examination (lethargy, mild hypotonia, overactive reflexes, myoclonus, weak suck, and weak Moro reflexes) and low-voltage activity by an electroencephalogram are at particular risk for seizures. The infant in this vignette is not at increased risk for seizure activity because the baby is well-appearing and without any signs of encephalopathy.

4. D. Minimal flexion of arms and legs at rest

Infants born preterm, full-term, and postterm have specific physical findings. A preterm infant's examination may have the following characteristics:

- Decreased or absent plantar creases
- Lack of recoil of ear pinna
- Lanugo
- Minimal flexion of arms and legs at rest
- Prominent labia minora in females
- Small or absent areola and breastbud
- Undescended testes and decreased/absent scrotal rugae in males

Postterm infants may have leathery, cracked, and wrinkled skin.

To calculate an infant's gestational age, a clinician can use the Ballard assessment scale (shown in the next column). A clinician provides a specific score to each physical and neuromuscular assessment and then tallies the total. This point total corresponds with a specific gestational age (in Figure 2C).

	0	1	2	3	4	5
Skin	Gelatinous red, trans-parent	Smooth, pink, visible veins	Superficial, peeling &/or rash, few veins	Cracking, pale area, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled
Lanugo	None	Abundant	Thinning	Bald areas	Mostly bald	
Plantar Creases	No crease	Faint red marks	Anterior transverse crease only	Creases ant. 2/3	Creases cover entire sole	
Breast	Barely percept.	Flat areola, no bud	Stippled areola, 1–2 mm bud	Raised areola, 3–4 mm bud	Full areola, 5–10 mm bud	
Ear	Pinna flat, stays folded	Sl. curved pinna, soft with slow recoil	Well-curv. pinna, soft but ready recoil	Formed & firm with instant recoil	Thick cartilage, ear stiff	
Genitals Male	Scrotum empty, no rugae		Testes descend-ing, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals Female	Prominent clitoris & labia minora		Majora & minora equally prominent	Majora large, minora small	Clitoris & minora completely covered	

A

	0	1	2	3	4	5
Posture						
Square Window (Wrist)	90	60	45	30	0	
Arm Recoil	180		100-180	90-100	<90	
Popliteal Angle	180	160	130	110	90	<90
Scarf Sign						
Heel to Ear						

B

Score	Wks
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

C

FIGURE 2. From Ballard JL. New Ballard score expanded to include extremely premature infants. *J Pediatr*. 1991;119: 417–423

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the components of the Apgar score
- Understand the significance of the one- and five-minute Apgar scores
- Know the physical characteristics of preterm, full-term, and postterm infants

SUGGESTED READINGS

American Academy of Pediatrics and American Heart Association. *Textbook of Neonatal Resuscitation*. 6th ed. American Academy of Pediatrics; 2011.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 10 ANSWERS

1. B. Establishment of a patent airway before applying positive-pressure ventilation

If an infant is not breathing after birth, a neonatal team needs to provide warmth, ensure airway patency, and stimulate the baby. If the baby, despite these measures, has a heart rate less than 100 beats per minute, has apnea, or is gasping, the neonatal team needs to begin positive-pressure ventilation. Continued stimulation is not appropriate because it will not induce breathing if the newborn has irreversible secondary apnea. For the first few assisted breaths, a *higher* pressure may be required to effectively inflate the neonate's lungs. Once a neonate is receiving respiratory support, the team needs to place a pulse oximeter probe on the newborn's right wrist to measure a preductal oxygen saturation.

2. B. Compress to a depth one-third the anterior–posterior diameter of the chest

The current neonatal resuscitation guidelines for chest compressions include the following:

- Apply compressions over the lower third of the newborn's sternum
- Compress to a depth one-third the anterior–posterior diameter of the chest
- Provide chest compressions and bag-mask breaths in a ratio of *3:1*
- Use the two-thumb-encircling-hands approach instead of the two-finger technique when possible

The two-thumb-encircling technique is preferred because of the likelihood that it generates greater coronary perfusion. However, if a neonate requires an umbilical line placement, the two-finger technique may need to be used to allow access to the umbilicus.

3. A. If the heart rate does not increase above 60 beats per minute despite effective ventilation with oxygen for 30 seconds

It is really important that assisted ventilation is being delivered effectively before starting chest compressions. If a newborn's heart rate does not increase above 60 beats per minute despite effective ventilation with oxygen for 30 seconds, chest compressions should be initiated.

If a newborn has a heart rate less than 30 beats per minute immediately after birth, the team should provide bag-mask ventilation.

If a newborn remains cyanotic despite appropriate bag-mask ventilation, a team member should intubate the baby.

Decreased perfusion is not an indication for chest compressions in a newborn. If a newborn's perfusion is extremely poor with pale skin color and weak pulses, volume expansion is indicated if the heart rate has not responded to other resuscitative approaches. Poor perfusion is not a specific indicator to start chest compressions.

4. C. Intubation and suctioning the infant's trachea if the infant was not vigorous immediately after birth

This infant's chest radiograph demonstrates bilateral, diffuse, patchy densities with overexpanded lungs. Areas of overdistension result from air trapping because of airway obstruction. These radiographic findings are most consistent with meconium aspiration pneumonia. Current neonatal resuscitation guidelines recommend that newborns with a history of intrauterine passage of meconium who emerge apneic, limp, and inactive should undergo endotracheal intubation to suction the trachea for meconium and try to decrease the risk for aspiration. This recommendation is independent of the thickness of the meconium.

Classic radiographic findings of surfactant deficiency include the following:

- Air bronchograms
- Diffuse reticulogranular pattern or ground-glass appearance
- Low lung volumes

Some options that might decrease the severity of surfactant deficiency include:

- Administration of maternal steroids prior to delivery
- Initiation of continuous airway pressure soon after birth
- Intratracheal administration of surfactant soon after birth

Although oxygen supplementation does lead to pulmonary inflammation, minimizing the use of supplemental oxygen would not have decreased the severity of this infant's disease.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Ventilation

- Recognize the need to establish a patent airway before applying positive-pressure ventilation
- Recognize that a newborn who has a slow heart rate and impaired ventilatory effort requires immediate positive-pressure ventilation
- Know that the initial lung inflation may require increased pressure for the first breath

Perfusion

- Know the proper technique for external cardiac massage in a newborn
- Recognize the indications for external cardiac massage of a newborn during resuscitation

Suctioning

- Recognize a newborn's larynx needs to be visualized and the trachea suctioned if meconium is present in the amniotic fluid and the infant is not vigorous

SUGGESTED READINGS

American Academy of Pediatrics and American Heart Association. *Textbook of Neonatal Resuscitation*. 6th ed. American Academy of Pediatrics; 2011.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 11 ANSWERS

1. D. Curves 1 and 2

Although the terms *intrauterine growth restriction or IUGR* and *small for gestational age or SGA* are often used interchangeably, they are actually distinct. A fetus or infant has growth restriction if the intrauterine rate of growth is less than the predetermined growth potential of the fetus. Curve 1 corresponds with a growth-restricted infant because the initial intrauterine growth along the 75th percentile was disrupted, preventing the infant from achieving his/her growth potential. At birth, the infant had a normal birth weight percentile of ~40%, which is appropriate for gestational age.

A neonate is described as being SGA if the baby's birth weight is lower than that of the standard population, typically lower than the 10th percentile of population-based weight data. Curve 3 represents an infant who is SGA because the birth weight percentile is below the 10th percentile. Because the fetal growth pattern was less than the 10th percentile throughout gestation, there was no interruption of intrauterine growth; thus, Curve 3 corresponds to an infant who is SGA but not growth-restricted.

An infant can have IUGR and be SGA if the intrauterine growth curve was disrupted and the infant's birth weight percentile is less than the 10th percentile. Curve 2 shows a growth-restricted infant because the infant's growth potential was never reached. The infant is also SGA because the birth weight percentile is less than the 10th percentile.

2. A. Familial short stature

The intrauterine growth curve of a fetus with familial short stature may appear similar to Curve 3 with a low growth percentile throughout the pregnancy. Fetuses with a genetic abnormality may have a similar growth curve because of their small size throughout gestation. However, some genetic abnormalities will cause IUGR, leading to an infant who is either SGA or an appropriate size for gestational age.

Maternal gestational diabetes may impact fetal growth by leading to a large-for-gestational-age infant (i.e., above the 90th percentile). This mechanism is caused by high maternal serum glucose concentrations that cross into the fetal circulation. The fetal pancreas responds by increasing insulin production. Because insulin is an important intrauterine growth hormone, infants born to women with gestational diabetes often have macrosomia. If a woman has severe type I diabetes mellitus with significant small vessel disease, the fetal growth pattern may be inhibited because of placental insufficiency. These fetuses may have a growth curve similar to Curve 1 or Curve 2.

A woman with pregnancy-induced hypertension may have associated placental insufficiency, which leads to a decrease in fetal growth. Although this decrease in fetal growth may occur in the second or third trimester, it most commonly occurs in the third trimester, similar to the pattern of growth shown in Curve 1 or Curve 2.

Multiple gestation will also lead to a decrease in fetal growth over time, partly because growth is limited by the size of the uterus. Examples of typical fetal growth curves for a twin, triplet, and quadruplet gestation are shown in Figure 2.

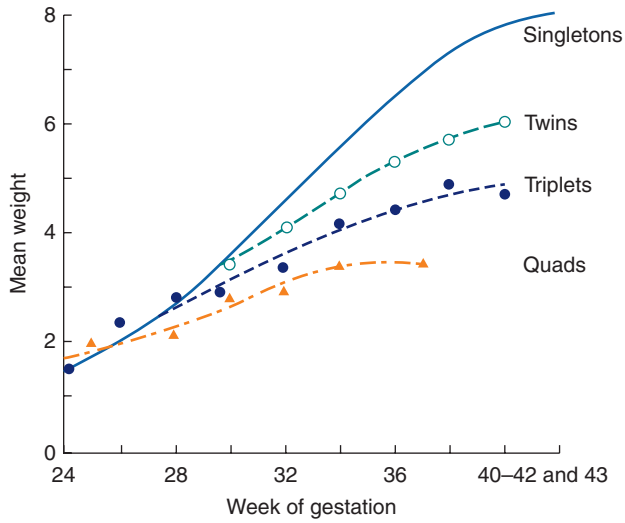

FIGURE 2. Adapted from McKeown T′ Record RG. Observation on foetal growth in multiple pregnancy in man. *J Endocrinol* 1952;8:386, with permission

Other causes of IUGR include maternal smoking, maternal undernutrition, and intrauterine infection.

3. D. Hypoglycemia

Similar to the fetus in this vignette, growth-restricted fetuses are at increased risk for intolerance of labor because uterine contractions cause additional stress to the fetus. This leads to a greater risk for cesarean delivery, need for neonatal resuscitation, and/or perinatal asphyxia.

The infant in this vignette had a decline in intrauterine growth, which led to a low birth weight (less than 10th percentile), characterizing the infant as IUGR and SGA. In general, SGA infants have a higher mortality and a greater risk for morbidities compared with appropriate-for-gestational-age infants. The two most common morbidities found in SGA infants include:

- Hypoglycemia because of decreased glycogen stores, decreased gluconeogenesis, and increased sensitivity to insulin

- Hypothermia because of decreased subcutaneous fat and a large surface area to body-weight ratio

Because of these risks, clinicians will typically monitor the initial serum glucose concentrations and temperatures of a SGA infant.

SGA infants are also at risk for polycythemia because of chronic intrauterine hypoxemia. Finally, SGA infants may have hypocalcemia because of decreased amount of calcium acquired in utero.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Distinguish between small for gestational age (SGA) and intrauterine growth restriction (IUGR)
- Know that SGA fetuses are seen in women with chronic systemic illnesses
- Know that perinatal asphyxia is a frequent complication of IUGR
- Recognize that SGA infants have a higher neonatal mortality rate than appropriate-for-gestational-age infants
- Know that SGA infants are prone to fasting hypoglycemia, polycythemia, and temperature instability

SUGGESTED READINGS

Brodsky D, Christou H. Current concepts in intrauterine growth restriction. *J Intensive Care Med*. 2004;19:307–319.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 12 ANSWERS

1. B. Very low-birth-weight (VLBW) infant

Premature birth (infant born less than 37 weeks' gestation) accounts for ~12% of all births in the United States. Independent of gestational age, infants can be categorized by birth weight:

- LBW infant = infant <2,500 g at birth
- VLBW infant = infant <1,500 g at birth
- ELBW infant = infant <1,000 g at birth
- Micropremie = infant <750 g at birth

The infant in this vignette is characterized as a VLBW infant because the birth weight is less than 1,500 g.

2. B. Neurologic immaturity

Premature infants often cannot achieve an Apgar score greater than 6 because they are neurologically immature with a greater likelihood of hypotonia and poor reflex irritability soon after birth.

While term infants may have a low resting heart rate, this finding is uncommon in premature infants.

Premature infants, especially those born less than 34 weeks' gestation, often have respiratory distress and cyanosis in the delivery room as a result of surfactant deficiency. However, these symptoms are unlikely to result from persistence of the fetal circulation because a preterm infant's pulmonary vessel musculature is inadequately developed.

Both term and preterm infants may have poor perfusion soon after birth, but this finding will not alter an infant's Apgar score.

3. A. Anemia of prematurity

Anemia of prematurity is a common complication found in many premature infants. Numerous factors contribute to this finding in preterm infants, including:

- Exposure to a relatively postnatal hyperoxic environment that leads to a decrease in erythropoietin production
- Need for multiple blood draws
- Shorter life span of red blood cells

Preterm infants usually develop anemia of prematurity at ~1 to 2 months of age. This finding is not apparent soon after birth.

Preterm infants have decreased glycogen and fat stores, increasing their risk for hypoglycemia. Thus, soon after birth, a neonatal nurse will measure a preterm infant's serum glucose concentration and start a continuous intravenous glucose infusion. To maximize the infant's nutrition, this intravenous fluid often contains total parenteral nutrition.

Preterm infants are at increased risk for hypothermia because of a(n):

- Decreased skin thickness
- Low amount of subcutaneous fat
- Immature nervous system
- Increased surface area to body weight ratio

Thus, premature infants require external heat and frequent monitoring of their temperature.

Premature infants are at increased risk for surfactant deficiency. Thus, it is important to monitor a preterm infant's respiratory status, including arterial oxygen and carbon dioxide concentrations, soon after birth. An infant with a significant respiratory acidosis may require additional respiratory assistance, such as endotracheal intubation and surfactant administration.

4. B. Complete blood cell count and blood culture

The reason for a spontaneous preterm birth is often unknown. However, because chorioamnionitis is a common known cause of preterm labor, neonatal providers will usually evaluate a preterm infant for infection by obtaining a complete blood cell count and blood culture. Preterm infants with

hypoglycemia, hypothermia, or respiratory distress usually are treated with antibiotics because of the possibility of a bacterial infection.

Serum electrolytes, blood urea nitrogen, and serum creatinine concentrations are not usually tested soon after birth because the values at this early age of life reflect maternal concentrations. These test results reliably correspond to a newborn's values by 24 hours of age. Because extremely premature infants have an increased risk for excessive fluid losses, the neonatal team often tests the newborn's concentration of serum electrolytes within 6 hours of age and then follows the electrolyte trend every 4 to 12 hours.

If neonatal providers are concerned that an infant might have hepatic injury because of perinatal depression or an infection, they may measure the newborn's serum transaminase concentration soon after birth.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that premature infants often cannot achieve an Apgar score greater than 6 because they are neurologically immature (e.g., hypotonic, blunted response to noxious stimuli)
- Plan the initial care of a premature infant (e.g., monitoring of blood glucose, administration of a parenteral glucose solution, maintenance of a thermoneutral environment, and monitoring of arterial oxygen concentrations)
- Recognize that initial care of the premature infant includes evaluation for sepsis, if appropriate

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

SECTION II

Pulmonology

CASE 1

Ventilator management

A neonatology team was called to evaluate a full-term male infant with severe respiratory distress and cyanosis at a few minutes of age. The infant had been born by vaginal delivery after his mother presented in spontaneous labor. Labor was complicated by maternal fever.

Upon arrival, the pediatric resident initiates continuous positive airway pressure (CPAP) with 21% FIO_2 using a bag-mask. The infant's work of breathing decreases and the baby appears pink with a right-arm pulse oximetry reading of 94%. The infant's physical examination reveals decreased aeration bilaterally. The infant is then admitted to the Neonatal Intensive Care Unit for further care.

In the intensive care unit, the baby is placed on a cardiovascular monitor. The infant's vital signs are:

- HR = 160 beats per minute
- RR = 84 breaths per minute
- BP = 60/40 mm Hg
- T = 100.9°F (38.3°C)

The nurse sends a complete blood count, blood culture, and an arterial blood gas. She also places an IV and administers intravenous ampicillin and gentamicin.

1. Of the following (noted in the table below), the normal arterial blood gas results in a newborn in room air are:

Option	pH	$PaCO_2$ (mm Hg)	PaO_2 (mm Hg)
A	7.37	40	30
B	7.39	44	70
C	7.40	30	90
D	7.42	42	140

The infant's arterial blood gas results while receiving CPAP with a positive end-expiratory pressure (PEEP) of 5 cm H_2O and 21% FIO_2 are shown below:

pH = 7.17, $PaCO_2$ = 75 mm Hg, PaO_2 = 32 mm Hg, HCO_3 = 26 mEq/L, base excess = –1.3 mEq/L

2. Of the following, the most likely interpretation of this infant's arterial blood is a:

   A. Metabolic acidosis
   B. Metabolic alkalosis
   C. Respiratory acidosis
   D. Respiratory alkalosis

The infant's clinical examination worsens, and the infant has severe respiratory distress and decreasing oxygen saturations. Even though the team increases the FIO_2 to 100% and increases the PEEP to 7 cm H_2O, the infant remains cyanotic and has persistent respiratory distress. The infant is then intubated and placed on spontaneous intermittent mechanical ventilation with the following settings:

- Peak inspiratory pressure (PIP) of 26 cm H_2O
- PEEP = 6 cm H_2O
- Rate = 25 breaths per minute
- FIO_2 = 100%

A chest radiograph shows that the endotracheal tube is appropriately positioned and the lung fields reveal bilateral pneumonia. There is no evidence of a pneumothorax or pleural effusions. An echocardiograph reveals a structurally normal heart with normal function and a patent ductus arteriosus with left-to-right (aorta to pulmonary artery) shunting.

A repeat arterial blood gas is obtained and the results are:

pH = 7.08, $PaCO_2$ = 95 mm Hg, PaO_2 = 38 mm Hg, HCO_3 = 27 mEq/L, base excess = –1.8 mEq/L

The infant's complete blood count results are:

- White blood cell count = 3×10^3/μl (neutrophils 20%, bands 20%, lymphocytes 60%)
- Hemoglobin = 11g/dL (mmol/L)
- Hematocrit = 33% (0.33)
- Platelet count = 150×10^3/μl (150×10^9/L)

3. Of the following, the *most* effective next step to improve this infant's oxygenation is to:

   A. Increase the inspiratory time
   B. Increase the PEEP
   C. Increase the PIP
   D. Increase the rate

4. Of the following, the *most* effective next step to decrease this infant's carbon dioxide concentration is to:

   A. Decrease the flow
   B. Decrease the PIP
   C. Increase the PEEP
   D. Increase the rate

In the setting of respiratory failure, the team attempts multiple strategies to improve this infant's oxygenation, including:

- Ventilator change to a high-frequency oscillator
- Frequent endotracheal suctioning
- Packed red blood cell transfusion to increase the infant's oxygen-carrying capacity

- Sedation to prevent the infant from breathing against the ventilator
- Placement of an arterial line for frequent arterial gas monitoring

Because this infant has severe respiratory failure with persistent hypoxemia that has not responded to any medical interventions, the neonatal team consults the pediatric surgeon to place the infant on extracorporeal membrane oxygenation (ECMO).

5. Of the following, the type of ECMO that is most indicated in this infant is:

   A. Arterio-arterial (AA)
   B. Arteriovenous (AV)
   C. Venoarterial (VA)
   D. Veno-venous (VV)

The infant is placed on ECMO for 5 days, and with resolution of the pneumonia, the baby is able to be decannulated without difficulty. The infant is discharged home at 3 weeks of age with close neurologic follow-up.

CASE 2

Apnea

A male infant is born at 30 weeks' gestation. He initially has some respiratory distress, which requires treatment with continuous positive airway pressure (CPAP) for 12 hours. He starts nasogastric feedings at 24 hours of age and feedings are advanced slowly. At 48 hours of age, he has several episodes of periodic breathing.

1. Of the following, the description that best describes periodic breathing is a:

   A. Pause in breathing associated with an inward movement of both the rib cage and the abdomen during inspiration
   B. Pause in breathing for longer than 20 seconds
   C. Pause in breathing that is usually associated with either cyanosis or a decrease in heart rate
   D. Pause in breathing that is less than 20 seconds followed by several rapid shallow breaths

During the infant's third and fourth day of life, he has three apneic events over a period of 24 hours.

2. Match the type of breathing pattern with the corresponding physiology:

A. Central apnea	1. Absent nasal airflow and absent breathing efforts
B. Mixed apnea	2. Absent nasal airflow while breathing efforts continue
C. Obstructive apnea	3. Absent nasal airflow and absent breathing efforts followed by absent nasal airflow while breathing efforts continued
D. Respiratory distress	4. Nasal airflow with increased work of breathing

On the fifth day of life, he has five pauses in breathing, each lasting 15 seconds, and followed by cyanosis and bradycardia. These apneic events occur over a period of 1 hour. The neonatology fellow meets with the baby's mother to discuss possible causes for this infant's breathing pattern.

3. Of the following, the *least* likely etiology for this infant's apnea is:

   A. Anemia
   B. Infection
   C. Prematurity
   D. Reflux

After a complete evaluation and several interventions including caffeine therapy, the infant's apnea decreases to 1 to 4 episodes per day.

4. Of the following, the *least* likely mechanism of caffeine therapy is a(n):

   A. Decrease in hypoxia-associated breathing depression
   B. Decrease in minute ventilation
   C. Increase in diaphragmatic activity
   D. Improvement in CO_2 sensitivity

At 35 weeks' postmenstrual age, the caffeine therapy is discontinued. The infant continues to have 1 to 2 apneic episodes per day that are associated with mild desaturations. By 38 weeks' postmenstrual age, the apneic events resolve and the infant is discharged to home 1 week later when his feeding ability is mature.

CASE 3

Stridor

A nurse pages a pediatric resident to evaluate a 1-hour-old full-term infant who is making a loud breathing noise. The resident assesses the baby and finds the following:

- A high-pitched upper airway sound that occurs during inspiration and expiration
- An upper airway noise that worsens with crying and improves when the infant is prone
- No respiratory distress
- No difficulty with feeding

1. Of the following, the most likely diagnosis in this infant is:

   A. Choanal atresia
   B. Laryngomalacia
   C. Macroglossia
   D. Tracheomalacia

The resident consults an otolaryngologist to help determine the cause of this infant's breathing. The specialist discusses that the infant's clinical findings often correspond to the location of the obstruction. The otolaryngologist speaks with the infant's parents and is optimistic about their infant's long-term prognosis.

2. Match the type of stridor with the most likely location of the obstruction:

A. Biphasic stridor	1. Intrathoracic obstruction
B. Expiratory stridor	2. Laryngeal obstruction
C. Inspiratory stridor	3. Supraglottic obstruction

A few weeks later, the same pediatric resident is rotating in the Neonatal Intensive Care Unit. A neonatal intensive care nurse calls him to the bedside to evaluate an infant with respiratory distress. The nurse reports that the female infant had been born at 25 weeks' gestation. Her clinical course had been complicated by severe lung disease requiring prolonged intubation. The infant had self-extubated a few minutes prior to the resident's arrival. Upon examination, the resident notices that the infant has biphasic stridor and respiratory distress. The resident asks the nurse to page the neonatologist. The neonatologist then intubates the infant after the second attempt, and an otolaryngologist evaluates the infant.

3. Of the following, the most likely cause of this infant's stridor is:

   A. Bronchospasm
   B. Pulmonary edema
   C. Retropharyngeal abscess
   D. Subglottic stenosis

CASE 4

Surfactant deficiency

A pregnant woman presents at 32 weeks' gestation with premature rupture of membranes. The obstetrician orders tocolytics, antibiotics, and dexamethasone. Despite tocolytic therapy, the labor progresses and she delivers later that day. After birth, the infant has severe respiratory distress and cyanosis, requiring intubation. The neonatology fellow meets with the infant's parents to discuss the infant's expected clinical course.

1. Of the following, the typical clinical course found in most infants with surfactant deficiency is:

   A. Delayed respiratory symptoms in infants exposed prenatally to steroids
   B. Peak severity of illness usually occurs at 12 to 24 hours of age
   C. Recovery begins at ~72 hours of age
   D. Respiratory symptoms are initially observed at 2 to 4 hours of age

A respiratory therapist administers surfactant through the infant's endotracheal tube.

2. Of the following, the most likely effect of synthetic surfactant administration is to:

   A. Decrease alveolar surface tension
   B. Increase the pressure needed to keep alveoli open
   C. Maintain bronchiolar patency
   D. Preferentially improve the surface tension of collapsed alveoli

The infant's chest radiograph at 15 minutes of age is shown in Figure 1.

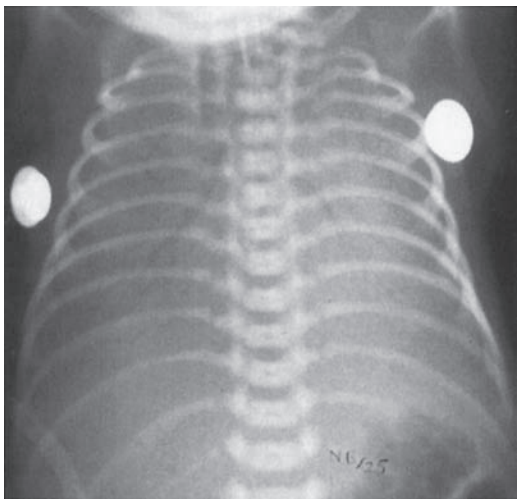

FIGURE 1. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005

3. Of the following, the radiographic finding that is most consistent with surfactant deficiency is (are):

   A. Air bronchograms
   B. Enlarged heart size
   C. Heterogeneous lung disease
   D. Hyperinflated lung fields

After surfactant therapy, the infant's ventilator support decreases significantly and the infant is extubated to continuous positive airway pressure (CPAP) at ~8 hours of age.

4. Of the following, the *least* likely strategy to decrease the severity of respiratory distress syndrome in preterm infants is:

   A. Antenatal steroid administration
   B. Avoidance of supplemental oxygen in the delivery room
   C. Early CPAP
   D. Tocolysis to delay preterm birth

CASE 5

Pulmonary air leaks

A pediatric resident is asked to evaluate a full-term infant who developed respiratory distress soon after birth. The resident examines the infant and finds the following:

- RR = 70, HR = 160s, BP = 60/46, T = 98.6°F (37°C)
- Oxygen saturation = 88% in room air
- Mild intercostal retractions
- Slightly decreased breath sounds on the left
- Slightly increased anterior–posterior diameter of the left chest

The resident suspects an air leak and brings the infant to the Neonatal Intensive Care Unit.

1. Of the following, the most likely diagnosis in this infant is:

   A. Bilateral pneumothoraces
   B. Left pneumothorax
   C. Pneumomediastinum
   D. Right pneumothorax

The infant has an oxygen saturation of 96% after being placed in an oxygen hood with 100% FIO_2. The neonatal nurse places an IV and starts D10W at 60 ml/kg/day. The resident is unable to identify an air leak by transillumination and orders a chest radiograph. While waiting for the results, the resident teaches the medical student about the radiographic findings found in infants with air leaks.

2. Match the chest radiograph (Figs. 1–4) with the corresponding diagnosis:

   A. Bilateral pneumothoraces
   B. Left pneumothorax
   C. Pneumomediastinum
   D. Right pneumothorax

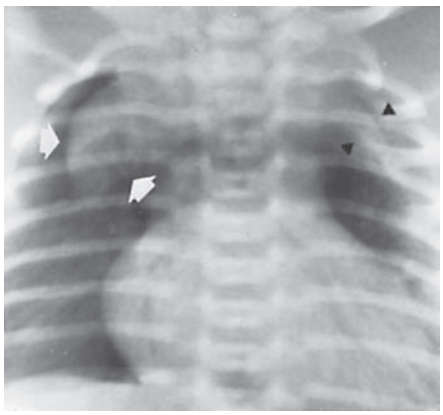

FIGURE 1. From Eisenberg L. Clinical Imaging: An Atlas of Differential Diagnosis. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 29.6A

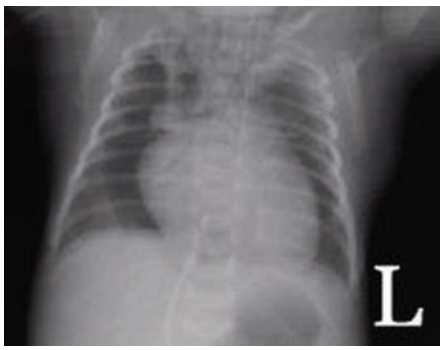

FIGURE 2. Courtesy of Brodsky D

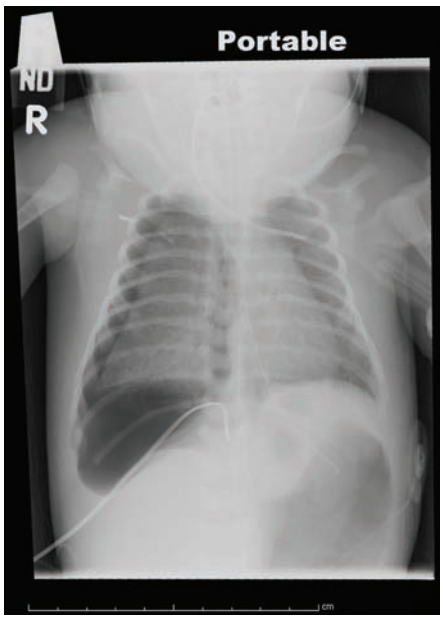

FIGURE 3. Courtesy of Dukhovny D

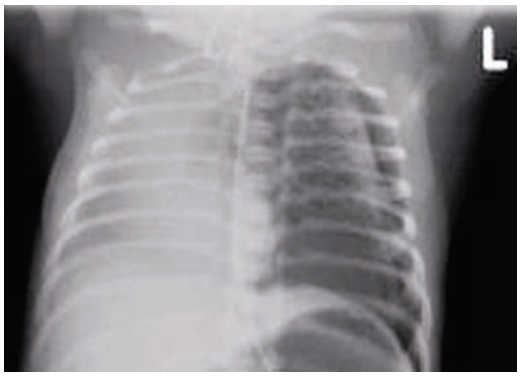

FIGURE 4. Courtesy of Brodsky D

The medical student asks the pediatric resident to review the possible causes of a pneumothorax in a newborn.

3. Of the following, the *least* likely cause of a pneumothorax in a newborn is:

   A. Esophageal atresia
   B. Excessive bag-mask ventilation
   C. Severe lung disease requiring high ventilator pressures
   D. Spontaneous occurrence

The infant's radiograph confirms that the infant has a small left pneumothorax. Because the infant has mild respiratory distress and a normal oxygen saturation in a 50% oxygen hood, the resident does not intervene. A few hours later, the neonatal nurse pages the resident because the infant has increased work of breathing. The infant's examination reveals the following:

- RR = 80, HR = 180s, BP = 40/32, T = 99°F (37.2°C)
- Oxygen saturation = 75% in 50% oxygen hood
- Severe respiratory distress
- Lack of breath sounds over the left lung
- Increased anterior–posterior diameter of the left chest
- Displaced point of maximal cardiac impulse to the right

4. Of the following, the preferred *next* step in the management of this infant is:

   A. Increase the F_{IO_2} to 100%
   B. Intubation
   C. Needle thoracentesis
   D. Normal saline bolus

CASE 6

Meconium aspiration syndrome

A neonatology team is called to the delivery of a full-term infant with thin meconium-stained amniotic fluid. The infant emerges without any respiratory effort, no activity, and a heart rate of 55.

1. Of the following, the most appropriate *next step* in the management of this infant is:

   A. Bag-mask ventilation
   B. Chest compressions
   C. Intratracheal suctioning
   D. Intubation and positive pressure ventilation

After initial resuscitation, the team observes that the infant has severe intercostal and subcostal retractions with decreased aeration and central cyanosis. The neonatology fellow intubates the infant and the team transports the baby to the Neonatal Intensive Care Unit. The infant is then placed on a synchronized intermittent mechanical ventilator with high settings. The infant's abdomen appears distended and the nurse places a nasogastric tube to remove air in the stomach. The infant's radiograph is shown in Figure 1.

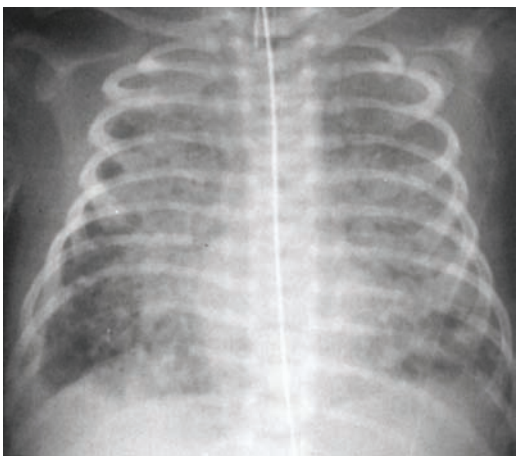

FIGURE 1. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 29.9

2. Of the following, the most likely diagnosis in this infant is:

   A. Meconium aspiration syndrome
   B. Pneumothorax
   C. Respiratory distress syndrome
   D. Retained fetal lung fluid

The neonatology fellow reviews the pathogenesis of this infant's disease with the pediatric resident.

3. Of the following, the pathophysiology that is *least* likely to be occurring in this infant is:

   A. Airway obstruction
   B. Chemical pneumonitis
   C. Pulmonary interstitial emphysema
   D. Surfactant dysfunction

CASE 7

Patchy lung fields

A male infant is delivered at 32 weeks' gestation after his mother develops a fever of 102°F (38.9°C) in the setting of ruptured membranes for 48 hours. The baby has respiratory distress soon after birth, evident by grunting, severe intercostal and subcostal retractions, and nasal flaring. His vital signs are:

- Heart rate = 130 beats per minute
- Respiratory rate = 70 breaths per minute
- Oxygen saturation (right arm, room air) = 80%
- Oxygen saturation (right arm, facial continuous positive airway pressure [CPAP] 40%) = 91%
- Blood pressure = 39/32 mm Hg

His initial arterial blood gas while on CPAP is: pH = 7.17, $Paco_2$ = 75 mm Hg, Pao_2 = 32 mm Hg, HCO_3 = 26 mEq/L, base excess = −1.3 mEq/L

His chest radiograph is shown in Figure 1.

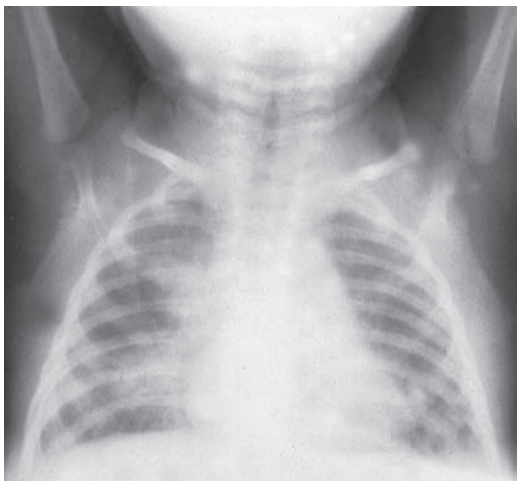

FIGURE 1. From Sweet RL, Gibbs RS. *Atlas of Infectious Diseases of the Female Genital Tract*. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 4.4

1. Of the following, the diagnosis that is most likely in this infant is:

   A. Congenital pneumonia
   B. Pneumothorax
   C. Surfactant deficiency
   D. Transient tachypnea of the newborn

The infant is then intubated and placed on synchronized intermittent mechanical ventilation. Additional laboratory data include the following:

- White blood cell count = $1.5 \times 10^3/\mu L$ ($1.5 \times 10^9/L$)
- Differential = 25% neutrophils, 25% bands, 50% lymphocytes
- Hemoglobin = 18.3 g/dL (11.3 mmol/L)
- Hematocrit = 55% (0.55)
- Platelet count = $90 \times 10^3/\mu L$ ($90 \times 10^9/L$)

2. Of the following, the pathophysiologic mechanism that can contribute to this infant's diagnosis is:

   A. Ascending vaginal flora
   B. Aspiration of contaminated amniotic fluid
   C. Transplacental acquisition
   D. All of the above

3. Of the following, the organism that is most likely responsible for this infant's illness is:

   A. *Chlamydia trachomatis*
   B. Flavobacteria
   C. *Listeria monocytogenes*
   D. Respiratory syncytial virus

CASE 8

Tachypnea

An obstetrician is closely monitoring a pregnant woman with insulin-dependent diabetes mellitus. At 40 weeks' gestation, a fetal ultrasound shows that the fetus is in a breech position and is macrosomic. The following day, the infant is delivered by cesarean. After birth, the baby is noted to have a bluish discoloration to the lips. The pediatric resident evaluates the infant and finds the following:

- Heart rate = 130 beats per minute
- Respiratory rate = 95 breaths per minute
- Oxygen saturation (right arm, room air) = 91%
- Oxygen saturation (right arm, 25% blow by oxygen) = 99%
- Blood pressure = 62/38 mm Hg

The infant's physical examination findings include the following:

- Active infant, appropriate during examination
- Slightly cyanotic lips in room air that become pink after 25% blow by oxygen is applied
- Rapid respiratory rate without retractions and no evidence of grunting or nasal flaring
- Symmetric breath sounds with good aeration
- Normal heart sounds without murmur, normal femoral pulses, and well-perfused
- Normal abdominal and neurologic examination

The infant's laboratory data include the following:

- Arterial blood gas (25% blow by oxygen): pH = 7.32, $Paco_2$ = 50 mm Hg, Pao_2 = 89 mm Hg, HCO_3 = 25 mEq/L
- Serum glucose = 65 mg/dL (3.6 mmol/L)

The baby's chest radiograph is shown in Figure 1:

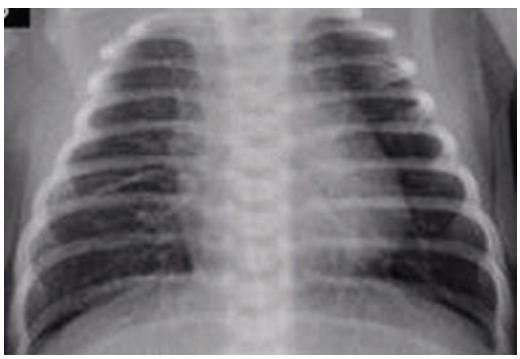

FIGURE 1. Courtesy of Brodsky D

1. Of the following, the most likely cause of this infant's tachypnea is:

   A. Cyanotic heart disease
   B. Metabolic acidosis
   C. Retained fetal lung fluid
   D. Surfactant deficiency

2. Of the following, the most appropriate next step in managing this infant is to:

   A. Administer a normal saline bolus and an intravenous $NaHCO_3$ bolus if repeated arterial pH is <7.35
   B. Avoid supplemental oxygen and start a prostaglandin infusion
   C. Initiate intravenous antibiotics
   D. Start maintenance intravenous fluid and provide supplemental oxygen

The pediatric resident meets with the family to discuss the infant's expected clinical course.

3. Of the following, the most likely clinical course for the infant in this vignette is:

   A. Decreased distal perfusion at 48 hours of age
   B. Increased severity of respiratory distress at 48 hours of age
   C. Resolution of tachypnea within 48 hours of age
   D. Worsening cyanosis at 48 hours of age

CASE 9

Cystic lung disease

A female infant born at 26 weeks' gestation had a complicated medical course. She received two doses of surfactant and initially required high ventilator settings on the high-frequency oscillator. She was able to transition to the conventional ventilator at 12 days of life and extubated at 3 weeks of age after a 7-day course of steroids. Her feeding advancement went slowly initially, but she was on full-volume enteral feedings by 3½ weeks of age. She was treated for 1 week with antibiotics for presumed chorioamnionitis. At 10 weeks of age, she required 1-L flow by nasal cannula with 30% FIO_2. Her most recent chest radiograph is shown in Figure 1.

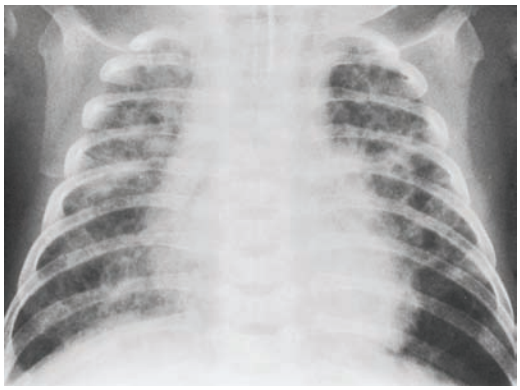

FIGURE 1. From Fleisher GR, Ludwig W, Baskin MN. *Atlas of Pediatric Emergency Medicine*. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. Figure 16.03

1. Of the following, the diagnosis that is most likely in this infant is:

   A. Bronchogenic cyst
   B. Bronchopulmonary dysplasia (BPD)
   C. Congenital cystic adenomatoid malformation (CCAM)
   D. Pulmonary interstitial emphysema (PIE)

At 42 weeks' postmenstrual age, the baby was able to take full oral feedings and was gaining weight on 24 calories per ounce. She was discharged home with supplemental oxygen and had follow-up arranged with several clinicians, including the pediatrician, a pediatric pulmonologist, Early Intervention, and the Infant Follow-up Clinic.

2. Of the following, the infant in this vignette is at increased risk of developing:

   A. Cor pulmonale
   B. Recurrent wheezing episodes
   C. Respiratory infections
   D. All of the above

Five months after discharge, the pediatrician is concerned because the infant's growth has been poor despite an increase to 26 calories per ounce. The family meets with a gastroenterologist to determine the approach to managing this infant's failure to thrive.

3. Of the following, the statement that the gastroenterologist is most likely to make to the family is:

   A. Failure to thrive is a rare complication in infants with BPD.
   B. Gastroesophageal reflux is unusual in infants with BPD.
   C. Infants with BPD are unlikely to develop an oral aversion.
   D. Poor growth in infants with BPD is often related to the infant's oxygenation status.

CASE 10

Tracheoesophageal abnormalities

A neonatology team is asked to attend a delivery of a term infant with a prenatal diagnosis of polyhydramnios of uncertain etiology. The infant emerges with good activity but has a large amount of oral secretions. A nasogastric tube is placed, and the radiograph is shown below (Figure 1). An abdominal radiograph reveals that air is located in the stomach and proximal intestines.

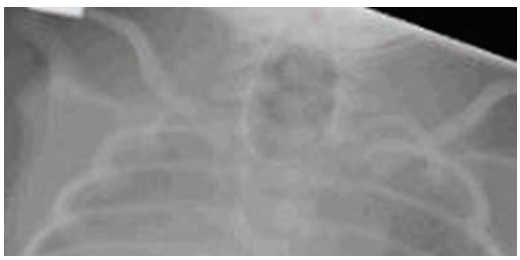

FIGURE 1. Courtesy of Brodsky D

1. Of the following, the type of tracheoesophageal abnormality that is most likely in this infant (Figure 2) is:

2. Of the following, the next best step in the management of this infant is to:

   A. Consult Interventional Radiology to place a nasogastric feeding tube into the infant's stomach
   B. Place a cuffed endotracheal tube in the infant's trachea and consult Pediatric Surgery
   C. Place a suction catheter into the esophageal blind pouch to remove secretions and consult Pediatric Surgery
   D. Start intravenous prostaglandin infusion and consult Pediatric Cardiology

The neonatologist meets with the family to discuss the management of TEF. The family has lots of questions about long-term outcome.

3. Of the following, the *least* likely complication after surgical repair of this infant's TEF is:

   A. Apneic episodes
   B. Dysphagia
   C. Esophageal stricture
   D. Leakage at point of anastomosis

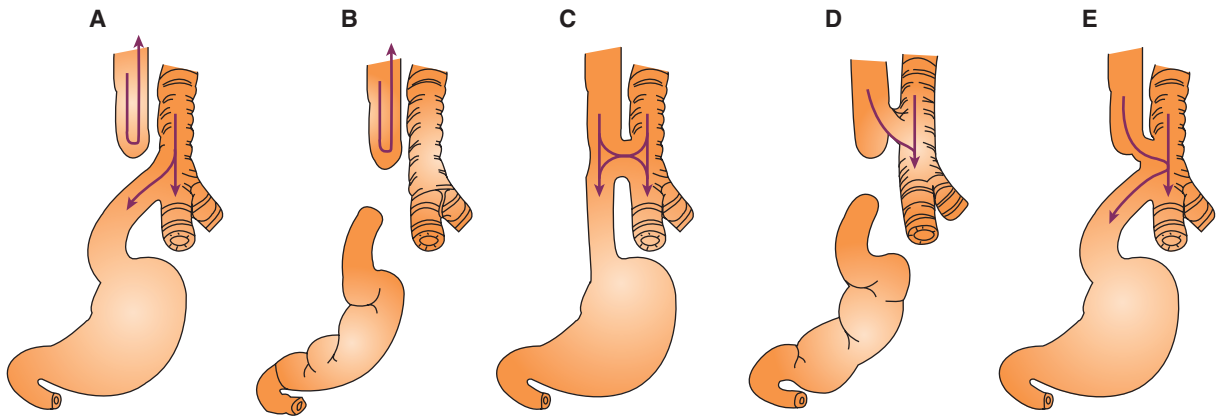

FIGURE 2. From Pillitteri, A. *Maternal and Child Nursing*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 39.05

CASE 11

Congenital malformations of the lung

A term male infant delivered by cesarean is noted to have mild to moderate respiratory distress at a few minutes of life. A pediatric resident transports the infant to the Neonatal Intensive Care Unit for further care. Initial evaluation shows that the infant has normal oxygen saturations in room air and the respiratory distress is improving. However, a chest radiograph does demonstrate an abnormality.

1. Match the diagnosis with the corresponding chest radiograph:

   A. Bronchogenic cyst
   B. Congenital cystic adenomatoid malformation (CCAM)
   C. Congenital diaphragmatic hernia (CDH)
   D. Pulmonary interstitial emphysema (PIE)

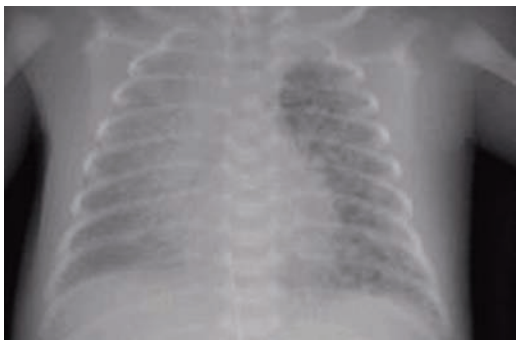

FIGURE 1. Courtesy of Brodsky D

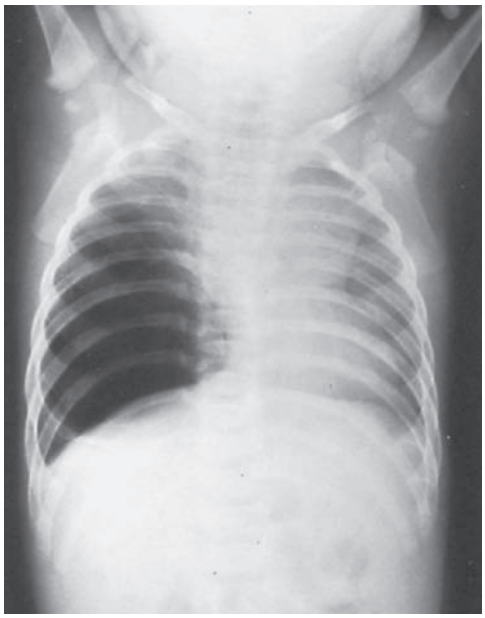

FIGURE 2. From Crapo JD, Glassroth J, Karlinsky JB, et al. *Baum's Textbook of Pulmonary Diseases*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. Figure 66.01A

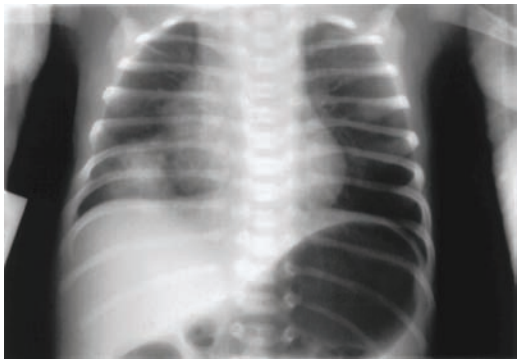

FIGURE 3. From Mulholland W, Maier V, et al. *Greenfield's Surgery: Scientific Principles and Practice*, 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. Figure 109.04

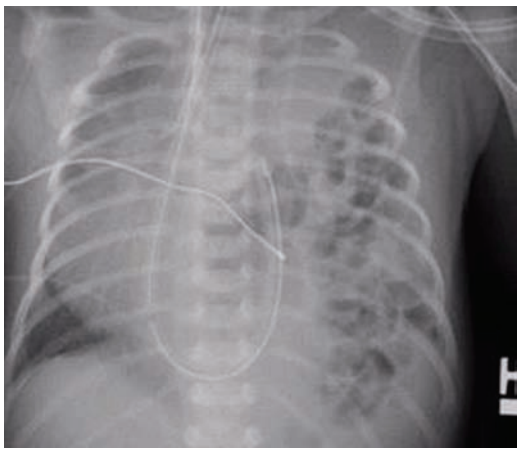

FIGURE 4. Courtesy of Dukhovny D

Upon further review of the infant's prenatal history, the pediatric resident learns that the infant had a prenatal diagnosis of a CCAM, which is found on the postnatal radiograph. Despite this prenatal diagnosis, the infant's respiratory distress resolves at 30 minutes of age.

2. Of the following, the most appropriate management of the infant in this vignette is:

   A. Administer antibiotics because of the high likelihood for intrapartum infection
   B. Intubate the infant in anticipation of worsening respiratory distress by 48 hours of age
   C. Nothing required because the mass will involute over time
   D. Reevaluate at 1 to 2 months of age with a computed tomography scan to evaluate the lesion in more detail

After the infant is discharged home, the same pediatric resident is called again to the delivery room to evaluate another term infant with respiratory distress. The pregnancy had been complicated by severe oligohydramnios at 20 weeks' gestation. The infant has severe retractions and appears cyanotic. The resident provides bag-mask ventilation and notes that the infant requires high peak inspiratory pressures and 100% FIO_2 to maintain a preductal oxygen saturation over 85%.

3. Of the following, a possible cause of this infant's respiratory distress is:

   A. Persistent pulmonary hypertension
   B. Pulmonary hypoplasia
   C. Septic shock
   D. All of the above

SECTION II

Answers

CASE 1 ANSWERS

1. B. pH = 7.39, $Paco_2$ = 44, Pao_2 = 70

The normal pH of a neonate ranges between ~7.35 and 7.43. Normal Pao_2 (i.e., arterial Po_2) values range between 60 and 90 mm Hg and $Paco_2$ (i.e., arterial Pco_2) values range between 35 and 45 mm Hg. Thus, the arterial blood gas with a pH = 7.39, $Paco_2$ = 44, and Pao_2 = 70 is normal for an infant.

An infant with an arterial Po_2 of 30, as shown in option A, has hypoxemia. Because an infant is unable to achieve a Pao_2 of 140 in room air, option D is not possible. However, if an infant receives supplemental oxygen, the Pao_2 can be greater than 150 if the baby does not have cardiac or respiratory disease. If an infant has an arterial Pco_2 that is too low, as in option C, this may lead to cerebral vasoconstriction.

2. C. Respiratory acidosis

The infant in this vignette has severe cyanosis and respiratory distress. An arterial blood gas is helpful to assess an infant's ventilation and oxygenation. If the pH is low (i.e., acidotic) and the $Paco_2$ is high, this is consistent with a respiratory acidosis and demonstrates that an infant is not ventilating effectively because of lung disease. This infant's blood gas is consistent with a respiratory acidosis.

In contrast, if the pH is high (i.e., alkalotic) and the $Paco_2$ is low, this is consistent with a respiratory alkalosis. A respiratory alkalosis is sometimes observed in infants with a urea cycle defect.

Metabolic acidosis is associated with a low pH and a low $Paco_2$. The infant's anion gap can be helpful to determine the cause of an infant's metabolic acidosis. The anion gap is calculated by the difference between cations and anions:

$$\text{Anion gap} = [Na^+] - ([Cl^-] + [HCO3^-])$$

A metabolic acidosis with an elevated anion gap is associated with shock, sepsis, renal failure, and metabolic disorders. A metabolic acidosis with a normal anion gap can result from renal tubular acidosis, diarrhea, and congenital adrenal hyperplasia.

A metabolic alkalosis is associated with an elevated pH and $Paco_2$. A metabolic alkalosis can be found in infants with emesis, diuretic use, and Bartter syndrome.

3. B. Increase the PEEP

Oxygenation is most dependent on mean airway pressure. The most effective way to increase mean airway pressure is by increasing the PEEP. However, as the PEEP increases, the tidal volume decreases and can compromise ventilation.

Increasing the PIP or increasing the inspiratory time will also increase mean airway pressures, but not as effectively. By increasing the flow or rate on a ventilator, a small increase in mean airway pressure may occur.

4. D. Increase the rate

There are several ventilator strategies to decrease an infant's $Paco_2$, including:

- Increase the rate
- Increase PIP (note: if the PEEP stays constant, an increase in PIP will increase tidal volume)
- Decrease PEEP (note: if the PIP stays constant, a decrease in PEEP will increase tidal volume)
- Increase flow
- Increase the expiratory time

However, each of these changes can lead to secondary consequences. For example, by increasing the ventilator rate, stacked breaths or inadvertent PEEP can occur, which may decrease tidal volume and increase $Paco_2$. An increase in PIP or flow can induce barotrauma. While an infant's tidal volume will increase with a decrease in PEEP, the mean airway pressure will also decrease, and this may lead to worsening hypoxemia. Similarly, an increase in expiratory time can decrease mean airway pressure and worsen an infant's oxygenation.

5. D. Veno-venous (VV)

Despite multiple strategies to treat the infant in this vignette, the infant remains hypoxemic. ECMO is an option for infants who fail maximal ventilator support with 100% Fio_2 and have an elevated alveolar–arterial O_2 gradient and a high oxygenation index. ECMO is contraindicated in the following infants:

- Premature infants (typically those infants who are <34 weeks' gestation)
- Irreversible lung disease
- Irreversible severe neurologic abnormalities
- Severe intraventricular hemorrhage
- Significant coagulopathy
- Congenital anomalies incompatible with a good long-term outcome

There are two types of ECMO: VV and VA. In VV ECMO, blood from an infant's vein is circulated outside of the infant, oxygenated, and returned back to the infant's venous circulation. In VA ECMO (see Figure 1), blood is similarly removed from an infant's vein and oxygenated outside of the body. However, blood is returned back to the infant's arterial circulation,

bypassing the infant's heart. VA ECMO is used when an infant's cardiac dysfunction is partly responsible for the infant's hypoxemia. Because the infant in this vignette has hypoxemia primarily resulting from a respiratory process, VV ECMO will be effective at oxygenating and ventilating this baby.

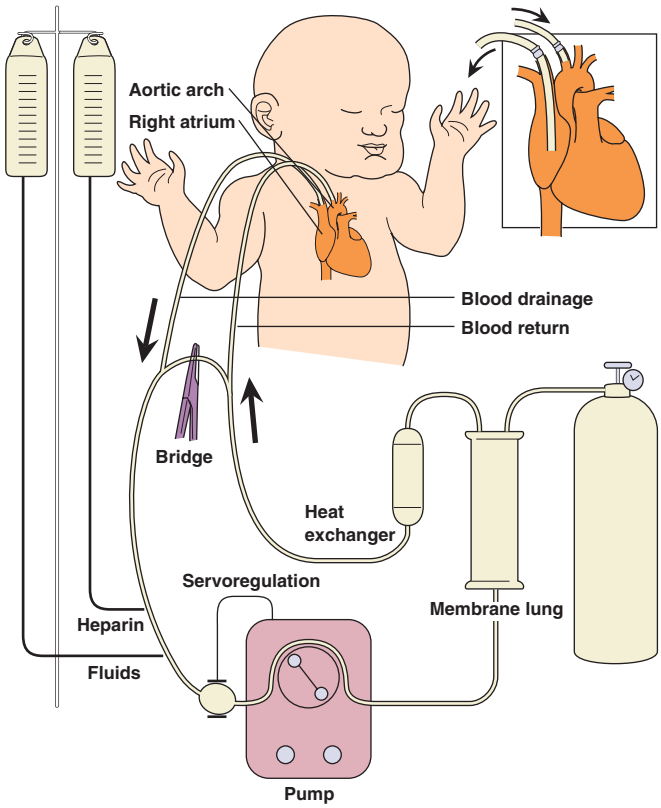

FIGURE 1. From Blackbourne LH. *Advanced Surgical Recall*. 2nd ed. Baltimore, MD: Lippincott Williams & Wilkins; 2004. Figure 64.2

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the normal arterial blood gas values for a newborn
- Review strategies to adjust mean airway pressure and improve oxygenation
- Review approach to ventilator if infant has elevated P_{CO_2}
- Recognize different modes of ventilation
- Plan the evaluation of a full-term infant who has severe respiratory failure at birth that does not respond to intubation and assisted ventilation

SUGGESTED READINGS

Aly H. Respiratory disorders in the newborn: Identification and diagnosis. *Peds Rev.* 2004. 25;201–208.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Goldsmith JP, Karotkin EH (eds). *Assisted Ventilation of the Neonate*. 5th ed. Philadelphia, PA; WB Saunders; 2010.

CASE 2 ANSWERS

1. D. Pause in breathing that is less than 20 seconds followed by several rapid shallow breaths

Infants with period breathing have pauses in breathing that are less than 20 seconds (typically a duration of 10–15 seconds) with interruptions of at least 3 seconds. Sometimes, an infant will have several rapid shallow breaths after a pause in breathing. Periodic breathing is not usually associated with cyanosis or a decrease in heart rate. This breathing pattern is a normal variation of breathing in infants.

Term, healthy infants can have paradoxical breathing, which describes the inward movement of the rib cage (i.e., collapse of chest wall) while the abdomen moves outward during inspiration. This typically happens during sleep.

2.

A. Central apnea	1. Absent nasal airflow and absent breathing efforts
B. Mixed apnea	3. Absent nasal airflow and absent breathing efforts followed by absent nasal airflow while breathing efforts continued
C. Obstructive apnea	2. Absent nasal airflow while breathing efforts continue
D. Respiratory distress	4. Nasal airflow with increased work of breathing

There are three types of apnea that can occur in premature infants:

- *Central apnea* is characterized by a complete absence of inspiratory efforts without any evidence of obstruction. In this type of apnea, an infant has absent nasal airflow and absent breathing efforts.
- *Obstructive apnea* is characterized by a breathing attempt against an obstructed upper airway (typically the pharynx or larynx). In this type of apnea, an infant has absent nasal airflow despite breathing efforts.
- *Mixed apnea* is characterized by central apnea followed by obstructive apnea. In this type of apnea, an infant has a period of absent nasal airflow and absent breathing efforts followed by absent nasal airflow despite breathing efforts. This is the most common type of apnea in premature infants.

Apnea of prematurity is defined as absence of breathing for more than 15 to 20 seconds, which is usually accompanied by an oxygen desaturation and/or bradycardia. Although periodic breathing is self-limited, an infant with apnea of prematurity may not be able to reinitiate ventilation.

3. D. Reflux

There are many possible causes of apnea in an infant, such as:

- Anemia
- Electrolyte disturbance, such as hypoglycemia
- Hypoxemia

- Infection, such as sepsis, meningitis, respiratory syncytial virus
- Intracranial process, such as an intraventricular hemorrhage
- Medications, such as sedatives, magnesium, prostaglandin E1
- Prematurity
- Seizures
- Spinal cord abnormalities

Although apnea and gastroesophageal refux often coexist in preterm infants, multiple studies have shown that these entities are not usually temporally related. When there is a relationship between the two, apnea typically comes before the reflux, perhaps because the loss of central respiratory drive is often accompanied by decreased lower esophageal tone.

4. B. Decrease in minute ventilation

Caffeine therapy decreases apnea in premature infants by many different mechanisms, including:

- Decreasing hypoxia-associated breathing depression
- Decreasing periodic breathing
- Enhancing diaphragmatic activity
- Improving CO_2 sensitivity
- Increasing minute ventilation

To start therapy, an infant first receives a loading dose of caffeine, which is followed by maintenance dosing. Caffeine can be administered by an oral or intravenous route. Caffeine has several advantages over theophylline therapy because it has a greater therapeutic index, decreasing the risk for toxicity. Caffeine also has a longer half-life than theophylline.

There are also some nonpharmacologic approaches to treat apnea of prematurity. Tactile stimulation of an infant with apnea may terminate a short episode of apnea. CPAP may help to splint the upper airway with positive pressure and decrease the obstructive component of the apnea. CPAP also may provide an added benefit by increasing an infant's functional residual capacity, which improves oxygenation and decreases hypoxia-associated breathing depression. For those infants with severe or extremely frequent apneic events, endotracheal intubation and ventilator assistance may be necessary. Finally, if an infant has apnea in the setting of anemia, a packed red blood cell transfusion may increase the infant's oxygen-carrying capacity and decrease hypoxia-induced respiratory depression.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Distinguish between apnea and periodic breathing
- Know the difference between central and obstructive apnea
- Know the differential diagnosis of central apnea in infancy
- Know the treatment of idiopathic recurrent apnea in premature infants
- Understand the association between apnea and anemia in premature infants

SUGGESTED READINGS

Baird TM, Martin RJ, Abu-Shaweesh JM. Clinical associations, treatment and outcome of apnea of prematurity. *NeoReviews*. 2002;3:e66–e70.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Martin RJ, Abu-Shaweesh JM, Baird TM. Pathophysiologic mechanisms underlying apnea of prematurity. *NeoReviews*. 2002;3:e59–e65.

CASE 3 ANSWERS

1. B. Laryngomalacia

The infant described in this vignette most likely has laryngomalacia, the most common cause of congenital stridor. Affected infants typically have inspiratory stridor that worsens with agitation and improves in the prone position. It is typically benign and self-limited. Conservative management is common, particularly when the infant does not have any associated respiratory distress or feeding difficulties. The table below compares the pathophysiology, clinical findings, diagnosis, management, and outcome of laryngomalacia and tracheomalacia.

	Tracheomalacia	Laryngomalacia
Pathophysiology	Cartilaginous rings supporting the trachea are soft and tend to collapse during expiration Can be associated with chronic ventilation	Collapse of epiglottis and/or arytenoids cartilages and/or larynx leading to prolapse into glottis during inspiration Unknown etiology
Clinical	Although most common cause of intrinsic congenital tracheal narrowing, it is rare Expiratory stridor	Most common cause of congenital stridor Coarse, inspiratory stridor that is worse with agitation and improved in prone position Can have expiratory component to stridor Typically benign, self-limited, male > female (2:1) Presents with stridor between birth and first month of life Majority without respiratory distress or feeding difficulties
Diagnosis	Bronchoscopy (anterior and posterior tracheal walls approximate during expiration)	Laryngoscopy

	Tracheomalacia	Laryngomalacia
Management	Consider CPAP If severe, may need tracheostomy	Conservative
Outcome	Majority with spontaneous resolution by 6–12 months of age	Spontaneous resolution by about 2 years of age Rare to require tracheostomy

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An infant with unilateral choanal atresia usually is asymptomatic unless the unaffected naris is obstructed with a suction catheter or a feeding tube. An infant with bilateral choanal atresia will have inspiratory stridor soon after birth that is associated with respiratory distress and cyanosis at rest. These symptoms often improve with crying because of air entry through the mouth.

Infants with macroglossia may have inspiratory stridor that is worse in the supine position because gravity moves the tongue posterior. Infants with macroglossia do not have an expiratory component to their stridor.

2. A. Biphasic stridor — 2. Laryngeal obstruction
B. Expiratory stridor — 1. Intrathoracic obstruction
C. Inspiratory stridor — 3. Supraglottic obstruction

The location of an infant's airway obstruction and associated type of stridor are summarized in the table below.

Type of Obstruction	Clinical Findings	Differential Diagnosis
Supraglottic obstruction (nose, nasopharynx, oropharynx, hypopharynx) This region *narrows during inspiration*	Inspiratory stridor Often less with crying Worse in supine position because gravity moves tongue posterior	Pierre Robin and Treacher Collins (both with micrognathia) Macroglossia (Beckwith–Wiedemann syndrome, hypothyroidism, glycogen storage diseases, trisomy 21) Choanal atresia Thyroglossal duct cyst (moves with swallowing due to attachment to base of tongue or hyoid bone)
Laryngeal obstruction (vocal cords, subglottis, extrathoracic trachea) This region is a *fixed* size during inspiration and expiration	Biphasic stridor Usually worse with agitation Because the larynx is the narrowest part of the neonate's airway, this type of stridor is most common	Laryngomalacia—most common congenital laryngeal anomaly Vocal cord paralysis—second most common laryngeal anomaly Congenital subglottic stenosis—often unable to handle secretions, recurrent pneumonias; if severe, tracheostomy and dilatations needed Laryngeal web, cyst
Intrathoracic obstruction (intrathoracic trachea and bronchi) This region *narrows during expiration*	Expiratory stridor Less common than laryngeal stridor but often more serious	Tracheomalacia Tracheal stenosis External compression (vascular rings, mediastinal mass)

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3. D. Subglottic stenosis

Subglottic stenosis is caused by a narrowing of the subglottic airway (below the vocal cords and above the trachea) that can be congenital or acquired. Acquired subglottic stenosis often occurs after a baby has had a long period of intubation. It is associated with biphasic stridor that worsens with agitation. The cause of this acquired stenosis is attributable to multiple factors, including:

- Endotracheal tube movement
- Gastroesophageal reflux
- Infection
- Multiple intubations
- Small cricoid region

The diagnosis of subglottic stenosis is confirmed by direct laryngoscopy under general anesthesia. In this procedure, tubes of increasing sizes are passed through the obstructed region to determine the precise size of the smaller portion of the airway. Possible treatment options include:

- Reintubation and continued observation with possible therapies such as antibiotics, antireflux medications, and steroids
- Tracheostomy
- Surgical treatment (including possible laser surgery, dilatation, anterior cricoid split)

Infants who require chronic ventilation are also at increased risk for tracheomalacia.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the differential diagnosis of congenital stridor
- Recognize subglottic stenosis as a complication of endotracheal intubation

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Daniel M, Cheng A. Neonatal stridor. *Int J Peds*. 2012; Article ID 859104, 5 pages, doi:10.1155/2012/859104.
Wei JL, Bond J. Management and prevention of endotracheal intubation injury in neonates. *Curr Opin Otolaryngol Head Neck Surg*. 2011; 19:474–477.

CASE 4 ANSWERS

1. C. Recovery begins at ~72 hours of age

Premature infants with surfactant deficiency can have respiratory distress syndrome, which is also known as hyaline membrane disease. Affected infants typically have respiratory distress soon after birth. The peak severity of illness usually occurs at 1 to 3 days of age. The recovery phase of this disease usually begins at ~3 days of age, coinciding with an increase in diuresis. Although prenatal exposure to steroids has been shown to decrease the risk and severity of illness, this antenatal therapy does not alter the timing of respiratory symptoms.

2. A. Decrease alveolar surface tension

There are various types of synthetic surfactant that can be administered through an endotracheal tube of an infant with respiratory distress syndrome. This exogenous surfactant is preferentially distributed to alveoli that have not yet collapsed. Once the compound reaches open alveoli, it can help to decrease the alveolar surface tension and decrease the pressure needed to keep those alveoli open. Exogenous surfactant does not have an impact on bronchiolar patency.

3. A. Air bronchograms

Radiographic findings in this disease include:

- Air bronchograms (visible because the air within the bronchi are outlined by the surrounding collapsed)
- Diffuse homogenous reticulogranular pattern, also known as a "ground-glass appearance" that corresponds with multiple collapsed alveoli
- Low lung volumes

All of these findings are evident in the chest radiograph of the infant in the vignette.

4. B. Avoidance of supplemental oxygen in the delivery room

There are multiple approaches to attempt to decrease the severity of hyaline membrane disease in preterm infants. Because the severity of surfactant deficiency correlates indirectly with gestational age, delaying preterm birth by tocolysis, when possible, is important. Prior to an infant's birth, antenatal steroid administration to the pregnant woman can help to decrease the severity of the disease. This effect is most evident when a woman delivers the baby 48 hours after she has received the first of two doses of steroids. Administering CPAP in the delivery room to premature infants with respiratory distress syndrome has been shown to decrease alveolar collapse and lessen the severity of the illness. If CPAP is administered to the infant after several hours of age, many alveoli lacking surfactant have had time to collapse, making CPAP less effective.

The use of supplemental oxygen to full-term infants in the delivery room has been shown to increase oxidative stress and increase mortality in full-term infants. Although oxygen administration has been shown to increase the preterm infant's risk for retinopathy of prematurity and chronic lung disease (i.e., bronchopulmonary dysplasia), it has not been shown to exacerbate respiratory distress syndrome.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the characteristic clinical and radiographic appearance of respiratory distress syndrome
- Understand the effects of surfactant administration in an infant with respiratory distress syndrome
- Know appropriate treatments for respiratory distress syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Warren JB, Anderson JM. Respiratory distress syndrome. *NeoReviews*. 2009;10:e351–e361.

CASE 5 ANSWERS

1. B. Left pneumothorax

Clinical findings in an infant with a pneumothorax include:

- Respiratory distress
- Cyanosis
- Affected side with decreased breath sounds
- Affected side with increased anterior–posterior diameter of the chest
- Acute decrease in blood pressure if pneumothorax under tension

An infant with bilateral pneumothoraces will have bilaterally decreased breath sounds and a symmetric anterior–posterior chest diameter. The symptoms of the infant described in this vignette are most consistent with a left pneumothorax that is not under tension. Only a minority of infants with a pneumomediastinum will have symptoms, which include tachypnea, distant heart sounds, and cyanosis.

2.	A. Bilateral pneumothoraces	2
	B. Left pneumothorax	4
	C. Pneumomediastinum	1
	D. Right pneumothorax	3

A chest radiograph is helpful to diagnose a pneumothorax by demonstrating a hyperlucent area without pulmonary parenchymal markings. If the anteroposterior radiographic view is not definitive, a lateral decubitus film with the suspected side of the pneumothorax positioned up will delineate the external air more clearly. Bilateral pneumothoraces are shown in the radiograph 2. In this anteroposterior chest radiograph, there is a large right-sided pneumothorax, a left-sided pneumothorax, and some mediastinal air extending into the neck region.

A pneumomediastinum is evident in the first radiograph. In this anteroposterior chest radiograph, the thymic lobes are elevated by mediastinal air (*white arrows* on the right side and *black arrowheads* on the left). This is often described as a "spinnaker sail sign" or "angel's wings sign."

A large right pneumothorax is evident on the third radiograph resulting in a collapsed right lung. The fourth chest radiograph is consistent with a moderate left pneumothorax, leading to a rightward shift of mediastinal structures. There is also a suggestion of pulmonary interstitial emphysema throughout the left upper and mid lung.

3. A. Esophageal atresia

A pneumothorax occurs when air enters the space between the parietal pleura that lines the chest wall and the visceral pleura that covers the lung. A pneumothorax occurs in the following situations:

- Excessive bag-mask ventilation
- Severe lung disease requiring high ventilator pressures
- Spontaneous occurrence
- Intubated infant with improving compliance
- Intubated infant with expiratory efforts that oppose the ventilator breaths

Infants with esophageal atresia can have various symptoms, depending on the communication with the trachea. Infants can present with excessive oral secretions, feeding intolerance, respiratory distress with feeding, and abdominal distention.

4. C. Needle thoracentesis

The left pneumothorax of the infant in this vignette has now increased in size. This is evident by the infant's symptoms of severe respiratory distress, hypotension, tachycardia, cyanosis, and a displaced point of maximal cardiac impulse to the right. These findings are consistent with a tension pneumothorax that requires emergent removal of air by a needle thoracentesis. If the leak is continuous after needle aspiration, placement of a chest tube may be necessary.

If an infant has minimal symptoms associated with a pneumothorax, conservative management is appropriate. This includes close observation for worsening symptoms.

Although this infant may ultimately need to be intubated, this is not the next best step in managing an infant with a tension pneumothorax because the pressures from the ventilator will increase the size of the pneumothorax. If an infant is already receiving ventilator-assisted breaths at the time of a pneumothorax, the pressures should be decreased.

The hypotension in the infant in this vignette is caused by the tension pneumothorax. Treatment with a normal saline bolus will not improve this infant's blood pressure. Instead, removal of the external air will improve the infant's blood pressure.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the characteristic clinical and radiographic appearance of a pneumothorax in a newborn
- Recognize that pulmonary air leaks are common in newborns who are treated with assisted ventilation

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Posner K, Needleman JP. Pneumothorax. *Peds Rev*. 2008;29:69–70.

CASE 6 ANSWERS

1. C. Intratracheal suctioning

The most recent Neonatal Resuscitation Program guidelines from 2012 recommend that an apneic, inactive infant born through meconium-stained amniotic fluid should undergo intratracheal suctioning immediately after delivery. This procedure is performed based on the newborn's degree of activity rather than the degree of thickness of the meconium-stained fluid. Meconium in an infant's trachea is then removed, preventing this meconium from being aspirated. It is uncertain if the amount of meconium in an infant's trachea is sufficient to cause meconium aspiration syndrome, and most studies have shown that the aspiration occurs prior to birth.

Bag-mask ventilation is indicated if the baby in the vignette remains apneic or bradycardic after the intratracheal intubation. Chest compressions are not indicated for initial bradycardia until effective ventilation with bag-mask ventilation has been established. If bag-mask ventilation is ineffective at improving the infant's respiratory or cardiovascular status, intubation to provide more effective positive pressure ventilation is indicated.

2. A. Meconium aspiration syndrome

Similar to the infant in this vignette, an infant with meconium aspiration syndrome typically presents soon after birth with

respiratory distress and cyanosis. This infant's chest radiograph shows the following:

- Coarse, diffuse infiltrates
- Hyperinflated lungs (the left and right diaphragms are located at ribs 10 and 11, respectively)
- Heterogenous lung disease
- Areas of overdistention as a result of air trapping from airway obstruction

These findings are consistent with meconium aspiration syndrome.

An infant with a pneumothorax will have a hyperlucent area in the lung region that does not have pulmonary parenchymal markings. Radiographic findings in an infant with respiratory distress syndrome include low lung volumes, diffuse reticulogranular pattern, and air bronchograms. An infant with retained fetal lung fluid (i.e., transient tachypnea of the newborn) has hyperinflated lung fields, fluid in the pleural effusion, perihilar linear densities, and, sometimes, pleural effusions evident on the chest radiograph.

3. C. *Pulmonary interstitial emphysema*

After experiencing intrauterine stress, a fetus may pass meconium. If the fetus becomes hypoxemic and has fetal gasping, the risk of intrauterine aspiration is increased. When meconium enters the infant's lung, it causes a(n):

- Acute airway obstruction
- Possible chemical pneumonitis
- Pulmonary vasoconstriction and pulmonary hypertension
- Surfactant dysfunction

Infants with severe chronic lung disease of prematurity (i.e., bronchopulmonary dysplasia) may have pulmonary interstitial emphysema; this complication is not typically found in infants with meconium aspiration syndrome. A general overview of the pathogenesis of meconium aspiration syndrome is outlined in Figure 2.

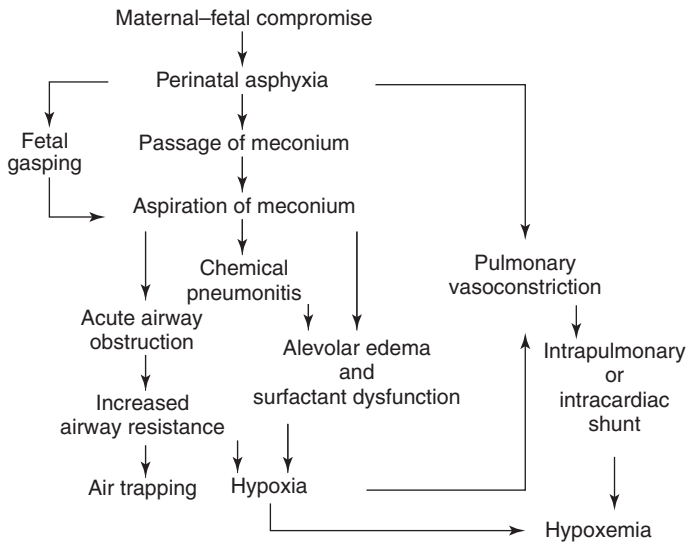


FIGURE 2. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 29.8

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the characteristic clinical and radiographic appearance of meconium aspiration syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Yeh TF. Meconium aspiration syndrome: Pathogenesis and current management. *NeoReviews*. 2010;11:e503–e512.

CASE 7 ANSWERS

1. A. *Congenital pneumonia*

The chest radiograph of the infant in this vignette is most consistent with pneumonia. Classic radiographic findings of congenital pneumonia include unilateral or bilaterally streaky densities, opacifications, a pleural effusion, and, sometimes, a granular appearance with air bronchograms. Because the radiographic findings of congenital pneumonia can mimic images of surfactant deficiency, it is often difficult to distinguish between these two diseases. Thus, premature infants with respiratory distress are often treated initially with antibiotics. The infant's clinical course and blood culture results will then help to determine the length of antibiotic treatment.

2. D. *All of the above*

The infant in this vignette has other findings consistent with pneumonia, including a low white blood cell count, an abnormal differential with increased immature white blood cells, and thrombocytopenia. Congenital pneumonia can be acquired by aspiration of contaminated amniotic fluid, ascending vaginal flora, or a transplacental route

3. C. *Listeria monocytogenes*

A newborn can acquire pneumonia in utero, intrapartum, or postnatally. Because this infant presented soon after birth, his pneumonia was most likely acquired during pregnancy or delivery. The specific organisms that are associated with intrauterine, intrapartum, and postnatal acquisition of pneumonia are summarized in the table below.

Acquisition Period	Associated Organisms
Intrauterine	Adenovirus, cytomegalovirus, herpes simplex virus, human immunodeficiency virus, rubella, mumps *Listeria monocytogenes* *Mycobacterium tuberculosis* *Toxoplasma gondii* *Treponema pallidum* *Varicella zoster*
Intrapartum	Group B *Streptococcus* *Escherichia coli*, *Klebsiella* sp *C. trachomatis* (clinical presentation typically at approximately age 3 weeks)

Acquisition Period	Associated Organisms
Postnatal	Adenovirus, respiratory syncytial virus Gram-positive bacteria (groups A, B, and G streptococci, *Staphylococcus*) Gram-negative enteric bacteria (*Klebsiella* sp, *Proteus* sp, *Pseudomonas aeruginosa*, flavobacteria, *Serratia marcescens*, *E. coli*)

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Differentiate between the normal results of a newborn's chest X-ray and the radiographic patterns that reflect pneumonia
- Recognize that neonatal pneumonia can mimic respiratory distress syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Flidel-Rimon O, Shinwell ES. Respiratory distress in the term and near-term infant. *NeoReviews*. 2005;6:e289–e297.

CASE 8 ANSWERS

1. C. Retained fetal lung fluid

The infant in this vignette is an infant of a diabetic mother who was born by cesarean and presents soon after birth with mild cyanosis that improves with a small amount of supplemental oxygen. The baby also has tachypnea without respiratory distress and is well-appearing with a normal blood pressure and normal perfusion. The chest radiograph demonstrates perihilar vascular densities, streaky opacities of interstitial edema, and fluid in the horizontal fissure of the right lung. The most likely cause of the infant's tachypnea is retained fetal lung fluid, also known as transient tachypnea of the newborn (TTN).

TTN is caused by a delay in fetal lung fluid reabsorption. Risk factors for developing TTN include:

- Cesarean birth without a period of labor
- Perinatal depression
- Maternal diabetes or asthma
- Anesthesia during labor

Affected infants present soon after birth with "comfortable tachypnea" (as high as 120 breaths per minute) without significant respiratory distress.

An infant with a metabolic acidosis can also have tachypnea without significant respiratory distress. Affected infants may have a gray or ashen color associated with poor perfusion and a low blood pressure because of decreased cardiac output. The infant in this vignette has an arterial blood gas that demonstrates an acute respiratory acidosis without a metabolic component (i.e., normal HCO_3).

In addition to TTN, a full-term infant born to a mother with insulin-dependent diabetes is also at increased risk for surfactant deficiency. Infants with surfactant deficiency typically have signs of respiratory distress and a chest radiograph that shows a reticulogranular pattern, air bronchograms, and decreased aeration. None of these findings were evident in this vignette.

Congenital heart disease is more likely to occur in an infant born to a mother with insulin-dependent diabetes. However, the infant in this vignette is unlikely to have cyanotic heart disease because the infant has a normal arterial Po_2 with a small amount of supplemental oxygen.

2. D. Start maintenance intravenous fluid and provide supplemental oxygen

Infants with TTN may need a small amount of oxygen supplementation to maintain a normal oxygen saturation; mechanical ventilation is rarely required. Because the infant in this vignette is breathing rapidly, most neonatologists would hold off on allowing the baby to feed and instead provide maintenance intravenous fluid.

For infants with a metabolic acidosis, treatment may include a normal saline bolus if the infant's cardiac output is decreased (evident by decreased distal pulses, poor perfusion, and a low blood pressure). Intravenous $NaHCO_3$ is indicated only if an infant has a significant metabolic acidosis with normal ventilation.

Supplemental oxygen is avoided in infants with a left-sided obstructive lesion (e.g., left hypoplastic heart syndrome, aortic stenosis, mitral stenosis) to prevent a decrease in pulmonary vascular resistance. By maintaining a high pulmonary vascular resistance, shunting across the patent ductus arteriosus can continue to be right-to-left (i.e., pulmonary artery to aorta) to provide systemic cardiac output. Infants with a left-sided cardiac obstruction will also require a prostaglandin infusion to maintain ductal patency.

Although antibiotics will not alter the clinical course of infants with TTN, they can be administered to treat a bacterial infection (e.g., pneumonia, sepsis, urinary tract infection).

3. C. Resolution of tachypnea within 48 hours of age

Infants with TTN typically have a normal respiratory rate within 1 to 5 days of life and usually by 48 hours of age. Infants may require oxygen and, in some cases, continuous positive airway pressure. It is unlikely that an infant with TTN will have decreased distal perfusion (as might occur with ductal closure in an infant with a ductal-dependent left-sided cardiac-obstructive lesion) or worsening cyanosis (as might occur with ductal closure in an infant with a ductal-dependent right-sided cardiac-obstructive lesion).

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Identify and manage transient tachypnea of the newborn

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Flidel-Rimon O, Shinwell ES. Respiratory distress in the term and near-term infant. *NeoReviews*. 2005;6:e289–e297.

CASE 9 ANSWERS

1. B. Bronchopulmonary dysplasia (BPD)

The infant described in this vignette has a postmenstrual age of 36 weeks' gestation. Her chest radiograph shows generalized overaeration, a heterogeneous pattern of lung disease, and multiple cystic regions bilaterally. These radiographic findings are consistent with BPD. BPD is caused by multiple factors that impact the prenatal (e.g., infection, intrauterine stress, glucocorticoid exposure) and postnatal (e.g., mechanical ventilation, glucocorticoid therapy, nutritional deficiencies, inflammation) development of the lung. An overview of the pathogenesis of BPD is shown in Figure 2.

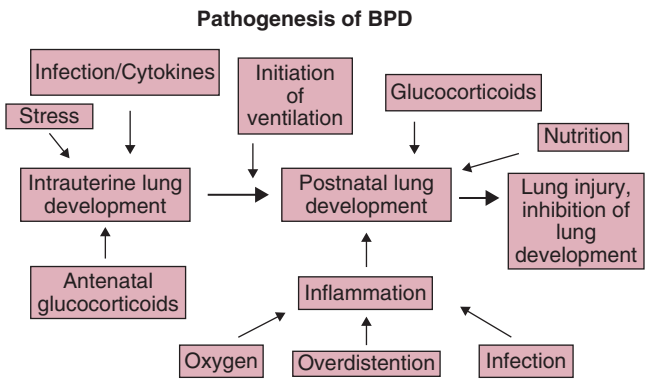


FIGURE 2. Adapted from Jobe AH. The new BPD: An arrest of lung development. *Pediatr Res*. 1999;46:641, with permission

Although most infants who develop BPD are born prematurely, this lung disease can develop in any newborn, regardless of gestational age, who has been treated with artificial ventilation and exposed to increased oxygen concentrations.

2. D. All of the above

Infants with severe BPD are prone to pulmonary artery hypertension that can lead to cor pulmonale (i.e., right heart failure). These outcomes result from both structural and functional changes of the infant's lung. Recurrent wheezing episodes are also common in children with BPD less than 2 years of age. Infants with BPD are also prone to respiratory infections, especially respiratory syncytial virus (RSV). Thus, infants with BPD receive a vaccination containing a monoclonal antibody against RSV during their first winter to decrease the risk of hospitalization if they acquire this virus.

3. D. Poor growth in infants with BPD is often related to the infant's oxygenation status

As exemplified by the infant in this vignette, failure to thrive is common in infants with BPD. Indeed, infants with BPD often require greater than 100% of the recommended dietary allowance of calories in order to grow. This is a result of increased energy expenditure associated with their respiratory disease. Poor growth in infants with BPD may be a sign of insufficient oxygenation.

Infants with BPD are also at greater risk of developing an oral aversion and of having gastroesophageal reflux that may worsen their respiratory status. In addition, affected infants are also at increased risk for neurodevelopmental disabilities.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that BPD can develop in a newborn, regardless of gestational age, who has been treated with artificial ventilation and an enriched oxygen concentration
- Recognize that infants with BPD may require home oxygen therapy
- Recognize that infants with BPD are prone to cor pulmonale, recurrent wheezing with infections, and severe respiratory infections
- Recognize that failure to thrive is common in infants with BPD
- Know that infants with BPD often require greater than 100% of the recommended dietary allowance of calories in order to grow
- Know that poor growth may be a sign of insufficient oxygenation in an infant with BPD
- Recognize that aversive oral motor behavior is associated with BPD
- Recognize that gastroesophageal reflux is a common association in infants with BPD and that it may aggravate their respiratory status

SUGGESTED READINGS

Adams JM, Stark AR. Outcome of infants with bronchopulmonary dysplasia. UpToDate. Accessed on March 1, 2013.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Jobe AH. The new BPD. *NeoReviews*. 2006;7:e531–e545.

CASE 10 ANSWERS

1. A. Esophageal atresia with a distal tracheoesophageal fistula (TEF)

The infant in this vignette presented with increased oral secretions and the neonatology team was unable to pass a nasogastric tube into the infant's stomach. This suggests that the infant has an esophageal atresia. This diagnosis explains the prenatal finding of polyhydramnios because of the fetus's inability to swallow amniotic fluid. Because air is noted in the infant's stomach and proximal intestines, a connection between the trachea and the distal esophagus must exist. Of the five types of tracheoesophageal abnormalities shown in the options, only

option A (esophageal atresia with a distal TEF) and option E (esophageal atresia with a distal and proximal TEF, a rare type of TEF) correlate with this infant's clinical findings. Because option A is more common, occurring in 86% of infants with a TEF, this is the infant's most likely diagnosis.

An infant with option B (esophageal atresia without a TEF, 5%–8%) or option D (esophageal atresia with proximal TEF, a rare type of TEF) will present with increased oral secretions but air will not be present in the stomach or intestines. Infants with an H-type TEF without esophageal fistula (option C, 2%–3%) may present later with recurrent pneumonias or difficulty with feedings. Infants with any of these types of tracheoesophageal abnormalities can also present with cyanosis, coughing or choking with feedings.

2. C. Place a suction catheter into the esophageal blind pouch to remove secretions and consult Pediatric Surgery

After an infant is diagnosed with a TEF, it is important to place a suction catheter into the esophageal blind pouch to continuously remove secretions. Following, the neonatology team should consult with a Pediatric Surgery.

The other options in this question are all incorrect. A nasogastric feeding tube cannot be placed in an infant with an esophageal atresia and distal TEF. Positive pressure ventilation should be avoided in the infant in this vignette because gastric distention will be excessive. Intravenous prostaglandin is indicated only if an infant with a TEF also has a ductal-dependent cardiac defect.

3. A. Apneic episodes

An infant with a TEF requires surgical repair to resect any fistula and anastomose any incongruent esophageal segments. After surgery, infants can have the following potential complications:

- Dysphagia because of impaired esophageal peristalsis
- Esophageal stricture as a result of acidic gastric fluid eroding the shortened esophagus
- Gastroesophageal reflux
- Leakage of esophageal contents at the point of anastomosis
- Recurrence of the fistula

Infants with a TEF may have respiratory complications (e.g., recurrent pneumonia, aspiration, poor coordination with feedings) as a result of reflux, tracheomalacia, recurrent fistula, and esophageal stricture.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the signs and symptoms of esophageal atresia with tracheoesophageal fistula
- Know how to evaluate an infant with a tracheoesophageal fistula
- Know that tracheoesophageal fistula may result in tracheomalacia

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Hansen TN, Cooper TR, Weisman LE. *Contemporary Diagnosis and Management of Neonatal Respiratory Diseases*. 2nd ed. Newtown, CT: Handbooks in Health Care; 1998.

Kovesi T, Rubin S. Long-term complications of congenital esophageal atresia and/or tracheoesophageal fistula. *Chest*. 2004;126;915–925.

CASE 11 ANSWERS

1.	A. Bronchogenic cyst	2
	B. Congenital cystic adenomatoid malformation (CCAM)	3
	C. Congenital diaphragmatic hernia (CDH)	4
	D. Pulmonary interstitial emphysema (PIE)	1

A bronchogenic cyst is evident in radiograph 2 because of a well-defined hyperaerated area within the right lower lobe. Radiograph 3 reveals a fluid-filled mass that appears as a density in the right hemithorax, which is consistent with a CCAM. A left-sided congenital diaphragmatic hernia is evident in radiograph 4 shown by intestinal contents within the left lung and a shift in the heart to the right side. Radiograph 1 demonstrates an infant with pulmonary interstitial emphysema in the left lung.

2. D. Reevaluate at 1 to 2 months of age with a computed tomography scan to evaluate the lesion in more detail

An infant with a prenatal diagnosis of a CCAM can have a variable outcome. If the mass is large, an infant may present with respiratory distress soon after birth. However, some lesions regress or disappear and, similar to the infant in this vignette, an affected infant may be asymptomatic after birth. Asymptomatic infants with a prenatal diagnosis of a CCAM should have a postnatal radiograph after birth and a computed tomography scan at 1 to 2 months of age to evaluate the lesion in more detail. Although ~20% of asymptomatic infants with radiographic evidence of a CCAM have complete regression of the abnormality, the remaining 80% have persistence of the lesions. Symptomatic infants will require surgical resection. Because of the concern that a persistent CCAM may lead to recurrent infections or pose a malignancy risk, most surgical centers resect the mass of asymptomatic infants as an elective procedure during childhood.

3. D. All of the above

A decrease in amniotic fluid volume (i.e., oligohydramnios) can be caused by renal agenesis, renal obstruction (associated with hydronephrosis), uteroplacental insufficiency, or a rupture of chorioamniotic membranes. Because maintenance of amniotic fluid is important for fetal lung growth, the fetus may develop pulmonary hypoplasia and extremity contractures if the oligohydramnios is prolonged and severe (see Figure 5). Infants with pulmonary hypoplasia often have persistent pulmonary hypertension because the pulmonary vasculature has

developed poorly. The infant in this vignette is also prone to septic shock from chorioamnionitis if the cause of the oligohydramnios results from rupture of membranes.

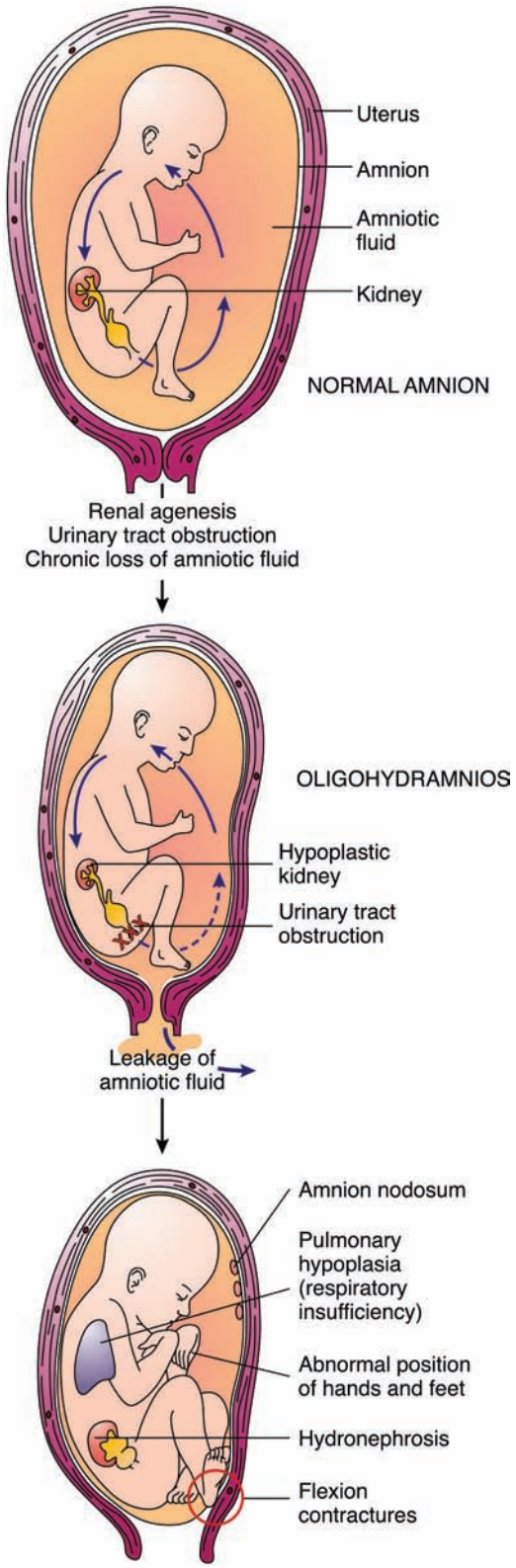


FIGURE 5. Image from Rubin E, Farber JL. *Pathology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999. Figure 6.04

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that congenital malformations of the lung (e.g., hypoplastic lung, cystic adenomatoid malformation) may cause respiratory signs and symptoms

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

DiPrima FA, Bellia A, Inclimona G, et al. Antenatally diagnosed congenital cystic adenomatoid malformations. *J Prenat Med*. 2012;6:22–30.

SECTION III

Cardiology

CASE 1

Congenital heart disease

A nurse in the Neonatal Intensive Care Unit (NICU) asks about the difference in the mean blood pressure of the infant born at 40 weeks' gestation she is caring for today compared to the 24-week-gestational-age infant she was caring for the day before. Although the gestational age-specific blood pressure that provides adequate organ perfusion is uncertain, you are aware that linear regression models for gestational age and blood pressure exist.

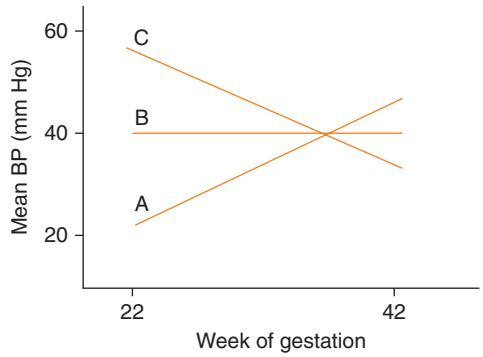


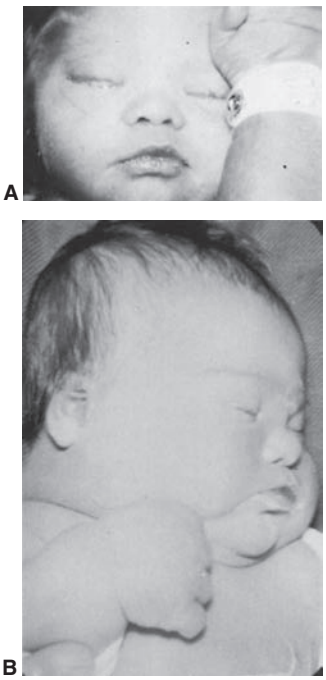
FIGURE 1.

1. Of the following, the line in the Figure 1 that best represents the correlation between mean blood pressure and gestational age is:

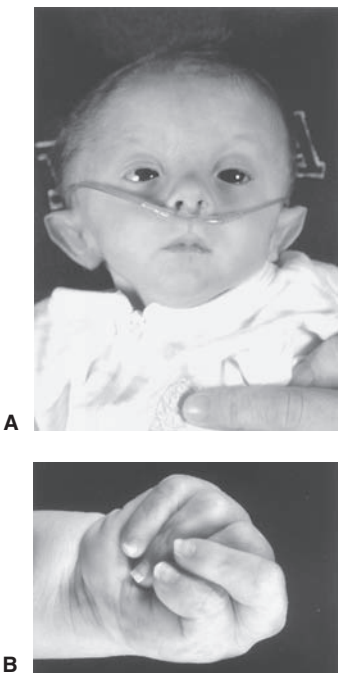
   A. Line A
   B. Line B
   C. Line C
   D. None of the above

The nurse then comments that the term infant has dysmorphic features and a murmur. You remember that some infants with dysmorphic features are at increased risk for congenital heart disease (CHD).

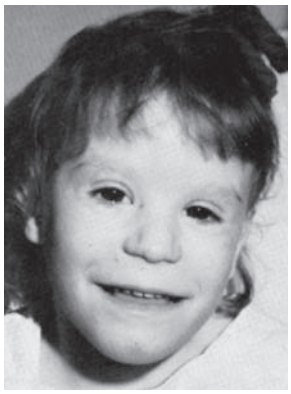
2. Match the following pictures of patients (Pictures A–E) with dysmorphic features to the appropriate CHD (listed as i–v):



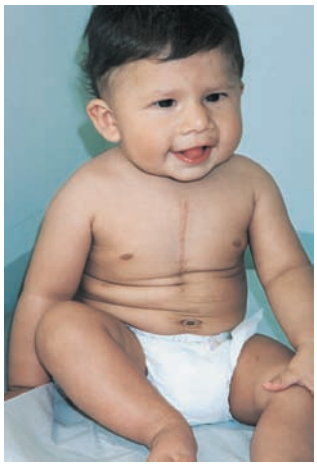
PICTURE A. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn.* 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 38.3AB



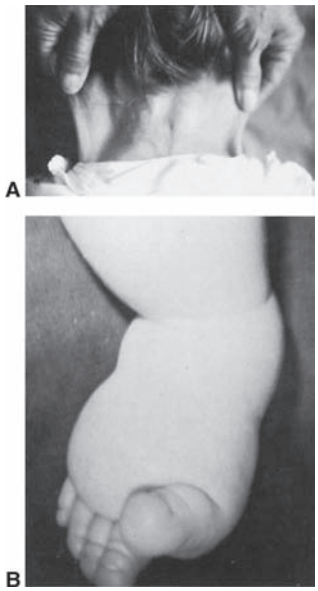
PICTURE B. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn.* 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 38.4AB



PICTURE C. From Sadler T. *Langman's Medical Embryology.* 9th ed. Image Bank. Baltimore, MD: Lippincott Williams & Wilkins; 2003. Figure 6.08B



PICTURE D. From Roberts R. *Atlas of Infectious Diseases.* Mandell G (series ed), Wilfert CM, eds. Philadelphia, PA: Current Medicine, Inc; 1998. Figure 21.2



PICTURE E. From MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn.* 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 38.6AB

A. _____	i. Atrioventricular canal
B. _____	ii. Coarctation of the aorta
C. _____	iii. Conotruncal defect
D. _____	iv. Atrial septal defect
E. _____	v. Ventricular septal defect

3. Match the syndrome with the corresponding increased risk for CHD:

A. CHARGE Association	i. 25%
B. Rubinstein-Taybi syndrome	ii. 45–50%
C. Trisomy 18	iii. 50–70%
D. Trisomy 21	iv. >90%

A. _____
B. _____
C. _____
D. _____

4. Of the following, the most appropriate evaluation of an infant with increased risk for CHD includes:

A. Physical examination, chest radiography, and electrocardiography
B. Pre- and postductal oxygen saturations and a hyperoxia test
C. Echocardiography
D. All of the above

CASE 2

Cyanosis

A full-term female infant in the well-baby nursery is noted to be cyanotic.

1. Which of the following statements about cyanosis in the newborn is true?

   A. Central cyanosis is evident in mucous membranes and is observed if there is >3 to 5 g of reduced hemoglobin per deciliter of capillary blood.
   B. Peripheral cyanosis (i.e., acrocyanosis) is a common finding in healthy full-term newborns.
   C. Peripheral cyanosis (i.e., acrocyanosis) is limited to the extremities.
   D. All of the above

The infant has cyanotic mucous membranes and a bluish-colored tongue but does not have any respiratory distress.

2. Select potential etiologies for this infant's central cyanosis:

   A. Idiopathic persistent pulmonary hypertension of the newborn (PPHN)
   B. Tetralogy of Fallot (TOF), pulmonary valve atresia, tricuspid atresia
   C. Surfactant deficiency
   D. A and B

The nurse places a pulse oximeter on the infant's right hand and the oxygen saturation is 60%. The infant's color does not improve after being placed in a 100%-oxygen hood.

3. Refer to the oxyhemoglobin dissociation curve below and select the most likely Pa_{O_2}:

   A. 15 mm Hg
   B. 30 mm Hg
   C. 50 mm Hg
   D. 70 mm Hg

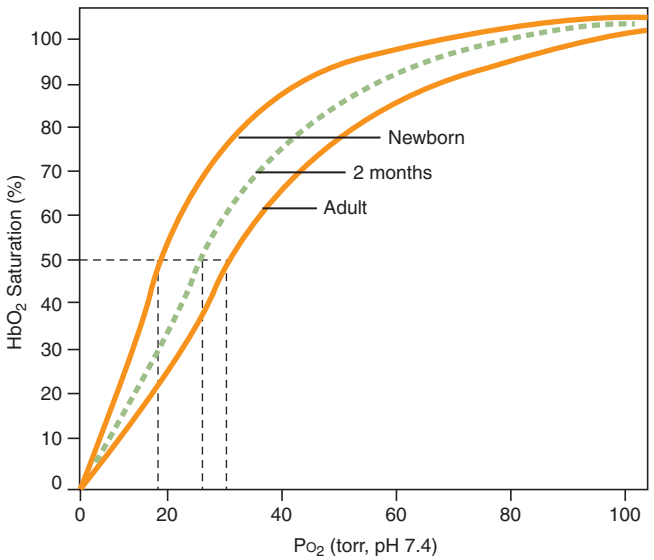


FIGURE 1. From Hodson WA, Truog WE. In: Avery GB, Fletcher MA, MacDonald MG, eds. *Neonatology: Pathophysiology and Management of the Newborn*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999, with permission

CASE 3

Cardiogenic shock

A 3-day-old full-term male infant, born via spontaneous vaginal delivery, was scheduled to go home when he is noted to be acutely cyanotic, tachypneic, and poorly perfused. His room air oxygen saturation (Sa_{O_2}) is 54% and his blood pressure is 40/28 (32).

1. Select the information you feel would be most helpful for your preliminary diagnosis:

   A. Complete blood count with differential and blood culture
   B. Electrolyte measurements and blood glucose concentration
   C. Family history
   D. Physical examination, four extremity blood pressures, pre- and postductal oxygen saturations, chest radiography, electrocardiography, and arterial blood gas

The infant's physical examination findings include central cyanosis, tachypnea, tachycardia, delayed capillary refill of 3 to 4 seconds, and cool extremities. Laboratory results and imaging for this infant reveal increased lung markings on the chest radiograph, arterial blood gas findings of metabolic acidosis and hypoxemia, pre- and postductal differential in oxygen content of 15 mm Hg, a complete blood count without a left shift, normal serum electrolytes, and a blood glucose of 62 mg/dL. The family history is not significant. Although you have ordered an electrocardiogram and echocardiography, the technician will not be available for one hour.

2. Select the initial therapeutic management for this infant:

   A. Administer bicarbonate bolus to correct the infant's metabolic acidosis
   B. Consider intubation and mechanical ventilation
   C. Consult with a cardiologist and start prostaglandin E_1 (PGE_1)
   D. All of the above

3. Because the infant in this vignette had of symptoms of cardiogenic shock on day 3 of life, the infant's most likely heart lesion is:

   A. Hypoplastic left heart syndrome (HLHS)
   B. Pulmonary valve stenosis
   C. Tetralogy of Fallot (TOF)
   D. Tricuspid atresia

CASE 4

Non-cardiogenic shock

A 25-year-old pregnant woman at 37 weeks' gestation presents to the labor and delivery floor with copious vaginal bleeding. Her pregnancy has been uncomplicated. The male infant is born via stat cesarean under general anesthesia. He emerges floppy with marked pallor, perioral cyanosis, and no pulse or respiratory rate.

1. With the limited data above, select the best choice for the infant's preliminary diagnosis:

   A. ABO blood type incompatibility
   B. Hypovolemic shock as a result of a placental abruption and blood loss
   C. Reaction to maternal general anesthesia
   D. Sepsis

The resuscitation team acts swiftly, following the Neonatal Resuscitation Program guidelines. The team intubates the infant, places an umbilical venous catheter (UVC), and administers two doses of intravenous epinephrine. The infant's heart rate (HR) is now 100.

2. From the choices below, select the next most appropriate therapy for this infant:

   A. Antibiotics
   B. Emergency administration of O-negative blood
   C. Normal saline (NS) bolus until O-negative blood arrives
   D. B and C

The infant's HR is now 170 beats per minute with a BP mean of 32 mm Hg. He remains extremely pale with cool extremities. His birth hematocrit is 21%. He has received a total of 20 ml/kg of NS and 10 ml/kg of O-negative blood.

3. From the choices below, select the next most appropriate therapy for this infant:

   A. Additional 10 ml/kg of NS
   B. Another 10 ml/kg of O-negative blood
   C. Intravenous 2 ml/kg bolus of glucose
   D. Intravenous 1 mEq/kg bolus of bicarbonate

CASE 5

Cyanotic heart disease: Diagnosis and management

A male infant was born via spontaneous vaginal delivery at 39 3/7 weeks' gestation to a 24-year-old G2 P0 woman with reassuring prenatal screens, including negative Group B *Streptococcus* status. The membranes had spontaneously ruptured 4 hours prior to delivery and the mother did not have a fever. The infant's Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The infant stayed with his mother and attempted breastfeeding. During the second breastfeeding attempt at 4 hours of age, the nurse noted that he had tachypnea and cyanosis.

1. Of the following, the preferred initial assessment to determine whether this infant's cyanosis results from a respiratory or cardiac cause is:

   A. Complete blood count, blood culture, and arterial blood gas (ABG)
   B. Echocardiography
   C. Family history
   D. Physical examination, chest radiograph, electrocardiogram, hyperoxia test

This infant's hyperoxia test results were consistent with cyanotic heart disease.

2. Of the following, the technique that best describes the hyperoxia test is:

   A. Assessment of the amount of supplemental oxygen required to obtain an oxygen saturation ≥95%
   B. Measurement of the infant's arterial Pa_{O_2} in room air
   C. Measurement of the infant's arterial Pa_{O_2} while receiving 50% F_{IO_2}
   D. Comparison of the infant's arterial Pa_{O_2} in room air with the infant's Pa_{O_2} while receiving 100% F_{IO_2}

3. Of the following, the congenital cardiac lesions that present with cyanosis are:

   A. Atrial septal defect (ASD), ventricular septal defect (VSD), aortic stenosis (AS), coarctation of the aorta
   B. Critical pulmonary stenosis (PS), truncus arteriosus, pulmonary atresia (PA) with intact ventricular septum, Ebstein anomaly, total anomalous pulmonary venous return (TAPVR) with obstruction
   C. Hypoplastic left heart syndrome (HLHS), transposition of the great arteries (TGA), tricuspid atresia, TOF with PA, TAPVR without obstruction, single ventricle
   D. B and C

4. Of the following, the congenital cardiac lesions associated with decreased pulmonary blood flow are:

   A. ASD, VSD, AS, coarctation of the aorta, atrioventricular canal (AVC) without PS
   B. Critical PS, tricuspid atresia, PA, TOF, Ebstein anomaly, TAPVR with obstruction
   C. HLHS, TGA, truncus arteriosus, TOF with PA, TAPVR without obstruction, single ventricle
   D. B and C

The infant's examination was notable for severe cyanosis, nondysmorphic features, and absence of murmur. He had a preductal oxygen saturation (right arm) that was 20% *lower* than his postductal oxygen saturation (leg). The infant's chest radiograph is shown in Figure 1. His electrocardiogram had a normal QRS axis. Echocardiography revealed a cyanotic heart defect.

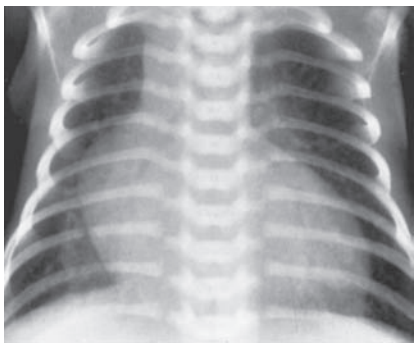


FIGURE 1. Eisenberg L. *An Atlas of Differential Diagnosis.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 10.2

5. Of the following, the most appropriate next step(s) in the management of this infant is (are):

   A. Consult the cardiology service
   B. Educate parents about the lesion and discuss that a Rashkind procedure may be needed to increase the size of the foramen ovale
   C. Initiate an intravenous prostaglandin (PGE_1) infusion to maintain patency of the ductus arteriosus
   D. All of the above

6. Of the following, the possible side effects of an intravenous PGE1 infusion is (are):

   A. Apnea
   B. Flushing
   C. Hypotension
   D. All of the above

CASE 6

Cyanotic heart disease: Outcomes

A full-term female infant was discharged to home on day 3 of life. Her course was unremarkable until 3 weeks of age when her mother noted that she was tiring with feedings and becoming tachypneic. Her mother also noted that when the baby awakened from sleep, her lips and face turned blue while crying. The mother brought the infant to the emergency room (ER) where her room air oxygen saturations with crying are found to be 70%. Her electrocardiogram shows right ventricular hypertrophy (RVH), and her chest radiograph is described as a "boot-shaped" heart with a right aortic arch.

1. Of the following, the diagnosis that most likely explains this infant's desaturation events while crying is:

   A. Foreign body aspiration
   B. Pneumonia
   C. Pulmonary edema
   D. "Tet" spell

The infant had a complete surgical repair and her symptoms resolved. She does not have an underlying genetic abnormality or any confounding risk factors.

2. From the choices below, select the statement that best reflects her prognosis:

   A. Good long-term survival and excellent quality life
   B. Progressive RVH and heart failure
   C. Unlikely to survive beyond age 30
   D. A and B

The infant is followed regularly in a cardiology clinic that monitors patients with cyanotic congenital heart disease (CHD).

3. From the choices below, select the statement that reflects the prognosis for cognitive development for patients seen in the cyanotic CHD clinic:

   A. Improved neurodevelopmental outcome as a result of environmental factors (e.g., early intervention programs and school programs, including tutoring, special education, and speech therapy)
   B. Increased risk for neurodevelopmental delay because of biologic risk factors (e.g., underlying genetic syndromes or developmental disorders)
   C. Potential for behavioral abnormalities with impaired social interaction, inattention, and impulsive behavior
   D. All of the above

CASE 7

Differential cyanosis

A 5-hour-old male infant born at 41 weeks' gestation via spontaneous vaginal delivery is noted to be cyanotic with retractions. He is brought to the Special Care Nursery, where his oxygen saturations are 80% in room air. His preductal oxygen saturations are ~10% higher than his postductal oxygen saturations.

1. Of the following, the diagnosis that is most likely in the infant in this vignette is:

   A. Cyanotic congenital heart disease (CHD)
   B. Persistent pulmonary hypertension
   C. Surfactant deficiency
   D. A or B

The rest of his history reveals that he was born through thick particulate meconium-stained amniotic fluid. His first chest radiograph after intubation is shown in Figure 1.

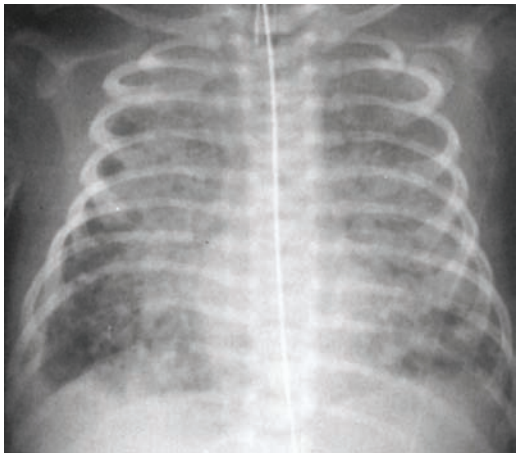


FIGURE 1. MacDonald G, Seshia MK, et al. *Avery's Neonatology: Pathophysiology & Management of the Newborn.* 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 29.9

He has a mixed acidosis on his arterial blood gas. Echocardiography shows pulmonary pressures greater than systemic pressures, evident by moderate tricuspid regurgitation, bowing of the ventricular septum into the left ventricle, and right-to-left (pulmonary artery to aorta) shunting across the patent ductus arteriosus.

2. Of the following, the most effective therapy to increase this infant's pulmonary blood flow is:

   A. Antibiotics
   B. Inhaled nitric oxide
   C. Thirty percent oxygen
   D. All of the above

CASE 8

Arrhythmias

A 37-year-old G4P0 pregnant woman presents for her regularly scheduled prenatal appointment at 28 weeks' gestation. Her obstetrician notes an intermittent fetal arrhythmia. She undergoes fetal echocardiography with Doppler imaging and, at a follow-up visit, also has fetal magnetocardiography to observe the fetal cardiogram signals. The woman's sister has lupus, and her sister's most recent pregnancy had been complicated by a fetal arrhythmia. This patient does not have lupus but has many questions about fetal arrhythmias.

1. Of the following, the most accurate statement about fetal arrhythmias is:

   A. About 1 to 2% of fetuses have fetal arrhythmias; of those, 10% have associated morbidity.
   B. Fetal supraventricular tachycardia (SVT) represents 70% to 80% of fetal tachyarrythmias.
   C. Lupus is associated with fetal or neonatal complete heart block.
   D. All of the above

The result of the fetal testing shows that the fetal arrhythmia is most consistent with intermittent SVT.

2. Match the EKG with the corresponding arrhythmia.

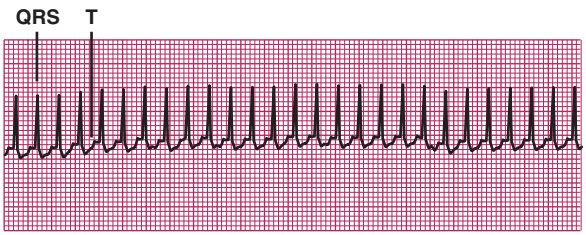
1. 

FIGURE 1. From Bickley LS, Szilagyi P. *Bates' Guide to Physical Examination and History-Taking*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 17.5

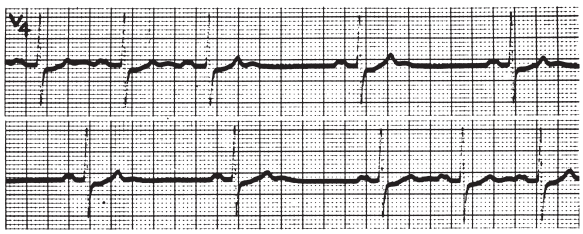
2. 

FIGURE 2. From Harwood-Nuss A, Wolfson AB, et al. *The Clinical Practice of Emergency Medicine*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001. Figure 134.4

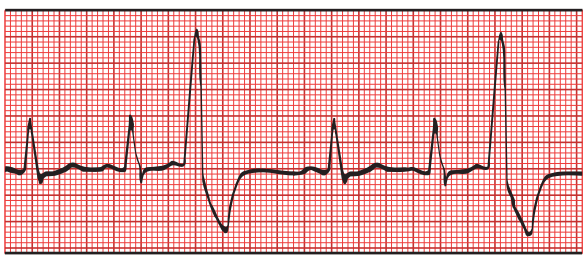
3. 

FIGURE 3. From LifeART © 2014 Lippincott Williams & Wilkins. All rights reserved

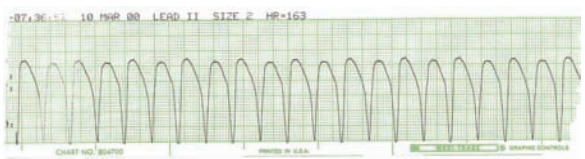
4. 

FIGURE 4. From AACN Clinical Simulations: Hemodynamic Monitoring. [CD-ROM]. Philadelphia, PA. Lippincott Williams & Wilkins, 2001.

A. Premature atrial contractions (PACs) ____
B. Premature ventricular contractions (PVCs) ____
C. Supraventricular ventricular tachycardia (SVT) ____
D. Ventricular tachycardia (VT) ____

During the rest of the pregnancy, the fetus remains healthy. The fetal arrhythmia is not sustained, and intrauterine interventions are not required. The baby is born at term and appears healthy. He is hemodynamically stable but continues to have SVT after delivery and needs treatment.

3. Select the first-line treatment for intrauterine treatment and the first-line treatment for postnatal treatment, respectively:

A. Adenosine, adenosine
B. Digoxin, vagal maneuvers
C. Sotalol, vagal maneuvers
D. Verapamil, adenosine

SECTION III

Answers

CASE 1 ANSWERS

1. A. Line A

Line A shows that an infant's mean blood pressure value increases with increasing gestational age. An infant's mean arterial blood pressure (MAP) can be calculated by the following formula:

$$MAP = ([2 \times \text{diastolic pressure}] + \text{systolic pressure})/3$$

In general, the normal mean arterial pressure in preterm infants and newborns can be calculated by taking the infant's gestational age (in weeks) and adding 2–5.

$$\text{Normal MAP} = \text{gestational age (weeks)} + 2\text{–}5$$

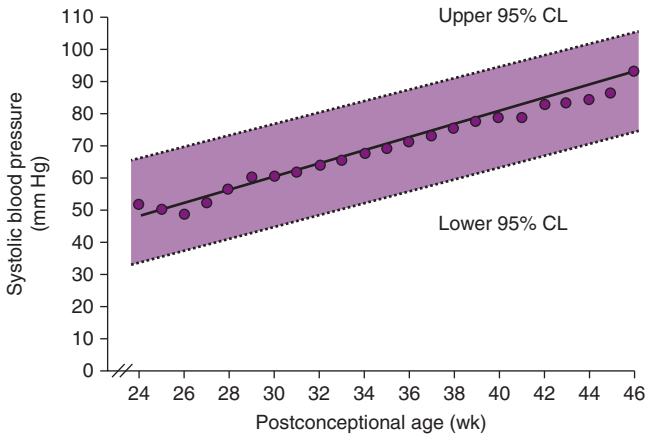


FIGURE 2. Linear regression of mean systolic blood pressure on postconceptional age (gestational age in weeks plus weeks after delivery). Data from Zubrow AB, Hulman S, Kushner H, et al. Determinants of blood pressure in infants admitted to Neonatal Intensive Care Units: A prospective multicenter study. Philadelphia Neonatal Blood Pressure Study Group. *J Perinatol*. 1995;15:470–479

2. A. i.
B. v.
C. iv.
D. iii.
E. ii.

Picture A represents an infant with facial stigmata of trisomy 21.

Picture B is of an infant with trisomy 18, also known as Edwards syndrome. This infant has a small head, micrognathia, and clenched fists.

Picture C represents a child with fetal alcohol syndrome with narrow, small eyes, and a smooth philtrum.

Picture D is a postoperative picture of an infant with 22q11 microdeletion, also known as DiGeorge syndrome. This infant has misshapen ears, a prominent nose, and micrognathia.

Picture E shows some findings in a patient with 45,XO or Turner syndrome, including pedal edema and a webbed neck.

3. A. CHARGE Association — iii. 50–70%
B. Rubinstein-Taybi syndrome — i. 25%
C. Trisomy 18 — iv. 90%
D. Trisomy 21 — ii. 45–50%

4. D. All of the above

The appropriate evaluation of an infant with increased risk for CHD includes a physical examination to evaluate the following:

- Dysmorphic features
- Presence or absence of murmur
- Quality of femoral pulses
- Presence or absence hepatomegaly
- Degree of capillary refill

In addition, the evaluation should include a(n):

- Chest radiography
- Electrocardiography
- Pre- and postductal oxygen saturations
- Hyperoxia test

When possible, an echocardiography is important to confirm the diagnosis and delineate the complete structure of the heart. For critically ill infants or those with severe cyanosis, echocardiography may need to be obtained emergently.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that blood pressure values vary directly with gestational age
- Recognize the increased risk and plan appropriate evaluation of congenital heart disease in a newborn with congenital anomalies (e.g., trisomy 21, trisomy 18, fetal alcohol syndrome, 22q11 microdeletion, 45,×0)

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Tschudy M, Arcara K; Johns Hopkins Hospital, Children's Medical and Surgical Center, eds. *The Harriet Lane Handbook: A Manual for Pediatrics House Officers*. 19th ed. Philadelphia, PA: Mosby Elsevier; 2012.

CASE 2 ANSWERS

1. D. All of the above

Differentiating central versus peripheral (i.e., acrocyanosis) is a fundamental first step in managing the cyanotic infant. When an infant has central cyanosis, the cyanosis is present throughout the body and is evident in the mucous membranes and tongue. Central cyanosis is observed if there is >3 to 5 g of reduced hemoglobin per deciliter of capillary blood. The presence of central cyanosis warrants immediate evaluation.

In contrast, peripheral cyanosis or acrocyanosis is limited to the extremities, is a common finding in healthy full-term newborns, and does not require further evaluation in the immediate newborn period.

2. D. A and B

Cyanosis can be secondary to cardiac, respiratory, hematologic, and metabolic causes. Severe cyanosis in the newborn is a prominent feature of congenital heart disease (CHD) and is associated with varying degrees of pulmonary blood flow (PBF). Infants who have cyanotic heart disease with decreased PBF may present with severe cyanosis without any respiratory distress while infants with CHD with increased PBF may present with respiratory distress. The table below lists cyanotic heart defects that are associated with varying degrees of PBF.

CHD and Cyanosis with Normal or Increased PBF (may have respiratory distress)	CHD and Cyanosis with Decreased PBF (usually without respiratory distress)
Transposition of the great arteries (TGA)	TOF
Truncus arteriosus	Tricuspid atresia
Double outlet right ventricle	Pulmonic atresia with intact septum or pulmonic stenosis
Ebstein anomaly of the tricuspid valve	Ebstein anomaly of the tricuspid valve

PPHN is the failure of the normal circulatory transition that occurs after birth and is characterized by significant pulmonary hypertension causing hypoxemia and right-to-left shunting across the foramen ovale and ductus arteriosus. PPHN most often occurs with parenchymal lung disease, such as meconium aspiration. PPHN can be idiopathic, thought to be in response to prolonged fetal stress. While infants with PPHN as a result of meconium aspiration syndrome present with respiratory distress, infants with idiopathic PPHN more often present without respiratory distress.

A rare extrapulmonary cause of cyanosis in the newborn is methemoglobinemia. In this disease, the iron within hemoglobin is oxidized from the ferrous state to the ferric state. Methemoglobinemia occurs when red blood cells contain greater than 1% methemoglobin and the oxygen-carrying capacity of blood is decreased.

Infants with surfactant deficiency typically present clinically with grunting, flaring, and retractions.

3. B. 30 mm Hg

Oxygen saturation is the percentage of hemoglobin that is combined with oxygen. The oxyhemoglobin dissociation curve represents the nonlinear tendency for oxygen to bind to hemoglobin. Thus, oxygen binding with hemoglobin increases as the partial pressure of oxygen increases in a nonlinear relationship. Below an oxygen saturation (Sao_2) of 90%, small differences in hemoglobin saturation reflect large changes in Pao_2. In a newborn, an Sao_2 of 60% would correlate with a Pao_2 of 30 mm Hg. Some practitioners describe this relationship as the 30-60-90 rule:

- At a Pao_2 of 30 mm Hg, the Sao_2 is ~60%
- At a Pao_2 of 60 mm Hg, the Sao_2 is ~90%
- At a Pao_2 of 90 mm Hg, the Sao_2 is ~95%

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that peripheral cyanosis is a common finding in healthy full-term newborns
- Distinguish between central cyanosis and acrocyanosis
- Know the common extrapulmonary causes of cyanosis: right-to-left shunt, methemoglobinemia
- Know how to validate and quantitate a clinical observation of cyanosis: arterial blood gases, oxyhemoglobin saturation
- Know that cyanosis is not a sensitive indicator of oxyhemoglobin desaturation

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Tschudy M, Arcara K; Johns Hopkins Hospital, Children's Medical and Surgical Center, eds. *The Harriet Lane Handbook: A Manual for Pediatrics House Officers*. 19th ed. Philadelphia, PA: Mosby Elsevier; 2012.

CASE 3 ANSWERS

1. D. Physical examination, four extremity blood pressures, pre- and postductal oxygen saturations, chest radiography, electrocardiography, and arterial blood gas

Although all of the possible options would be part of the complete evaluation for the infant in this vignette, this infant's clinical findings most likely result from cardiogenic shock, which may be the initial finding in a newborn with cyanotic heart disease.

2. D. All of the above

This infant has all of the cardinal findings of neonatal shock. Shock occurs when there is inadequate blood flow to the tissues

to meet tissue metabolic requirements. This leads to tissue hypoxemia, metabolic acidosis, irreversible cellular changes, and possibly subsequent cellular death. Shock can be classified as hypovolemic, distributive, or cardiogenic; common causes of each include placental abruption/massive bleeding, sepsis, and critical congenital heart disease (CHD), respectively. The most common types of CHD causing shock are left-sided obstructive lesions. Blood shunting from the pulmonary artery to aorta across a patent ductus arteriosus will assist with providing systemic blood flow, lessening the symptoms of an infant with a left-sided obstructive lesion. With closure of the ductus arteriosus (typically by 48 hours of age), an affected infant will develop severe symptoms. The initial therapeutic management in an infant with cardiogenic shock includes:

- Consulting with a cardiologist
- Starting PGE_1 with consideration for intubation because of a potential side effect of apnea
- Correcting any metabolic acidosis with an intravenous bicarbonate bolus or intravenous fluids with added acetate
- Initiating inotropic agents to improve myocardial function.

3. A. Hypoplastic left heart syndrome (HLHS)

The most common types of CHD causing shock are left-sided obstructive lesions, such as:

- Aortic atresia or severe aortic stenosis
- Coarctation of the aorta
- Interrupted aortic arch
- Mitral valve atresia or severe mitral stenosis (a type of HLHS)
- Total anomalous pulmonary venous return (TAPVR) with obstruction.

It is important to be aware that PGE_1 is indicated in most cases where a newborn is critically ill with a presumed ductal-dependent lesion. However, it is important to recognize that in a newborn with TAPVR with obstruction, PGE_1 may worsen symptoms by increasing pulmonary blood flow, further increasing pulmonary congestion with an associated worsening of systemic perfusion.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that an electrocardiogram and echocardiography should be part of the evaluation of a patient with possible cardiogenic shock
- Know that cardiogenic shock may be the initial finding in a newborn with congenital heart disease
- Recognize the findings of cardiogenic shock in the newborn
- Know the treatment of cardiogenic shock in the newborn
- Know what important lesions are associated with the shock-like presentation in a newborn

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 4 ANSWERS

1. B. Hypovolemic shock as a result of a placental abruption and blood loss

Hypovolemic shock is characterized by decreased blood volume below a critical level. There is decreased ventricular filling and decreased stroke volume (SV) with subsequent decreased cardiac output (CO) unless the infant is able to compensate with increased HR. Infants have poor peripheral perfusion, decreased distal pulses, hypotension, and decreased urine output.

In contrast to hypovolemic shock, cardiogenic shock is characterized by cardiac failure with impaired filling, poor ventricular emptying, and decreased contractility. Distributive shock is characterized by inadequate relative intravascular volume secondary to vasodilation. A comparison of these three types of shock is shown in the table below.

Hypovolemic Shock	Distributive Shock	Cardiogenic Shock
Decreased blood volume below a critical level Most common type of shock in neonate	Inadequate relative intravascular volume secondary to vasodilation	Cardiac failure
Decreased ventricular filling and decreased SV Decrease in CO unless able to compensate with increased HR	Normal circulating blood volume but insufficient for adequate cardiac filling	Impaired filling, impaired ventricular emptying, impaired contractility
Presents initially with decreased urine output, decreased BP, increased HR (note: premature infants may actually have decreased HR), no congestive heart failure (CHF)	Presents with decreased urine output, increased HR, decreased BP Often with bounding pulses	Presents with decreased urine output, increased HR, decreased BP CHF/pulmonary edema Often with hepatomegaly, cardiomegaly

Hypovolemic Shock	Distributive Shock	Cardiogenic Shock
Severe hemorrhage Severe fluid loss Can also be associated with sepsis (capillary leakage into third spaces and/or interstitial spaces)	Sepsis Anaphylaxis Vasodilators Toxins	Metabolic (e.g. hypocalcemia and hypoglycemia) Congenital heart disease Cardiac tamponade Severe perinatal depression Arrhythmias, myocarditis, cardiomyopathy, myocardial ischemia/infarction Can also be associated with sepsis (decreased contractility)

Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:117

2. D. B and C

This infant has hypovolemic shock as a result of a placental abruption and massive blood loss. Clinicians need to follow the appropriate Neonatal Resuscitation Program steps. The infant should be given emergency release of O-negative blood as soon as it is available. After an UVC is placed, a NS bolus may be administered while awaiting arrival of the blood.

3. B. Another 10 ml/kg of O-negative blood

It must be recognized that immediate volume resuscitation of an infant in hypovolemic shock may require more than 20 ml/kg to improve the infant's clinical status. This infant is profoundly anemic and his body is attempting to compensate for his decreased ventricular filling and SV by increasing his HR. Frequent clinical assessment of this infant is mandatory to provide ongoing appropriate medical management.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical signs of shock due to fluid loss
- Know the type of fluids to be administered in the treatment of shock
- Recognize that frequent clinical assessment is required in the treatment of shock
- Recognize that immediate fluid resuscitation of infants in shock may require more than 20 mL/kg of fluid to improve their clinical conditions

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 5 ANSWERS

1. D. Physical examination, chest radiograph, electrocardiogram, hyperoxia test

To distinguish between cardiac and respiratory causes of cyanosis, the physical examination can be helpful. Infants with cyanotic heart disease typically have milder respiratory distress compared with infants with respiratory disease. Infants with heart disease may have additional cardiac-specific findings, such as a hyperactive precordial impulse, delayed capillary refill, a gallop rhythm, a single second heart sound, hepatomegaly, and/or a murmur.

The chest radiograph is also useful in distinguishing cardiac from respiratory disease. Infants with respiratory disease typically have lung disease evident on the radiograph. Infants with cardiac disease may have cardiomegaly, a distinctive shape of the heart border, and increased or decreased pulmonary vascular markings.

An electrocardiogram may also be helpful to assess for the type of cyanotic heart disease. Infants with a complete atrioventricular canal or tricuspid atresia typically have a left superior QRS axis.

The hyperoxia test is the most sensitive and specific method to diagnose cyanotic heart disease.

2. D. Comparison of the infant's arterial PaO_2 in room air with the infant's PaO_2 while receiving 100% FIO_2

The hyperoxia test is a useful tool for diagnosing cyanotic heart disease. In this test, an ABG is obtained from the right radial artery (preductal) while the infant is in room air. Another ABG is obtained after the infant has inspired 100% oxygen for a minimum of 15 minutes. If an infant has cyanotic heart disease, there is little to no rise in PaO_2 with 100% FIO_2 (usually $<$100 torr), leading to a "failed" hyperoxia test result. Infants receiving 100% FIO_2 with a PaO_2 between 100 and 250 torr *may* have structural heart disease with intracardiac mixing and increased pulmonary blood flow. However, an infant receiving 100% FIO_2 with a PaO_2 $>$250 torr has "passed" the hyperoxia test, indicative of the absence of cyanotic heart disease.

3. D. B and C

Lesions with right-to-left shunting at the intracardiac level cause infants to have cyanosis because blood is shunted away from the lungs. These cyanotic lesions can be remembered by the "five T's rule":

- TOF
- Tricuspid atresia

- TGA
- TAPVR
- Truncus arteriosus

Other cardiac lesions that lead to cyanosis include the following:

- Double outlet right ventricle
- Ebstein anomaly
- HLHS
- PA or severe PS
- Single ventricle

4. B. Critical PS, tricuspid atresia, PA, TOF, Ebstein anomaly, TAPVR with obstruction

These types of cyanotic heart disease are associated with decreased PBF. These lesions are associated with a greater severity of cyanosis, and chest radiographs will reveal dark lung fields.

5. D. All of the above

TGA is the most likely cardiac defect in this infant. This infant's difference in oxygen saturations with a preductal saturation being lower than the postductal saturation is consistent with reversed differential cyanosis. This occurs when an infant has TGA, an intact ventricular septum, and a patent ductus arteriosus with shunting from the pulmonary artery to the aorta.

The infant described in this vignette also has the classic "egg on a string" chest radiograph finding that is consistent with TGA. This shape illustrates the narrowing of the superior mediastinum as a result of the anterior–posterior aorta and main pulmonary artery relationship. A diagram of TGA is shown in Figure 2.

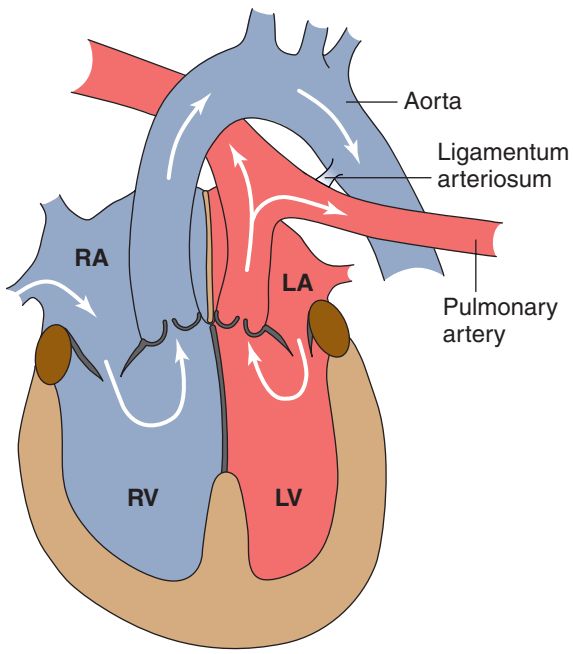


FIGURE 2. Rubin R, Strayer DS. *Rubin's Pathology: Clinicopathologic Foundations of Medicine*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008. Figure 11.10

If a physician suspects that an infant has cyanotic heart disease, he/she should immediately consult the cardiology service. The infant should receive PGE_1, a prostaglandin analog that relaxes arterial smooth muscle and maintains ductal patency. Blood then shunts across the patent ductus based on vascular resistance in the distal aorta and pulmonary artery. For infants with increased pulmonary vascular resistance, ductal shunting will occur from the pulmonary artery to aorta, increasing systemic cardiac output. For infants with decreased pulmonary vascular resistance compared to systemic vascular resistance, ductal shunting will occur from the aorta to pulmonary artery, increasing pulmonary blood flow.

Infants with TGA and an intact ventricular septum may not receive a tremendous benefit from PGE_1 and may also require an emergent Rashkind procedure, a technique developed in 1966. In this technique, a catheter with a deflated balloon at the tip is inserted through the foramen ovale. The balloon is then filled with air and the catheter is rapidly pulled back through the foramen to create a large septostomy between the right and left atria. This opening increases intra-atrial mixing until arterial switch surgery can be performed.

6. D. All of the above

Although PGE_1 is a life-saving treatment, it has several potential side effects. These include flushing, hypotension, and apnea. It is important to consider intubating any infant who is receiving PGE_1.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the cardiac causes of cyanosis in the newborn
- Recognize that the absence of improvement in arterial oxygen content with 100% oxygen in comparison with room air is compatible with the diagnosis of cyanotic congenital heart disease
- Recognize the clinical features and management of transposition of the great arteries
- Understand the role of ductus arteriosus in cyanotic congenital heart disease and the use of prostaglandin E1 in treatment

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

Long WA (ed). *Fetal and Neonatal Cardiology*. Philadelphia, PA: WB Saunders; 1990.

CASE 6 ANSWERS

1. D. "Tet" spell

Tetralogy of Fallot (TOF) is a congenital heart defect that involves the following four anatomic abnormalities:

- Ventricular septal defect
- Obstruction of the right ventricular outflow tract
- Overriding of the ventricular septum by the aortic root
- Right ventricular hypertrophy

This cardiac defect is depicted in Figure 1.

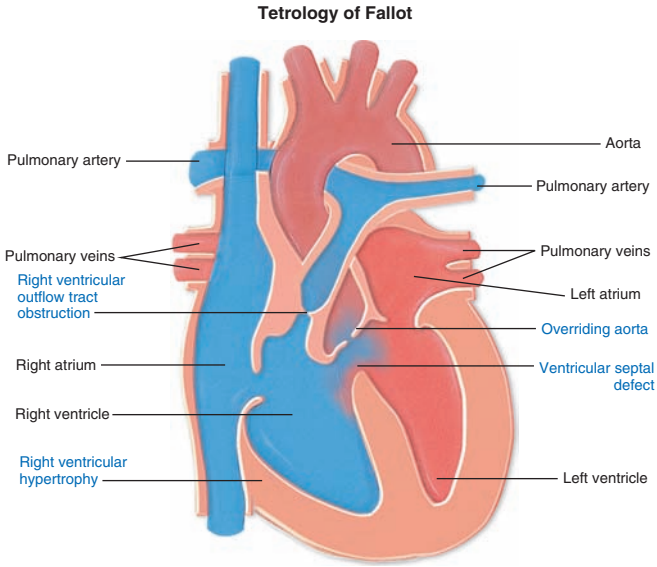


FIGURE 1. Courtesy of Anatomical Chart Co. © 2014 Lippincott Williams & Wilkins. All rights reserved

"Tet" spells or hypercyanotic spells can be described as an imbalance between pulmonary and systemic vascular resistance favoring decreased pulmonary flow and increased right-to-left (i.e., pulmonary artery to aorta) shunting. Hypoxemia, metabolic acidosis, hyperpnea, increased systemic venous return, excessive catecholamines, and pulmonary vasoconstriction are thought to be involved in an interaction that results in a continuous cycle. The proposed mechanism for a "tet" spell is shown in Figure 2.

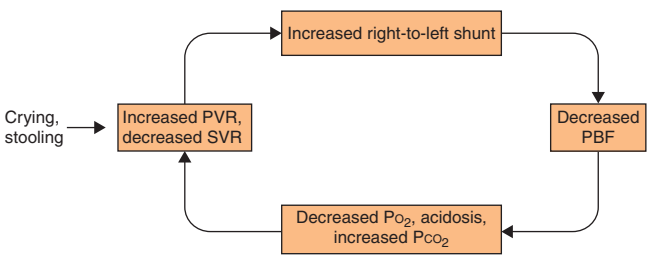


FIGURE 2. Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:120

2. A. Good long-term survival and excellent quality life

Ninety percent of patients with complete repair of TOF during infancy develop a progressively leaky pulmonary valve in adulthood. These patients have a good overall long-term survival and they have an excellent quality of life. Affected infants who are not surgically repaired will have progressive right ventricular hypertrophy and heart failure.

3. D. All of the above

Children with cyanotic CHD are at increased risk of developmental disability or developmental delay. Developmental disorders are common in infants with CHD, especially those infants who require open heart surgery in the first year of life or those with cyanotic CHD who are not repaired in the first year of life. These high-risk patients require periodic developmental surveillance, screening, evaluation, and reevaluation throughout childhood. This surveillance may enhance identification of significant deficits, allowing for appropriate therapies and education to enhance later academic, behavioral, psychosocial, and adaptive functioning.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Identify the clinical characteristics of a tetralogy spell
- Understand the prognosis for a patient with tetralogy of Fallot
- Understand the prognosis for cognitive development in patients with cyanotic congenital heart disease

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Marino B, Lipkin PH, Newburger JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: Evaluation and management—a scientific statement from the American Heart Association. *Circulation*. 2012;126:1143–1172.

CASE 7 ANSWERS

1. D. A or B

Persistent pulmonary hypertension of the newborn (PPHN) occurs in ~1 to 2 per 1,000 births. It is caused by a failure of transition from intrauterine to extrauterine pulmonary physiology. Thus, affected infants have a persistent elevation in their pulmonary vascular resistance (PVR). This increase in PVR leads to right-to-left shunting at the atrial (i.e., right-atrium-to-left-atrium shunting) or ductal level (i.e., pulmonary-artery-to-aorta shunting), with the resultant decrease in pulmonary blood flow leading to hypoxemia. PPHN can be divided into two groups:

- Maladaptation—normal structure of the pulmonary vascular bed with elevated PVR (e.g., meconium aspiration syndrome, pneumonia, sepsis, hypoxia, perinatal depression)

- Maldevelopment—abnormal structure of the pulmonary vascular bed leading to vascular smooth muscle hypertrophy (e.g., CHD, pulmonary hypoplasia, diaphragmatic hernia)

A newborn with cyanosis, low oxygen saturations, and a significant differential in pre- and postductal oxygen saturations requires further evaluation to establish a definitive diagnosis. In the absence of meconium aspiration syndrome, it is difficult to distinguish between PPHN and cyanotic CHD.

2. B. Inhaled nitric oxide

The infant described in this vignette should have an echocardiograph to rule out CHD and to confirm the presence of PPHN. There are several strategies that are used to treat PPHN, including:

- Administration of 100% oxygen to increase pulmonary vasodilation
- Use of inhaled nitric oxide, a selective pulmonary vasodilator
- Use of sedation medications
- Maximization of an infant's oxygen-carrying capacity by transfusing with packed red blood cells if the infant is anemic
- Maintenance of cardiac output
- Avoidance of acidosis
- Administration of antibiotics as PPHN may be associated with sepsis/pneumonia
- Utilization of ventilator support
- Option of extracorporeal membrane oxygenation (ECMO) in term infants should all else fail

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that it is difficult to distinguish between persistent pulmonary hypertension without meconium aspiration and cyanotic congenital heart disease
- Recognize the clinical presentation of a neonate with persistent pulmonary hypertension following meconium aspiration
- Know the strategy to manage persistent pulmonary hypertension of the newborn

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 8 ANSWERS

1. D. All of the above

The conduction of the fetal heart is functionally mature by 16 weeks' gestation, yielding a normal fetal heart rate of 110 to 160 beats per minute for the remainder of the pregnancy. Fetal arrhythmias represent deviations from this norm. Approximately 1% to 2% of fetuses have fetal arrhythmias; of those, 10% have associated morbidity. The most common cause of a fetal arrhythmia is premature atrial contractions (PACs) where there is most often a 1:1 conduction of ectopic beats yielding early ventricular contractions as well. PACs are most often benign and intermittent. In any fetus with frequent ectopy, the fetal heart rate should be auscultated at each prenatal visit and an ultrasound should be done to evaluate structural abnormality of the fetal heart. Pregnant women with lupus are at increased risk of having a fetus or neonate with complete heart block.

2.

A	2
B	3
C	1
D	4

3. B. Digoxin, vagal maneuvers

A fetus with sustained SVT warrants treatment. First-line intrauterine treatment is digoxin administered intravenously to the pregnant woman. If the fetus is sick, second-line treatment is amiodarone, while second-line treatment for a healthier fetus can be procainamide, flecainide, or sotalol. Lastly, delivery is an option for the fetus with mature lungs.

A newborn with SVT warrants treatment if the SVT is sustained or if there are any signs or symptoms of cardiovascular compromise. If the infant is unstable, clinicians can perform synchronized cardioversion at a dose of 0.5 to 2 J/kg. If the infant is stable, clinicians can perform vagal maneuvers (crushed ice to face; rectal stimulation) and administer adenosine intravenously if the arrhythmia persists.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Understand the significance and plan the management of fetal arrhythmias
- Using electrocardiographic patterns, identify premature atrial contractions, premature ventricular contractions, supraventricular tachycardia, and ventricular tachycardia
- Understand the treatment of supraventricular tachycardia

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Strasburger JF. Prenatal diagnosis of fetal arrhythmias. In: Wernovsky G, Berger S, Rubenstein SD, eds. *Congenital Heart Disease: Impact on the Fetus, Pregnancy, Neonate and Family*. Philadelphia, PA: W B Saunders; 2005:891–912. *Clinics in Perinatology*; vol 32.

SECTION IV

Neurology

CASE 1

Head growth

During a night shift, four full-term infants are admitted to the Special Care Nursery. The next day, the neonatologist reviews each infant's head circumference (HC). Her findings are shown below:

Baby boy Banks	HC = 37 cm
Baby girl Gray	HC = two to three standard deviations below the mean
Baby boy Scott	HC > three standard deviations above the mean
Baby girl Smith	HC = 40 cm

1. Match the infant with the corresponding description (the descriptions may be used more than once):

A. Baby boy Banks ____	1. Macrocephaly
B. Baby girl Gray ____	2. Microcephaly
C. Baby boy Scott ____	3. Normal HC
D. Baby girl Smith ____	

The continued head growth of one of these infants is plotted on the growth chart (Figure 1). Referring to this growth chart, please answer the next question.

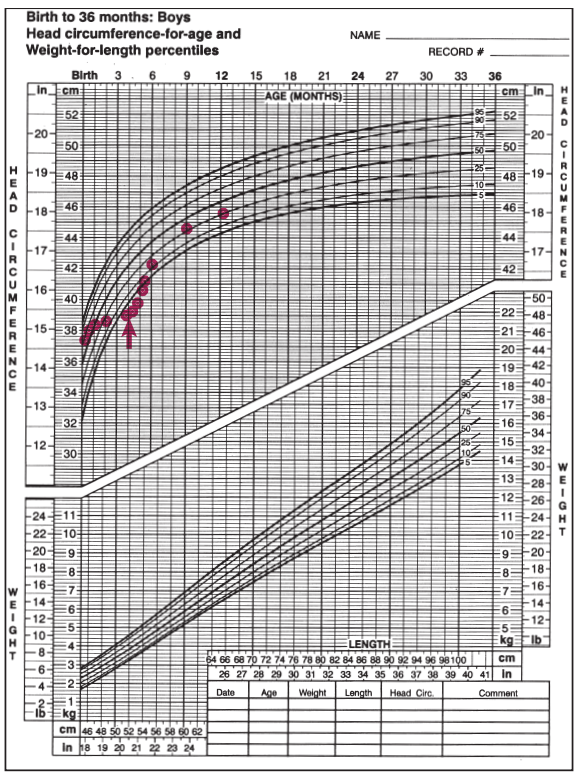


FIGURE 1. Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000). http://www.cdc.gov/growthcarts

2. Of the following, a possible etiology of this baby's head growth from birth until 4 months of age is:

   A. Acquired microcephaly as a result of craniosynostosis
   B. Acquired microcephaly from a perinatal insult
   C. Progressive microcephaly as a result of a neurodegenerative or neurogenetic process
   D. All of the above

One of the babies in the scenario above has craniosynostosis that requires surgery at age 4 months.

3. Review the diagrams (Figure 2) and match the type of craniosynostosis to the corresponding head shape:

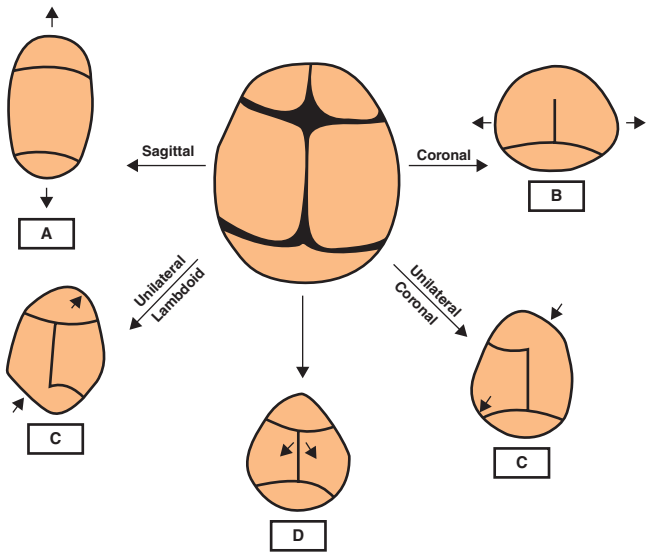


FIGURE 2. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005

A. _____	1. Brachycephaly
B. _____	2. Plagiocephaly
C. _____	3. Scaphocephaly or dolichocephaly
D. _____	4. Trigonocephaly

4. For the baby in the Special Care Nursery who had macrocephaly, what is the most likely etiology of this infant's abnormal head growth?

   A. Beckwith–Wiedemann syndrome, neurofibromatosis, Sotos syndrome, or fragile X syndrome
   B. Benign familial macrocephaly
   C. Intracranial mass
   D. Posthemorrhagic hydrocephalus

CASE 2

Brachial plexus injury at birth

You are called stat to labor room 2 due to possible shoulder dystocia. A large-for-gestational-age baby girl is delivered using McRobert's maneuver assistance. She is vigorous and crying at the perineum. She is brought to the warmer, where you provide routine care. You palpate her clavicles, and they are intact. However, she has decreased movement of her right arm.

1. Match the following clinical signs and symptoms with the two types of brachial plexus injury listed to the right:

   A. C5–C7 ____
   B. Less common ____
   C. "Waiter's tip" ____
   D. Absent shoulder Moro reflex with presence of hand Moro reflex ____

   i. Erb–Duchenne (proximal) palsy
   ii. Klumpke (distal) palsy

The infant was diagnosed with an Erb palsy. You are asked to explain the management and prognosis to the parents.

2. Select the most appropriate management and prognosis below:

   A. Physical therapy; likely full recovery by 4 months
   B. Immediate surgery; likely full recovery by 4 months
   C. Physical therapy and Botox injections; variable recovery
   D. Neurosurgical consultation; if no improvement by 2 weeks, likely will persist

CASE 3

Seizures

A full-term female infant was born by an uncomplicated repeat cesarean delivery. Her Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. She had been doing well until day 5 of life when her mother noted that she had brief jerking movements of her legs. As the covering pediatrician, you evaluate the infant.

1. What would be your differential diagnosis?

   A. Benign sleep myoclonus
   B. Exaggerated startle response, jitteriness
   C. Seizure
   D. All of the above

The infant is admitted to the Neonatal Intensive Care Unit (NICU). While you are observing her, she has another event.

2. All of the following possible clinical findings would support a diagnosis of seizure with the exception of:

   A. Abnormal chewing
   B. Bicycling or "swimming" movement of the extremities
   C. Eye deviation
   D. Sudden hypotension

The infant undergoes the following laboratory tests and studies:

- A sepsis evaluation, including a lumbar puncture
- Electrolytes, calcium, magnesium, phosphorus
- An electroencephalography (EEG)
- Magnetic resonance imaging (MRI)

She develops unifocal clonic seizure activity and is diagnosed with a right middle cerebral arterial (MCA) infarct.

3. Which statement(s) below is(are) true?

   A. Abnormal interictal EEG has less favorable outcome
   B. Overall outcome for infants with seizures after arterial or venous vaso-occlusive disease is favorable
   C. Seizures are the most common presentation of stroke in the newborn period, and stroke is the second most common cause of neonatal seizures
   D. All of the above

CASE 4

Hypoxic-ischemic encephalopathy

A 43-year-old primigravida woman presents to Labor and Delivery 1 hour after feeling a decrease in fetal movement. The fetal tracing is flat, prompting an emergent cesarean delivery. After birth, the baby girl requires resuscitation with intubation, chest compressions, epinephrine, and volume. Her Apgar scores are 1, 3, and 4 at 1, 5, and 10 minutes, respectively. The cord pH is 6.82 in the umbilical artery and 6.93 in the umbilical vein. While being observed in the Neonatal Intensive Care Unit (NICU), the infant has a seizure.

1. The most common timing of seizure activity in this infant with hypoxic-ischemic encephalopathy (HIE) is:

   A. 0 to 6 hours of life
   B. Within the first 24 hours of life
   C. 24 to 48 hours of life
   D. >72 hours of life

2. Multisystem organ effects may occur in the setting of severe intrapartum asphyxia. Chose the answer below that reflects the type of end-organ injury seen as a result of severe HIE:

   A. Hypotonia, seizures, hypertension, ventricular dysfunction, tricuspid regurgitation, polyuria with sodium wasting, pulmonary hypertension, intestinal ischemia
   B. Hypotonia, seizures, other organ effect uncommon
   C. Hypotonia, seizures, transient myocardial ischemia, ventricular dysfunction, tricuspid regurgitation, oliguria and acute tubular necrosis (ATN), pulmonary hypertension, intestinal ischemia
   D. Hypotonia, seizures, transient myocardial ischemia, ventricular dysfunction, tricuspid regurgitation, oliguria and ATN, respiratory distress with shunting from left to right across the patent ductus arteriosus (PDA) and patent foramen ovale (PFO), intestinal ischemia

The infant is undergoing therapeutic hypothermia. Her seizures have quelled with phenobarbital; she remains on dopamine at 5 mcg/kg/min; her laboratory values peaked with aspartate aminotransferase (AST) of 800 mg/dL and alanine aminotransferase of 675 mg/dL, blood urea nitrogen (BUN) of 12 mg/dL, creatinine (Cr) of 1.3 mg/dL, and a platelet nadir of 72×10^9/L. She remains critically ill.

3. The nurse has been talking with the father at the bedside. He is devastated and believes that his daughter will have a terrible outcome. The nurse suggests a family meeting as soon as possible. Before the meeting, the neonatology attending discusses HIE and outcomes with the pediatric residents. Which statement(s) below is(are) true?

   A. More individualized outcome predictors for infants with HIE depend on the severity of the encephalopathy, the presence or absence of seizures, EEG findings, and neuroimaging results
   B. The majority of term infants with seizures due to HIE do not manifest long-term neurodevelopmental sequelae
   C. Therapeutic hypothermia in term infants with moderate/severe encephalopathy reduces mortality and/or neurodevelopmental outcomes (measured at 18 months of age)
   D. All of the above

CASE 5

Intracranial hemorrhage

The attending on service has selected three infants in the Neonatal Intensive Care Unit (NICU) for you to follow this week. He has asked you to prepare a presentation on intracranial hemorrhage by the end of the week. He suggests you design a case-based presentation based on the following four patients.

i. A male infant was born at 24 weeks' gestation to a mother with chorioamnionitis. His hospital course has been complicated by respiratory distress syndrome, severe hypotension, a patent ductus arteriosus (PDA), and sepsis. His neurologic examination is currently appropriate for gestational age.
ii. A full-term female infant had a difficult delivery. Her neurologic examination is significant for hypotonia, lateral eye deviation, unequal pupil size, and irregular respirations.

iii. A full-term male infant was born via uncomplicated spontaneous vaginal delivery. He had been well until his second postnatal day when he developed seizures. He is currently hemodynamically stable and remains in room air.
iv. A preterm infant was born via emergent cesarean delivery for fetal distress. He required cardiopulmonary resuscitation after birth and now is showing signs of brainstem compression.

1. Match the above cases to potential head imaging results based on the risk factors in the short vignettes above:

   A. Bilateral germinal matrix hemorrhages (GMH) on postnatal day 3, followed by periventricular leukomalacia (PVL) noted on imaging at 1 month
   B. Cerebellar hemorrhage
   C. Subarachnoid hemorrhage
   D. Subdural hemorrhage

2. Select the radiographic study that is most accurate at detecting a specific neurologic finding (select one best answer for each finding; answers may be used more than once or not at all):

   A. GMH and PVL
   B. Cerebellar hemorrhage
   C. Hypoxic-ischemic encephalopathy
   D. Subdural hemorrhage

   i. Computed tomography (CT)
   ii. Magnetic resonance imaging (MRI)
   iii. Ultrasonography

3. The critically ill patients described in vignettes ii and iv need intervention. What steps would you take to evaluate and manage these infants?

   A. Call neurology stat, but hold off on calling neurosurgery as you do not have imaging results yet
   B. Follow guidelines for neonatal stabilization; secure the airway (intubate); provide blood products and volume; start inotropes; obtain complete blood count with differential, blood culture, electrolytes, disseminated intravascular coagulation panel; call neurosurgery stat and arrange for head imaging urgently
   C. Monitor vital signs and call neurosurgery
   D. Send the infant urgently to radiology as there is no time to secure the airway

CASE 6

Neonatal encephalopathy

A full-term male infant was born at a community hospital via repeat cesarean delivery to a 30-year-old gravida 3 para 2 now 3 Caucasian woman with reassuring prenatal screens aside from Group B *Streptococcus* colonization. The infant did well in the delivery room, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively.

On postnatal day 3, the infant was unable to breast-feed and became hypothermic and jittery. Within an hour, his clinical condition deteriorates rapidly with tachypnea, tachycardia, and extreme lethargy. The pediatric hospitalist calls the transport team to transfer the infant to the closest level 3 Neonatal Intensive Care Unit (NICU). You are the resident who will be admitting the infant to the NICU.

1. Based on the clinical history thus far, you have created a differential diagnosis. What studies will you order upon admission?

   A. Ammonia level, electrolytes, blood urea nitrogen (BUN), creatinine (Cr), glucose
   B. Arterial blood gas (ABG), complete blood count (CBC), blood culture
   C. Radiograph of chest and abdomen
   D. All of the above

The infant is now intubated and receiving intravenous fluids. He also received a normal saline bolus, a 10% dextrose bolus, and has been started on ampicillin and gentamicin. Test results are as follows:

- ABG: pH = 7.17, $Paco_2$ = 55 mm Hg, Pao_2 = 147 mm Hg, base deficit = –15 mEq/L
- Na = 149 mEq/L, K = 6.9 mEq/L, Cl = 111 mEq/L
- Blood glucose = 90 mg/dL
- Plasma ammonia level > 2,000 µM/L

- CBC within normal limits
- Chest radiograph within normal limits
- Newborn state screen pending

The metabolism consult service has recommended sending quantitative plasma amino acids, urine amino acids, urine ketones, liver function tests (LFTs), and frequent repeat serum ammonia levels via arterial puncture. The results lead to a diagnosis of a urea cycle defect. Despite maximal therapy with hemodialysis, the infant remains in a coma for 3 days.

2. Which statement(s) is(are) true regarding neurologic sequelae and outcomes in infants diagnosed with a urea cycle defect?

   A. Most patients with urea cycle defects live well into adulthood
   B. Neurologic sequelae and survival depend on the length of the hyperammonemic coma
   C. There is a low risk for neurologic sequelae if the coma lasts for 4 days
   D. All of the above

SECTION IV

Answers

CASE 1 ANSWERS

1. A 3. Normal HC
B 2. Microcephaly
C 1. Macrocephaly
D 1. Macrocephaly

If a pregnancy is complicated by placental insufficiency, head growth is initially preserved and is the last growth parameter to be adversely affected. The average HC for full-term infants is 33 to 38 cm. After 3 weeks of life, an infant's HC increases ~1 cm/week.

Microcephaly describes an infant with a HC that is greater than two to three standard deviations *below* the mean. Congenital microcephaly, also known as primary microcephaly, is microcephaly that is present at birth. Congenital microcephaly is more common than postnatal microcephaly (also known as acquired or secondary microcephaly). This latter type of microcephaly occurs when there is failure of normal brain growth in an infant who had a normal-sized brain at birth.

Macrocephaly describes an infant with a HC that is greater than three standard deviations *above* the mean. Macrocephaly results from an increase in size of any component of the cranium (brain, cerebral spinal fluid [CSF], blood, skull), increased intracranial pressure, or presence of a mass (cyst, tumor, abscess).

Hydrocephaly occurs when the cerebral ventricular system contains excessive CSF, resulting in increased ventricular dilatation and possibly increased ventricular pressure.

2. D. All of the above

The growth chart shown in Figure 1 corresponds with an infant with postnatal microcephaly. This infant's decrease in head growth can be caused by:

- A hemorrhagic or ischemic stroke
- A neurodegenerative or neurogenetic process, such as an inborn error of metabolism or a genetic syndrome (e.g., Miller–Dieker syndrome, Rett syndrome, ataxia–telangiectasia)
- A perinatal insult, such as hypoxic ischemic encephalopathy
- Other etiologies such as craniosynostosis

Infants with craniosynostosis have premature closure of one or more cranial sutures, resulting in a decrease in head growth noted at birth or, more often, postnatally. The baby who had the growth curve shown in Figure 1 was diagnosed with premature closure of the sagittal sutures. The baby's pediatrician initially suspected this diagnosis by physical examination findings and confirmed the diagnosis by a three-dimensional computed tomography (CT) scan. The baby underwent surgical repair at 4 months of age, which resulted in improved head growth.

The management of an infant with craniosynostosis involves imaging and neurosurgical consultation. Head ultrasound has been used as a diagnostic tool for craniosynostosis, but it requires an experienced technician for maximum utility. Three-dimensional CT now serves as the standard diagnostic tool for complete visualization of the skull and sutures. Indications for surgery include:

1. Prevention of intracranial hypertension and associated complications
2. Prevention of progressive skull and facial deformity
3. Optimization of brain growth potential

As most of an infant's brain growth occurs in the first year of life, it is important to recognize craniosynostosis as early as possible with neurosurgical corrective repair at age 3 to 9 months of life.

3. A 3. Scaphocephaly or dolichocephaly
B 1. Brachycephaly
C 2. Plagiocephaly
D 4. Trigonocephaly

Scaphocephaly or dolichocephaly involves premature closure of the sagittal suture and is the most common type of craniosynostosis. Frontal plagiocephaly, resulting from premature closure of a unilateral coronal suture, is the next most common type of craniosynostosis and is associated with Crouzon and Apert syndrome. Brachycephaly involves premature closure of the bilateral coronal sutures; it occurs infrequently and can be observed in infants with Carpenter syndrome. Occurring even less frequently, trigonocephaly involves premature closure of the metopic suture and is seen more often in males.

4. B. Benign familial macrocephaly

Fifty percent of cases of macrocephaly are associated with benign familial macrocephaly, which typically has an autosomal dominant inheritance pattern and affects males more often than females. Macrocephaly may also be associated with genetic syndromes/disorders such as Beckwith–Wiedemann syndrome, neurofibromatosis, Sotos syndrome, and fragile X syndrome. In addition, intracranial tumors and posthemorrhagic hydrocephalus can lead to macrocephaly as a result of obstructive hydrocephalus.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the normal head circumference of a full-term infant at birth
- Recognize the growth pattern of acquired microcephaly
- Recognize normal and abnormal variations in head shape
- Craniosynostosis
  - Recognize the clinical findings of premature closure of a cranial suture
  - Distinguish between the closure of cranial sutures secondary to failure of brain growth (small, normally shaped head) and premature closure of a single cranial suture
  - Plan appropriate management for a patient with craniosynostosis

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Tschudy M, Arcara K (Children's Medical and Surgical Center, Johns Hopkins Hospital), eds. *The Harriet Lane Handbook: A Manual for Pediatric House Officers*. 19th ed. Philadelphia, PA: Mosby Elsevier; 2012.

CASE 2 ANSWERS

1. A. i. Erb–Duchenne
B. ii. Klumpke
C. i. Erb–Duchenne
D. i. Erb–Duchenne

Figure 1 compares the clinical findings of an infant with an Erb–Duchenne palsy and those of an infant with a Klumpke palsy.

	Erb–Duchenne Palsy (proximal)	Klumpke Palsy (distal)
Nerve roots	C5–C7	C8–T1
Clinical signs and symptoms	Most common (90%) "Waiter tip" position with arm adducted, internally rotated arm, extension of elbow, pronation of forearm, flexed wrist and fingers Biceps reflex absent Intact palmar grasp Absent shoulder moro while hand moro is present	Least common Rare to be isolated (often upper roots involved as well, leading to total palsy) Weakness of flexors of wrist and fingers, and finger abduction C4/C5—phrenic nerve paralysis, respiratory distress, decreased diaphragm movement, CXR with elevated hemidiaphragm C7—flexion deformity of the hand, winging of the scapula, absent Moro, intact grasp reflex, cutaneous sensory loss over the deltoids and radial aspect of upper arm, decreased temperature and perspiration Wrist, fingers extended, digits in neutral position Biceps reflex absent Grasp reflex absent Complete moro absent T1—unilateral Horner syndrome with miosis, ptosis, anhidrosis, decreased pigmentation of the iris

FIGURE 1. Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:173

Figure 2 shows an infant with an Erb palsy.

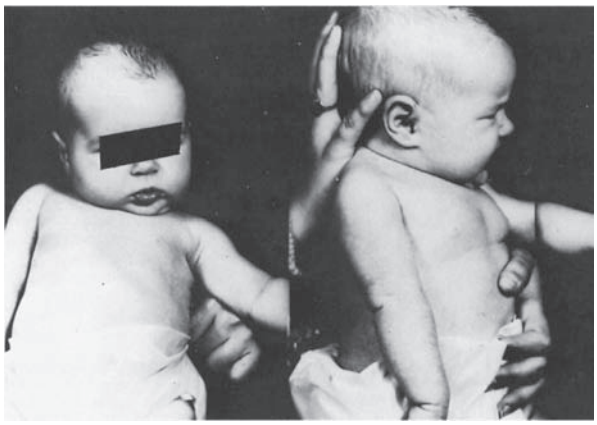


FIGURE 2. This picture shows an infant with Erb palsy. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 52.17

Figure 3 shows how a brachial plexus injury can occur after excessive stretching of the neck during delivery.

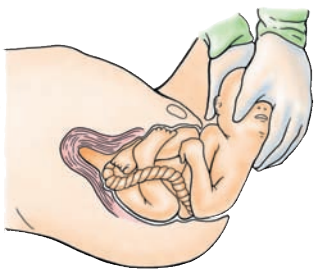


FIGURE 3. From Moore KL, Agur AM, eds. *Essential Clinical Anatomy*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002. Figure 7.6

2. A. Physical therapy; likely full recovery by 4 months

Some brachial plexus injuries heal without treatment; others improve or recover by 3 to 4 months of age. Treatments used for brachial plexus injuries are physical therapy and, in certain cases, surgery. Prognosis is based on location and type of injury. For avulsion and rupture injuries, surgical intervention is needed in a timely fashion to offer an opportunity for complete recovery.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical manifestations of neonatal brachial plexus injuries
- Know the management and prognosis of neonatal brachial plexus injuries

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Tschudy M, Arcara K (Children's Medical and Surgical Center, Johns Hopkins Hospital), eds. *The Harriet Lane Handbook: A Manual for Pediatric House Officers*. 19th ed. Philadelphia, PA: Mosby Elsevier; 2012.

CASE 3 ANSWERS

1. D. All of the above

"Seizure mimics" in the newborn period can make it difficult to distinguish between normal immature activity, abnormal nonseizure activity, and true seizures.

- True epileptic seizures are not usually stimulus-sensitive
- Epileptic seizures cannot be stopped by repositioning or passive restraint
- Epileptic seizures most often have associated autonomic changes or ocular manifestations

Some "seizure mimic" examples are nonnutritive sucking, jitteriness, and an exaggerated startle response.

2. D. Sudden hypotension

All of the following are potential manifestations of seizure activity in the neonate:

- Abnormal chewing
- "Bicycling" or "swimming" movement of the extremities
- Eye deviation
- Tachycardia
- Apnea
- Sudden hypertension

Hypotension would be unusual unless the infant had prolonged apnea with bradycardia and subsequent low blood pressure.

The clinical diagnosis of neonatal seizures can be categorized into five subtypes, as summarized in the table below.

Seizure Subtype	Clinical Manifestations	Preterm or Term Infant
Subtle	Oral, facial, or ocular activity; "swimming" or "bicycling" limb movements; autonomic changes with tachycardia, apnea, and increased blood pressure	Occurs in both (most frequent neonatal subtype)
Multifocal clonic	Clonic activity of one limb with movement to another part of body in a nonordered manner; may look like jitteriness; not usually associated with apnea or ocular movements	Term infant
Focal clonic	Well-localized, repetitive, usually one limb, conscious throughout, may represent focal or diffuse disease (i.e., metabolic disorder)	Term infant > preterm infant
Tonic	Abrupt change in tone that leads to change in posture; described as "posturing," "stiffening," "rigidity"; may have associated apnea and ocular movements	Preterm infant
Myoclonic	Rapid, sudden, "shock-like" jerks of flexion of both arms and/or legs; events may occur in brief series	Term and preterm

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:177–178

3. D. All of the above

Seizures are a marker for potential adverse neurologic outcome. The overall prognosis for survival in an infant with neonatal seizures is ~85% with a morbidity that varies between 35% and 60%. The three major predictors of outcome after a neonatal seizure are:

- Underlying etiology
- EEG
- Gestational age

Infants with hypoxic-ischemic encephalopathy and seizure activity have a 50% chance of normal neurologic development. Infants diagnosed with bacterial meningitis accompanied by seizures also have ~50% chance for a normal neurologic outcome. Overall outcome for infants with seizures after arterial or

venous vaso-occlusive disease is favorable. In infants with arterial strokes, those with an abnormal interictal EEG background have a less favorable outcome. Infants with benign neonatal seizures, also known as "fifth day fits," have normal background EEG patterns with seizure resolution usually by day 15 of life; as the name implies, infants have a normal neurologic outcome. Intracranial hemorrhage and subsequent seizure are seen in both term and preterm infants, but the outcome depends on parenchymal injury and gestational age with lower-gestational-age infants at risk for significantly worse neurologic outcome.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the differential diagnosis of neonatal seizures
- Know the clinical manifestations of neonatal seizures
- Know the prognosis following neonatal seizures

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Olson D. Neonatal seizures. *NeoReviews*. 2012;13:e213–e222.

CASE 4 ANSWERS

1. B. Within the first 24 hours of life

HIE is the most frequent cause of neonatal seizure in a full-term infant, occurring in 20% to 50% of these infants. Seizures related to HIE most often start between 6 and 24 hours after the insult.

2. C. Hypotonia, seizures, transient myocardial ischemia, ventricular dysfunction, tricuspid regurgitation, oliguria and ATN, pulmonary hypertension, intestinal ischemia

Intrapartum asphyxiation can lead to multiorgan injury. Acute asphyxia elicits the diving reflex where blood preferentially flows to the most vital organs, such as the brain, heart, and adrenal glands. Vasoconstriction occurs in organs such as the kidneys, liver, lungs, and intestines. The kidney is the most common organ affected in perinatal asphyxia as decreased perfusion to the proximal tubule leads to ATN. Cardiac dysfunction is caused by transient myocardial ischemia with clinical findings of *hypotension*, ventricular dysfunction (right ventricle worse than left ventricle), and tricuspid regurgitation. There is increased risk for bowel ischemia and necrotizing enterocolitis. Hematologic effects include thrombocytopenia due to poor production in the bone marrow, poor production of clotting factors due to liver dysfunction, and disseminated intravascular coagulation due to damage to blood vessels. Peak laboratory values for liver function studies, BUN, and serum Cr usually occur 1 to 4 days after the insult.

Figure 1 shows the brain of a full-term infant with severe HIE. Figure 1A and Figure 1B are computed tomographic images, and Figure 1C is a magnetic resonance image. The progression of the images represents changes at day 3, at 4 months of age, and at 2 years of life. Figure 1A shows generalized, decreased tissue attenuation in both cerebral hemispheres. Figure 1B and Figure 1C reveal multicystic encephalomacia and cerebral atrophy.

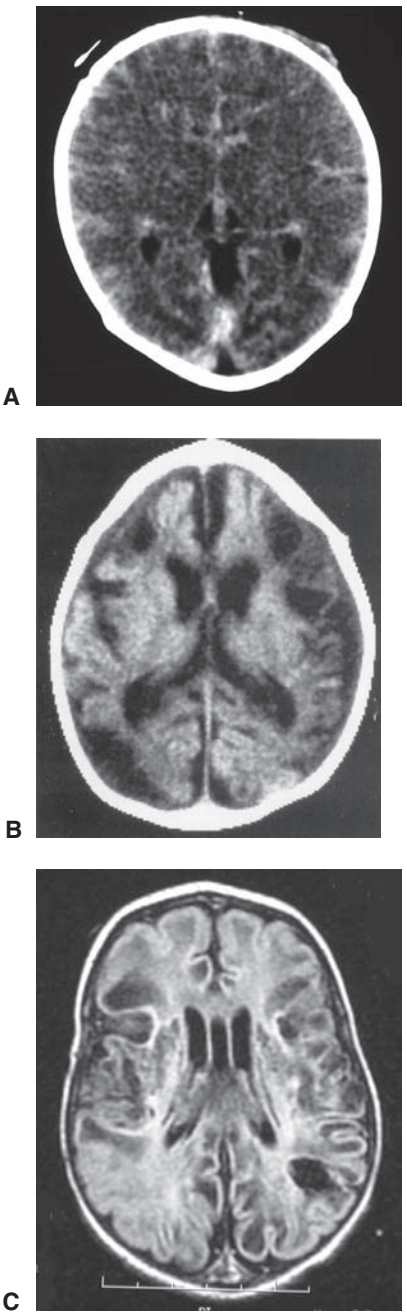


FIGURE 1ABC. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 50.1ABC

3. D. All of the above

The overall mortality rate in infants with HIE is 10% to 30%, and the incidence of neurodevelopmental sequelae is 15% to 45% in surviving infants. Therapeutic hypothermia in term infants with moderate/severe encephalopathy

reduces mortality and/or neurodevelopmental outcomes when measured at 18 months of age. Attempts to predict individual patient outcomes depend on the severity of the encephalopathy, the presence or absence of seizures, EEG results, neuroimaging findings, and the infant's clinical examination.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that hypoxic-ischemic encephalopathy is the most frequent cause of neonatal seizure in a full-term infant
- Recognize that neonatal seizures secondary to hypoxic-ischemic encephalopathy characteristically occur within 24 hours of birth
- Recognize that intrapartum asphyxiation can cause injury to multiple organ systems (e.g., kidney, lung, intestine, liver, brain, heart)
- Recognize that the majority of full-term newborns who have neonatal seizures secondary to hypoxic-ischemic encephalopathy do not manifest long-term neurodevelopmental sequelae

SUGGESTED READINGS

Allan W. The clinical spectrum and prediction of outcome in hypoxic-ischemic encephalopathy. *NeoReviews*. 2002;3:e108–e114.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 5 ANSWERS

1. A i
B iv
C iii
D ii

Vignette i describes a 24-week-gestational-age infant who has bilateral GMH (or a grade 1 intraventricular hemorrhage [IVH]) on his initial head ultrasound. The incidence of IVH in an infant at this gestation is 30%. Approximately 78% of IVHs are ultrasonographically visible by postnatal day 3, and 90% of IVH are visible by one week of age. As described in this case, this infant develops PVL. His risks for developing PVL include prematurity, IVH, chorioamnionitis, and initial profound hypotension.

Figure 1 depicts the various grades of IVH.

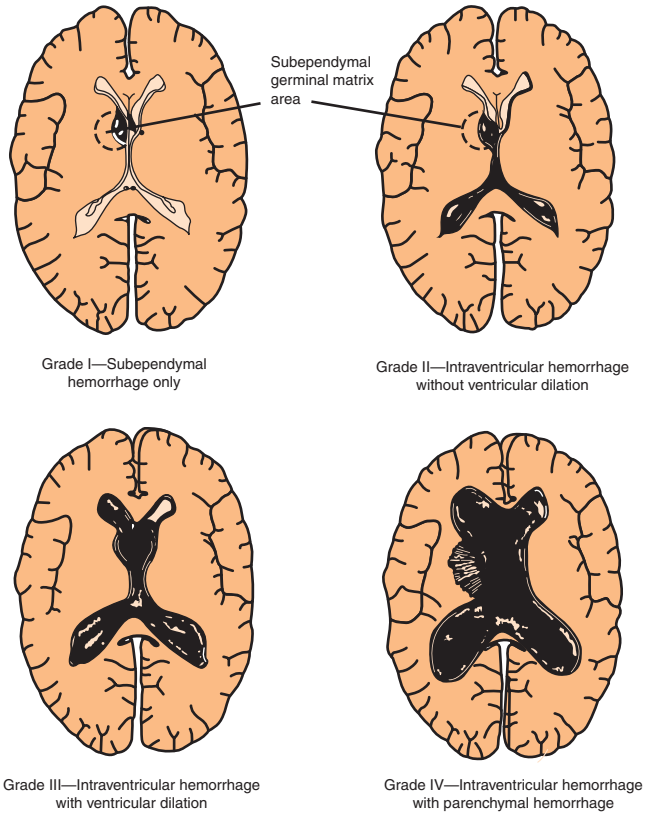


FIGURE 1. From Rozmus C. Periventricular-intraventricular hemorrhage in the newborn. *Matern Child Nurs*. 1992;17:672, with permission

Vignette iv describes a preterm infant showing signs of brainstem compression that can be associated with a cerebellar hemorrhage. Although uncommon, cerebellar hemorrhage can be serious and can lead to long-term neurodevelopmental deficits.

Vignette iii depicts a term infant with seizures on day 2. A subarachnoid hemorrhage is the most frequent intracranial hemorrhage and rarely is of clinical significance. If symptomatic, infants may have early onset refractory seizures.

Vignette ii describes a term infant who withstood a traumatic delivery resulting in a subdural hemorrhage caused by trauma and tearing of the veins and venous sinuses. Figure 2 shows an extensive left subdural hemorrhage covering the frontal lobe (*arrows*) and extending into the midline along the falx cerebri.

2. A ii. and iii. MRI and Ultrasonography
B i. CT
C ii. MRI
D i. CT

IVH is best visualized via ultrasonography or MRI. It is routine to obtain head ultrasound imaging for infants born <32 weeks' gestation. For extremely premature infants, testing is usually obtained on day 1 to 3, day 10, day 30, and

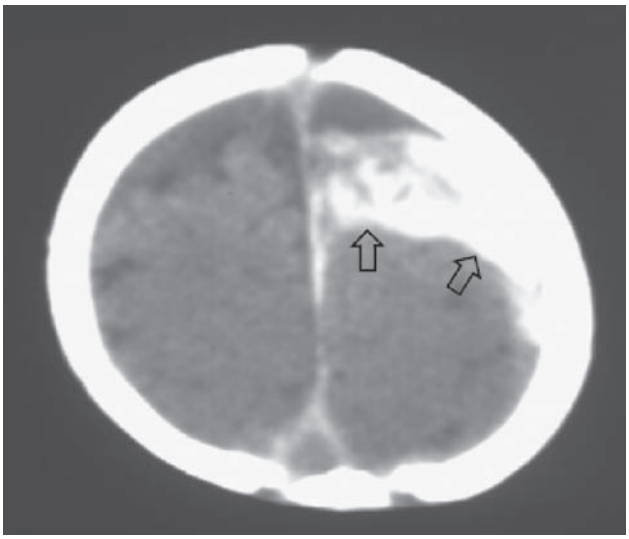


FIGURE 2. Courtesy of Robert A. Zimmerman, MD

term gestational age, with more frequent testing if an infant is acutely ill or has abnormal radiographic findings.

Subdural, subarachnoid, and cerebellar hemorrhages are best visualized via CT. Although CT delivers radiation to the infant as opposed to ultrasound and MRI, newer protocols have been developed to minimize radiation exposure. However, because of these radiation concerns, MRI is sometimes used for detection of these hemorrhages.

3. B. Follow guidelines for neonatal stabilization; secure the airway (intubate); provide blood products and volume; start inotropes; obtain complete blood count with differential, blood culture, electrolytes, disseminated intravascular coagulation panel; call neurosurgery stat and arrange for head imaging urgently

The two infants described in vignettes ii and iv represent neurosurgical emergencies until proven otherwise. They need urgent stabilization and neurosurgery needs to be consulted. In the case of a subdural hemorrhage with severe neurologic decompensation, surgical evacuation must be performed.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical and laboratory findings associated with intracranial hemorrhage in a neonate
- Plan the evaluation and management of a neonate with intracranial hemorrhage

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

Whitelaw A. Core concepts: Intraventricular hemorrhage. *NeoReviews*. 2011;12:e94–e101.

CASE 6 ANSWERS

1. D. All of the above

A newborn presenting at postnatal day 3 with poor feeding, hypothermia, jitteriness, followed by tachypnea, tachycardia, and extreme lethargy, prompts a vast differential diagnosis. There are two broad categories that initially should be considered:

- Disorders resulting from infection, cardiorespiratory compromise, congenital brain abnormalities, trauma (intracranial hemorrhage versus other), or toxins
- Disorders caused by an inborn error of metabolism (including carbohydrate disorders, protein abnormalities, organic acidemias, fatty acid abnormalities, lysosomal storage diseases, mitochondrial disorders)

Thus, all the studies listed in the options would be helpful initial tests to narrow the differential diagnosis.

The initial laboratory findings that may lead to a diagnosis of an inborn error of metabolism are acidosis and hyperammonemia. A mild increase in ammonia (typically <500 µM/L) may be seen in sepsis, perinatal asphyxia, or disseminated herpes simplex infection. A moderate increase in ammonia (>500 µM/L) may be seen in:

- Deficiencies of urea cycle enzymes
- Organic acidemias
- Lysinuric protein intolerance
- Hyperammonemia–hyperornithinemia–homocitrullinemia syndrome
- Transient hyperammonemia of the newborn
- Congenital hyperinsulinism with hyperammonemia

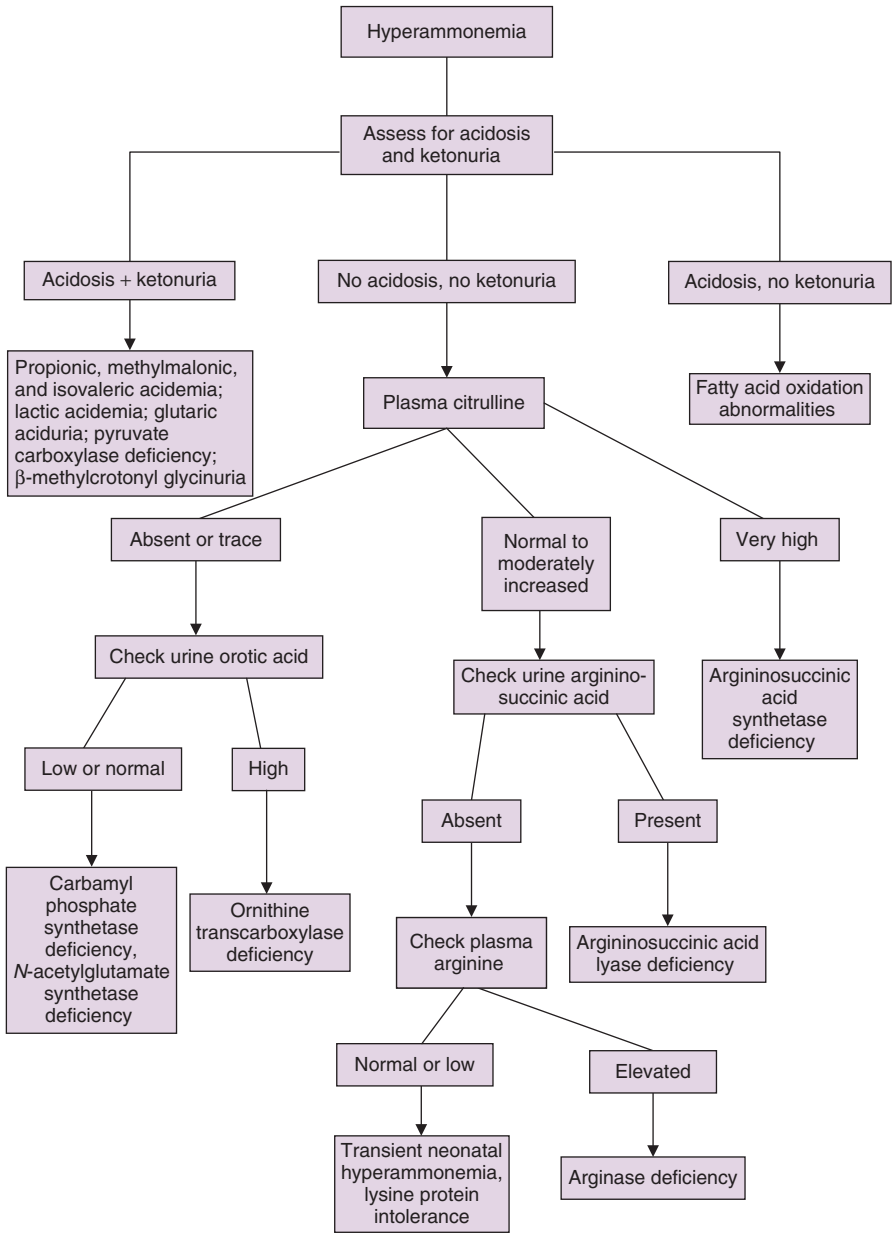


FIGURE 1. Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:420; Modified from: Ward JC. Inborn errors of metabolism of acute onset in infancy. *Pediatr in Rev*. 1990;11:210 and An Approach to Inborn Errors of Metabolism in the Neonate. Lecture by Korson M. Children's Hospital, Boston, MA. August 1990

See Figure 1 for the workup and steps to further delineate the etiology of hyperammonemia:

2. B. Neurologic sequelae and survival depend on the length of the hyperammonemic coma

Infants diagnosed with a urea cycle defect at a few days of life may succumb to their illness unless management is swift. Neurologic sequelae and survival depend on the length of the hyperammonemic coma. In infants with a duration of hyperammonemia coma that is <2 days, there is potential for minimal neurologic sequelae. Many infants who survive the newborn period have developmental delay, cognitive deficits, seizures, cortical atrophy, and spastic quadriparesis. Further morbidity or death may result from acute illness due to protein intake or infection.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Formulate a differential diagnosis of lethargy and coma in the neonate

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Enns G, Packman S. Diagnosing inborn errors of metabolism in the newborn: Clinical features. *NeoReviews*. 2001;2:e183–e191.
Joseph M, Hageman J. Neonatal transport: A 3-day-old neonate with hypothermia, respiratory distress, lethargy, and poor feeding. *J Perinat*. 2002;22:506–509.

SECTION V

Musculoskeletal System

CASE 1

Clubfoot

A 32-year-old pregnant woman has a benign prenatal course with a normal early risk assessment and 16-week fetal ultrasound. She delivers a full-term female infant with a left-sided foot abnormality. The infant's pediatrician is unable to manipulate the foot back to the midline position. A diagram of this infant's feet is shown in Figure 1.

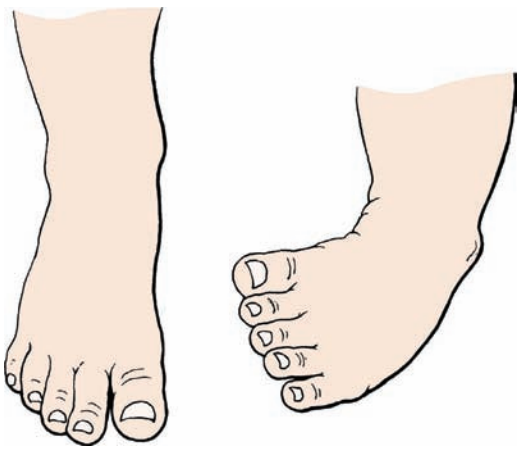


FIGURE 1. Courtesy of LifeArt © 2014 Lippincott Williams & Wilkins. All rights reserved

1. Of the following, the most likely structural abnormality in this newborn is:

   A. Talipes equinovarus
   B. Talipes equinus
   C. Talipes valgus
   D. Talipes varus

2. Of the following, the most likely classification for this infant's deformity is:

   A. Genetic
   B. Isolated
   C. Positional
   D. Syndromic

The pediatrician meets with the infant's family to discuss the management of clubfoot. A pediatric orthopedist is consulted, who suggests an intervention to prevent long-term disability, deformity, and pain.

3. Of the following, the most appropriate next best management for this infant is:

   A. Casting
   B. Observation
   C. Surgical correction
   D. All of the above

The family wants to discuss the likelihood of having a second child with a clubfoot. Neither parents had this abnormality.

4. Of the following, the recurrence risk that is most likely in this baby girl's future sibling is:

   A. 0%
   B. 2% to 5%
   C. 10%
   D. 15%

CASE 2

Developmental dysplasia of the hips

A pediatrician is rounding with a third-year medical student in the newborn nursery. This is the student's second day of his clinical rotation in the nursery. He expresses interest in learning more about the newborns' hip examination. The pediatrician and medical student review the perinatal histories and then examine the 15 neonates who are currently in the nursery.

Four newborns have a distinct perinatal history, as described below; all have a normal hip examination:

i. Female full-term infant with a history of breech position between 24 and 26 weeks' gestation but then changed to vertex position and was delivered vaginally
ii. Female infant born at 36 weeks' gestation by cesarean delivery because of breech presentation
iii. Male full-term infant born by cesarean delivery because of breech presentation
iv. Male infant who was born to a mother with developmental dysplasia of the hips (DDH)

1. Of the following, match the infant scenarios listed above (i–iv) with the most appropriate *next* management:

A. No actions required, routine newborn care
B. Obtain hip radiographs
C. Schedule hip ultrasonography at 4 to 6 weeks of age
D. Obtain a hip ultrasound and consult a pediatric orthopedist

Six newborns have specific physical examination findings:

v. Male infant with asymmetric thigh and posterior gluteal folds
vi. Male infant with disproportionate length of legs
vii. Female infant with bilateral hip clicks
viii. Female infant with unilateral hip clunk
ix. Male infant with bilateral hip clunks
x. Female infant with abnormal Barlow maneuver but normal Ortolani test

2. Of the following, match the infant scenarios listed above (v–x) with the most appropriate *next* management:

A. No actions required, routine newborn care
B. Obtain hip radiographs
C. Schedule hip ultrasonography at 4 to 6 weeks of age
D. Obtain a hip ultrasound and consult a pediatric orthopedist

The remaining five newborns have a benign perinatal history and a completely normal hip examination.

3. Which statement is true about the risk of DDH in the five remaining newborns?

A. If an orthopedist confirms that the hip examinations are normal, the infants have no risk of DDH.
B. It would be extremely rare that these infants later have a diagnosis of DDH.
C. Only the female infants need to be monitored for a potential risk of DDH.
D. The pediatricians will still need to monitor the infants' hip examinations because they are still at risk for DDH.

CASE 3

Torticollis

A full-term male infant is born by cesarean delivery because of breech presentation. The baby does well in the newborn nursery and is discharged after 2 days. At a routine appointment at 2 weeks of age, the pediatrician observes that the infant prefers to hold his head toward the right side. The pediatrician is able to move the infant's head to the left side without difficulty but movement toward the right side is restricted and seems to cause pain to the infant. The infant is pictured in Figure 1.

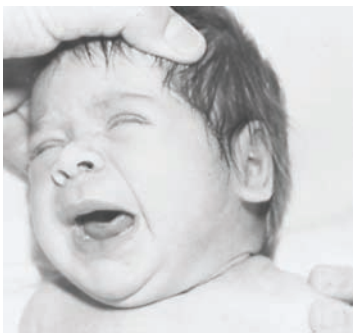


FIGURE 1. From Avery GB, Fletcher MA, MacDonald MG. *Neonatology: Pathophysiology and Management of the Newborn*, 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999. Figure 13.23

1. Of the following, the most likely cause of this infant's physical examination finding is injury to the right:

A. Clavicle
B. Facial nerve
C. Sternocleidomastoid muscle
D. Trapezius muscle

The pediatrician needs to determine if this infant's torticollis is congenital or acquired. He recalls that there are different reasons for acquired torticollis, including the following:

- Brachial plexus palsy
- Brain abnormalities, such as posterior fossa syndrome
- Cervical spinal abnormalities
- Craniosynostosis
- Klippel–Feil syndrome
- Ocular dysfunction

However, based on a complete physical examination of the infant, the pediatrician believes that this infant most likely has isolated congenital torticollis.

2. Of the following, the finding that is most consistent with congenital, instead of acquired, torticollis is:

   A. A low posterior hairline
   B. A palpable neck mass
   C. Microcephaly
   D. Strabismus

The pediatrician discusses management options with the infant's mother.

3. Of the following, the management that is most likely to be helpful in this infant is:

   A. Await spontaneous resolution (i.e., no treatment required)
   B. Passive stretching exercises
   C. Surgical removal of any neck mass
   D. Temporary stabilization of the neck

CASE 4

Contractures

A neurologist is asked to evaluate a full-term male infant who was born with contractures of all his extremities. A photograph of the infant is shown in Figure 1.

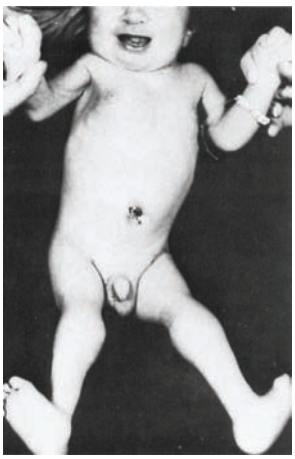


FIGURE 1. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 52.15

1. Of the following, the most accurate name for this infant's findings is:

   A. Achondrogenesis
   B. Achondroplasia
   C. Arthrochondritis
   D. Arthrogryposis

The neurologist meets with the infant's parents to obtain a detailed prenatal and family history.

2. Of the following, the intrauterine history that corresponds with this infant's findings is a(n):

   A. Abnormal maternal glucose tolerance test
   B. Decrease in fetal movements
   C. Low resting heart rate
   D. All of the above

The neurologist also discusses the possible causes of the infant's joint contractures.

3. An abnormality in which of the following organ systems can lead to joint contractures?

   A. Connective tissue
   B. Muscular system
   C. Neurologic system
   D. All of the above

CASE 5

Osteogenesis imperfecta

A full-term male newborn has the following radiograph (Figure 1) on the first day of life.

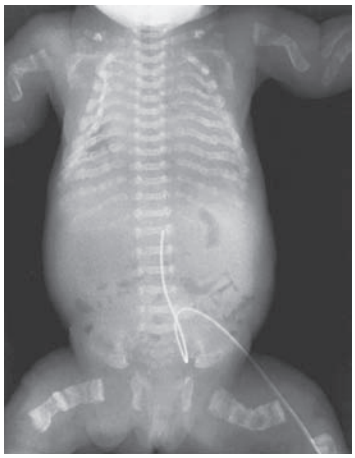


FIGURE 1. Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 6.11

1. Of the following, the abnormal findings that are consistent with osteogenesis imperfecta (OI) type II in this radiograph are:

   A. Deformed and crumpled femurs
   B. Diffuse osteoporosis
   C. Multiple rib fractures with callus formation
   D. All of the above

Indeed, OI type II had been diagnosed prenatally.

2. Of the following, the statement that is most consistent with OI type II is:

   A. Most affected newborns have deep blue sclerae
   B. OI type II has an X-linked recessive inheritance pattern
   C. The majority of affected patients survive to adulthood
   D. This disorder is caused by a mutation in the fibroblast growth factor receptor 3 gene

The neonatologist obtains a complete skeletal survey, with the skull film shown in Figure 2.

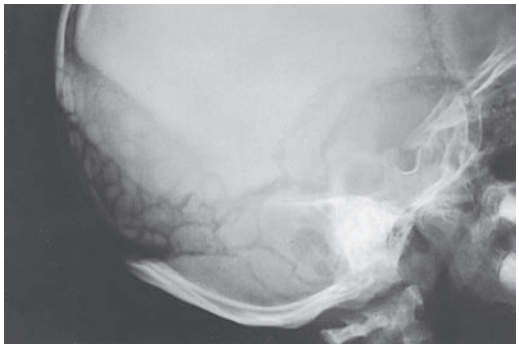


FIGURE 2. Courtesy of C.H. Quay, MD, Melbourne, Australia

3. Of the following, the finding that is exemplified in this radiograph is:

   A. Cloverleaf skull shape
   B. Craniosynostosis
   C. Widely split sutures
   D. Wormian bones

Genetic testing confirms that the neonate has OI type II. The neonatologist discusses the infant's prognosis with the family. The parents had been counseled about this likely diagnosis prenatally. However, because they have a distant relative with OI who is doing well at age 48, they are surprised by their infant's prognosis. They inform the neonatologist that their relative has OI type I evident by blue sclerae, several fractures during childhood but only two since puberty, easy bruisability, and hyperextensible joints.

4. Of the following, the most likely additional finding in this adult relative with type I OI is (are):

   A. Cataracts
   B. Early menopause
   C. Hearing loss
   D. Mitral valve prolapse

CASE 6

Achondroplasia

A geneticist is following several children with achondroplasia in her outpatient clinic. All of her patients have the same mutation in the fibroblast growth factor receptor 3 (*FGFR3*) gene. They also have similar clinical characteristics, including the following:

- Flat vertebrae with abnormally shaped pelvis
- Hearing loss
- Hypotonia during early infancy
- Macrocephaly
- Short limbs with relatively normal trunk length
- "Trident" hand shape with short, wide, and cone-shaped phalanges

1. Of the following, the skeletal dysplasia that is also caused by a mutation in the *FGFR3* gene and has similar clinical features as achondroplasia is:

   A. Achondrogenesis
   B. Hypochondrogenesis
   C. Osteogenesis imperfecta
   D. Thanatophoric dysplasia

Children with achondroplasia require frequent monitoring to assess for potential complications.

2. Of the following, the most likely potential complication of children with achondroplasia is:

   A. Cognitive disabilities
   B. Fractures
   C. Retinal detachment
   D. Spinal complications

None of the parents or siblings of the affected children whom the geneticist is following up has achondroplasia.

3. Of the following, the inheritance pattern that is associated with achondroplasia is:

   A. Autosomal dominant
   B. Autosomal recessive
   C. X-linked dominant
   D. X-linked recessive

CASE 7

Limited neck movements

A neonatologist is asked to evaluate a 6-hour-old full-term infant with limited neck movements. The neonatologist finds that the infant also has a low posterior hairline and a short neck.

1. Of the following, the most likely diagnosis in this infant is:

   A. Ellis–van Creveld syndrome
   B. Klippel–Feil syndrome
   C. Stickler syndrome
   D. Thanatophoric dysplasia

The neonatologist speaks with the family about the infant's likely diagnosis. Lateral flexion-extension radiographs of the infant's cervical spine reveal fused cervical vertebrae. Because of possible associated findings, the neonatologist recommends additional testing.

2. Of the following, the most likely associated finding in this infant is (are):

   A. Deafness
   B. Genitourinary abnormalities
   C. Structural heart defects
   D. All of the above

SECTION V
Answers

CASE 1 ANSWERS

1. A. *Talipes equinovarus*

The infant in this vignette has a left clubfoot, which is caused by abnormal bone formation that also involves the local muscles, nerves, tendons, and blood vessels. There are several structural abnormalities that can lead to a clubfoot, including:

- Talipes varus—the foot is turned inward, leading to the appearance of the leg and foot of the letter "J"
- Talipes valgus—the foot rotates outward, leading to the appearance of the letter "L"
- Talipes equinus—the foot points downward, similar to a ballerina's position
- Talipes calcaneus—the foot points upward with the heel pointing downward

The infant in this vignette has talipes equinovarus, the most common cause of clubfoot. In this deformity, the foot appears to be pointed downward (i.e., equinus) and inward (i.e., varus). Clubfoot can be unilateral or bilateral and involve a mild or severe deformity.

2. B. *Isolated*

Clubfoot can be classified into three types:

1. Isolated: the most common type (80%), often first identified after birth
2. Positional: caused by a fixed intrauterine position of the foot, often associated with a restricted uterine environment (e.g., uterine anomalies, oligohydramnios); this is not a "true" clubfoot because the foot is structurally normal
3. Syndromic or genetic: associated with other anomalies, usually attributable to a multifactorial etiology

While a positional clubfoot is flexible and can be moved back to midline easily, infants with an isolated or syndromic clubfoot have fixed abnormalities.

3. A. *Casting*

Even for mild deformities, all affected newborns require treatment. For neonates with isolated clubfoot, the ideal initial management is serial casting or splinting of the affected foot. This should be initiated within the first week of life with cast changes every few weeks for 2 to 3 months. Most infants will then require surgery with a tenotomy to release and lengthen the Achilles heel. Following, a bracing regimen is instituted for several years to minimize recurrence.

Conservative treatment with stretching exercises is recommended for infants with positional clubfoot.

4. B. *2% to 5%*

If an affected infant's parents did not have a clubfoot, as in this vignette, then the overall risk of an isolated clubfoot in the siblings depends on the sex of the affected child. If the affected child is male, the recurrence risk is 2%. If the affected child is female, the recurrence risk is 5%.

If an affected infant (without respect to gender) has a parent who had a clubfoot, the recurrence risk is ~3% to 4%. If both parents had a clubfoot, this risk increases to 15%. It is likely that a single gene is involved, but both autosomal recessive and X-linked recessive inheritance patterns have been described in affected families. Less commonly, variably penetrant autosomal dominant inheritance has also been observed.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that the most common component of clubfoot is equinovarus deformity
- Be aware that early treatment of clubfoot is critical
- Recognize that the treatment for talipes equinovarus is casting or splinting of the affected foot

SUGGESTED READING

Magriples U. Prenatal diagnosis of talipes equinovarus (clubfoot). UpToDate (Subscription required). http://www.uptodate.com/contents/prenatal-diagnosis-of-talipes-equinovarus-clubfoot. Accessed March 21, 2013.

CASE 2 ANSWERS

1. A. i, iii
B. none
C. ii, iv
D. none

When determining a newborn's risk for DDH, a pediatrician needs to assess the infant's perinatal history, observe the baby's movements at rest and with activity, and perform a hip examination. There are several easily identifiable risk factors for DDH, including:

- Extended breech positioning, particularly in late gestation
- Female infant (females have a 4- to 8-fold risk of DDH compared with males because of their increased sensitivity to maternal relaxin)
- Maternal hip dysplasia because genetic factors increase the offspring risk

In the setting of a normal hip examination, the recognition of these risk factors, such as the infants in scenario ii and scenario iv, should prompt a hip evaluation by ultrasonography at 4 to 6 weeks of age. Hip ultrasonography is preferred over radiographies because it is the most precise imaging modality to confirm the diagnosis of DDH in infants.

For the infant in scenario i with a short intrauterine period of breech positioning and for the male infant in scenario iii who was born breech, further actions are not required because these infants are at low risk for DDH.

2. A. vii
B. none
C. none
D. v, vi, viii, ix , x

An infant with DDH can have one or more abnormal physical examination findings, including:

- Asymmetry of the thigh and posterior gluteal folds
- Limited abduction of the affected hip
- Galeazzi test (also known as the Allis sign): with knee flexion, while the infant's feet are flat on a surface, the knee on the affected side appears lower

Thus, the infants in scenarios v and vi require a hip ultrasound and a pediatric orthopedist consult. These findings are shown in Figure 1. Figure 1A shows increased folds on the affected right side, Figure 1B shows limited abduction of the right leg, and Figure 1C shows a lower knee position of the affected left side.

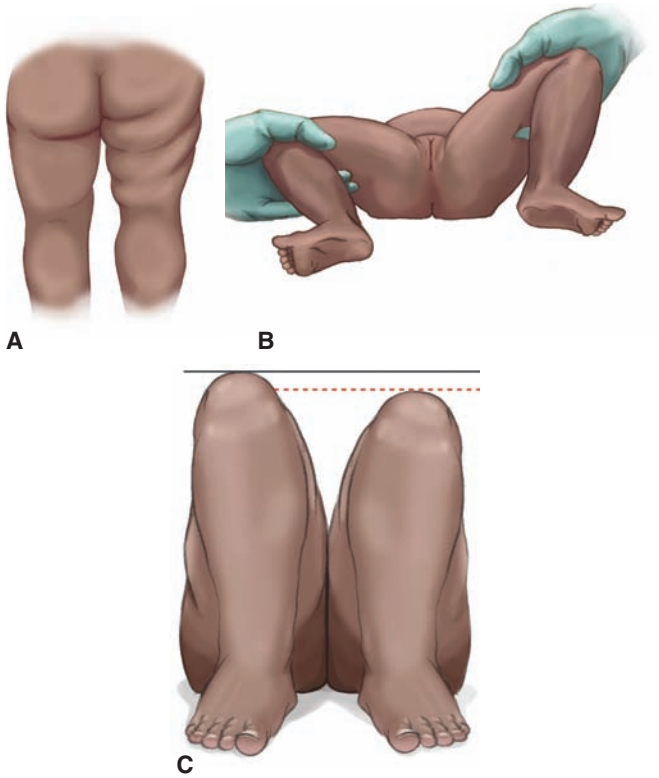


FIGURE 1ABC. Klossner NJ, Hatfield NT. *Introductory Maternity and Pediatric Nursing*. 2nd ed. Philadelphia , PA: Lippincott Williams & Wilkins; 2009. Figure 21.24AC

Finally, when the infant is in a supine position, the Ortolani and Barlow tests are helpful in the detection of DDH. In the *Barlow maneuver* (shown in Figure 2B), the clinician's fingers are placed over the greater trochanters and the hips and knees are flexed at 90 degrees. Following, a gentle backward pressure is applied while adducting the thighs. If the femoral head dislocates out of the acetabulum, the test is positive. In the *Ortolani test*, the clinician's fingers are placed on the infant's greater trochanters and the thumbs grip the femurs (shown in Figure 2A). While applying upward pressure over the trochanters, the thighs are abducted. If the femoral head is dislocated, this can be felt as a "clunk." Thus, the Barlow maneuver dislocates a dislocatable hip and the Ortolani test relocates a dislocated hip. Any male or female infant with a unilateral or bilateral positive Barlow and/or Ortolani test (e.g., scenarios viii, ix, and x) requires a hip ultrasound and a pediatric orthopedist consult.

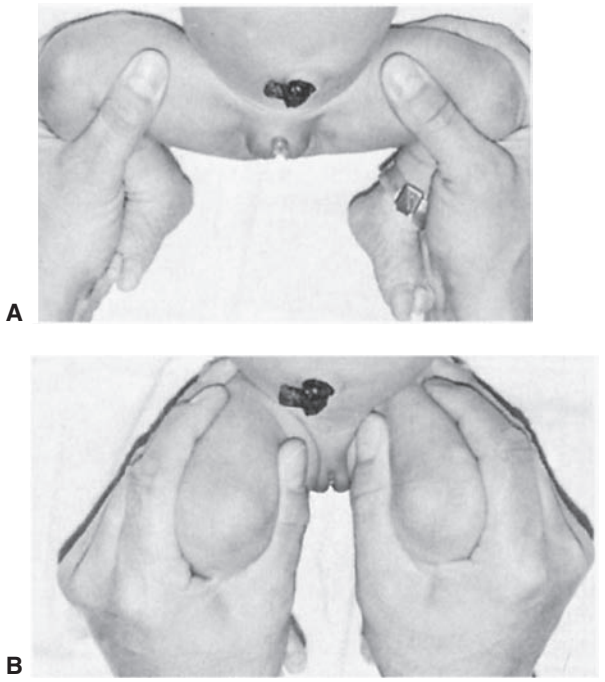


FIGURE 2AB. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 52.1AB

Isolated hip clicks are unlikely indicators of DDH, and without any other concerning signs for DDH, the infant in scenario vii should receive routine newborn care.

3. D. The pediatricians will still need to monitor the infants' hip examinations because they are still at risk for DDH.

The term "congenital hip dislocation" had previously been used to describe DDH. However, because neonates may not have any abnormal findings of hip dislocation initially, the term was changed to "developmental dysplasia of the hips." During newborn visits, pediatricians still need to monitor

the infants' hip examinations even if prior examinations were normal because the babies are still at risk for DDH.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that developmental dysplasia of the hips is more likely in girls and in infants who are born by breech presentation
- Know that ultrasonography is the most precise imaging modality for confirmation of the diagnosis of developmental dysplasia of the hip(s) in young infants
- Recognize asymmetry of the gluteal and thigh folds as a sign of possible subluxation of the hip
- Know that isolated hip clicks are unlikely indicators of dysplasia
- Know that initially there may be no abnormal signs of subluxation of the hip in developmental dysplasia of the hip(s)

SUGGESTED READING

Wilkinson AG, Wilkinson S. Neonatal hip dysplasia: A new perspective. *NeoReviews*. 2010;11:e349–e362.

CASE 3 ANSWERS

1. C. Sternocleidomastoid muscle

The infant described in this vignette most likely has congenital muscular torticollis. Although the precise etiology is unknown, most affected infants have an injury to and shortening of the sternocleidomastoid muscle.

2. B. A palpable neck mass

The diagnosis of congenital torticollis can usually be made clinically. Infants typically present in the first 2 to 4 weeks of age with head tilting to the affected side. A characteristic circumscribed and firm mass may be palpable in the inferior part of the affected sternocleidomastoid muscle. Radiographs of the cervical spine may be helpful to assess for C1-C2 subluxation and other bone abnormalities. In addition, an ultrasound of the neck mass may be helpful to confirm that it is part of the muscle.

A low posterior hairline with a short neck is found in infants with Klippel–Feil syndrome. Microcephaly is not associated with torticollis. Strabismus may contribute to the development of acquired torticollis.

3. B. Passive stretching exercises

Infants with congenital torticollis can be treated by conservative therapy with passive and active stretching therapy. It is ideal if passive stretching is initiated prior to 1 month of age. Parents are taught specific exercises to attempt to stretch the shortened sternocleidomastoid muscle. In addition, environmental therapy, such as placing visual effects on the side of the torticollis, will help encourage infants to rotate their head in that direction. A physical therapist may also be involved in monitoring an infant's progress. After 6 months of age, additional active stretching movements are recommended. If children continue to have limited neck motion, severe plagiocephaly, or facial asymmetry beyond 6 to 12 months of age, surgical intervention may be warranted.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Understand the etiology of congenital torticollis
- Recognize that the differential diagnosis of torticollis includes head tilt secondary to malformation of the cervical spine, a visual disturbance, and a posterior fossa tumor
- Differentiate between congenital and acquired torticollis
- Understand that physical therapy (stretching) of the neck by a pediatric physical therapist and/or a parent may be successful treatment for torticollis

SUGGESTED READING

Macias CG, Gan V. Congenital muscular torticollis. UpToDate (Subscription required). http://www.uptodate.com/contents/congenital-muscular-torticollis. Accessed March 18, 2013.

CASE 4 ANSWERS

1. D. Arthrogryposis

The infant described in this vignette has contractures of his joints, known as arthrogryposis. This term describes joints (i.e., arthro) that are curved or hooked (i.e., gryposis).

Achondrogenesis is an autosomal dominant skeletal dysplasia associated with short limbs caused by a defect in type II collagen.

Achondroplasia is an autosomal dominant skeletal dysplasia leading to abnormal formation of cartilaginous tissues with short limbs. It is caused by a mutation in the fibroblast growth factor receptor 3 gene.

Arthrochondritis is an inflammation of articular cartilage; this condition is not typically found in newborns.

2. B. Decrease in fetal movements

The prenatal history of an infant with arthrogryposis may identify one or more of the following:

- Abnormal amniotic fluid volume—polyhydramnios or oligohydramnios
- Infants with a neurologic abnormality may have joint contractures because of lack of fetal movements. These infants may also have associated polyhydramnios because of decreased fetal swallowing as a result of abnormal neurologic function. In contrast, infants with severe oligohydramnios may develop joint contractures as a result of fetal crowding.

- Decreased fetal movements
- Intrauterine breech positioning

The maternal glucose tolerance test and fetal resting heart rate will be unaffected in infants with arthrogryposis.

3. D. All of the above

Joint contractures in a fetus can be caused by *intrinsic* fetal abnormalities in the fetal neurologic, muscular, or connective tissue systems. A neurologic problem is the most common cause of arthrogryposis. Potential neurologic abnormalities include meningomyelocele, motor horn cell deficiency, and structural brain abnormalities, such as anencephaly, hydranencephaly, and holoprosencephaly. Muscular abnormalities, such as muscle agenesis, myopathy, and myotonic dystrophy, can also lead to arthrogryposis. A fetus with a significant connective tissue disorder (e.g., synostosis, lack of joint development, abnormal fixation of joints) is at increased risk for developing arthrogryposis. All of these abnormalities can lead to decreased intrauterine joint mobility resulting in joint fixations.

In addition to intrinsic fetal abnormalities, arthrogryposis can occur because of an *extrinsic* etiology leading to fetal crowding or constraint. Examples of these external/environmental causes are:

- Multiple births
- Severe oligohydramnios as a result of renal agenesis or early persistent amniotic fluid leakage; affected infants may have a Potter facies with abnormal ear lobation, micrognathia, flattened nose, and infraorbital folds

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize the clinical features of arthrogryposis

SUGGESTED READINGS

Jones K. *Smith's Recognizable Patterns of Human Malformation*. 6th ed. Philadelphia, PA: Saunders; 2006.
Swarr DT, Sutton VR. Skeletal dysplasias in the newborn: Diagnostic evaluation and development genetics. *NeoReviews*. 2010;11:e290–e305.

CASE 5 ANSWERS

1. D. All of the above

The abnormal findings that are evident in this radiograph are:

- Deformed and crumpled femurs and humeri
- Diffuse osteoporosis
- Multiple rib fractures with callus formation leading to a beaded or wavy rib appearance
- Short ribs and long bones

These radiographic findings are consistent with OI. OI is a heterogeneous disorder of increased bone fragility that is categorized into nine types.

2. A. Most affected newborns have deep blue sclerae

Type II is the most severe form of OI with a high intrauterine mortality or death in early infancy as a result of respiratory failure. Affected infants have short broad long bones, short limbs, multiple fractures, and deep blue sclerae. The skull is often poorly mineralized with a soft calvarium and large fontanels. This type of OI typically has an autosomal dominant inheritance pattern (although some rare subtypes have an autosomal recessive inheritance pattern) and is usually caused by an abnormality in type I collagen genes.

3. D. Wormian bones

This skull film demonstrates multiple Wormian bones, which are small bony fragments along a suture line. As shown in this radiograph, these bones are often observed along the lambdoid suture. Wormian bones can be found as a normal variant or in infants with OI or cleidocranial dysplasia.

4. C. Hearing loss

Even though OI types I and II are both autosomal dominant disorders that impact the same collagen gene, patients have different clinical manifestations. This occurs because type I OI is caused by a quantitative defect in the type I collagen genes (*COL1A1* or *COL1A2*), while type II OI results from a qualitative defect of the same genes. While OI type 2 is associated with a poor prognosis, patients with OI type 1 have an excellent prognosis. Individuals with type I OI have blue sclerae, Wormian skull bones, a normal stature, hyperextensibility, and infrequent fractures that often decrease after puberty. Approximately 50% of affected patients have adult-onset hearing loss as a result of osteosclerosis.

There are a total of nine types of OI. Type I is the mildest form; type II is the most severe form; types III through IX lead to moderate or severe bone fragility. All types have an autosomal dominant or recessive pattern of inheritance.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the clinical features of osteogenesis imperfecta
- Recognize the association of deafness with osteogenesis imperfecta

SUGGESTED READINGS

Jones K. *Smith's Recognizable Patterns of Human Malformation*. 6th ed. Philadelphia, PA: Saunders; 2006.
Swarr DT, Sutton VR. Skeletal dysplasias in the newborn: Diagnostic evaluation and development genetics. *NeoReviews*. 2010;11:e290–e305.

CASE 6 ANSWERS

1. D. Thanatophoric dysplasia

Mutations in the *FGFR3* gene can cause three different types of skeletal dysplasias:

1. Thanatophoric dysplasia
2. Achondroplasia
3. Hypochondroplasia

The most significant difference between these disorders is the severity of the dysplasia. Infants with thanatophoric dysplasia have a high mortality rate in the first few days of life because of respiratory failure from pulmonary hypoplasia. In contrast, infants with achondroplasia have an excellent prognosis and typically survive into adulthood. In both of these disorders, affected infants have a large head and short limbs with a normal-sized trunk. Hypochondroplasia is the mildest of the three dysplasias, with onset during the second decade of life.

Achondrogenesis and hypochondrogenesis are collagen disorders with mutations in the type 2 collagen gene (*COL2A1*). Affected infants have abnormalities of the spine and epiphyses of the long bones. The vast majority (90%) of infants with osteogenesis imperfecta have a mutation in a gene for type I collagen (either *COL1A1* or *COL1A2*), which leads to an increase in bone fragility.

2. D. Spinal complications

Approximately 46% of patients with achondroplasia have spinal complications, and close follow-up by an orthopedist and neurologist is important. While almost all children with achondroplasia have a small foramen magnum, brainstem or upper cervical cord compression leading to respiratory failure and sudden death occurs rarely.

Although affected children can have speech delay, their cognitive abilities are typically normal. While bone compression can occur in children with achondroplasia, osteoarthritis and fractures are not commonly found. Children with achondroplasia may have short eustachian tubes, resulting in middle-ear infections and conductive hearing loss. However, their vision is normal without risk for retinal detachment.

3. A. Autosomal dominant

Achondroplasia has an autosomal dominant inheritance pattern. However, parents and siblings are not usually affected because 90% of cases are caused by new mutations.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical features and complications of achondroplasia
- Recognize the inheritance pattern of achondroplasia

SUGGESTED READINGS

Jones K. *Smith's Recognizable Patterns of Human Malformation*. 6th ed. Philadelphia, PA: Saunders; 2006.

Swarr DT, Sutton VR. Skeletal dysplasias in the newborn: Diagnostic evaluation and development genetics. *NeoReviews*. 2010;11:e290–e305.

CASE 7 ANSWERS

1. B. Klippel–Feil syndrome

The infant described in this vignette has the classic clinical triad of Klippel–Feil syndrome:

- Low hairline
- Short neck
- Limited neck movements

These symptoms are attributable to fused cervical vertebrae. Klippel–Feil syndrome is also commonly associated with other skeletal abnormalities, with more than half of affected children having scoliosis.

Ellis–van Creveld syndrome, also known as chondroectodermal dysplasia, is associated with skeletal abnormalities, such as a narrow thorax, polydactyly, and fused metacarpals or phalanges. In addition, affected individuals can have pelvic dysplasia, gingival frenulum, congenital heart defects, hypoplastic nails, and dental abnormalities.

Infants with Stickler syndrome typically have midfacial hypoplasia, micrognathia, joint hypermobility, cleft palate, sensorineural hearing loss, and ophthalmologic abnormalities.

Infants with thanatophoric dysplasia typically have the following clinical features:

- Central nervous system malformations (e.g., megalencephaly, neuronal migration disorders)
- Depressed nasal bridge with a prominent forehead
- Narrow thorax, often associated with pulmonary hypoplasia
- Very short extremities with a normal trunk length

The infant in Figure 1 has thanatophoric dysplasia, evident by frontal bossing and short limbs and fingers.

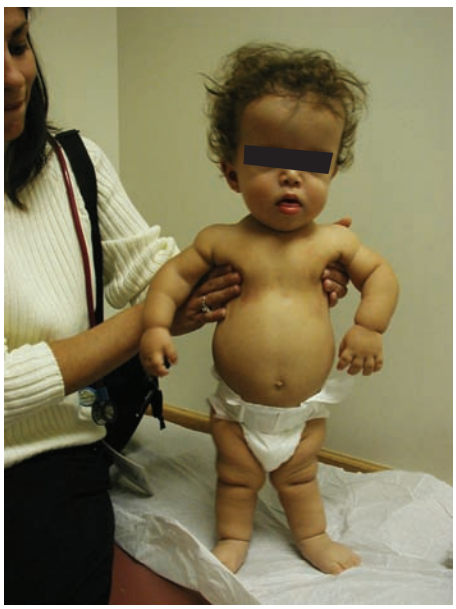


FIGURE 1. Courtesy of Paul S. Matz, MD

Infants with thanatophoric dysplasia type II have a characteristic "cloverleaf" skull deformity, shown in Figure 2.

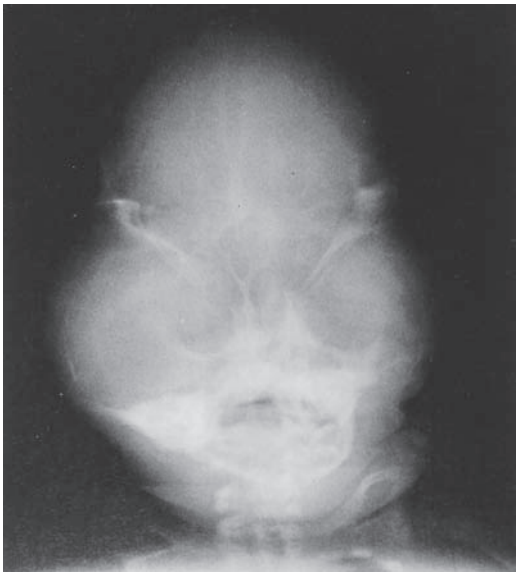


FIGURE 2. Reprinted with permission from: Stevenson RE, Hall JG, Goodman RM (eds). *Human Malformations and Related Anomalies*. New York, NY: Oxford University Press;1993

2. D. All of the above

Approximately 30% of infants with Klippel–Feil syndrome also have conductive or neural deafness. Affected infants can have congenital heart defects, with ventricular septal defect being the most common. Genitourinary abnormalities are also found in infants with Klippel–Feil syndrome. The most common renal abnormalities include renal agenesis, renal ectopia, or a pelvic kidney.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Know the clinical and radiologic features of Klippel–Feil syndrome congenital abnormalities

SUGGESTED READINGS

Jones K. *Smith's Recognizable Patterns of Human Malformation*. 6th ed. Philadelphia, PA: Saunders; 2006.

Swarr DT, Sutton VR. Skeletal dysplasias in the newborn: Diagnostic evaluation and development genetics. *NeoReviews*. 2010;11:e290–e305.

SECTION VI

Genetics

CASE 1

Postnatal genetic testing

A 40-year-old gravida 6 para 0 woman is currently pregnant at 12 weeks' gestation. Her past medical history is complicated by five spontaneous abortions with one fetus with a postmortem diagnosis of Turner syndrome. The prenatal fetal ultrasound for this pregnancy is concerning for a thickened nuchal fold. The parents have declined prenatal testing. Six months later, a male infant is born at term, and his examination reveals dysmorphic features.

1. Which of the following gene defects could be diagnosed via fluorescent in situ hybridization (FISH) to provide the family with information as soon as possible?

   A. 22q11 deletion
   B. Down syndrome
   C. Trisomy 18 syndrome
   D. All of the above

The infant's clinical features are not consistent with any of the common gene defects, and the FISH results are normal. Further testing will need to be done. The consulting geneticist recommends sending comparative genomic hybridization (CGH).

2. Which of the following statements is true regarding CGH?

   A. CGH has replaced high-resolution chromosomal analysis.
   B. CGH is inexpensive.
   C. CGH is less likely than karyotype analysis to provide a genetic diagnosis.
   D. CGH only detects large deletions.

CASE 2

Inheritance patterns

A 42-year-old woman is pregnant. Her family history is reviewed and is significant for a maternal uncle with Marfan syndrome, a paternal aunt with cystic fibrosis, and a cousin with intellectual disability. To understand the implications to the fetus, you need to review the inheritance patterns in the woman's family.

1. Match the inheritance pattern (A–D) with the descriptions below:

   A. Autosomal dominant
   B. Autosomal recessive
   C. X-linked dominant
   D. X-linked recessive

   i. An affected father will transmit the carrier state to his daughters but cannot transmit the disease or carrier state to his sons
   ii. An affected female has a 50% chance of passing the disease to her sons or daughters
   iii. If both parents are affected, recurrence risk is 75%
   iv. If both parents are affected, recurrence risk is 100%

The pregnant woman signs a medical release form so that you can obtain and review records from a genetics consultation she had 3 years ago after recurrent pregnancy losses and one fetus with a postmortem diagnosis of Turner syndrome. You also learn that her cousin with intellectual disability was diagnosed with fragile X syndrome and her father had hemophilia.

The medical records include the pedigree charts (Figure 1A–D).

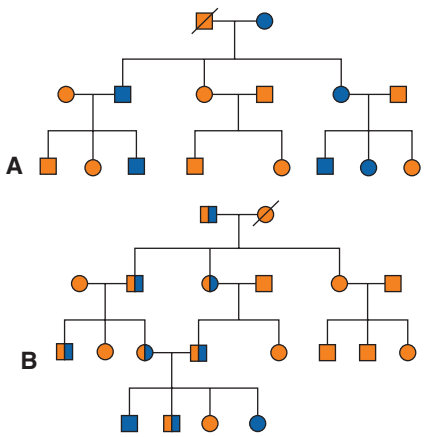


FIGURE 1. **A–C:** From Topol EJ, Califf RM, et al. *Textbook of Cardiovascular Medicine*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. **D:** Courtesy of Genica Pharmaceuticals Corporation, Worcester, MA

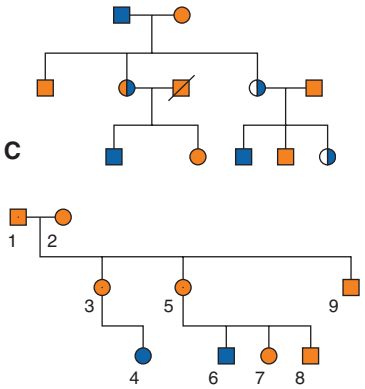


FIGURE 1. **A–D:** (*Continued*)

2. Match the potential inheritance patterns indicated by the pedigree charts (Figures 1A-D) to the diseases listed below. The inheritance patterns can be used more than once or not at all:

   i. Cystic fibrosis
   ii. Fragile X syndrome
   iii. Hemophilia B
   iv. Marfan syndrome

CASE 3

Autosomal trisomy syndromes

A full-term male infant is born via spontaneous vaginal delivery to a 27-year-old primigravida woman. Her pregnancy was unremarkable, and she declined prenatal testing. As the pediatric resident covering the delivery room, you are called to evaluate the infant shortly after birth because of a concern for dysmorphic features. On your examination, you find that the baby has features consistent with trisomy 21 syndrome.

1. Match the trisomy (A–C) with the descriptions (i through iv) below. Of note, i, ii, iii, or iv may be used more than once:

A. Trisomy 13 (Patau syndrome)	i. Duodenal atresia, increased risk of Hirschsprung disease
B. Trisomy 18 (Edward syndrome)	ii. Hypoplastic nails, clenched hand, overlapping of second finger over third finger or fifth finger over fourth finger, rocker-bottom feet, micrognathia, small mouth, malformed low-set ears, occipital prominence
C. Trisomy 21 (Down syndrome)	iii. Transverse palmar crease, cutis aplasia, polydactyly, cleft lip/palate, colobomas, narrow hyperconvex fingernails
	iv. Transverse palmar crease; flat facies; upslanting palpebral fissures; wide gap between first and second toes; broad, short hands and feet; inner epicanthal folds; large protruding tongue; nuchal redundancy; hypotonia

2. Match the trisomy (A–C) with the most commonly associated cardiac lesion (i through iv). Of note, i, ii, iii, or iv may be used more than once:

A. Trisomy 13 (Patau syndrome)	i. Endocardial cushion defect, ventricular septal defect (VSD), patent ductus arteriosus (PDA), cardiac anomalies seen in 40% to 50% of patients
B. Trisomy 18 (Edward syndrome)	ii. Mitral valve prolapse, aortic regurgitation, anomalous subclavian artery
C. Trisomy 21 (Down syndrome)	iii. VSD, PDA, bicuspid aortic valve, pulmonary stenosis, coarctation of the aorta, tetralogy of Fallot, cardiac anomalies seen in 95% to 99% of patients
	iv. VSD, PDA, cardiac anomalies seen in 80% to 90% of patients

The infant's karyotype is shown in Figure 1.

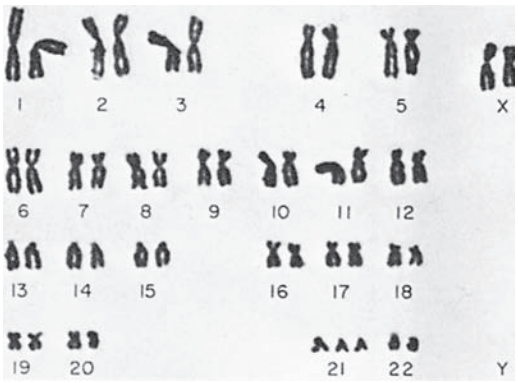


FIGURE 1. Klossner NJ, Hatfield NT. *Introductory Maternity and Pediatric Nursing*. 2nd ed. Philadephia, PA: Lippincott Williams & Wilkins; 2009. Figure 21.27

He has a VSD but otherwise is doing well, tolerating feedings and has a normal stooling pattern. He is at risk for several medical problems.

3. Match the clinical finding that can be observed in infants with this diagnosis with the corresponding incidence. Of note, i, ii, iii, and iv may be used more than once or not at all:

A. Atlantoaxial subluxation with spinal cord compression	i. 1%
B. Early Alzheimer disease by 60 years of age	ii. 2% to 5%
C. Hearing loss (associated chronic otitis media effusions or sensorineural)	iii. 70% to 75%
D. Hypothyroidism	iv. 100%

The parents ask about future pregnancies and whether they have an increased risk of having another child with Down syndrome. You recall that the mother and father are 27 and 29 years old, respectively.

4. Select the true statement(s) below about recurrence risk and trisomy 21 syndrome:

   A. Fifty percent of new diagnoses are sporadic.
   B. Three percent to 4% result from an unbalanced translocation between chromosome 21 and another acrocentric chromosome, usually chromosome 14.
   C. If both parents have normal karyotypes, recurrence risk is 10%.
   D. Recurrence risk is higher in a 45-year-old woman than for a 25-year-old woman with a balanced translocation.

CASE 4

Turner syndrome

A 33-year-old pregnant woman has a finding of a cystic hygroma observed by fetal ultrasonography at 16 weeks' gestation. A fetal ultrasound at 35 weeks' gestation shows that the hygroma is decreasing in size. Fetal echocardiography is unremarkable. The woman declines any invasive testing. She delivers a full-term female infant with dysmorphic features that are suggestive of Turner syndrome.

1. Select the collection of clinical findings that are most consistent with Turner syndrome:

   A. Coloboma, genital hypoplasia, ear anomalies, murmur, microcephaly, anal atresia
   B. Edema of hands and feet, short stature, broad chest with wide-spaced nipples, webbed neck, low posterior hairline
   C. Micrognathia, glossoptosis, cleft palate
   D. Short/webbed neck, low posterior hairline, hypertelorism, low-set ears, low nasal bridge, pectus excavatum, ptosis

The infant in the vignette has an evaluation that includes echocardiography, a renal ultrasound, and a genitourinary ultrasound. The parents ask about their daughter's ability to have children in the future.

2. Select the correct statement about fertility in a patient with Turner syndrome:

   A. Gonadal dysgenesis is universal in patients with Turner syndrome; about 50% will bear children.
   B. Gonadal dysgenesis is universal in patients with Turner syndrome; however, fertility is unaffected.
   C. Gonadal dysgenesis is universal in patients with Turner syndrome; infertility is most likely.
   D. None of the above.

The pediatrician meets with the family to describe the physical features and relay the presumptive diagnosis of Turner syndrome. He tells them that a definitive diagnosis of Turner syndrome requires chromosomal analysis.

3. Select the karyotype below that would be mostly likely in this vignette:

A. Figure 1
B. Figure 2
C. Figure 3
D. Figure 4

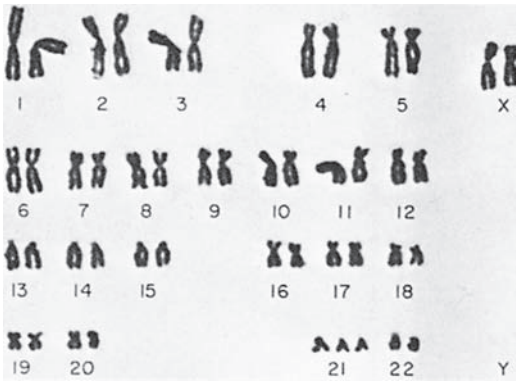


FIGURE 1. Klossner NJ, Hatfield NT. *Introductory Maternity and Pediatric Nursing*. 2nd ed. Philadephia, PA: Lippincott Williams & Wilkins; 2009. Figure 21.27

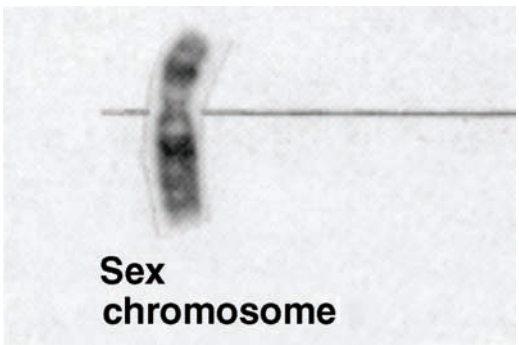


FIGURE 2. From Beckmann CRB, Ling FW, Laube DW, et al. *Obstetrics and Gynecology*. 4th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2002

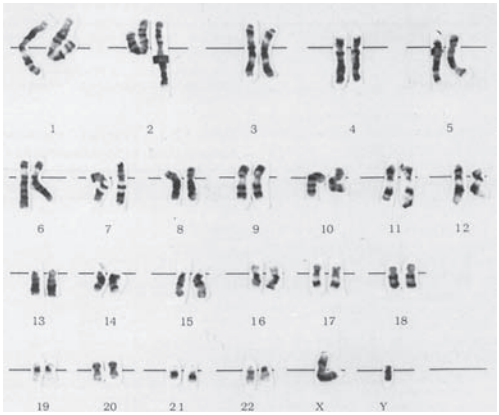


FIGURE 3. Scott JR, Gibbs RS, Karlan BY, et al. *Danforth's Obstetrics and Gynecology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 6.03

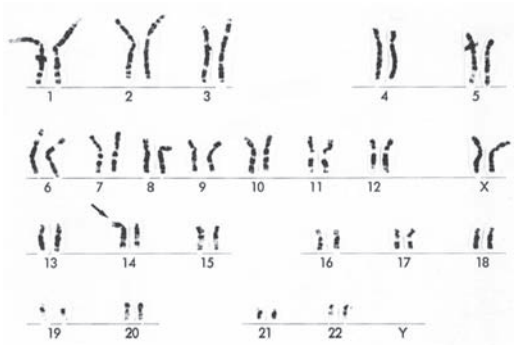


FIGURE 4. Reprinted with permission from Gelehrter TD, Collins FS, Ginsburg D. *Principles of Medical Genetics*. 2nd ed. Baltimore, MD: Lippincott Williams & Wilkins; 1998:166. Figure 1.6B

4. Select the therapy that is recommended in patients with Turner syndrome as soon as their height falls below the fifth percentile:

A. Androgen
B. Estrogen
C. Growth hormone
D. No therapy should be initiated

CASE 5

Syndromes of tall stature

A 45-year-old woman delivers a full-term nondysmorphic, average-weight male infant via cesarean for failure to progress. The infant does well throughout the neonatal period and early childhood. By age 6, he is diagnosed with autism. By age 15, he is significantly taller than anyone in his class and the class above his. His mother and father are average height. At his next pediatrician appointment, his physician notes his growth velocity and detects small testes by physical examination.

1. Select the syndrome below that would be most consistent with the presentation above:

A. Ehlers–Danlos syndrome
B. Klinefelter syndrome
C. Marfan syndrome
D. None of the above

CASE 6

Genetic associations

A 27-year-old primigravida woman from Korea presents to Labor and Delivery with a cervical dilation of 8 cm. All of her prenatal care has been in Korea. She tells the obstetrician on call that her pregnancy was uncomplicated except for intrauterine growth restriction. The neonatologist is called to attend the delivery. The infant is born with multiple congenital anomalies, including a cardiac defect and renal/genitourinary anomalies.

1. Select the syndrome(s)/association that would most likely fit this description:

   A. Alagille syndrome and VACTERL association
   B. CHARGE syndrome and VACTERL association
   C. Holt–Oram syndrome and CHARGE syndrome
   D. None of the above

Further workup and examination of the infant reveal hemivertebrae, anal atresia, single umbilical artery, dysplastic kidneys, and thumb hypoplasia.

2. Select whether the infant's diagnosis is consistent with a syndrome or an association and the corresponding likely neurological outcome and recurrence risk:

   A. Association, as there is currently no known genetic cause; it is not associated with developmental disabilities; there is a low recurrence risk.
   B. Syndrome, as it represents a pattern of congenital anomalies with a known genetic cause; it is often associated with developmental disabilities; there is a significant recurrence risk.
   C. Both A and B
   D. None of the above

CASE 7

Deletion syndromes

A 39-year-old gravida 6 para 0 woman pregnant with twins presents with spontaneous rupture of membranes at 35 weeks' gestation. The twins are delivered via cesarean because of breech presentation in the presenting twin. The mother's medical history is significant for infertility, and this pregnancy had been conceived by in vitro fertilization. One of the twins (twin A) has hypotonia, almond-shaped palpebral fissures, and undescended testes. Although his twin brother (twin B) currently has no stigmata of a syndrome, each twin has a distinct syndrome. One has a microdeletion of maternal origin, while the other has a microdeletion of paternal origin.

1. Explain the most plausible etiology for the syndromes in the vignette above by completing the following sentence: The two distinct syndromes may represent:

   A. Autosomal dominant inheritance
   B. Contiguous gene syndromes
   C. Single-gene defects
   D. None of the above

2. Select the syndrome (A–D) with the pictures below. Each syndrome can be used only once:

   A. Angelman syndrome
   B. Beckwith–Wiedemann syndrome
   C. DiGeorge syndrome
   D. Prader–Willi syndrome

   i. Figure 1
   ii. Figure 2
   iii. Figure 3
   iv. Figure 4

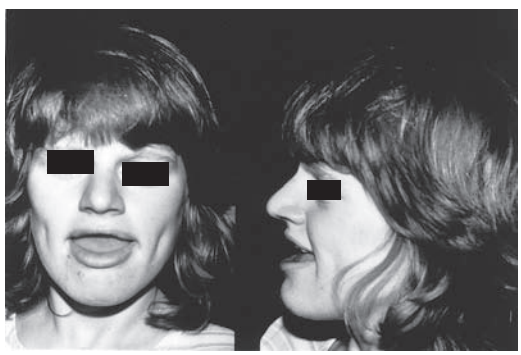


FIGURE 1. Courtesy of Gorlin RJ. Department of Oral Pathology and Genetics, University of Minnesota

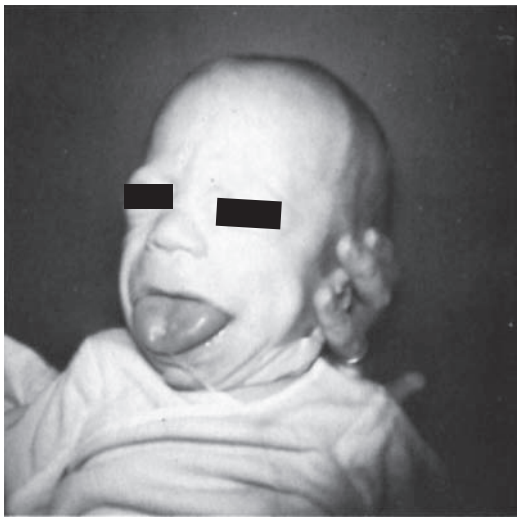


FIGURE 2. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 38.13

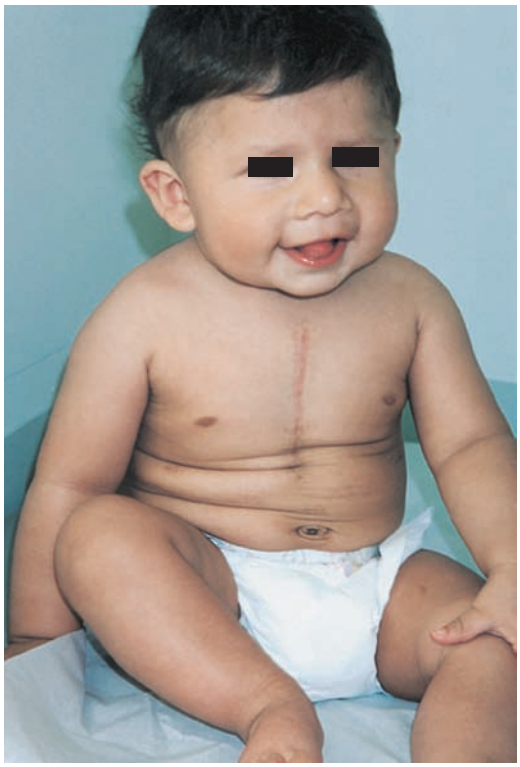


FIGURE 3. From Roberts R. *Atlas of Infectious Diseases*. Mandell G (series ed.), Wilfert CM, ed. Philadelphia, PA: Current Medicine, Inc; 1998. *Pediatric Infectious Diseases*, vol 11

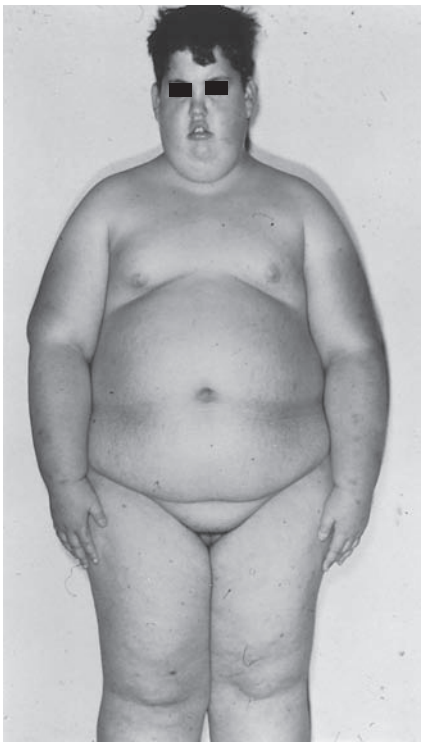


FIGURE 4. Courtesy of Gorlin RJ. Department of Oral Pathology and Genetics, University of Minesota

3. Match the syndrome (A–D) with an appropriate management. All cases will require genetics consultation and close follow-up. Each syndrome can be used only once:

A. Angelman syndrome	i. Monitor for delayed developmental milestones and risk for seizure
B. Beckwith–Wiedemann syndrome	ii. Monitor for hypocalcemia
C. DiGeorge syndrome	iii. Monitor for hypoglycemia
D. Prader–Willi syndrome	iv. Monitor for risk of failure to thrive in infancy

The twins were diagnosed with Prader–Willi syndrome (twin A) and Angelman syndrome (twin B), as represented by Figure 5 on the next page. This Southern blot analysis shows that the patient with Prader–Willi syndrome has a 6.0-kb fragment from the mother but lacks the 4.4-kb fragment from the father. This results from either a deletion on the paternal chromosome 15 or maternal uniparenteral disomy. In contrast, the patient with Angelman syndrome has a 4.4-kb fragment from the father but lacks the maternal 6.0-kb fragment. This results from either a deletion on the maternal chromosome 15 or a paternal uniparental disomy (see Figure 5).

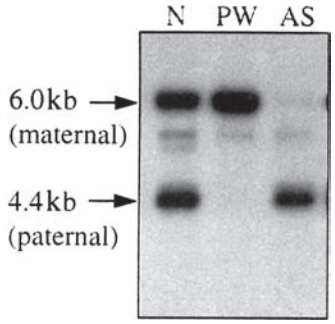


FIGURE 5. From Schad CR, Jalal SM, Thibodeau SN. Genetic testing for Prader–Willi and Angelman syndromes. *Mayo Clin Proc.* 1995;70:1195–1196, with permission

The nurse caring for the twins assists with a blood draw for an infant in the adjacent bed space. She notices that the infant is markedly jittery and has dysmorphic facial features consisting of hypertelorism, short palpebral fissures, a small mouth, and a prominent nose with a square nasal root and narrow alar base. The infant's ionized calcium result is 0.69 mmol/L.

4. Select the genetic syndrome that best fits the description above:

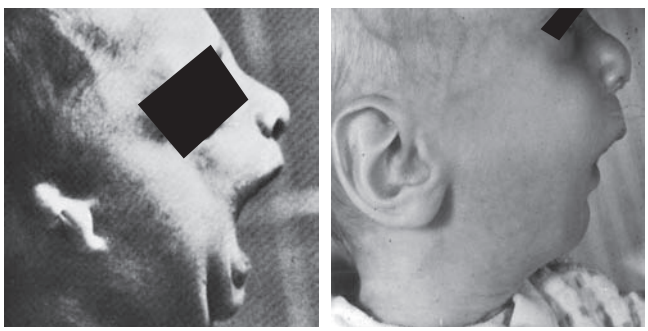
   A. Angelman syndrome
   B. Beckwith–Wiedemann syndrome
   C. DiGeorge syndrome
   D. Prader–Willi syndrome

CASE 8

Treacher Collins syndrome and Pierre–Robin sequence

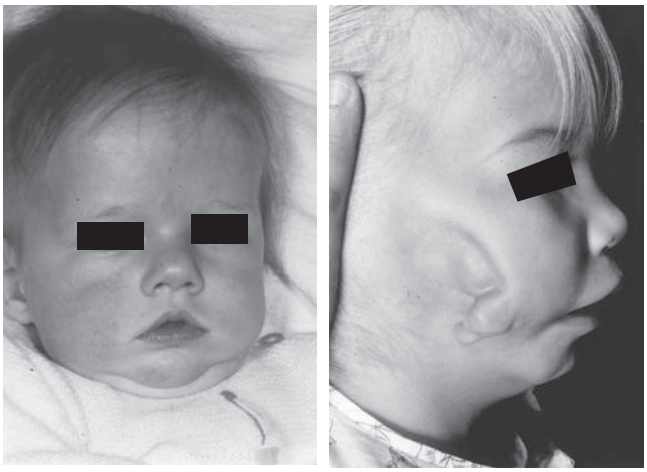
An 18-year-old gravida 1 para 0 woman presents in active labor at term gestational age. The fetal heart rate tracing is reassuring, but there is meconium-stained amniotic fluid. The neonatologist is present at the delivery. Intubation is attempted, following the Neonatal Resuscitation Program guidelines for an infant born floppy, without respiratory effort, in the presence of meconium-stained amniotic fluid. The intubation attempt is unsuccessful likely because of the infant's physical findings of micrognathia, glossoptosis, and a U-shaped cleft palate. The infant begins to cry vigorously at 40 seconds of life, and routine care is resumed.

1. Of the craniofacial defects shown (Figure 1A–D), select the defect that is thought to result from hypoplasia of the mandible, occurring before the ninth week of development:



A B

FIGURE 1. A: Courtesy of Warkany J. Reprinted with permission from Warkany J. *Congenital Malformations*. Chicago, IL: Yearbook publishers; 1971. B–D: Courtesy of Gorlin RJ. Department of Oral Pathology and Genetics, University of Minnesota



C D

FIGURE 1. (*Continued*)

2. Match the photographs (Figure 1A–D) with the corresponding syndromes (i–iv):

   i. DiGeorge syndrome ____
   ii. Goldenhar syndrome ____
   iii. Pierre–Robin sequence ____
   iv. Treacher Collins syndrome ____

3. Select the true statement(s) below regarding the infants in photographs A and B above:

   A. One is a sequence and one is a syndrome.
   B. One is caused by a single-gene defect, while the other is a condition secondary to hypoplasia of the mandible before the ninth week of development.
   C. A and B
   D. None of the above

The infant in the vignette is diagnosed with Pierre–Robin sequence. After several weeks in the hospital, he was discharged to home on a monitor, stable in room air, with nasogastric tube feedings. Close follow-up was arranged, with plans for cleft palate repair at a later date. Parents were also told that he may need a gastrostomy tube and tongue–lip adhesion, depending on his clinical course. By 5 weeks of life, he develops rapid weight gain, progressive respiratory difficulty, and cyanosis in room air. He is admitted to the hospital with the following findings:

- Heart rate = 180 beats per minute
- A third heart sound
- A systolic murmur
- Coarse breath sounds bilaterally

An electrocardiography is consistent with biventricular hypertrophy.

4. From the list below, which is the most likely clinical diagnosis?

   A. Aspiration pneumonia
   B. Cyanotic congenital heart disease
   C. Sepsis
   D. Upper airway obstruction leading to cor pulmonale

SECTION VI

Answers

CASE 1 ANSWERS

1. D. All of the above

FISH is a laboratory technique where a single-stranded DNA probe, complementary to the sequence of interest, is tagged with a fluorescent marker. The cultured cells from the patient are exposed to the fluorescent probe. The signal is easily identified using ultraviolet light. FISH is available for the following:

- Angelman syndrome
- Chromosome 4p deletion
- Cri du chat syndrome
- DiGeorge syndrome/velocardiofacial syndrome
- Miller–Dieker syndrome
- Trisomy 13
- Trisomy 18
- Trisomy 21
- Prader–Willi syndrome
- Williams syndrome

2. A. CGH has replaced high-resolution chromosomal analysis

CGH, or chromosomal microarray analysis, is a molecular-cytogenetic method for the analysis of copy number changes (gains/losses) in the DNA content in a patient's DNA. CGH detects only unbalanced chromosomal changes. This technique has replaced high-resolution chromosomal analysis, is still relatively expensive, is more likely to provide a genetic diagnosis than karyotyping, and is able to detect very small deletions or duplications of genetic material.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

FISH

- Know the common gene defects that can be diagnosed with fluorescent in situ hybridization

Comparative genomic hybridization

- Understand that comparative genomic hybridization has replaced high-resolution chromosome analysis to screen patients suspected of having a chromosome abnormality

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Schrijver I, Zehnder JL, Cherry AM. Cytogenetic and molecular genetic diagnostic tools. UpToDate (Subscription required). http://www.uptodate.com/contents/cytogenetic-and-molecular-genetic-diagnostic-tools. Accessed March 30, 2013.

CASE 2 ANSWERS

1.

A.	Autosomal dominant	iii
B.	Autosomal recessive	iv
C.	X-linked dominant	ii
D.	X-linked recessive	i

Single-gene disorders refer to Mendelian inheritance. The table below characterizes some common features that occur in autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive disorders.

Mendelian Inheritance Patterns	Incidence	Characteristics	Recurrence Risk
Autosomal dominant	1/200 individuals	Wide variation of expression Vertical transmission of disease phenotype No skipped generations Males and females equally likely to transmit to offspring	For offspring of one carrier parent, recurrence risk is 50% If both parents are affected, recurrence risk is 75%
Autosomal recessive	Rare in population	Less variation in expression than autosomal dominant diseases Clustering of the disease among siblings Males and females are equally likely to transmit the disease to offspring	For offspring of two carrier parents, recurrence risk is 25% If an affected homozygote mates with a heterozygote, recurrence risk is 50% If both parents are affected homozygotes, recurrence risk is 100%

Mendelian Inheritance Patterns	Incidence	Characteristics	Recurrence Risk
X-linked dominant	Rarer than X-linked recessive diseases	Twice as common in females than in males Fathers cannot transmit the disease to sons Rare to have skipped generations Heterozygote females may be less severely affected than affected males An affected female has a 50% chance of passing the disease to her sons or daughters	Dependent on genotype of each parents and the sex of their offspring
X-linked recessive	More common than X-linked dominant diseases	Since females have two copies of the X chromosome and males have only one, X-linked recessive diseases are usually clinically evident in males Fathers cannot transmit the disease to sons Can have skipped generations An affected father will transmit the disease to all of his daughters, who will be carriers and pass the disease onto ~ half of their sons	Dependent on genotype of each parents and the sex of their offspring

Adapted from Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:162–163

2. A iv. Marfan syndrome (Autosomal dominant)
B i. Cystic fibrosis (Autosomal recessive)
C iii. Hemophilia B (X-linked recessive)
D ii. Fragile X syndrome (X-linked dominant)

Affected individuals in the pedigree charts are shown as filled circles or squares and unaffected individuals are shown as empty symbols. Figure 1D represents a pedigree of a family with fragile X syndrome. Figure 1D also has symbols with a central dot, representing a premutation. All of these genetic disorders (i.e., cystic fibrosis, fragile X syndrome, hemophilia B, and Marfan syndrome) can be diagnosed prenatally.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Autosomal dominant
- Recognize the inheritance pattern associated with an autosomal dominant disorder with incomplete penetrance

Autosomal recessive
- Recognize the clinical and laboratory features associated with an autosomal recessive disorder

X-linked recessive
- Recognize the inheritance patterns of X-linked recessive disorders
- Recognize the clinical features associated with an X-linked recessive disorder
- Know that Factor VIII and IX deficiencies can be diagnosed prenatally
- Recognize that fragile X syndrome is associated with X-linked mental retardation

X-linked dominant
- Recognize the inheritance patterns of X-linked dominant disorders

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Jorde LB, Carey JC, Bamshad MJ. *Medical Genetics*. 3rd ed. St. Louis, MO: Mosby; 2009.

CASE 3 ANSWERS

1. A. Trisomy 13 Answer is iii.
B. Trisomy 18 Answer is ii.
C. Trisomy 21 Answer is i and iv.

Figure 2 shows an infant with trisomy 21.

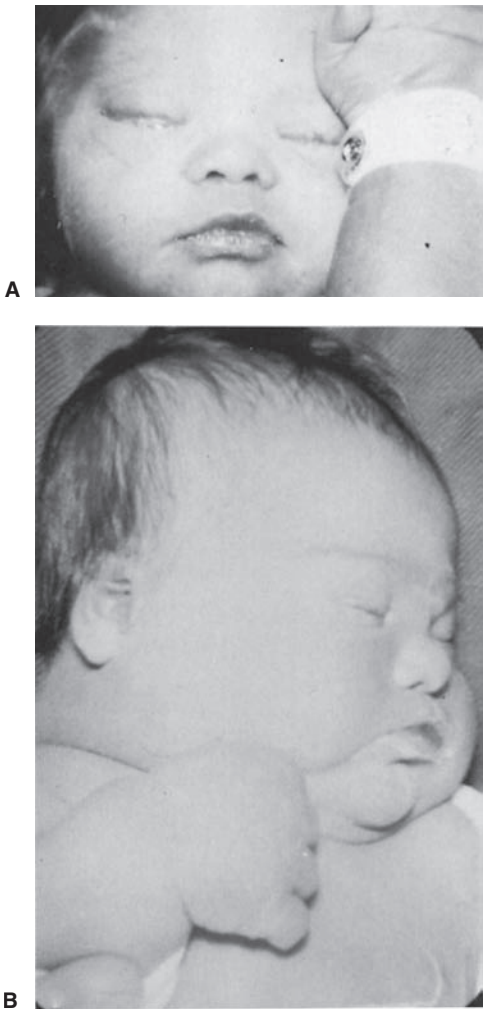


FIGURE 2. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 52.15

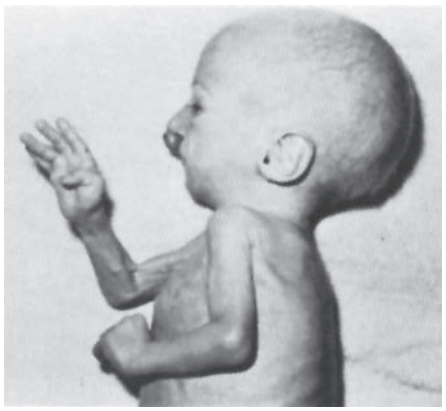


FIGURE 3. From Sadler T. *Langman's Medical Embryology*. 9th ed. Image Bank. Baltimore, MD: Lippincott Williams & Wilkins; 2003. Figure 1.9

An infant with trisomy 18 syndrome is shown in Figure 3; clinical findings include a prominent occiput, micrognathia, low-set ears, and a flexed finger.

Figure 4 shows an infant with trisomy 13 syndrome who has a cleft lip and palate, a sloping forehead, microphthalmia, and polydactyly.

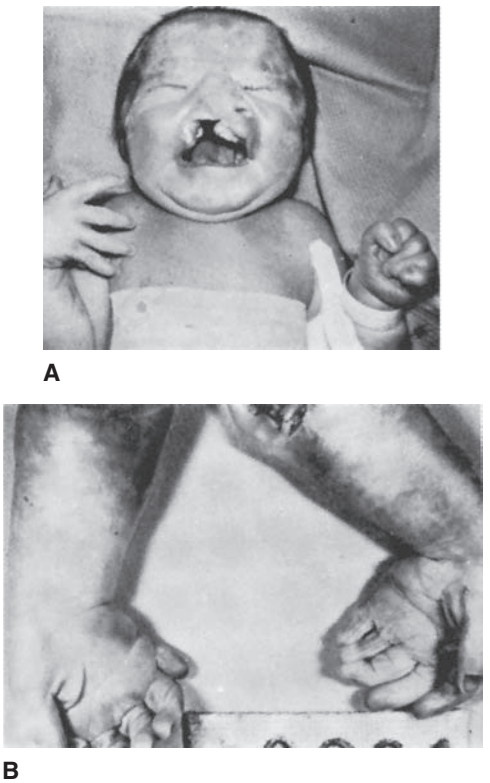


FIGURE 4. From Sadler T. *Langman's Medical Embryology*. 9th ed. Image Bank. Baltimore, MD: Lippincott Williams & Wilkins; 2003. Figure 1.10AB

2. A. Trisomy 13 — Answer is iv
B. Trisomy 18 — Answer is iii
C. Trisomy 21 — Answers are i and ii

Cardiac lesions are found in 40% to 50% of patients with Down syndrome, with endocardial cushion defects predominating. Cardiac anomalies are found in the vast majority (95%–99%) of patients with Edward Syndrome. The associated cardiac defects include a VSD, PDA, bicuspid aortic valve, pulmonary stenosis, coarctation of the aorta, and tetralogy of Fallot. In patients with trisomy 13, cardiac lesions are also very common (80%–90% of affected individuals) and most often are either a VSD or a PDA.

3. A — i. 1%
B — iii. 70% to 75%
C — iii. 70% to 75%
D — ii. 2% to 5%

The karyotype of this infant confirms the diagnosis of trisomy 21 syndrome. There is an increased incidence of congenital malformations and acquired diseases in patients with Down

syndrome. The two leading causes of death for these patients are congenital heart disease and pneumonia. Hearing loss and ophthalmologic disorders occur in 70% and 60% of patients, respectively. Early Alzheimer disease affects 75% of patients by age 60. Atlantoaxial subluxation with spinal cord compression occurs with an incidence of <1%. Other medical complications include epilepsy (5%–10%), gastrointestinal problems (duodenal atresia and Hirschsprung disease, 5%), hypothyroidism (5%), and leukemia (1%).

4. B. Three percent to 4% result from an unbalanced translocation between chromosome 21 and another acrocentric chromosome, usually chromosome 14.

It is imperative that the practitioner be able to explain recurrence risk and trisomy 21, as this information may be very important to families. Ninety-five percent of cases are sporadic. If both parents have normal karyotypes, the recurrence risk is 1%. Three to 5% of cases result from an unbalanced translocation between chromosome 21 and another acrocentric chromosome, usually chromosome 14; seventy-five percent of these translocations are de novo while the remainder occurs because of familial translocations. The risk of having another child with Down syndrome is greater for a young woman with a balanced translocation than for a middle-aged woman with normal chromosomes.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the prominent features of trisomy 21 in a newborn
- Recognize the prominent features of trisomy 13 in a newborn
- Recognize the prominent features of trisomy 18 in a newborn
- Know the associated medical problems in children with Down syndrome
- Recognize that the risk of having another child with Down syndrome is greater for a young woman who is a balanced translocation carrier than for a middle-aged woman

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Bull M. Health supervision for children with Down syndrome. *Pediatrics*. 2011;128(2):393–406.

Newberger D. Down syndrome: Prenatal risk assessment and diagnosis. *Am Fam Physician*. 2000;62(4):825–832.

CASE 4 ANSWERS

1. B. Edema of hands and feet, short stature, broad chest with wide-spaced nipples, webbed neck, low posterior hairline

A newborn with Turner syndrome often demonstrates minimal to no findings at birth and subsequently is diagnosed after an evaluation for growth failure or failure to enter puberty. The classic features that may be present at birth include:

- Cardiac (35%)—coarctation of the aorta, bicuspid aortic valve, aortic stenosis, mitral valve prolapse
- Extremities—cubitus valgus, knee anomalies
- Facial/neck—cystic hygroma in utero, short/webbed neck (especially posteriorly), low posterior hairline
- Genitourinary—gonadal dysgenesis with subsequent infertility (majority of patients)
- Renal—horseshoe kidney
- Other—edema of hands and feet (congenital lymphedema), short stature, broad chest with wide-spaced nipples, bone dysplasia

As affected individuals get older, additional clinical manifestations can be found, including the following:

- Aortic dissection
- Hypertension
- Increased risk for gonadoblastoma
- Poor coordination
- Visual spatial deficits

Importantly, Noonan syndrome can sometimes be confused with Turner syndrome, as these syndromes have some overlapping features. Infants with Noonan syndrome often have short/webbed neck, low posterior hairline, hypertelorism, low-set ears, low nasal bridge, pectus excavatum, and ptosis. More than 50% of patients with Noonan syndrome have cardiac anomalies, which most often include dysplastic pulmonary valve, atrial septal defect, and cardiomyopathy. In utero, patients with Noonan syndrome may also have a cystic hygroma.

Micrognathia, glossoptosis, and a cleft palate are found in patients with Pierre–Robin sequence.

CHARGE syndrome is described as:

- *C*oloboma (80%)
- *H*eart defect (50%–70%)
- *A*tresia of choanae (60%)
- *R*etarded growth (90%, most often noted postnatally)
- Genital hypoplasia (in males, 75%)
- *E*ar anomalies (90%), often with deafness

Figure 5 depicts features of Turner syndrome.

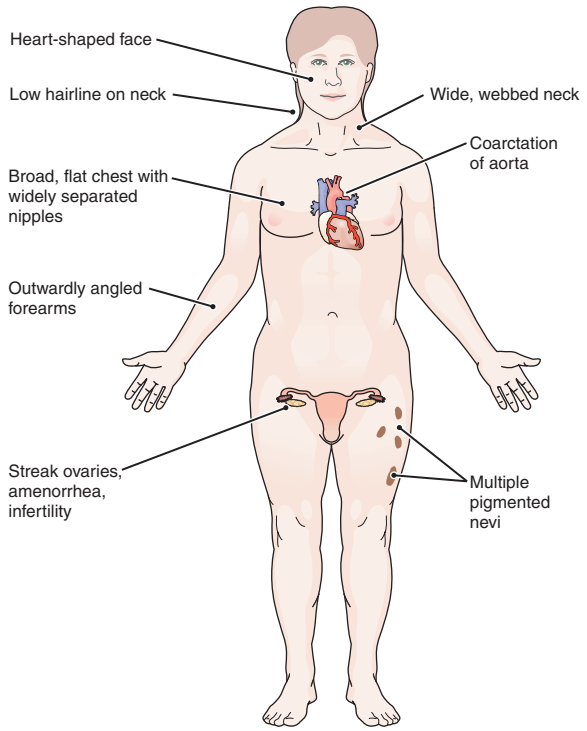


FIGURE 5. From McConnell TH. *The Nature of Disease Pathology for the Health Professions*. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. Figure 7.17

Figure 6 shows two features of Turner syndrome: webbed neck and pedal edema.

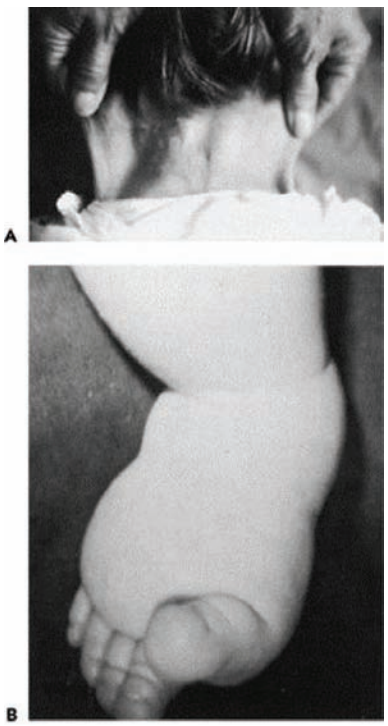


FIGURE 6. From MacDonald MG, Mullett MD, Seshia MM. *Avery's Neonatology*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

2. C. Gonadal dysgenesis is universal in patients with Turner syndrome; infertility is most likely.

Spontaneous fertility is rare among patients with Turner syndrome. If a woman with Turner syndrome successfully becomes pregnant, the woman's karyotype would most likely represent mosaicism for a normal 46, XX cell lineage or 47, XXX cell lineage. In addition, it is unlikely she would carry the fetus to term.

3. B. Figure 2

Figure 2 shows a karyotype in a patient with Turner syndrome, demonstrating 45, X with one of the X chromosomes missing. The karyotype in Figure 1 is consistent with trisomy 21 because there are three chromosomes in the 21st position. Figure 3 shows a normal male human karyotype. The karyotype in Figure 4 depicts translocation of chromosome 21 into 14, resulting in Down syndrome.

4. C. Growth hormone

Growth hormone may be an effective treatment in patients with Turner syndrome to increase final height at adulthood. It should be initiated as soon as the patient's height falls below the fifth percentile for age. The combination of growth hormone with low-dose estrogen replacement therapy may improve growth in addition to other benefits. Ninety percent of patients with Turner syndrome will require estrogen therapy to initiate puberty and complete growth. An added health benefit of estrogen therapy in women with Turner syndrome who do not have spontaneous puberty is a reduced risk for osteoporosis and heart conditions. Adding an androgen to growth hormone therapy at age 9 to 12 years should be considered in girls with Turner syndrome who have extreme short stature.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the features of the Turner phenotype in a newborn
- Recognize that growth retardation may be the only clinical manifestation of Turner syndrome
- Know that gonadal dysgenesis is uniformly present in Turner syndrome
- Know that a definitive diagnosis of Turner syndrome requires chromosomal analysis
- Recognize that growth hormone may be an effective treatment for Turner syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Saenger P. Management of Turner syndrome (gonadal dysgenesis). UpToDate (Subscription required). http://www.uptodate.com/contents/management-of-turner-syndrome-gonadal-dysgenesis. Accessed April 8, 2013.

Sybert V, McCauley E. Turner's syndrome. *N Engl J Med*. 2004;351:1227–1238.

CASE 5 ANSWERS

1. B. Klinefelter syndrome

Klinefelter syndrome (47, XXY) has an incidence of 1 in 500 to 1,000 male births and is derived equally from maternal or paternal errors. The mother in this vignette is 45 years old. Importantly, if Klinefelter is maternally derived, there is a higher risk with advanced maternal age. Male infants with Klinefelter syndrome are phenotypically normal as the manifestations do not appear until after the newborn period. Figure 1 depicts a male patient with clinical features of Klinefelter syndrome.

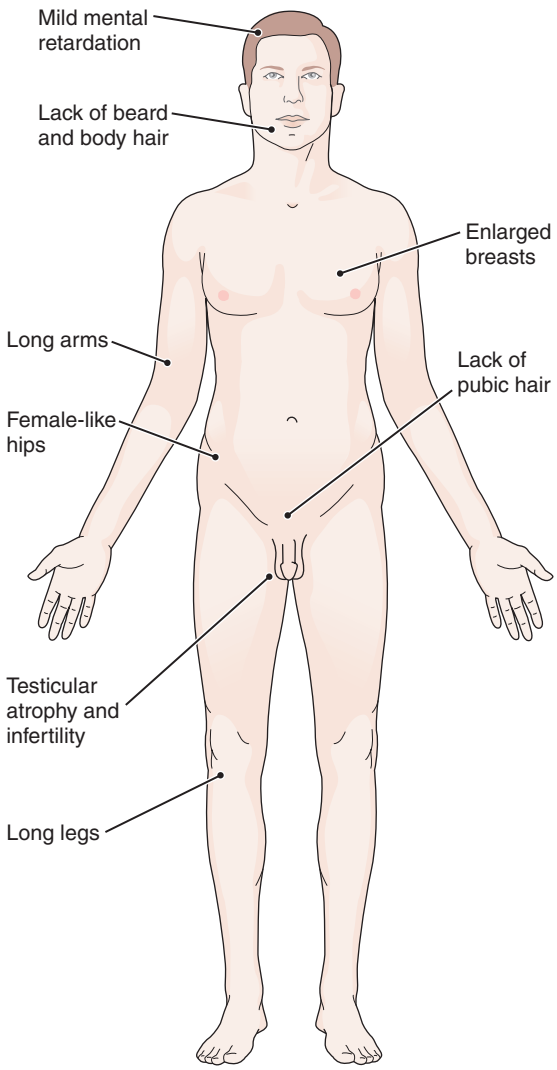


FIGURE 1. From McConnell TH. *The Nature of Disease Pathology for the Health Professions*. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. Figure 7.16

Patients with Klinefelter syndrome are at higher risk for behavioral difficulties (immaturity, shyness), learning disabilities, and autism.

Ehlers–Danlos is an inherited connective-tissue disorder caused by a defect in the synthesis of collagen. These patients may be tall and have joint hypermobility and skin hyperextensibility, among other findings.

Marfan syndrome is also a connective-tissue disorder and is secondary to abnormal fibrillin gene. Patients with Marfan syndrome tend to be unusually tall, with long limbs and long, thin fingers. Marfan syndrome is an autosomal dominant condition that may be associated with advanced paternal age.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Know the major clinical manifestations of Klinefelter syndrome

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Snyder P. Causes of primary hypogonadism in males. UpToDate (Subscription required). http://www.uptodate.com/contents/causes-of-primary-hypogonadism-in-males. Accessed April 8, 2013.

CASE 6 ANSWERS

1. B. CHARGE syndrome and VACTERL association

CHARGE syndrome is described as:

- *C*oloboma (80%, usually involving the retina)
- *H*eart defect (50%–70%, tetralogy of Fallot, double-outlet right ventricle, ventricular septal defect, atrial septal defect, patent ductus arteriosus, right-sided aortic arch)
- *A*tresia of choanae (60%)
- *R*etarded growth (90%, most often noted postnatally)
- Genital hypoplasia (in males, 75%)
- *E*ar anomalies (90%, often with deafness)
- Other findings: neurocognitive impairment, cranial nerve dysfunction

VACTERL/VATER is described as:

- *V*ertebral (70%, e.g., hemivertebrae)
- *A*nal atresia (80%, may have fistula)
- *C*ardiac (50%, ventricular septal defect more common than tetralogy of Fallot or coarctation of the aorta)
- *T*racheoesophageal fistula (70%, typically with *E*sophageal atresia)
- *R*enal anomalies (90%, most often noted postnatally)
- *L*imb dysplasia (65%, typically radial, may also have preaxial polydactyly or syndactyly)
- Other findings: intrauterine growth restriction, ear anomalies, spinal anomalies

VATER association was first named in the early 1970s; shortly thereafter, the "C" and the "L" were added, with the subsequent change to the acronym VACTERL. Vertebral and cardiac anomalies are features of patients with either CHARGE or VACTERL syndrome.

Alagille syndrome is a genetic disorder that predominantly affects the liver, heart, and kidney and is associated with bile duct paucity and cholestasis. Renal anomalies have been reported in Alagille syndrome but are uncommon. Holt–Oram syndrome is a disorder that affects bones in the upper limbs, most typically with absent radial bones, and may also cause cardiac conduction defects. Holt–Oram typically does not have associated genitourinary abnormalities.

2. A. Association, as there is currently no known genetic cause; it is not associated with developmental disabilities; there is a low recurrence risk.

The additional findings in the infant in this vignette suggest a diagnosis of VACTERL association. Affected individuals are unlikely to have developmental disabilities, and there is a low risk of recurrence. VACTERL is an association because there is currently no known genetic cause for the clinical manifestations.

Syndromes represent a pattern of congenital anomalies with a known genetic cause. They are often associated with developmental disabilities, and there can be a significant recurrence risk for the parents or the affected individual. CHARGE syndrome was known as an association until 2004 when the responsible gene (*CHD7*) was identified.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize the clinical manifestations of genetic associations (e.g., CHARGE, VACTERL)

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Kaplan J, Hudgins L. Neonatal presentations of CHARGE syndrome and VATER/VACTERL association. *NeoReviews*. 2008;7:e299–e305.

CASE 7 ANSWERS

1. B. Contiguous gene syndromes

Microdeletions are chromosomal deletions that are too small to be detected by conventional cytogenetic methods. They are usually only a few megabases (Mb) long and involve contiguous genes. The twins in the vignette have a small deletion between 15q11 and 15q13, resulting in two completely different syndromes depending on the parental origin of the chromosome. In contrast to contiguous gene syndromes, single-gene disorders (Mendelian inheritance) include the following inheritance patterns: autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive.

2.

A.	Angelman syndrome	i.	Figure 1
B.	Beckwith–Wiedemann syndrome	ii.	Figure 2
C.	DiGeorge syndrome	iii.	Figure 3
D.	Prader–Willi syndrome	iv.	Figure 4

Table 1 summarizes the clinical features in these syndromes.

TABLE 1. Clinical Features

Syndrome	Features
Angelman syndrome	Profound intellectual disability Postnatal microcephaly Gait ataxia ("puppet-like" gait) Happy demeanor Large mouth Protruding tongue Widely spaced teeth Seizures
Beckwith–Wiedemann syndrome	Macroglossia Macrosomia Midline abdominal wall defects (omphalocele, umbilical hernia, diastasis recti) Ear creases or pits Neonatal hypoglycemia
DiGeorge syndrome	Hypoplasia of thymus and/or parathyroid gland Neonatal hypocalcemia Susceptibility to infection Predisposition to autoimmune diseases Mild/moderate learning disabilities
Prader–Willi syndrome	Hypotonia Poor feeding in infancy Increased appetite and obesity in adolescence Genital hypoplasia Small hands and feet Almond-shaped eyes Mild intellectual disability in two-third of cases

3.

A.	Angelman syndrome	i.	Monitor for delayed developmental milestones and risk for seizure
B.	Beckwith-Wiedemann syndrome	iii.	Monitor for hypoglycemia
C.	DiGeorge syndrome	ii.	Monitor for hypocalcemia
D.	Prader-Willi syndrome	iv.	Monitor for risk of failure to thrive in infancy

Table 2 below summarizes the management of these syndromes.

TABLE 2. Management

Syndrome	Management
Angelman syndrome	Genetics consultation May be asymptomatic in newborn period Monitoring for delayed developmental milestones and seizures
Beckwith–Wiedemann syndrome	Genetics consultation If omphalocele present, surgical consultation Close monitoring for neonatal hypoglycemia
DiGeorge syndrome	Genetics and cardiology consultations Monitoring for hypocalcemia
Prader–Willi syndrome	Genetics consultation Monitoring for failure to thrive in infancy Risk for obesity in adolescence

4. C. DiGeorge syndrome

Newborn infants with DiGeorge syndrome can have the following physical findings:

- Cleft palate
- Hypertelorism
- Micrognathia
- Misshapen ears
- Murmur
- Prominent nose with square nasal root and narrow alar base
- Short palpebral fissures
- Short philtrum

Hypoplastic parathyroid glands in patients with DiGeorge syndrome result in hypocalcemia with clinical findings of jitteriness. None of the other syndromes fit with the clinical picture of the infant in this vignette.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Understand the cause(s) of contiguous gene syndromes
- Appreciate that contiguous gene syndromes (deletion or alteration of multiple gene pairs that are adjacent to one another) can cause syndromes with multiple apparent unconnected defects (e.g., Angelman, Prader–Willi)
- Recognize contiguous gene syndromes, including Prader–Willi, Angelman, Beckwith–Wiedemann, and DiGeorge, and manage appropriately
- Recognize the signs of DiGeorge syndrome

SUGGESTED READINGS

Bacino C. Microdeletion syndromes (chromosomes 12 to 22). UpToDate (Subscription required). http://www.uptodate.com/contents/microdeletion-syndromes-chromosomes-12-to-22. Accessed April 8, 2013.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 8 ANSWERS

1. B. Pierre–Robin sequence is thought to result from mandibular hypoplasia occurring prior to 9 weeks of development.

The other photographs represent the following syndromes: A. Treacher Collins syndrome, C. DiGeorge syndrome, and D. Goldenhar syndrome.

2.

i.	DiGeorge syndrome	Figure 1C
ii.	Goldenhar syndrome	Figure 1D
iii.	Pierre–Robin sequence	Figure 1B
iv.	Treacher Collins syndrome	Figure 1A

Features of each are listed in Table 1.

TABLE 1. Syndrome/Sequence Features

Syndrome/ Sequence	Features
DiGeorge syndrome	• Majority with 22q11.2 deletion • Also described as Velocardiofacial syndrome • CATCH 22 (Cardiac, Abnormal facies, Thymic hypoplasia, Cleft palate, Hypocalcemia) • Autosomal dominant with variable expression
Goldenhar syndrome	• Hemifacial microsomia • Short neck, low posterior hairline, limited movement of head, facial asymmetry, deafness (conductive or neural) • Abnormal cervical vertebrae (typically fused) • Unknown etiology
Pierre–Robin sequence	• Triad: micrognathia; glossoptosis (normally sized tongue in a small oral cavity); cleft palate (U-shaped) • Feeding intolerance • Conductive hearing loss; normal intelligence • Posterior airway obstruction with potential for cor pulmonale • May be isolated or associated with genetic disorders such as Treacher Collins syndrome

Syndrome/ Sequence	Features
Treacher Collins syndrome	• Lower eyelid coloboma; down-slanting of palpebral fissures; malformed ears; mandibular hypoplasia; malar hypoplasia with or without a cleft in the zygomatic bone; absence of lower eyelashes; possible cleft palate; scalp hair that may extend to lateral cheek • Conductive hearing loss; visual deficit; normal intelligence • Respiratory difficulties as a result of a narrow airway • Results from a single gene defect; autosomal dominant with variable expression; 60% because of a new mutation

3. C. A and B

Pierre–Robin is a sequence, while Treacher Collins is a syndrome. A sequence occurs when a single primary developmental defect results in a chain of secondary defects. The primary defect in Pierre–Robin sequence is mandibular hypoplasia leading to posterior displacement of the tongue, which does not allow closure of the palatal arches. This sequence is secondary to hypoplasia of the mandible before the ninth week of development.

Treacher Collins is a syndrome, which represents a pattern of many primary malformations as a result of one etiology. Treacher Collins syndrome is caused by a single-gene defect from a mutation in the *TCOF1* gene (chromosome 5).

4. D. Upper airway obstruction leading to cor pulmonale

The infant in this vignette has clinical findings consistent with cor pulmonale. The most likely cause of cor pulmonale in an infant with Pierre–Robin sequence is severe and persistent upper airway obstruction.

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- Know that the features of Pierre–Robin sequence are secondary to micrognathia
- Know the clinical features of Treacher Collins syndrome and that it is due to a single-gene defect
- Know that upper airway obstruction caused by glossoptosis may cause cor pulmonale in infants with Pierre–Robin sequence

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Buchanan E, Cole P, Hollier L. Syndromes with craniofacial abnormalities. UpToDate (Subscription required). http://www.uptodate.com/contents/syndromes-with-craniofacial-abnormalities. Accessed April 8, 2013.

SECTION VII

Infectious Diseases

CASE 1

Sepsis

A 28-year-old pregnant woman contacts her obstetrician after her "water breaks" at 25 weeks' gestation. Her obstetrician urges her to come to the hospital for an evaluation. Testing in the hospital confirms that the woman has experienced rupture of the membranes of the amniotic sac and chorion, leading to complete loss of amniotic fluid. The fetus appears active with a normal heart rate tracing. The woman is afebrile and is not having any contractions. She is admitted to the hospital for observation and bed rest. She meets with the neonatology team to discuss the prognosis of an infant born at this gestational age.

1. Of the following, a potential complication in a newborn with preterm premature rupture of membranes (PPROM) is:

   A. Infection
   B. Pulmonary hyperplasia
   C. Renal dysfunction
   D. All of the above

Four weeks later, the woman is noted to have a high fever, abdominal pain, and contractions. Her obstetrician suspects chorioamnionitis, and the infant is born at 29 weeks' gestation after unstoppable preterm labor. The baby has severe respiratory distress requiring intubation and surfactant administration, hypotension requiring volume and inotropic support, and a coagulopathy requiring platelet and fresh frozen plasma transfusions. The infant receives total parenteral nutrition (TPN) by an umbilical venous catheter. The neonatology team treats the baby with antibiotics for presumed early-onset sepsis.

2. Of the following, the antibiotic regimen that is most appropriate for this infant is:

   A. Ampicillin and gentamicin
   B. Cefotaxime
   C. Gentamicin
   D. Vancomycin and gentamicin

3. If this pregnant woman also had a flu-like illness and brown-colored amniotic fluid, the most likely organism involved would be:

   A. Group B *Streptococcus* (GBS)
   B. *Escherichia coli*
   C. *Enterococcus*
   D. *Listeria monocytogenes*

After 2 days, the infant stabilizes. The infant's blood culture is negative and cerebrospinal fluid testing is normal. However, because of initial clinical concerns for sepsis, the infant receives 14 days of antibiotics. Because of some initial intolerance of enteral feedings and a need for slow feeding advancement, a percutaneous central-line catheter is placed to provide TPN. At 2 weeks of age, the infant has an increase in apneic events and appears lethargic. The neonatology team is concerned about late-onset sepsis.

4. Match the characteristics listed below with the type of sepsis (of note, some characteristics may be found in both types of sepsis):

A. Presents in the first week of life	i. Early-onset sepsis
B. Acquired from the maternal genital tract	ii. Late-onset sepsis
C. Acquired from the postnatal environment	
D. Caused by GBS	
E. Caused by *Staphylococcus* coagulase-negative	
F. Focal involvement more common than multisystem involvement	
G. Associated with central-line catheter	
H. Mortality between 15% and 45%	

CASE 2

Group B *Streptococcus*

At 36 weeks' gestation, a pregnant woman has a vaginal culture that is positive for Group B *Streptococcus* (GBS). The woman is concerned about the possibility that her infant will develop a GBS infection.

1. Of the following, the time period that an infant can acquire a GBS infection is:

   A. Shortly before delivery
   B. During delivery
   C. Postnatally
   D. All of the above

The obstetrician discusses the factors that would increase the baby's risk of acquiring a GBS infection in the first week of life.

2. Of the following, the characteristic that is *least* likely to increase this baby's risk for early-onset GBS infection is:

   A. Advanced maternal age
   B. Maternal GBS bacteriuria
   C. Preterm birth
   D. Sibling with invasive GBS disease in the neonatal period

To minimize the risk of acquisition of GBS disease in this infant, the obstetrician describes the approach to and impact of maternal intrapartum antimicrobial prophylaxis (i.e., chemoprophylaxis).

3. Chemoprophylaxis is indicated in all of the following scenarios *except* for a woman with:

   A. A prior infant with invasive GBS disease, regardless of current GBS status
   B. GBS bacteriuria during current pregnancy
   C. GBS colonization during a prior pregnancy, regardless of current GBS status
   D. Unknown GBS status and is in preterm labor

4. Of the following, the optimal intravenous antibiotic for intrapartum chemoprophylaxis is:

   A. Cefazolin
   B. Clindamycin
   C. Penicillin
   D. Vancomycin

5. Of the following, the most likely impact of chemoprophylaxis in a GBS-positive pregnant woman is:

   A. A decreased incidence of late-onset neonatal GBS disease by 50%
   B. A lower incidence of early-onset neonatal GBS disease by 80%
   C. A lower risk of early-onset neonatal GBS disease in future pregnancies
   D. Prolongation of labor by 2 to 4 hours

The pregnant woman remains extremely anxious about the possibility of GBS infection in her baby. Thus, the obstetrician asks a neonatologist to discuss care of her infant after birth. The neonatologist reviews the three possible options that may occur after delivery:

- Observation of the baby and/or
- Evaluation of the baby with blood tests and/or
- Initiation of antibiotic therapy

6. Match the clinical description (A through F) with the *initial* approach in the neonate (i, ii, or iii):

   A. Asymptomatic, well-appearing infant born to a GBS-positive woman with adequate intrapartum GBS prophylaxis and no signs of chorioamnionitis
   B. Asymptomatic, well-appearing infant born to a GBS-positive woman with inadequate intrapartum GBS prophylaxis with duration of membrane rupture <18 hours and no maternal fever
   C. Asymptomatic, well-appearing infant born to a GBS-positive woman with inadequate GBS prophylaxis with duration of membrane rupture ≥ 18 hours
   D. Asymptomatic, well-appearing infant born to a GBS-positive woman with adequate intrapartum GBS prophylaxis and signs of chorioamnionitis
   E. Asymptomatic, well-appearing infant born to a GBS-positive woman with inadequate intrapartum GBS prophylaxis and signs of chorioamnionitis
   F. Symptomatic, ill-appearing infant born to a GBS-positive woman with adequate intrapartum GBS prophylaxis

   i. Observation (i.e., no evaluation or antibiotic initiation)
   ii. Observation and evaluation with blood tests
   iii. Observation, evaluation, and initiation of antibiotics

After the infant is born and the appropriate approach is taken, the infant is discharged home. At 3 weeks of age, the infant is admitted to the hospital with late-onset GBS disease.

7. Of the following, the clinical manifestation(s) that is (are) more common in late- rather than early-onset GBS disease is (are):

   A. Meningitis
   B. Pneumonia
   C. Septicemia
   D. All of the above

8. Of the following, the most appropriate management approach in an infant with GBS infection is:

   A. Change broad-spectrum antibiotic coverage to intravenous penicillin G after isolation of the GBS organism
   B. Length of treatment is dependent on the location of infection
   C. Use of oral penicillin is inadequate in the treatment of GBS disease in an infant
   D. All of the above

CASE 3

Herpes simplex virus

A pregnant woman presents to the hospital in labor at 32 weeks' gestation. She reports that her water had broken 6 hours ago and she is now having contractions every 2 minutes. On examination, her obstetrician observes a genital lesion that is most consistent with herpes simplex virus (HSV). This is the first time the woman has had a genital lesion.

1. Which of the following statements is (are) *true*?

   A. A pregnant woman with a primary genital herpes lesion during delivery has a greater than 25% chance of having a neonate who is infected.
   B. A pregnant woman with a secondary genital herpes lesion during delivery has a greater than 25% chance of having a neonate who is infected.
   C. The majority of neonates who acquire a herpes infection are born to women without a history of genital herpes.
   D. The majority of neonates who acquire a herpes infection are born to women who are asymptomatic.
   E. B and C
   F. A, C, and D
   G. All of the above

The woman's labor progresses rapidly and a male infant is born by vaginal delivery 10 minutes after the mother's arrival to the hospital. This neonate has several risk factors for acquiring a herpes infection.

2. For each of the following, determine which scenario is associated with a higher risk of a neonate acquiring HSV if the mother has a genital herpes lesion:

   A. Cesarean birth vs. vaginal delivery
   B. Maternal genital lesion in the first trimester vs. maternal genital lesion at delivery
   C. Premature infant vs. term infant
   D. Rupture of membranes for less than 2 hours prior to delivery vs. rupture of membranes more than 6 hours prior to delivery
   E. Use of a fetal scalp monitor vs. noninvasive fetal monitoring

The neonatology team is asked to evaluate the baby because of his mother's primary genital herpes lesion.

3. Of the following, the most appropriate management of an *asymptomatic* infant born to a mother with a *primary active genital lesion* at the time of delivery is:

   A. Consider empirical intravenous acyclovir
   B. Monitor infant closely
   C. Obtain surface cultures at 12 to 24 hours of age
   D. All of the above

4. Of the following, the most appropriate management of an *asymptomatic* infant with a maternal history of genital herpes but *no active lesions* at the time of delivery is:

   A. Consider empirical intravenous acyclovir
   B. Monitor the infant closely
   C. Obtain surface cultures at 12 to 24 hours of age
   D. B and C
   E. All of the above

The infant described in the vignette has surface cultures that are positive for HSV, confirming HSV *infection*. However, the infant needs to be assessed for HSV *disease*; the neonatologist orders the following studies:

- Complete blood cell count with differential
- Lumbar puncture for cerebrospinal fluid (CSF) indices and HSV polymerase chain reaction (PCR)
- Serum hepatic transaminases
- Whole blood for PCR

The neonatologist meets with the infant's family to discuss the different approach for HSV infection and HSV disease. He explains that their neonate has HSV infection and requires 10 to 14 days of intravenous acyclovir to prevent progression to HSV disease. If the baby's test results are consistent with HSV disease, longer treatment with acyclovir will be needed.

The neonatologist meets with the family a few days later because the CSF and whole blood PCR tests are consistent with HSV disease. The baby does indeed develop clinical symptoms consistent with HSV disease.

5. Of the following, the most likely timing of neonatal symptoms caused by peripartum acquisition of HSV is:

   A. Immediately after delivery
   B. Forty-eight hours of age
   C. Two to 3 weeks of age
   D. Four months of age

6. Of the following, the examination finding(s) that is (are) consistent with HSV disease in an infant is:

   A. Encephalitis leading to lethargy and seizures
   B. Conjunctivitis, chorioretinitis, papulovesicular lesions, mucous membrane involvement
   C. Systemic findings, including coagulopathy, shock, pneumonitis
   D. All of the above

7. Of the following, the appropriate management of an infant with HSV disease with central nervous system (CNS) involvement is:

   A. Oral acyclovir × 3 weeks
   B. Intravenous acyclovir × 3 weeks
   C. Oral acyclovir × 3 weeks, followed by oral acyclovir suppressive therapy × 6 months
   D. Intravenous acyclovir × 3 weeks, followed by oral acyclovir suppressive therapy × 6 months

CASE 4

Lower respiratory tract infections

An infant born at 27 weeks' gestation has a postnatal course significant for:

- Intubation and surfactant therapy
- Transition to continuous positive airway pressure (CPAP) on the second day of life
- Continuation of CPAP for 6 weeks, then transitioned to room air
- Apnea of prematurity that resolved
- Feeding immaturity that resolved
- Mild retinopathy of prematurity that resolved

The baby is discharged home in June. Initially, the baby's mother is the primary care provider. However, the mother returns to work in September and enrolls the baby in full-time daycare. At the end of March, the parents bring the baby to the pediatrician because of a low-grade fever, tachypnea, cough, wheezing, and nasal congestion.

1. Of the following, the most common cause of lower respiratory infections in infants is:

   A. Chlamydia
   B. Influenza
   C. Respiratory syncytial virus (RSV)
   D. *Ureaplasma*

The infant has an evaluation and is found to have an RSV infection. The parents are surprised by their infant's diagnosis because the baby had been receiving monthly palivizumab since November to protect against RSV. The pediatrician explains the benefit of this prophylaxis.

2. Of the following, the benefit of palivizumab prophylaxis in premature infants is to *decrease* the:

   A. Mortality rate
   B. Rate of acquisition
   C. Rate of hospitalization
   D. Rate of transmission

3. Of the following, the population that should receive RSV prophylaxis during the first winter season includes:

   A. All infants with a small ventricular septal defect
   B. All infants with cystic fibrosis
   C. All premature infants with a diagnosis of chronic lung disease
   D. All premature infants born less than 35 weeks' gestation

CASE 5

Hepatitis B virus

A full-term 3,400-g female infant is born by vaginal delivery to a mother with an unknown hepatitis B surface antigen (HBsAg) status.

1. Of the following, the most appropriate management of this infant is to:

   A. Administer hepatitis vaccine (HBV) by 12 hours of age
   B. Administer hepatitis immune globulin (HBIG) as soon as possible if the mother is positive for HBsAg or by 1 week of age if she remains HBsAg-unknown
   C. Test the infant's mother for HBsAg
   D. All of the above

2. If this infant had weighed 1,900 g at birth, the most appropriate management for this infant would have been to:

   A. Administer HBV by 12 hours of age
   B. Administer HBIG by 12 hours of age
   C. Test the infant's mother for HBsAg
   D. All of the above

The mother's HBsAg status is negative. However, she converts to a positive HBsAg status during her second pregnancy. She delivers this second baby at term gestational age.

3. Of the following, the most appropriate management of this infant is to:

   A. Administer HBV and HBIG by 12 hours of age
   B. Administer HBV by 12 hours of age and HBIG by 1 week of age
   C. Test the infant for HBsAg and antibodies to HBsAg (anti-HBs) at 1 month of age
   D. B and C

The infant receives the appropriate management after birth.

4. Of the following, the transmission of hepatitis B infection to this mother's second child is highest during:

   A. Breast-feeding
   B. Gestation (i.e., in utero)
   C. Labor and delivery
   D. Postpartum

CASE 6

Syphilis

A female infant is born at 35 weeks' gestation by vaginal delivery. The pregnancy had been complicated by a diagnosis of syphilis in the infant's mother at 32 weeks' gestation.

1. Of the following, the scenario in which this infant would require an evaluation for syphilis is:

   A. If the mother was appropriately treated during pregnancy and had a twofold decrease in viral titers
   B. If the mother was appropriately treated during pregnancy less than 4 weeks prior to delivery
   C. If the mother was treated with a nonpenicillin antibiotic
   D. All of the above

At 1 month of age, the infant has clinical findings that are consistent with syphilis, including the following:

- Copious nasal secretions
- Hemolytic anemia
- Lymphadenopathy
- Pneumonia

2. Of the following, the route by which this 1-month-old infant most likely acquired syphilis is during:

   A. Breast-feeding
   B. Direct contact with the mother
   C. Gestation (by transplacental route)
   D. Labor and delivery

3. Additional clinical findings in this infant with syphilis include all of the following, *except*:

   A. Desquamating maculopapular rash
   B. Hepatosplenomegaly
   C. Hutchinson triad
   D. Osteochondritis

To confirm the diagnosis of syphilis in this infant, the neonatologist orders an RPR (rapid plasma reagin) test and a fluorescent treponemal antibody absorption (FTA) test on the infant and compares these findings with the mother's test results. The maternal and neonatal testing are consistent with neonatal infection.

4. Of the following, the test results most consistent with congenital syphilis is:

   A. Mother: negative RPR, positive FTA; infant: negative RPR, positive FTA
   B. Mother: positive RPR, negative FTA; infant: positive RPR, negative FTA
   C. Mother: positive RPR, positive FTA; infant: negative RPR, positive FTA
   D. None of the above

The neonatologist also performs a complete evaluation for syphilis, including the following:

- Complete blood count
- Direct bilirubin
- Liver function tests
- Cerebrospinal fluid (CSF) examination for cell count, protein, and quantitative VDRL (Venereal Disease Research Laboratory) test
- Chest radiograph
- Long-bone radiographs
- Ophthalmologic examination

All of these test results are abnormal and consistent with systemic and neurologic evidence of syphilis.

5. Of the following, the most effective treatment for this infant is:

   A. Ampicillin administered intravenously × 10 days
   B. Aqueous crystalline penicillin G administered intravenously × 10 days
   C. Penicillin G benzathine administered intramuscularly once per week × three doses
   D. All of the above are acceptable options

CASE 7

Toxoplasmosis

A full-term male infant is born to a woman with normal prenatal screening tests. He is discharged to home after 2 days in the hospital. The pediatrician meets with the infant's parents the day after discharge to discuss a positive toxoplasmosis result that was found on the infant's state screening test. The infant's examination is normal. The pediatrician reviews the maternal history and learns that the woman had been healthy throughout her pregnancy and is currently asymptomatic.

1. Of the following, the most accurate statement by the pediatrician about this baby is:

   A. Congenital toxoplasmosis is unlikely because the baby is asymptomatic.
   B. Congenital toxoplasmosis is unlikely because the mother is asymptomatic.
   C. The baby most likely has congenital toxoplasmosis from a primary maternal infection.
   D. The baby most likely has congenital toxoplasmosis from a secondary maternal infection.

The parents have many questions for the pediatrician. In particular, the mother wants to know how she might have acquired toxoplasmosis.

2. Of the following, the mode of transmission that might have led this mother to acquire toxoplasmosis is:

   A. Oocyst from contaminated food
   B. Oocyst from contaminated water
   C. Tissue cyst from undercooked meat
   D. All of the above

Maternal *Toxoplasma gondii*-specific IgG and IgM antibody levels and neonatal *T. gondii*-specific IgG, IgM, and IgA antibody levels confirm that the baby has congenital toxoplasmosis. The infant is asymptomatic and has normal ophthalmologic, auditory, and neurologic evaluations.

3. Of the following, the clinical issues that are likely to develop in this infant several months to years later include the following:

   A. Hearing impairment
   B. Mental deficiency
   C. Visual impairment
   D. All of the above

The pediatrician consults with infectious diseases experts to determine the management plan.

4. Of the following, the appropriate management of this infant is:

   A. Close monitoring but no medications until the infant becomes symptomatic
   B. Pyrimethamine only × 1 year
   C. Sulfadiazine only × 1 year
   D. Pyrimethamine and sulfadiazine × 1 year

The parents are concerned that the infant's 3-year-old sibling might have acquired toxoplasmosis.

5. Of the following, the clinical manifestation of *T. gondii* infections acquired after birth is:

   A. Easy bruisability, petechial rash, hematochezia
   B. Fever, rash, myalgia, cervical lymphadenopathy
   C. Lethargy, seizures, hearing loss
   D. Nausea, emesis, diarrhea

CASE 8

Human immunodeficiency virus

A 32-year-old pregnant woman has routine blood testing during the first trimester. Her testing reveals the following:

- Blood type O positive
- Rapid plasma reagin nonreactive
- Hepatitis B surface antigen negative
- Rubella immune
- Human immunodeficiency virus (HIV) antibody positive

The woman's HIV-positive status is confirmed with additional testing. The woman's obstetrician reviews these new findings, discusses the preventive strategies to decrease the risk of HIV transmission to her baby, and refers her to an infectious disease specialist.

1. Of the following, the most likely period of mother-to-child transmission of HIV in the United States is:

   A. During the first trimester
   B. During the third trimester
   C. Intrapartum
   D. Postnatally

2. Of the following, the approach(es) to minimize the risk of transmission is:

   A. Oral antiretroviral medication to the pregnant woman during pregnancy
   B. Intravenous antiretroviral medication to the pregnant woman during delivery
   C. Oral antiretroviral medication to the infant postnatally for 6 weeks
   D. All of the above

After following all of the recommendations by the infectious disease specialist to attempt to minimize HIV transmission to her infant, the woman delivers a full-term infant girl.

3. Of the following, the preferred method to diagnosis HIV infection in a newborn is:

   A. Detection of p24 antigen
   B. Enzyme immunoassay
   C. Nucleic acid amplification
   D. Viral isolation by culture

While waiting for the infant's test results, the woman asks the pediatrician to describe the most likely clinical presentation in an infant with a maternally acquired HIV infection.

4. Of the following, the most likely clinical diagnosis in an *untreated infant* with a maternally acquired HIV infection is:

   A. Disseminated candidiasis
   B. *Pneumocystis jirovecii* pneumonia
   C. Toxoplasmosis
   D. All of the above

CASE 9

Cytomegalovirus

A 6-month-old female infant with a diagnosis of cytomegalovirus (CMV) infection has an appointment in the Pediatric Infectious Diseases Clinic. The pediatric resident rotating in the clinic reviews the infant's medical records prior to the visit.

1. Of the following, acquisition of CMV infection may have occurred in this infant:

   A. By a blood transfusion
   B. During delivery
   C. Via infected breast milk
   D. All of the above

The resident learns that the infant acquired CMV by transplacental passage in utero.

2. Of the following, the most accurate statement about the intrauterine transmission of CMV is:

   A. A fetus is at greater risk of acquiring CMV infection if maternal infection occurs during the second half of pregnancy instead of the first half of pregnancy.
   B. CMV is the most common intrauterine infection worldwide.
   C. More than 80% of infants with congenital CMV are symptomatic and have clinical sequelae.
   D. All of the above

The infant was symptomatic with classic findings of congenital CMV infection after birth.

3. Of the following, the most likely clinical finding in the infant in this vignette is:

   A. Large for gestational age
   B. Macrocephaly
   C. Periventricular intracerebral calcifications
   D. Thrombocytosis

Upon further review of the infant's records, the resident finds that the infant had three normal hearing screens (day of life 2, age 2 months, and age 4 months). The parents report that their baby is able to hear noises and have no concerns about her hearing.

4. Of the following, this infant's risk of hearing loss is:

   A. 1% to 5% because the infant's hearing screen was normal soon after birth
   B. 10% to 15% because the 6-month-old infant's hearing seems appropriate to the parents
   C. 30% to 40% because of the diagnosis of symptomatic congenital CMV infection
   D. 80% to 90% because of the diagnosis of symptomatic congenital CMV infection

CASE 10

Immunizations

A male infant is born at 28 weeks' gestation with a birth weight of 960 g. He has a typical clinical course in the Neonatal Intensive Care Unit (NICU), complicated by surfactant deficiency, apnea of prematurity, feeding immaturity, anemia of prematurity, and mild retinopathy of prematurity. He is discharged home at 35½ weeks' postmenstrual age, weighing 1,995 g. At his first pediatric appointment at 36 weeks' postmenstrual age, the pediatrician meets with the family and discusses the approach to immunizations in a former preterm infant.

1. Of the following, the *least* accurate statement is:

   A. Most preterm infants have an adequate immune response postvaccination to prevent disease.
   B. Preterm infants should receive a lower vaccine dose than term infants.
   C. Preterm infants should receive inactivated vaccines while in the hospital.
   D. Very-low-birth-weight infants may have an increase in cardiorespiratory events postvaccination.

The pediatrician then plans the vaccination schedule for this infant.

2. Of the following, the most appropriate timing of this infant's 2-month set of vaccinations is:

   A. Simultaneously at 36 weeks' postmenstrual age (i.e., at 2 months' chronologic age)
   B. Simultaneously at 48 weeks' postmenstrual age (i.e., 2 months after the estimated due date)
   C. Simultaneously once the infant's weight is over 2,500 g
   D. Separation of vaccines in 1-week intervals, starting at 36 weeks' postmenstrual age

To protect the preterm infant until he can be vaccinated against influenza and receive the complete set of pertussis vaccinations, the pediatrician also discusses that household members should receive influenza each year and an acellular pertussis booster dose.

SECTION VII

Answers

CASE 1 ANSWERS

1. A. Infection

Premature rupture of membranes (PROM) describes the rupture of the amniotic sac prior to the onset of labor. If the rupture occurs prior to 37 weeks' gestation and prior to labor, this is termed "preterm premature rupture of membranes" (PPROM). In either situation, the fetus becomes susceptible; bacteria from the maternal vaginal flora can ascend and lead to chorioamnionitis and a fetal infection. If a woman's membranes rupture prematurely, she will need to be monitored closely for signs of infection. If there is a concern for chorioamnionitis, the obstetrician will need to deliver the baby.

For infants born after several weeks of PPROM without reaccumulation of the amniotic fluid, there is an increased risk for pulmonary *hypo*plasia. Renal function in these infants is not usually affected.

2. A. Ampicillin and gentamicin

For a newborn with suspected sepsis, the appropriate antibiotic regimen should provide a broad coverage of gram-negative and gram-positive organisms that are present in the maternal genital tract. These organisms include the following:

- *Group B Streptococcus*
- *Escherichia coli*
- *Listeria monocytogenes*
- Nontypeable *Haemophilus influenzae*
- *Enterococcus*

Because *Listeria monocytogenes* is a possible cause of neonatal sepsis, coverage with ampicillin is important.

3. D. Listeria monocytogenes

A pregnant woman can acquire a *Listeria monocytogenes* infection by consuming unpasteurized milk, unpasteurized soft cheeses, unwashed raw vegetables, or uncooked meat. Approximately 65% of pregnant women infected with *Listeria* will have a prodromal flu-like illness with headache, malaise, fever, and gastrointestinal symptoms. Infants can then acquire early-onset disease by transplacental transmission (most common) of the gram-positive rod or by ingestion or aspiration of infected amniotic fluid. The amniotic fluid of infected infants may have a brown-colored appearance, sometimes mistaken for meconium. Infants can also acquire a late-onset *Listeria* infection by a nosocomial route or from a colonized mother.

4.

A	i
B	i and ii
C	ii
D	i and ii
E	ii
F	ii
G	ii
H	i

The characteristics of early-onset and late-onset sepsis are compared in Table 1.

TABLE 1. Early-Onset and Late-Onset Comparisons

	Early-Onset Sepsis	Late-Onset Sepsis
Timing	Presents 0 to 6 days of life (some studies narrow to 0–3 days)	Presents 7 to 10 days of life (may occur later in premature infant)
Acquisition	From maternal genital tract	Either maternal genital tract or postnatal environment
Organisms	GBS, *E. coli*, *Listeria*, nontypeable *H. influenzae* (*H flu*), and *Enterococcus*	*Staphylococcus* (*Staph*) coagulase-negative, *Staph aureus*, *Pseudomonas*, GBS, *E Coli*, and *Listeria*
Clinical	Fulminant Multisystem involvement (greater risk of pneumonia)	Usually slowly progressive Focal involvement (greater risk of meningitis)
Mortality	Greater mortality (15%–45%)	Lower mortality (10%–20%)

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AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the significance for infection of prolonged premature rupture of the membranes
- Know the appropriate antibiotic treatment for suspected sepsis in the immediate newborn period
- Recognize *Listeria monocytogenes* as a cause of neonatal sepsis
- Understand the risk of sepsis from the use of intravascular catheters

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 2 ANSWERS

1. D. All of the above

GBS can be found in human gastrointestinal and genitourinary tracts. Between 15% and 35% of pregnant women are colonized with this organism. Transmission of GBS from a colonized mother to her infant can occur:

- Shortly before delivery
- During delivery
- Postnatally from a colonized caregiver or healthcare professional with inadequate hand hygiene

Because of the high risk of neonatal GBS disease, all pregnant women are screened for GBS vaginal/rectal colonization between 35 and 37 weeks' gestation.

2. A. Advanced maternal age

Early-onset GBS disease is characterized by a systemic infection in a neonate less than 7 days of age. In contrast, late-onset GBS disease usually occurs at 3 to 4 weeks of age with a range between 7 and 89 days of life. Risk factors of early-onset disease include the following:

- Black race
- Chorioamnionitis
- High inoculum of maternal genital GBS
- Intrauterine fetal monitoring
- Low maternal antibody concentration to the capsular polysaccharide of the infecting strain
- Maternal age less than 20 years
- Maternal GBS bacteriuria during the current pregnancy
- Maternal fever ≥ 38°C (100.4°F)
- Preterm birth (i.e., <37 weeks' gestation)
- Rupture of membranes >18 hours
- Sibling with invasive GBS disease in the neonatal period

3. C. GBS colonization during a prior pregnancy, regardless of current GBS status

To minimize the risk of neonatal GBS disease, 2010 guidelines from the Centers for Disease Control and Prevention and the American Academy of Pediatrics recommend maternal intrapartum chemoprophylaxis in the following scenarios:

- A woman with GBS bacteriuria during current pregnancy
- A woman with prior infant with invasive GBS disease, regardless of current GBS status
- A woman with unknown GBS status and any of the following:
  - Preterm labor
  - Duration of membrane rupture for 18 hours or longer
  - Intrapartum temperature ≥ 38°C (100.4°F)

A woman with GBS colonization during a prior pregnancy does *not* require intrapartum chemoprophylaxis unless she is GBS-positive in the current pregnancy. For those women who have a cesarean prior to the onset of labor and have intact amniotic membranes, intrapartum antimicrobial prophylaxis is not indicated.

4. C. Penicillin

To obtain adequate intrapartum GBS prophylaxis, the pregnant woman needs to receive the appropriate antibiotic 4 or more hours prior to delivery. The preferred antibiotic for maternal intrapartum chemoprophylaxis is intravenous penicillin G because of its high efficacy and narrow antimicrobial activity. Alternatively, intravenous ampicillin can be administered. For women who are mildly allergic to penicillin, intravenous cefazolin can be used to prevent early-onset neonatal GBS disease. For those women at high risk for anaphylaxis with penicillin exposure, intravenous clindamycin can be administered if the GBS isolate is sensitive to clindamycin. For those women with unknown GBS sensitivity or clindamycin-resistant GBS, intravenous vancomycin can be used. However, the efficacy of clindamycin or vancomycin is uncertain. Oral antimicrobials are not appropriate for chemoprophylaxis.

5. B. A lower incidence of early-onset neonatal GBS disease by 80%

Prior to the implementation of GBS chemoprophylaxis, the incidence of early-onset GBS neonatal disease was 1 to 4 cases per 1,000 live births and 1 to 2 infants per 100 colonized women. After implementing widespread maternal intrapartum antibiotic prophylaxis, this incidence of early-onset disease decreased by ~80% to 0.28 cases per 1,000 live births (2008 data). In contrast, maternal chemoprophylaxis has not had any impact on the incidence of late-onset disease, the risk of neonatal disease in future pregnancies, or the length of labor.

6. A i
B i
C ii
D iii
E iii
F iii

In a symptomatic newborn, the clinician should perform a complete diagnostic evaluation (complete blood count with differential, blood culture, and lumbar puncture) and initiate antibiotics, regardless of adequacy of intrapartum GBS prophylaxis (option F). However, for well-appearing infants who are born to a GBS-colonized mother, the approach is more targeted. If the mother received adequate intrapartum prophylaxis and there are no signs of chorioamnionitis (option A) or the mother had inadequate intrapartum prophylaxis with duration of membrane rupture less than 18 hours without a maternal fever (option B), observation of the infant is recommended. If the infant is born <37 weeks' gestation or the duration of membrane rupture is ≥18 hours with inadequate prophylaxis (option C), then the infant requires a limited evaluation (complete blood count/differential and blood culture) and observation for a minimum of 48 hours. If the culture is positive or the infant's clinical status changes, antibiotic therapy is needed. If chorioamnionitis is suspected, a limited evaluation with a complete blood count with differential and a blood culture and initiation of antibiotics is warranted, regardless of whether there is adequate intrapartum GBS prophylaxis (options D and E).

7. A. Meningitis

Early-onset GBS disease is characterized by systemic infection in a neonate less than 7 days of age. Newborns with early-onset GBS disease typically have the following clinical manifestations:

- Apnea
- Pneumonia
- Respiratory distress
- Septicemia
- Shock

Meningitis occurs less frequently (5%–10% of affected newborns).

In contrast, late-onset GBS disease usually occurs at 3 to 4 weeks of age with a range between 7 and 89 days of life. Affected infants typically have bacteremia or meningitis. Less frequently, late-onset GBS disease can manifest with focal infections, including cellulitis, osteomyelitis, pneumonia, and/or pyogenic arthritis.

8. D. All of the above

When an infant has a presumptive GBS infection, use of intravenous ampicillin and an aminoglycoside is the initial preferred antimicrobial regimen. Once the GBS organism has been identified, intravenous penicillin G can be administered. Oral penicillin is inadequate in the treatment of GBS disease in infants.

The length of treatment of a GBS infection in an infant depends on the location of the infection. For example, a 10-day course of antibiotics is appropriate for an infant with bacteremia, while a minimum of 14 days is recommended for uncomplicated meningitis, and an infant with septic arthritis or osteomyelitis requires 3 to 4 weeks of therapy.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the mode of transmission of Group B *Streptococcus*
- Understand the importance of maternal screening for Group B *Streptococcus* and the appropriate treatment of women with positive results
- Know the recommendations for evaluation of an infant whose mother is colonized with Group B *Streptococcus* and how the administration of intrapartum antibiotic therapy affects the evaluation
- Recognize the major clinical manifestations of Group B streptococcal infection: early-onset septicemia and pneumonia; late-onset bacteremia, pneumonia, meningitis, pyogenic arthritis, osteomyelitis
- Know the treatment of Group B *Streptococcus* infection

SUGGESTED READING

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

CASE 3 ANSWERS

1. F. A, C, and D

A pregnant woman with a primary genital herpes lesion at delivery has a 25% to 60% chance of having a neonate who is infected with herpes. This high risk is because of the following:

- High viral replication
- Longer excretion of virus from a primary lesion (3 weeks if primary infection vs. 2–5 days of shedding if recurrent herpes)
- Lack of maternal antibodies transferred to neonate

In contrast, a pregnant woman with a secondary genital herpes lesion during delivery has less than a 5% chance of having a neonate who is infected because of protective maternally transmitted antibodies. More than 75% of neonates who acquire a herpes infection are born to women who are asymptomatic or without a history of genital herpes.

2. Higher risk is associated with:

A. Vaginal birth
B. Maternal genital lesion at delivery
C. Premature infant
D. Rupture of membranes more than 6 hours prior to delivery
E. Use of a fetal scalp monitor

The risk of a neonate acquiring HSV is greatest if the mother has a primary genital lesion at the time of a vaginal delivery. Additional risk factors include the following:

- Prematurity because of low transplacental antibodies
- Fetal scalp monitoring because of the potential that an infant's skin barrier is broken, allowing easier entry of herpetic cells
- Rupture of membranes more than 4 hours because of the increased risk of ascending infection

3. D. All of the above

For an asymptomatic infant born by vaginal delivery to a woman with a primary active genital lesion, infectious diseases experts recommend the following:

- Obtain surface cultures of conjunctivae, nasopharynx, mouth, and rectum at 12 to 24 hours of age; the delay in obtaining surface cultures in an asymptomatic infant will allow the cultures to reflect viral replication instead of contamination from an exposure.
- Monitor the infant closely.
- Some experts suggest empirical intravenous acyclovir after surface cultures are obtained.

For asymptomatic infants born by vaginal delivery to a woman with a secondary genital lesion at the time of delivery, most experts would *not recommend* intravenous acyclovir unless surface cultures are positive.

4. B. Monitor the infant closely

For an asymptomatic infant born by vaginal delivery to a woman with a history of genital herpes but no active lesions at the time of delivery, the following is recommended:

- Monitor the infant closely and educate the family to monitor for signs and symptoms of HSV disease during the first 6 weeks of life.
- It is not necessary to obtain surface cultures for HSV.
- Empiric acyclovir therapy is not indicated.

5. C. Two to 3 weeks of age

The most likely timing of neonatal symptoms from perinatal acquisition of HSV is between 2 and 3 weeks of age. In contrast, infants with congenital HSV will be symptomatic immediately after delivery.

6. D. All of the above

There are three types of clinical presentations of neonatal herpes:

1. Disseminated (systemic) disease
2. Encephalitis (CNS involvement)
3. Skin, eye, mucous membranes (SEM)

There is some overlap with each of these disorders. Table 1 compares the timing, incidence, clinical features, morbidity, and mortality of these three types. Of note, while skin findings are common, they are not always present in neonates with herpes.

TABLE 1. Neonatal Herpes Disease

	Disseminated (Systemic)	SEM	Encephalitis (CNS)
Timing	4 to 10 days of life	6 to 9 days of life	10 to 18 days of life
Incidence	20%	40% to 45%	30% to 35%
Clinical	Fever, lethargy, irritability, poor oral intake Respiratory distress may be presenting sign in ~20% secondary to pneumonitis Hepatomegaly, adrenal gland involvement Coagulopathy, shock ~60% with skin involvement May also have CNS (60%–75%, results from hematogenous spread) or SEM (80%)	Most common Eyes: conjunctivitis, keratitis, chorioretinitis, retinal dysplasia Skin (80%–85%): papulovesicular lesions, often pustular and with erythematous base, often occurs at sites of trauma, risk of scar formation	Initially with fever, lethargy, and seizures Irritability, apnea Bulging fontanel Pyramidal tract signs ~60% with skin involvement CNS involvement (probably results from retrograde axonal transmission to brain)
Morbidity	~30% to 80% normal development if treated	Treatment minimizes risk of progression to disseminated or CNS disease Normal development in >90% if treated Greatest risk of neurologic sequelae if ≥3 skin recurrences	30% with normal development Increased risk of microcephaly, spasticity, blindness, chorioretinitis, developmental delay
Mortality	~30% (despite treatment)	Minimal	~4% to 10% (despite treatment)

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7. D. Intravenous acyclovir × 3 weeks, followed by oral acyclovir suppressive therapy × 6 months

Infants with SEM disease require intravenous acyclovir for 2 weeks. Those with CNS disease or disseminated disease should be treated for a minimum of 3 weeks. Oral acyclovir suppressive therapy for 6 months after treatment of acute HSV disease has been shown to improve neurodevelopmental outcomes in those infants with HSV CNS disease. This approach also has been shown to prevent additional skin lesions, regardless of the type of HSV. Infants with ophthalmologic involvement require a topical ophthalmologic medication in addition to intravenous acyclovir.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that newborns of mothers with primary herpes infections are more likely to be infected than infants born to mothers with recurrent genital herpes simplex infections
- Recognize that herpes simplex virus can be transmitted from a person with a primary or recurrent infection regardless of whether any symptoms are present
- Know the appropriate tests for the diagnosis of herpes simplex infection
- Recognize the clinical manifestations of herpes simplex virus infection in the neonatal period and that skin lesions are not always present
- Plan the appropriate management of a neonatal herpes simplex infection

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Westhoff GL, Little SE, Caughey AB. Herpes simplex virus and pregnancy: A review of the management of antenatal and peripartum herpes infections. *Obstet Gynecol Surv*. 2011;66:629–638.

CASE 4 ANSWERS

1. C. Respiratory syncytial virus (RSV)

RSV is the most common cause of lower respiratory infections in infancy. Most children acquire this infection during the first year of life. Affected infants typically have an upper respiratory illness, and ~20% to 30% also have a lower respiratory illness, such as bronchiolitis or pneumonia. Infants often present with the following symptoms:

- Cough
- Low-grade fever
- Nasal congestion
- Respiratory distress
- Tachypnea
- Wheezing

Preterm infants who acquire RSV during the first few weeks to months of life often present with lethargy, irritability, poor oral intake, and apnea.

2. C. Rate of hospitalization

Palivizumab has been shown to decrease the rate of RSV-associated hospitalizations in infants at high risk for RSV. Trials have not shown a significant decrease in mortality attributable to an RSV infection, in the rate of recurrent wheezing after an RSV infection, or in the transmission rate of RSV. Palivizumab administration is not helpful in the treatment of RSV disease.

3. C. All premature infants with a diagnosis of chronic lung disease

The American Academy of Pediatrics *Red Book* summarizes the most recent eligibility criteria for RSV prophylaxis of high-risk infants. The 2012 guidelines recommend RSV prophylaxis with palivizumab during the first winter season in the following infants:

- All infants with a diagnosis of chronic lung disease (i.e., receiving supplemental oxygen, bronchodilator, diuretic, or chronic corticosteroid treatment); those infants with severe disease who continue to need these therapies during their second winter season may benefit from a second prophylactic course.
- All infants born ≤31 6/7 weeks' gestation
- Infants born at 32 0/7 weeks' gestation and <35 weeks' gestation who attend child care or have a sibling <5 years of age (prophylaxis should be continued until the infant is 3 months of age for a maximum of three doses)
- Infants with airway abnormalities or neuromuscular disease
- Infants with cyanotic heart disease, symptomatic heart disease requiring medication to treat congestive heart failure, and moderate or severe pulmonary hypertension

Prophylaxis is *not* recommended for infants with any of the following:

- Mild cardiomyopathy without requiring medications
- Mild coarctation of the aorta
- Patent ductus arteriosus
- Pulmonic stenosis
- Secundum atrial septal defect
- Small ventricular septal defect
- Surgically corrected structural heart disease unless medication is still required to treat congestive heart failure
- Uncomplicated aortic stenosis

Infants with severe immunodeficiencies may benefit from RSV prophylaxis. Because of limited data in patients with cystic fibrosis, there is no current recommendation for routine RSV prophylaxis in this population.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that respiratory syncytial virus is the most common cause of lower respiratory infections in infancy
- Identify patients at high risk for morbidity and mortality from respiratory syncytial virus infection (e.g., those with congenital heart disease, bronchopulmonary dysplasia, prematurity) and those who may benefit from prophylaxis

SUGGESTED READING

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

CASE 5 ANSWERS

1. D. All of the above

The management of a full-term infant who weighs over 2,000 g at birth and is born to a woman with an unknown HBsAg status includes the following:

- Test the infant's mother for HBsAg as soon as possible
- Administer the first HBV within 12 hours of age to the infant
- Administer HBIG as soon as possible if the mother is positive for HBsAg or *by 1 week of age* if she remains HBsAg-unknown
- Complete hepatitis B immunization series with a total of three doses

This rationale for delaying the HBIG is because the vaccine is effective at preventing hepatitis infection in term infants.

2. D. All of the above

The management of an infant who weighs less than 2,000 g at birth and is born to a woman with an unknown HBsAg status includes the following:

- Test the infant's mother for HBsAg as soon as possible
- Administer the first HBV within 12 hours of age to the infant
- Administer HBIG *within 12 hours of age* if the mother is positive for HBsAg or if she remains HBsAg-unknown
- Complete hepatitis B immunization series with a total of *four doses*

Earlier administration of HBIG in this lower-birth-weight population is recommended because the immune response of these infants is less reliable.

3. A. Administer HBV and HBIG by 12 hours of age

The management of an infant who is born to a woman with a positive HBsAg status includes the following:

- Administer the first HBV to the infant within 12 hours of age, regardless of birth weight
- Administer HBIG to the infant within 12 hours of age, regardless of birth weight
- Complete the hepatitis B immunization series with a total of three doses for infants with a birth weight ≥2,000 g and provide a total of four doses for infants with a birth weight <2,000 g
- Test the infant for HBsAg and anti-HBs at 9 to 18 months of age; earlier testing leads to false-positive results because of possible detection of antibodies from the HBIG administration after birth. In addition, earlier testing may not detect late-onset Hepatitis B virus infections.

Concurrent dosing of HBV and HBIG should be administered at different anatomic sites.

A positive maternal HBeAg status *increases* the chance of transmission because of the associated high degree of replication. Without prophylaxis, an infant's risk of acquiring hepatitis B from a mother who is HBsAg-positive and HBeAg-positive is 70% to 90%. For women who are HBsAg-positive but HBeAg-negative, the risk of neonatal transmission is 5% to 20%. Infants born to an HBsAg-positive woman receive two types of immunoprophylaxis: HBV and HBIG. While the HBV provides long-term protection, the HBIG provides short-term protection (up to 1 week after administration).

4. C. Labor and delivery

Transmission of hepatitis B virus from an infected mother to her baby typically occurs by blood exposure during labor and delivery. There is no additional risk of hepatitis B viral transmission to infants who have been breast-fed by HBsAg-positive mothers and have received appropriate immunoprophylaxis with HBV and HBIG. Intrauterine transmission of this virus is very small, accounting for less than 2% of perinatal infections. Postpartum transmission of hepatitis B is unlikely for infants who have received the appropriate HBV.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Plan the treatment of an infant born to a woman who is a hepatitis B carrier (e.g., combination of hepatitis vaccine and hepatitis B immune globulin [HBIG] at birth)

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 6 ANSWERS

1. D. All of the above

A neonate must be evaluated for syphilis soon after birth in the following scenarios:

- If the baby is born to a seropositive mother with untreated syphilis
- If the mother is treated for syphilis during pregnancy with a nonpenicillin antibiotic
- If the mother was appropriately treated during pregnancy but this treatment occurred less than 4 weeks prior to delivery; evaluation is necessary because of the potential for a treatment failure
- If the mother was appropriately treated during pregnancy but did not show a fourfold (or more) decrease in viral titers.
- If the mother was appropriately treated during pregnancy but had insufficient follow-up
- If the baby has symptoms that are consistent with syphilis

2. C. Gestation (by transplacental route)

The transplacental route is the most common mode of acquisition of syphilis in the neonate. If a pregnant woman has primary syphilis that is untreated, there is a 70% to 100% risk of fetal acquisition.

An infant can acquire syphilis by contact with an active vaginal lesion during delivery, but this is less common than intrauterine acquisition. Transmission of syphilis by direct maternal contact and breast-feeding is unlikely. Acquired syphilis in children and adults almost always occurs through sexual contact with infected lesions or mucous membranes

3. C. Hutchinson triad

Congenital syphilis can result in prenatal findings, including stillbirth, hydrops fetalis, or preterm birth. Affected infants can be asymptomatic at birth (⅔) or have clinical findings that present within the first 2 months of age (⅓). These symptoms include the following:

- Chorioretinitis and/or uveitis
- Copious nasal secretions (also known as snuffles)
- Desquamating maculopapular rash involving the palms and soles or bullous eruptions
- Erb palsy
- Hemolytic anemia
- Hepatosplenomegaly
- Leptomeningitis
- Lymphadenopathy
- Nephrotic syndrome
- Osteochondritis
- Pneumonia
- Pseudoparalysis
- Thrombocytopenia

Untreated infants with congenital syphilis have additional findings that are evident after 2 years of age, including:

- Anterior bowing of shins (known as saber shins)
- Clutton joints (symmetric, painless knee swelling)
- Cognitive deficits
- Eighth cranial nerve deafness (evident at 10 to 40 years of age)
- Frontal bossing
- Hutchinson teeth (peg-shaped, notched central incisors)
- Interstitial keratitis (evident at 5 to 20 years of age)

Hutchinson triad refers to the combination of eighth cranial nerve deafness, Hutchinson teeth, and interstitial keratitis. These late findings of congenital syphilis can be prevented with appropriate early treatment.

4. C. Mother: positive RPR, positive FTA; infant: negative RPR, positive FTA

The RPR or VDRL test is a nontreponemal antibody test that detects cell membrane cardiolipin nonspecific IgG antibodies. It is reported as a titer, and it correlates with disease activity. In contrast, FTA detects a specific antibody to *Treponema pallidum*, remains active for life, and does not correlate with disease activity. Because of potential false-positive results, a diagnosis of syphilis requires both nontreponemal and treponemal testing.

If a mother tests positive for RPR and FTA with an infant who is negative or positive for RPR and positive for FTA, this is consistent with a mother with syphilis and an infected neonate.

If a mother tests negative for RPR and positive for FTA with an infant who is negative for RPR and positive for FTA, the mother has been successfully treated for syphilis or has a false-positive serology.

If a mother tests positive for RPR and negative for FTA with an infant who is also positive for RPR and negative for FTA, this is consistent with a false-positive nontreponemal test. Thus, the mother does not have syphilis and there has been passive transfer of RPR antibodies to the neonate.

5. B. Aqueous crystalline penicillin G administered intravenously × 10 days

For neonates with a definite or likely diagnosis of congenital syphilis, the most appropriate treatment is aqueous crystalline penicillin G administered intravenously for 10 days. An alternative treatment is procaine penicillin G administered intramuscularly for 10 days; although procaine penicillin G has low entry into the CSF, treatment failures have not been reported. For neonates who are at risk for congenital syphilis but have a benign examination with normal radiographic imaging and laboratory testing, some infectious diseases experts recommend treatment with penicillin G benzathine intramuscularly for 10 days. There is no data to support ampicillin for the treatment of congenital syphilis. After treatment, infants need to be followed closely with serum and CSF VDRL tests.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the mode of transmission of *Treponema pallidum*
- Recognize the clinical manifestations of congenital and acquired syphilis
- Plan the laboratory diagnosis of congenital syphilis
- Know the treatment of congenital syphilis (i.e., penicillin), and that CNS involvement must always be considered when planning the treatment

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 7 ANSWERS

1. C. The baby most likely has congenital toxoplasmosis from a primary maternal infection.

Almost all infants with congenital toxoplasmosis acquire the illness from a primary maternal infection during pregnancy. Most women are asymptomatic or have mild symptoms during this infection. Approximately 70% to 90% of infants with congenital toxoplasmosis are asymptomatic at birth.

2. D. All of the above

The organism that causes toxoplasmosis is a protozoan and an intracellular parasite. Members of the cat family serve as primary hosts. Cats usually acquire this parasite by eating infected animals (e.g., mice), uncooked household meats, or water or food contaminated with their own feces that contain oocysts. After replication in the cat's intestinal epithelium, oocysts are excreted for up to 2 weeks. These excreted oocysts can then become sporulated in a maturation process that takes 1 to 2 days. Once sporulated, oocysts can survive in soil for months to years. Sheep, pigs, and cattle can be intermediate hosts and have cysts located in their tissues.

Humans can acquire toxoplasmosis by eating undercooked animal tissues containing cysts or by ingesting sporulated oocysts found in soil, water, or contaminated food. In addition, transmission of *T. gondii* can occur by organ transplantation, laboratory accidents, or blood transfusions. Human-to-human transmission can occur only from a pregnant woman to her fetus. The life cycle of the *T. gondii* parasite is shown in Figure 1.

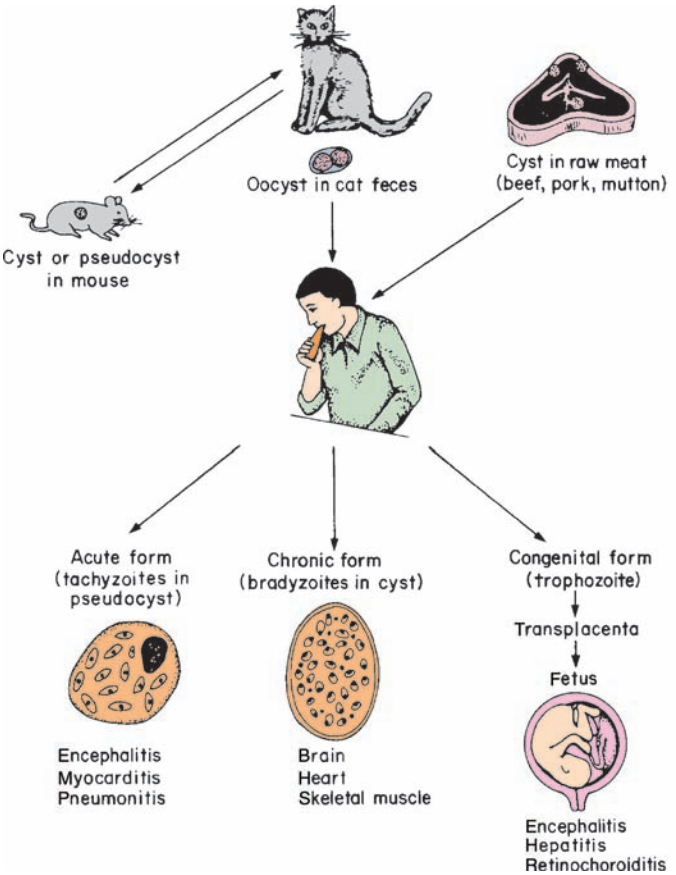

FIGURE 1. From Tsieh S. *Parasitic Disorders: Pathology, Diagnosis, and Management*. 2nd ed. Baltimore, MO: Lippincott Williams & Wilkins; 1999. Figure 14.1

3. D. All of the above

Infants with congenital toxoplasmosis have two possible clinical presentations:

1. Clinical findings in the neonatal period (least common)
2. Subclinical infection in the neonatal period with symptoms during the first few months to years of life (most common)

Infants with congenital toxoplasmosis usually present with visual impairment, hearing loss, learning disabilities, or mental deficiency during the first few months to years of life.

Clinical findings in the neonatal period are less common. Affected neonates may have neurologic findings, such as:

- Chorioretinitis
- Cortical brain calcifications
- Hydrocephalus
- Meningoencephalitis
- Microcephaly
- Seizures

The triad of chorioretinitis, cortical brain calcifications, and hydrocephalus is highly suggestive of congenital toxoplasmosis. Affected neonates may also have a blueberry muffin rash from dermal erythropoiesis, hearing loss, growth restriction, hepatosplenomegaly, lymphadenopathy, maculopapular rash, and thrombocytopenia.

4. D. Pyrimethamine and sulfadiazine × 1 year

For both symptomatic and asymptomatic infants with congenital toxoplasmosis, treatment with pyrimethamine and sulfadiazine is recommended. Infants need to be followed by an infectious diseases expert to determine the dose and length of treatment; typically, infants are treated for 1 year. Folinic acid is recommended while infants are receiving sulfadiazine. For those infants with mild toxoplasmosis, sometimes this regimen is alternated monthly with spiramycin during treatment months 7 to 12.

5. B. Fever, rash, myalgia, cervical lymphadenopathy

Infants, children, or adults who acquire a *T. gondii* infection after birth are usually asymptomatic. For those who develop symptoms, findings include the following:

- Arthralgia
- Fever
- Headache
- Lymphadenopathy, cervical (this is the most common sign)
- Malaise
- Myalgia
- Sore throat

Some patients may present with isolated ocular toxoplasmosis with chorioretinitis, leading to visual changes or visual disturbances. Less common symptoms include a mononucleosis-like illness, macular rash, and hepatosplenomegaly. Affected individuals typically have a self-limited clinical course. Immunocompromised patients may have more severe effects, such as myocarditis, myositis, hepatitis, pericarditis, pneumonia, or brain abscesses.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that the majority of newborns with congenital toxoplasmosis are asymptomatic in the neonatal period
- Know the epidemiology of toxoplasmosis: hosts, intermediate hosts, modes of transmission (vertical transmission from mother to infant, ingestion of cysts from contaminated food or soil)
- Know the clinical manifestations of congenital toxoplasmosis
- Recognize the importance of prompt treatment of congenital toxoplasmosis
- Identify the clinical manifestations of *Toxoplasma gondii* infections acquired after birth

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 8 ANSWERS

1. C. Intrapartum

Maternal transmission of HIV to an infant can occur by the following routes:

- Breast-feeding
- Intrapartum route (most common mode of transmission in the United States)
- Transplacentally throughout gestation

Breast-feeding is not recommended for HIV-positive women in the United States because formula is a safe alternative to human milk. However, for HIV-positive women in underdeveloped countries, the 2010 World Health Organization recommends breast-feeding because a safe alternative to human milk is not available.

2. D. All of the above

The risk of transmission of HIV infection from an untreated HIV-positive mother to her infant is 21% to 25% in the United States. Table 1 summarizes the highest risks associated with transmission of HIV from an HIV-positive pregnant woman to her infant.

TABLE 1. High Risks Associated with Transmission of HIV From an HIV-Positive Pregnant Woman to Her Infant

Maternal-disease specific risks	Advanced maternal illness
	Low maternal CD4 T-lymphocyte count
	Increased maternal viral load
	Newly acquired infection during the last trimester of pregnancy (because a primary infection is associated with a greater viral load)
Labor-specific risks	Chorioamnionitis
	Fetal scalp electrode
	Preterm delivery
	Prolonged labor
	Prolonged rupture of membranes, regardless of delivery mode
	Vaginal delivery (particularly if prolonged rupture of membranes)
Postnatal	Breast-feeding
Other	Increased exposure of fetus to maternal blood in utero
	Mother–infant human leukocyte antigen concordance

Approaches to decrease the transmission rate of HIV from an HIV-positive mother to her infant include the following:

- Oral antiretroviral medications to the woman during pregnancy
- Intravenous antiretroviral medication to the woman during delivery
- Oral antiretroviral prophylaxis to the infant for 6 weeks after birth
- Avoidance of breast-feeding (recommended approach in the United States)
- Cesarean delivery before the onset of labor and before rupture of membranes if maternal viral load > 1,000 copies/mL or unknown viral load

Because these approaches have markedly decreased the risk of perinatal HIV transmission, the American Academy of Pediatrics currently recommends that all pregnant women, with their consent, undergo HIV testing. For those women with an unknown HIV status, clinical providers should obtain rapid HIV antibody testing on the mother or infant after state-specific consent is obtained.

3. C. Nucleic acid amplification

Nucleic acid amplification by HIV-DNA polymerase chain reaction (PCR) assay is the preferred method of diagnosis of HIV infection in a neonate. Although ~30% of HIV-infected neonates will test positive for HIV-DNA by PCR at 48 hours of age, almost all HIV-infected neonates will have a positive DNA PCR assay result at 1 month of age. When an infant has a positive HIV-DNA PCR result, repeat testing is recommended at 1 to 2 months of age and again at 2 to 4 months of age. An infant is diagnosed with an HIV infection if two separate samples are positive by DNA PCR assays. In non-breast-feeding infants, two negative HIV DNA PCR assays confirm that the infant is not infected.

Detection of p24 antigen is less sensitive than testing by HIV-DNA PCR and may yield false-negative results because of a low amount of circulating antigen in asymptomatic infected infants. Detection of HIV antibody by enzyme immunoassay may yield false-positive results because of passively acquired maternal antibodies remaining in the infant until 18 months of age. Viral isolation by culture is not an ideal test in neonates because it is expensive and often requires up to 1 month to attain positive results.

4. B. Pneumocystis jirovecii pneumonia

P. jirovecii (previously known as *Pneumocystis carinii*) pneumonia is the most likely clinical presentation in an untreated infant with a maternally acquired HIV infection, occurring in approximately one-third of affected infants. Other clinical manifestations in an infant infected with HIV include the following:

- Lymphocytic interstitial pneumonitis (~25%)
- Recurrent bacterial infections (~20%)
- Encephalopathy (~15%)
- *Candida* esophagitis (~15%)
- Cytomegalovirus infection (~10%)
- *Mycobacterium avium* infection (~10%)
- Herpes simplex virus infection (~5%)
- Cryptosporidiosis (~5%)

A child's risk of acquiring these opportunistic infections is significantly decreased with highly active antiretroviral therapy.

Unless an infant is receiving total parenteral nutrition or has a central venous catheter, disseminated candidiasis is uncommon in an HIV-infected child. Similarly, toxoplasmosis is not a common illness in HIV-infected children.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the means of maternal transmission of HIV to her infant (e.g., vaginal delivery, breast-feeding, transplacentally, intrapartum)
- Know that cesarean delivery and treatment of an HIV-positive mother with antiretroviral drugs decrease the risk of transmission of virus to her infant
- Know the preferred method of diagnosis of HIV infection in infancy (i.e., nucleic acid amplification test)
- Know the effect of a mother's HIV-positive status on her infant's HIV test
- Know the clinical manifestations of human immunodeficiency virus infection in neonates

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D. Clinical presentation of neonatal HIV. *NeoReviewsPlus*. April 5, 2008:Q7.

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Maldonado YA. Acquired immunodeficiency syndrome in the infant. In: Remington JS, Klein JO, Wilson CB, et al. , eds. *Infectious Disease of the Fetus and Newborn Infant*. 6th ed. Philadelphia, PA: Elsevier Inc; 2006:667–692.

CASE 9 ANSWERS

1. D. All of the above

An infant can acquire CMV by different modes, including:

- By a blood transfusion (less common because of use of CMV-negative blood)
- By intrauterine transmission (all trimesters)
- During delivery (from cervical secretions; term infants usually asymptomatic because of passively transferred maternal antibodies; preterm infants at risk for clinical findings)
- Secretions (requires close contact)
- Via infected breast milk (term infants are usually asymptomatic because of passively transferred maternal antibodies; preterm infants are at risk for clinical findings)

2. B. CMV is the most common intrauterine infection worldwide.

Worldwide, CMV is the most common intrauterine infection. Seroconversion from a positive to a negative status during pregnancy is not very common, occurring in 1% to 4% of pregnant women and the majority of these women are asymptomatic. Approximately 40% of fetuses will acquire CMV if the pregnant woman acquires a primary CMV infection. The risk of neonatal disease and the severity of the neonate's illness are highest if the pregnant woman acquires an infection during the first half of gestation. Of those fetuses who become infected with CMV, 85% to 90% will be *asymptomatic* and have normal development. These infants have asymptomatic congenital CMV. Of the remaining 10% to 15% who become infected, ~90% will have clinical sequelae (i.e., symptomatic congenital CMV).

3. C. Periventricular intracerebral calcifications

Infants with symptomatic congenital CMV infection can have the following findings:

- Chorioretinitis
- Coagulopathy
- Dermal hematopoiesis
- Growth restriction
- Hearing loss, sensorineural (most common clinical sequela of congenital CMV infection)
- Hepatosplenomegaly
- Indirect hyperbilirubinemia
- Microcephaly
- Periventricular intracerebral calcifications
- Thrombocytopenia

The computed tomography image in Figure 1 reveals periventricular calcifications, enlarged ventricles, and white matter volume loss in an infant with congenital CMV infection. Approximately half of affected infants are at risk for neurologic sequelae, including cognitive deficits, developmental delays, and seizures.

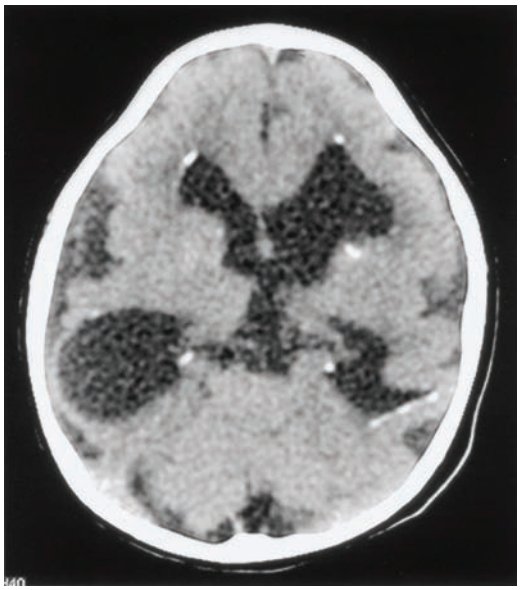


FIGURE 1. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 48.3

In contrast, infants who acquire CMV infection intrapartum or postnatally from infected breast milk or blood products typically are asymptomatic. However, some infants, such as preterm infants, may have clinical manifestations, such as pneumonitis, thrombocytopenia, hepatitis, poor head growth, and/or hearing loss.

4. C. 30% to 40% because of the diagnosis of symptomatic congenital CMV infection

Sensorineural hearing loss is the most common clinical consequence of symptomatic congenital CMV infection, occurring in 30% to 40% of affected children. In contrast, hearing loss occurs in 5% to 10% of children with asymptomatic congenital CMV. In those children with symptomatic congenital CMV and hearing loss, half will be identified during the newborns' hearing screening test and the remainder will be diagnosed during childhood. Thus, frequent audiology screening is necessary to identify children with late-onset CMV-related hearing loss.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that perinatal infection with cytomegalovirus may be acquired in utero, during delivery, or in the neonatal period (e.g., breast milk, blood transfusion)
- Recognize the clinical manifestations of symptomatic congenital cytomegalovirus disease, including congenital hearing loss and mental retardation

SUGGESTED READINGS

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 10 ANSWERS

1. B. Preterm infants should receive a lower vaccine dose than term infants

Preterm infant should receive the *same total vaccine dosage* as term infants. Clinicians should not divide the vaccine into multiple doses.

While data do show that some preterm infants (born $<$ 1,500 g and/or $<$ 29 weeks' gestation) have a decreased immune response to some of the vaccines, most preterm infants have an adequate immune response postvaccination to prevent disease.

If a preterm infant remains in the hospital at the time of vaccination, inactivated vaccines should be administered to medically stable infants (i.e., without current infection or acute illness).

Preterm infants have a similar tolerance to vaccines as term infants. However, very-low-birth-weight infants (i.e., weight < 1,500 g) have a higher incidence of cardiorespiratory events (apnea, bradycardia, and/or desaturation) after being vaccinated. These events are more likely if the infant has had apnea within 24 hours prior to being vaccinated, is of younger postmenstrual age, or has a current weight < 2,000 g.

2. A. Simultaneously at 36 weeks' postmenstrual age (i.e., at 2 months' chronologic age)

Preterm infants and infants should receive routine childhood vaccinations at the same chronologic age as do term infants. Thus, the infant in this vignette should receive the 2-month set of vaccinations at 36 weeks' postmenstrual age (i.e., at 2 months' chronologic age). Unless an infant is medically unstable or lacks vaccination sites, the 2-month set of vaccinations should be administered simultaneously.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that preterm infants should be immunized at the same postnatal age as full-term infant
- Plan an immunization schedule for a patient born three months prematurely

SUGGESTED READING

Baker CJ, Long SS, Pickering LK, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

SECTION VIII

Fluids, Electrolytes, and Nutrition

CASE 1

Fluid, caloric, and nutritional requirements

Two infants with respiratory distress are admitted to the Neonatal Intensive Care Unit soon after birth. One infant is born at 28 weeks' gestation, and the other infant is born at term. Both infants are started on maintenance intravenous fluids.

1. Select the most appropriate initial total fluid order for the infant born at 28 weeks' gestation and the infant born at term, respectively:

   A. 60 mL/kg/day for both
   B. 60 mL/kg/day and 100 mL/kg/day
   C. 100 mL/kg/day and 60 mL/kg/day
   D. 100 mL/kg/day for both

2. Match the findings below (A–F) with the appropriate gestational age (i–iv):

   A. Decreased ability to digest fats and absorb fat-soluble vitamins
   B. Greater fluid requirement per kilogram of body weight
   C. Greater insensible water loss (IWL)
   D. Greater protein requirement for adequate growth
   E. Lower caloric requirement per kilogram for adequate growth
   F. Most regain birth weight by 2 weeks of life

   i. Both full-term and preterm infants
   ii. Full-term infants
   iii. Preterm infants
   iv. Neither full-term nor preterm infants

CASE 2

Acidosis and alkalosis

A 1,300-g male infant is born at 30 5/7 weeks' gestation after unstoppable preterm labor. His mother is a 28-year-old woman with unremarkable prenatal screens aside from unknown Group B *Streptococcus* status. The infant is treated for respiratory distress syndrome with intubation and administration of surfactant. He is extubated to continuous positive airway pressure (CPAP) on postnatal day 2 and begins enteral feedings. On postnatal day 5, he has pronounced, frequent apnea and bradycardia episodes. The results of the sepsis evaluation and abdominal radiograph are reassuring. His serum electrolytes, blood gas, and urinalysis are as follows:

- Sodium = 137 mEq/L
- Potassium = 4.2 mEq/L
- Chloride = 108 mEq/L
- Bicarbonate = 15 mEq/L
- Arterial blood gas: pH = 7.2, P_{CO_2} = 41 mm Hg, bicarbonate = 15 mEq/L
- Urinalysis: pH = 7.5, no glucose, no protein

The neonatology team stops his enteral feedings, starts antibiotic therapy, and provides more supplemental alkali. His bicarbonate normalizes, and the team restarts enteral feedings.

1. Using the laboratory results from above, calculate the anion gap:

   A. 12
   B. 14
   C. 18
   D. 44

2. For each of the causes of metabolic acidosis (A–I), choose the corresponding selection (i, ii):

A. Acute renal failure	i. Elevated anion gap
B. Congenital adrenal hyperplasia	ii. Normal anion gap
C. Congenital hypothyroidism	
D. Galactosemia	
E. High-protein formula	
F. Inborn errors of metabolism	
G. Lactic acidosis	
H. Organic acidemias	
I. Toxins	

The infant in the next bed space was born at 28 weeks' gestation, is now postnatal day 5, and remains on the ventilator. His course has consisted of treatment for surfactant deficiency, a 48-hour rule-out sepsis with antibiotics, and phototherapy for indirect hyperbilirubinemia. His current settings on synchronized intermittent mandatory ventilation are:

- Peak inspiratory pressure = 20 mm Hg
- Peak end-expiratory pressure = 5 mm Hg
- Rate = 40 breaths per minute

He continues to breathe above the set rate of 40 breaths per minutes. His blood gas is as follows:

pH = 7.5, P_{CO_2} = 30 mm Hg, bicarbonate = 16 mEq/L

3. Select the most likely acid–base disorder:

A. Acute metabolic acidosis
B. Acute respiratory alkalosis
C. Chronic metabolic acidosis with compensation
D. Chronic respiratory alkalosis with compensation

CASE 3

Electrolyte abnormalities

A 690-g female infant is born at 24 weeks' gestation after unstoppable preterm labor. She is born to a 21-year-old woman with unremarkable prenatal screens aside from unknown Group B *Streptococcus* status. "Starter" parenteral fluid is initiated and consists of dextrose, sodium, and protein. The infant's serum electrolytes at 36 hours are as follows:

- Sodium = 143 mEq/L
- Potassium = 8.2 mEq/L
- Chloride = 110 mEq/L
- Bicarbonate = 18 mEq/L

1. Select the most likely etiology of her hyperkalemia:

A. Excess exogenous potassium
B. Necrotizing enterocolitis
C. Potassium shifts from the intracellular fluid (ICF) to the extracellular fluid (ECF) space
D. Renal failure

Soon after these results are reported, the bedside nurse notices a possible arrhythmia on the cardiorespiratory monitor.

2. Select the EKGs below (see Figure 1A–D) that would be consistent with cardiac changes in the setting of hyperkalemia:

A. Figure 1A
B. Figure 1B
C. Figure 1C
D. Figure 1D

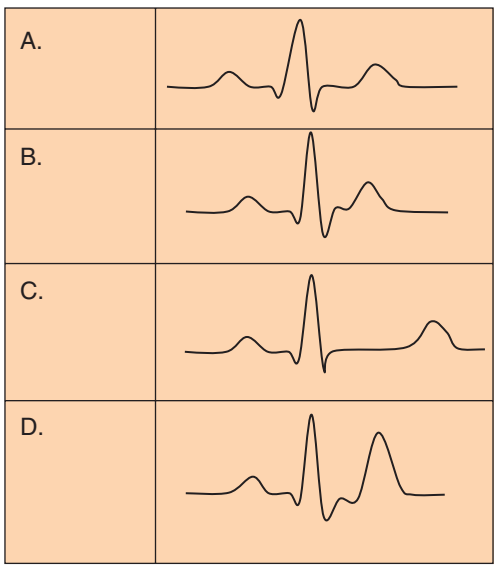


FIGURE 1.

3. Choose the next step(s) in medical management for this patient:

   A. Defibrillation
   B. Remove all exogenous potassium sources; give 10% calcium gluconate; give glucose and insulin; consider Lasix, $NaHCO_3^-$, and Kayexalate
   C. Synchronized cardioversion
   D. Vagal maneuvers; administration of adenosine; consider digoxin, propranolol, procainamide, flecanide, or verapamil

The infant is stabilized, and her serum potassium normalizes. A week later, she develops necrotizing enterocolitis and has a prolonged course of hyperalimentation. At 1 month of age, she is on full feedings and her nutrition laboratory values are notable for:

- Phosphorus = 3 mg/L
- Ionized calcium = 1.9 mg/L

4. Of the following, the most likely cause(s) of this infant's laboratory findings is:

   A. Congenital hyperparathyroidism
   B. Prolonged hyperalimentation with inadequate balance of calcium and phosphorus
   C. Transition to breast milk with limited nutritional supplementation
   D. All of the above

CASE 4

Mineral deficiencies

An 880-g male infant born at 28 weeks' gestation is now 6 months old and has hypochromic anemia unresponsive to iron therapy, neutropenia, and osteoporosis. In addition, he has decreased skin pigmentation, diarrhea, and failure to thrive (FTT).

1. Select the most likely mineral deficiency that is consistent with this infant's clinical findings:

   A. Chromium
   B. Copper
   C. Magnesium
   D. Zinc

2. Match the clinical findings below (A–D) with the most appropriate trace mineral deficiency (i–iv). Each mineral deficiency may be used more than once or not at all:

   A. Erosive skin changes, alopecia, diarrhea, FTT, and oral candidiasis — i. Chromium
   B. Often diagnosed as eczema or impetigo — ii. Copper
   C. Often seen with late-onset hypocalcemia — iii. Magnesium
   D. Wiry hair — iv. Zinc

CASE 5

Vitamin deficiencies

A 760-g male infant born at 27 weeks' gestation is now approaching 2 months old. He is status-post necrotizing enterocolitis at 4 weeks of age and has now reached full-volume enteral feedings with unfortified breast milk. He remains on mechanical ventilation because of severe chronic lung disease. His laboratory values and radiographs reveal that he has metabolic bone disease (MBD) consistent with rickets.

1. Select the primary risk factor for the development of MBD in this infant:

   A. Chronic lung disease
   B. Necrotizing enterocolitis
   C. Prematurity
   D. Prolonged NPO (nothing by mouth) status

2. Select the signs or symptoms that would *not* typically be present in an infant or child with MBD:

   A. Frontal bossing, craniotabes, prominence of costochondral junction (rachitic rosary)
   B. Manifestation between 6 and 12 weeks of age
   C. Nonpainful fractures
   D. Poor weight gain and failure to wean off mechanical ventilation because of excessive chest wall compliance

3. Choose the most appropriate management once a diagnosis of MBD of prematurity has been established:

   A. Ask the infant's mother to double her intake of multivitamins if she is breast-feeding
   B. Give preterm or transitional formula and human milk fortification, consider supplementation with calcium and phosphorus, and avoid administration directly to milk to prevent precipitation
   C. Offer breast milk at a higher volume
   D. All of the above

The medical student rotating in the Neonatal Intensive Care Unit (NICU) this month presents a talk about breast milk. He reviews the importance of supplementing breast-fed infants with Vitamin D. Next, he discusses that breast-fed infants have lower vitamin K levels when compared with infants receiving cow's milk.

4. Choose the additional neonatal risk factor(s) that predispose(s) the newborn to vitamin K deficiency:

   A. An immature newborn liver
   B. Initial lack of gastrointestinal (GI) microorganisms that synthesize vitamin K
   C. Maternal medications (e.g. anticonvulsants, warfarin, and antituberculosis medications)
   D. All of the above

CASE 6

Breast-feeding

A primigravida 26-year-old woman is wondering if she should breast-feed or formula-feed her newborn. The pediatrician rounding in the nursery explains the differences between breast milk and infant formula. He also describes the benefits of breast milk and the limited contraindications.

1. Match each description below (A–J) with the most appropriate type of milk (i–iv):

   A. Contains bile salt-dependent lipase
   B. Contains consistent caloric density
   C. Contains secretory IgA
   D. Increases lactobacilli growth
   E. Has consistent protein content
   F. Has fewer long-chain unsaturated fatty acids
   G. Lactose is the source of carbohydrate
   H. Provides protective and bactericidal enzymes
   I. Recommended as primary source of enteral feeding until 6 months, followed by introduction of cow's milk
   J. Yields lower incidence of gastrointestinal (GI) and respiratory infections

   i. Breast milk
   ii. Formula
   iii. Both
   iv. Neither

Further discussion with the mother and detailed chart review reveal that the mother has taken lithium for a bipolar disorder. In addition, under medical history, "cold sores" and a positive postpartum depression (PPD) are listed.

2. For the clinical scenarios below (A–D), select the most appropriate choice (i–iii). You may use each selection more than once or not at all:

   A. Mother continues to take lithium.
   B. Mother had an oral herpes simplex virus (HSV) infection 2 weeks prior to delivery, was treated with Valtrex, and the lesion has healed. She took Lithium for 5 years as a teenager and she has no symptoms of active tuberculosis with a negative chest radiograph.
   C. Mother has several open HSV lesions on her breasts.
   D. Mother stopped taking lithium prior to this pregnancy. She has no current HSV lesions (oral, breast, or genital). She had a positive PPD 3 years ago and is currently asymptomatic with a negative chest radiograph.

   i. Breast milk is contraindicated.
   ii. Breast milk is recommended.
   iii. There is no American Academy of Pediatrics (AAP) guideline for this clinical scenario.

Ultimately, breast milk is recommended for the mother in this case. The pediatrician asks the medical student to review protein, electrolyte, and iron concentrations in colostrum, mature breast milk, and cow's milk.

3. Refer to the table below and fill in the correct heading (i–iv) for the columns listed A, B, and C:

	A	B	C
Protein (g/L)	22.9	10.6	32.5
Whey:casein	80:20	55:45	20:80
Lactalbumin (g/L)	–	3.6	2.4
Na (mg/dL)	48	15	58
K (mg/dL)	74	55	138
Cl (mg/dL)	85	43	103
Ca (mg/dL)	39	35	130
Fe (μg/dL)	70	100	70

Modified from: Behrman RE, Kliegman RM, Arvin AM, eds. *Nelson Textbook of Pediatrics*. 15th ed. Philadelphia, PA: WB Saunders; 1996:158 and Lawrence RA, Lawrence RM. *Breastfeeding: A Guide for the Medical Profession*. 5th ed. St. Louis, MO: Mosby; 1999:128–129

i. Cow's milk
ii. Human colostrum
iii. Mature breast milk
iv. None of the above

CASE 7

Formula-feeding

A full-term male infant was born to a 19-year-old woman with a family history of asthma, allergies, and colic. The infant's mother decided that she did not want to breast-feed and sought out advice from family and friends to help guide her on what to feed her newborn infant. Her neighbor told her to give fresh goat's milk from the family's farm; her aunt said to use cow's milk; her sister told her to use soy formula, while her uncle, who is a phlebotomist in the local community hospital, said to use protein hydrolysate infant formula.

At 3 months of age, the infant was brought to the Emergency Department with failure to thrive (FTT), pallor, and lethargy. His laboratory values revealed megaloblastic anemia, severe hypernatremia, and azotemia.

1. Which feeding regimen would be most likely to lead to the above laboratory findings?

   A. Cow's milk
   B. Fresh goat's milk
   C. Protein hydrolysate infant formula
   D. Soy formula

After being hospitalized for a week with normalization of his physical examination and laboratory values, the infant was discharged to home on Neocate 24 calories per ounce. The neonatologist's decision to choose Neocate 24 calories per ounce was based on carbohydrate source, protein source, iron fortification, mineral content, and caloric density.

2. Identify the carbohydrate source (i–iii), protein source (iv–vii), fat source (viii–ix), and iron fortification (x–xii) for Neocate:

   A. Carbohydrate source _____
   B. Protein source_____
   C. Fat source_____
   D. Iron fortification_____

   i. Lactose
   ii. Sucrose and glucose polymers
   iii. Glucose polymers
   iv. Cow's milk protein
   v. Soy protein
   vi. Hydrolysate
   vii. Free amino acids
   viii. Long-chain triglycerides
   ix. Medium-chain and long-chain triglycerides
   x. Low dose
   xi. High dose
   xii. Formula without any iron

At age 3 months, the infant reaches the 15th percentile for weight on the growth chart, after having been at less than the 3rd percentile. He tolerates this new formula well.

His cousin, now 3 weeks old, is having frequent episodes of regurgitation, followed by crying, after his feedings of Enfamil. By 4 weeks of life, the regurgitation and crying after feedings continues and his stools have become more frequent and watery. His weight is 4,150 g, and he is gaining only 10 g per day over the past week. He has also developed a rash on his cheeks and buttocks. His pediatrician suspects milk protein allergy (MPA).

3. Select true or false (i–ii) for the following statements related to MPA in infants:

   i. True
   ii. False

   A. An infant with MPA may appear healthy but have a history of fussiness, regurgitation, increased frequency of stools, and presence of blood-tinged and/or mucous stools.
   B. Some infants demonstrate extreme irritability as the only symptom of MPA.
   C. The prevalence of MPA in infants is low.
   D. Skin prick testing and in vitro immunoassays (commonly called RAST tests) are recommended.
   E. It is not recommended that an infant with cow's MPA be changed to soy formula as the initial next step, as a significant percentage of infants are sensitive to both proteins.
   F. Up to 50% of infants with cow's MPA or soy-induced proctitis are intolerant to hydrolysated cow's milk formula.
   G. Lactose intolerance is the same as MPA, as both involve the immune system.
   H. Almost all infants will be able to tolerate cow's milk and soy products by 1 year of age.

SECTION VIII

Answers

CASE 1 ANSWERS

1. C. 100 mL/kg/day and 60 mL/kg/day

Knowledge of a neonate's insensible water losses (IWLs) is required to provide the appropriate maintenance fluid. IWL increases as gestational age decreases because immature infants have a high surface area to body mass ratio and water-permeable skin. Table 1 summarizes the mechanisms of IWL in neonates.

TABLE 1. Mechanisms of IWL

Neonatal evaporative water loss	1/3 via respiratory tract, 2/3 via skin
Factors leading to increased IWL	Increased environmental and body temperature Decreasing gestational age Skin breakdown Congenital skin defects Radiant warmer Phototherapy
Factors leading to decreased IWL	Humidity Plastic heat shield

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:269

Although there is some variation in fluid requirements because of an infant's individual clinical status, in general, the estimated total fluid requirement at birth for an infant born at 28 weeks' gestation ranges from 80 mL/kg/d for infants in incubators to 100 mL/kg/day for infants placed on radiant warmers. In contrast, the estimated total fluid requirement for an infant born at term is about 60 mL/kg/day.

2.
A iii. Preterm infants
B iii. Preterm infants
C iii. Preterm infants
D iii. Preterm infants
E ii. Full-term infants
F ii. Full-term infants

Premature infants have a decreased ability to digest fats and absorb fat-soluble vitamins. Premature infants have reduced bile salt content and decreased secretion of pancreatic lipase, which leads to fat malabsorption. In addition, body fat is increased in late gestation; thus, preterm infants are born with fewer fat-soluble vitamins and minimal caloric reserves.

Premature infants have a greater fluid requirement per kilogram of body weight than full-term infants because of greater IWL. Figure 1 shows the relationship of IWL and birth weight.

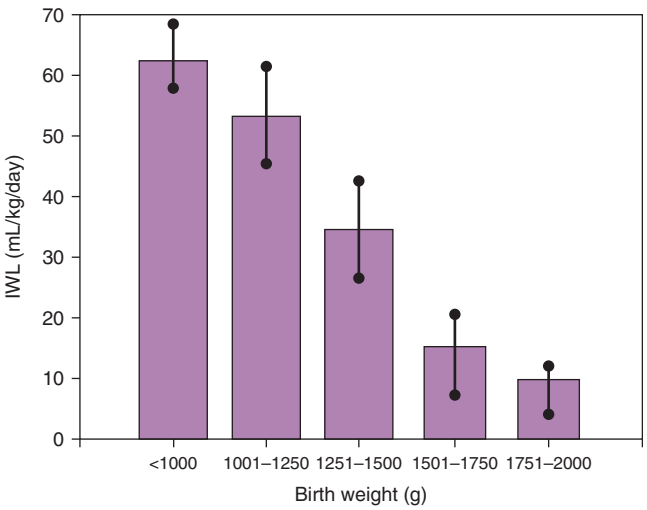


FIGURE 1. Data from Wu PY, Hodgman JE. Insensible water loss in preterm infants: Changes with postnatal development and nonionizing radiant energy. *Pediatrics*. 1974;54:704–712, as redrawn in Shaffer SG, Weismann DN. Fluid requirements in the preterm infant. *Clin Perinatol*. 1992;19: 233–250, with permission

Premature infants also have greater caloric requirements per kilogram to attain adequate growth. A term infant's protein requirement ranges between 1.8 g/kg/day to 2.2 g/kg/day, while the very-low-birth-weight (VLBW) infant requires 3 g/kg/day to 3.5 g/kg/day. Full-term infants generally regain their birth weight by 2 weeks of life. Preterm infants who are fed enterally (i.e., without intravenous fluids or parenteral nutrition) usually require longer than 2 weeks to regain their birth weight.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that preterm infants have a greater daily fluid requirement per kilogram of body weight than full-term infants
- Recognize that insensible water loss is increased with prematurity
- Recognize the difference in preterm and full-term infant's ability to digest fat and absorb fat soluble vitamins
- Know the protein requirements for premature and full-term infants
- Know the caloric requirements for infant
- Recognize that the caloric requirement per kilogram for adequate growth is greater for preterm infants than for full-term infants
- Know that most full-term infants will regain their birth weight within two weeks

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Poindexter B, Denne S. Protein needs of the preterm infant. *NeoReviews*. 2003;4:e52–e59.

CASE 2 ANSWERS

1. B. 14

This presentation is consistent with a normal anion gap hyperchloremic acidosis caused by renal tubular acidosis (RTA). RTA is generally caused by decreased renal reabsorption of bicarbonate ion or impaired urinary acidification.

Metabolic acidosis is defined as a loss of bicarbonate or a gain of hydrogen ions resulting in an arterial pH less than 7.4. It is a concern in preterm infants because of the effect on tissue metabolism and is a potential initial marker for underlying pathology.

The formula for calculating a metabolic acidosis anion gap is:

$$\text{Anion gap} = [Na^+] - ([Cl^-] + [HCO_3^-])$$

2.

A	i
B	ii
C	ii
D	i
E	ii
F	i
G	i
H	i
I	i

Metabolic acidosis may coincide with a normal anion gap acidosis or an elevated anion gap acidosis. Normal anion gap acidosis is caused by loss of bicarbonate via the gastrointestinal tract or the urinary system or by failure to excrete hydrogen ions. An elevated anion gap acidosis is usually caused by increased organic acid production, inborn errors of metabolism, or decreased excretion of acid in the setting of renal failure.

Table 1 lists the causes of metabolic acidosis (normal anion gap and elevated anion gap):

TABLE 1. Causes of Metabolic Acidosis

Metabolic Acidosis with Normal Anion Gap	Metabolic Acidosis with Elevated Anion Gap
Renal—RTA; acetazolamide administration, renal dysplasia, obstructive uropathy, early uremia	Lactic acidosis (hypoxemia, shock, sepsis)
Gastrointestinal—diarrhea; ileal drainage, cholestyramine administration, small-bowel drainage	Acute renal failure
Decreased aldosterone—congenital adrenal hyperplasia	Inborn errors of metabolism
Hyperalimentation and administration of excess acid and amino acids	Organic acidemias—e.g., methylmalonic acidemia
High-protein formula	Lactic acidosis—e.g., pyruvate dehydrogenase or carboxylase deficiency
Congenital hypothyroidism	Mitochondrial respiratory chain abnormalities
	Glycogen storage disease type 1
	Galactosemia
	Hereditary fructose intolerance
	Toxins

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:277

3. D. Chronic respiratory alkalosis with compensation

There are many causes of respiratory alkalosis, including:

- Hypoxia
- Parenchymal lung disease
- Medications (salicylate, xanthine, catecholamine)
- Mechanical ventilation
- Central nervous system disorders
- Metabolic disorders
- Hyperventilation syndrome

The infant in this vignette is being overventilated with a set rate of 40 breaths per minute (in addition to his own breaths), and his CO_2 is being "blown off." If the respiratory alkalosis persists for more than 2 to 6 hours, renal compensatory changes occur, such as decreased hydrogen secretion and increased bicarbonate excretion. Renal compensation results in a 4-mEq/L reduction in plasma $[HCO_3^-]$ for every 10 mm Hg reduction in P_{CO_2}.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know how to calculate the anion gap
- Formulate a differential diagnosis of acidosis with a normal anion gap
- Know the renal compensatory changes seen in primary respiratory alkalosis

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Ringer S. Renal tubular acidosis. *NeoReviews*. 2010;11(5);e252–e256.
Schwaderer A, Schwartz G. Back to basics: Acidosis and alkalosis. *Ped Rev*. 2004;25:350–357.

CASE 3 ANSWERS

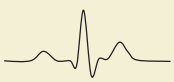
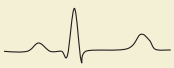
1. C. Potassium shifts from the intracellular fluid (ICF) to the extracellular fluid (ECF) space

Up to 25% to 50% of very-low-birth-weight (VLBW) infants develop hyperkalemia in the first 24 to 72 hours of life, even without receiving any exogenous potassium intake or renal failure. The hyperkalemia results from a potassium shift from the ICF to the ECF space, and the magnitude of the shift seems to correlate with the degree of prematurity. The underlying physiologic explanation is unknown. Generally, adding potassium to intravenous fluids or parenteral fluids for VLBW infant is not recommended until adequate urine output is established and potassium values are checked and are within normal limits.

2. D. Figure 1D

Table 1 describes the EKG findings that correlate with the corresponding electrolyte abnormalities.

TABLE 1. EKG Findings and Correlations to Electrolyte Abnormalities

Electrolyte Abnormality	EKG	EKG Findings
Normal		PR = 0.08–0.11 sec QRS = 0.04–0.07 sec
Hypercalcemia		Shortened QT interval
Hypocalcemia		Prolonged QT interval
Hyperkalemia >6.0 mEq/L		Tall peaked T Wave Shortened QT interval Depressed ST segment
>7.5 mEq/L		Prolonged PR interval Widened QRS complex Flattened P wave
>9.0 mEq/L		Absent P wave Sinusoidal QRS wave Asystole and ventricular fibrillation can occur
Hypokalemia <2.5 mEq/L		Slightly widened QRS complex Depressed ST segment Biphasic T wave attributable to visible U wave
~1.0 mEq/L		Prominent U wave Flat T wave If sustained, may develop prolonged PR interval and sinoatrial block

Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:143

3. B. Remove all exogenous potassium sources; give 10% calcium gluconate; give glucose and insulin; consider Lasix, $NaHCO_3^-$, and Kayexalate

Initial treatment of symptomatic hyperkalemia includes the following:

- Remove all exogenous potassium sources
- Give 10% calcium gluconate
- Give glucose and insulin
- Consider Lasix, $NaHCO_3^-$, and Kayexalate

Options C and D may be warranted in an infant with supraventricular tachycardia (SVT). A newborn with SVT warrants treatment if the SVT is sustained or if there are any signs or symptoms of cardiovascular compromise. If the infant is unstable, clinicians can perform synchronized cardioversion at a dose of 0.5 to 2 J/kg. If the infant is stable, clinicians can perform vagal maneuvers (crushed ice to face, rectal stimulation) and administer adenosine intravenously if the arrhythmia persists. Additional therapeutic agents are sometimes warranted if first-line medication fails.

4. D. All of the above

The etiology of hypophosphatemia and hypercalcemia in a 1-month old preterm infant could be consistent with congenital hyperparathyroidism, prolonged hyperalimentation with inadequate calcium and phosphorus, or transition to breast milk with limited nutritional supplementation. Further workup is warranted.

Hypophosphatemia is a common finding in preterm infants with osteopenia of prematurity (or rickets) and results from insufficient intake of calcium and phosphorus. Enteral intake selection in preterm infants is crucial as breast milk is low in phosphorus and full-term formula also has lower phosphorus content than preterm formula. Therefore, careful calculation of phosphorus and calcium content and ratio is needed to provide sufficient supplementation to the preterm infant. Calcium to phosphorus ratios should be in the 1.2:1 to 1.7:1 range; ratios <1:1 are not recommended. Congenital hyperparathyroidism is a rare cause of hypophosphatemia.

In contrast, hyperphosphatemia can be caused by:

- Ingestion of formula with high phosphorus concentration
- Excessive phosphorus concentration in parenteral nutrition
- Impaired phosphorus excretion as a result of renal failure

Metastatic calcifications and hypocalcemia can develop if hyperphosphatemia is severe and untreated.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Hyperkalemia

- Recognize that severe cardiac rhythm changes may begin abruptly in patients with hyperkalemia
- Know the signs of hyperkalemia
- Know the emergency treatment of hyperkalemia
- Plan the treatment for a patient with hyperkalemia

Phosphorus

- Know the problems associated with inadequate and excessive amounts of phosphorus in the diet of a premature infant

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Kenner C. *Comprehensive Neonatal Care: An Interdisciplinary Approach*. ST. Louis, MO: Saunders (Elsevier); 2007.

CASE 4 ANSWERS

1. B. Copper

The neonate in the scenario has copper deficiency, which can manifest with findings of:

- FTT
- Pallor/decreased pigmentation
- Hypothermia
- Apneic events
- Hypotonia
- Poor feeding
- Skeletal changes
- Abnormal elastic connective tissue
- Anemia
- Hypoceruloplasminemia
- Hepatosplenomegaly
- Diarrhea

Most fetal accretion of copper occurs during the third trimester. Thus, preterm infants are born deficient. The exact neonatal requirements are unknown, but reasonable guidelines have been made on the basis of current evidence.

Almost all cases of copper deficiency in neonates result from a nutritional deficiency or genetic disorder of copper metabolism. The X-linked recessive lethal multisystem disorder is called Menkes disease, which consists of neurodegeneration, connective tissue disturbances, and peculiar kinky hair. The levels of copper and ceruloplasmin are low, and the confirmatory test is presence of mutation analysis of the *ATP7A* gene.

Figure 1A–C reveals features of Menkes disease, including frayed and split internal elastic lamina (A), "cherubic" facies (B), and abnormal hair shaft (C).

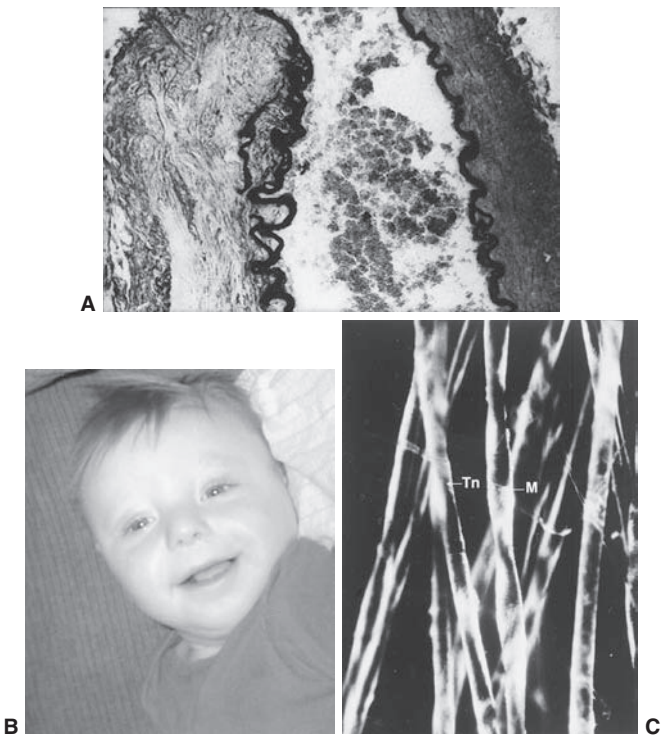


FIGURE 1. Menkes JH, Sarnat HB, Maria, BL. *Child Neurology*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 1.32

2.

A	iv
B	iv
C	iii
D	ii

Chromium deficiency in an infant is most often caused by long-term parenteral nutrition and may manifest with impaired glucose tolerance, weight loss, peripheral neuropathy, and confusion.

Copper deficiency is described in Answer 1.

Magnesium deficiency in a neonate is often a manifestation of late-onset hypocalcemia and can cause hypokalemia, vomiting, arrhythmia, tremor, muscle spasm, and tetany.

Similar to copper, Zinc is mostly accumulated in the fetus during the third trimester when liver stores are established. Typical manifestations of *zinc deficiency* are:

- Dermatitis
- Alopecia
- FTT
- Oral candidiasis
- Irritability

Manifestations later in life may include delayed sexual maturation, reduced taste sensitivity, poor night vision, immune compromise, and impaired wound healing.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Know the diseases that are associated with trace mineral deficiency (zinc, copper, magnesium, chromium)

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Giles E, Doyle L. Copper in the extremely low-birthweight or very preterm infants. *NeoReviews*. 2007;4: e159–e164.
Giles E, Doyle L. Zinc in the extremely low-birthweight or very preterm infants. *NeoReviews*. 2007;4: e165–e171.

CASE 5 ANSWERS

1. C. Prematurity

Prematurity is the single most important risk factor for the development of MBD. There is an inverse relationship to gestational age and birth weight and the frequency of MBD. Additional risk factors for MBD are:

- Enteral feeding practices (delayed initiation of enteral feedings, prolonged parenteral nutrition, use of breast milk without fortification)
- Lack of movement (e.g. sedation/paralysis, neuromuscular disorders)
- Malabsorption of vitamin D or vitamin D deficiency
- Medications (steroids, caffeine, Lasix)

2. C. Nonpainful fractures

MBD typically manifests between 6 and 12 weeks of age. Rapidly growing premature infants with low intake of either calcium or phosphorus are at high risk. The primary nutritional reason for MBD in preterm infants is a deficiency of vitamin D. Vitamin D is a prohormone essential for normal absorption of calcium from the intestines. When vitamin D deficiency occurs, growing children may develop MBD or rickets while adults may develop osteomalacia.

Infants may demonstrate poor weight gain, failure to thrive, and can have respiratory difficulties with potential for difficulty weaning off mechanical ventilation as a result of excessive chest wall compliance. Physical findings may include the following:

- Generalized hypotonia
- Pain in spine, pelvis, and legs
- Painful fractures
- Bowing of the legs
- Thickening of the skull
- Delayed anterior fontanelle closure
- Long-bone abnormalities with cupping or flaring of the metaphyses because of uncalcified osteoid formation

Infants with severe hypocalcemia may present with seizures. Children older than 2 years of age may succumb to greenstick fractures, kyphoscoliosis, and short stature. They may also be at increased risk for autoimmune disease as vitamin D is a modulator for B- and T-lymphocyte function.

Figure 1 demonstrates some radiographic features of MBD, including profound demineralization, frayed, irregular cupping of the end of the metaphysis, and poorly defined cortex. The chest radiograph (Figure 2) shows an 11-month with rickets, evident by demineralization and cupping of the distal end of ribs and humerus.

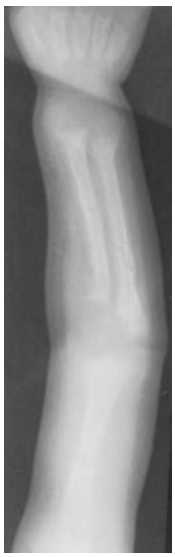


FIGURE 1. From Fleisher GR, Ludwig S, Baskin MN. *Atlas of Pediatric Emergency Medicine*. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. Figure 7.14

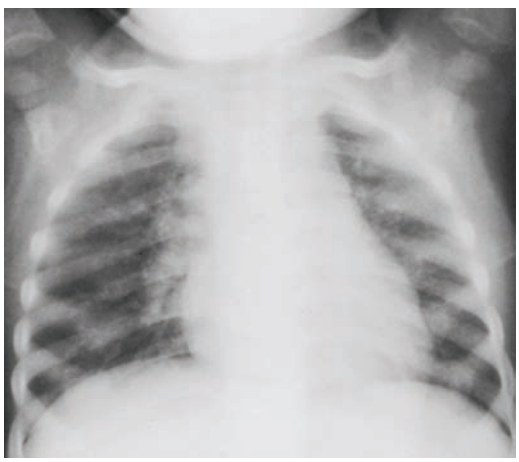


FIGURE 2. From Fleisher GR, Ludwig S, Baskin MN. *Atlas of Pediatric Emergency Medicine*. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. Figure 7.15

3. B. Give preterm or transitional formula and human milk fortification, consider supplementation with calcium and phosphorus, and avoid administration directly to milk to prevent precipitation

Option B is the most appropriate management, as administration of unfortified breast milk provides very little vitamin D and not enough for catch-up of bone mineralization. In fact, feeding preterm infants unfortified breast milk or term formula can lead to MBD in up to 50% of very-low-birth-weight infants. Vitamin D intake in pregnant women is important to prevent fetal vitamin D deficiency, but doubling a woman's multivitamin intake would not be the appropriate management for a breast-feeding infant with MBD. The AAP recommends daily supplementation of 400 international units (IU) of vitamin D for all breast-fed infants and for nonbreast-fed infants and children who do not ingest at least 1 L of vitamin D-fortified milk daily.

4. D. All of the above

Receiving an intramuscular dose of vitamin K at birth is strongly recommended for every newborn to prevent hemorrhagic disease of the newborn (HDN). Vitamin K is an essential cofactor for factors II, VII, IX, and X and for proteins C and S. Deficiency of vitamin K leads to a bleeding diathesis with classic HDN findings presenting at 2 to 7 days of life with GI bleeding, umbilical cord bleeding, intracranial hemorrhage, and/or prolonged bleeding after circumcision.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the presenting signs and symptoms of rickets and manage appropriately
- Recognize the effects of vitamin D deficiency in children of various ages, including breast-fed infants and older children
- Know that rickets may develop in rapidly growing premature infants with low intake of either calcium or phosphorus
- Recognize the clinical manifestations of vitamin K deficiency

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

Misra M, Pacaud D, Petryk A, et al.; Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: Review of current knowledge and recommendations. *Pediatrics*. 2008;122:398–417.

Vachharajani A, Mathur A, Rao R. Metabolic bone disease of prematurity. *NeoReviews*. 2009;10:e402–e411.

CASE 6 ANSWERS

1.	A. Contains bile salt-dependent lipase	i. Breast milk
	B. Contains consistent caloric density	ii. Formula
	C. Contains secretory IgA	i. Breast milk
	D. Increases lactobacilli growth	i. Breast milk
	E. Has consistent protein content	ii. Formula
	F. Has fewer long-chain unsaturated fatty acids	ii. Formula
	G. Lactose is the source of carbohydrate	iii. Both
	H. Provides protective and bactericidal enzymes	i. Breast milk
	I. Recommended as primary source of enteral feeding until 6 months, followed by introduction of cow's milk	iv. Neither
	J. Yields lower incidence of gastrointestinal (GI) and respiratory infections	i. Breast milk

The composition of breast milk provides many benefits to the newborn. Breast milk contains immunologic and antibacterial factors such as secretory IgA that can:

- Bind to viruses and bacteria to prevent invasion of mucosa
- Provide protective and bactericidal enzymes
- Increase lactobacilli growth

Colostrum has increased amounts of lymphocytes, macrophages, and immunoglobulins. Breast milk contains bile salt-dependent lipase that can aid with digestion. As breast milk matures, protein levels decrease in conjunction with advancing gestational age of the infant. Whey-to-casein ratio in colostrum is 80:20, while that in mature breast milk is 55:45. The whey-to-casein ratio of cow's milk is consistently 20:80.

The predominant carbohydrate in breast milk is lactose and is greater in foremilk versus hind milk. Many but not all formulae have lactose as the carbohydrate source.

The AAP supports breast-feeding until an infant is at least 12 months. If an infant is weaned off breast milk prior to age 12 months, iron-fortified formula is recommended. Cow's milk may be introduced after 1 year of life. The AAP also recommends daily supplementation of 400 international units (IU) of vitamin D for all breast-fed infants and for non–breast-fed infants and children who do not ingest at least 1 L of vitamin D-fortified milk daily.

2. A i
B ii
C i
D ii

Table 1 summarizes breast-feeding contraindications in the United States.

TABLE 1. Contraindications to Breast-Feeding in the United States

Infection	Maternal human immunodeficiency virus
	Mother with herpes simplex lesions on breast
	Symptomatic mother with positive PPD and chest radiograph
	Active breast abscess
	Relative infection contraindications
	Premature very-low-birth-weight infant and cytomegalovirus-seropositive mother, maternal oral HSV lesion
Galactosemia	Caused by lactose being the predominant carbohydrate in breast milk
Drugs	Cocaine
	Cyclosporine
	Lithium
	Methotrexate
	Phencyclidine
	Radioactive agents

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:306

3. A ii
B iii
C i

Component	Human Colostrum	Mature Breast Milk	Cow's Milk
Protein (g/L)	22.9	10.6	32.5
Whey:casein	80:20	55:45	20:80
Lactalbumin (g/L)	–	3.6	2.4
Na (mg/dL)	48	15	58
K (mg/dL)	74	55	138
Cl (mg/dL)	85	43	103
Ca (mg/dL)	39	35	130
Fe (μg/dL)	70	100	70

Obtained from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010. Modified from: Behrman RE, Kliegman RM, Arvin AM, eds. *Nelson Textbook of Pediatrics*. 15th ed. Philadelphia, PA: WB Saunders; 1996:158 and Lawrence RA, Lawrence RM. *Breastfeeding: A Guide for the Medical Profession*. 5th ed. St. Louis, MO: Mosby; 1999:128–129

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Breast milk

Content

- Understand the qualitative and quantitative differences between human milk and infant formulas
- Recognize that human and cow milk proteins differ in quality and quantity
- Know that breast milk is deficient in vitamin D

Benefits

- Know that human milk contains antibodies against certain bacteria and viruses, including high concentrations of secretory IgA antibodies
- Know that ingested antibodies from human colostrum and milk provide local gastrointestinal immunity against organisms entering the body via this route
- Understand that human milk provides protection against many gastrointestinal and respiratory infections
- Know that there is a lower incidence of gastrointestinal infections in infants fed with human milk

Contraindications

- Know the drugs that are contraindicated in breast-feeding
- Know that maternal ingestion of drugs with sedative properties has the potential to cause sedation in breast-feeding infants
- Know the disorders of the breast that may interfere with breast-feeding
- Judge for which maternal breast infections breast-feeding should be interrupted
- Know for which maternal chronic viral infections breast-feeding is not recommended

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Lulu. 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 7 ANSWERS

1. B. Fresh goat's milk

False and potentially dangerous information can lead parents to select an inappropriate feeding regimen for their newborn. It is important for pediatricians and neonatologists to dispel any myths about unsafe feeding practices. Fresh goat's milk is not an appropriate selection for enteral feedings in a newborn. Goat's milk contains 50 mg sodium and 3.56 g of protein per 100 ml, which is almost three times that in breast milk. A newborn requires ~100 mg/day to 200 mg/day of sodium and 9 g/day to 11 g/day of protein. The laboratory values for the infant in

this case reveal megaloblastic anemia (see Figure 1) as a result of folate deficiency (6 mcg folate/L in fresh goat's milk vs. 50 mcg/L in human breast milk). Figure 1 demonstrates hypersegmented neutrophils and well-hemoglobinized macrocytes, consistent with megaloblastic anemia.

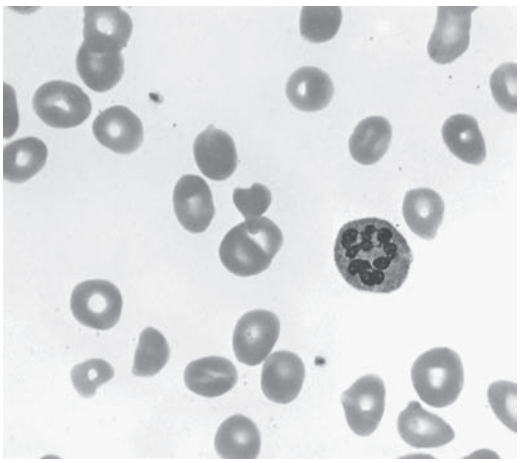


FIGURE 1. From McClatchey KD. *Clinical Laboratory Medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002. Figure 41.10

Soy protein-based formulas are recommended in the following limited clinical scenarios:

- Galactosemia
- Hereditary lactase deficiency
- Desire for strict vegetarian-based diet

The AAP recommends that all infants fed with breast milk or iron-fortified formula should receive iron supplementation for the first year of life.

2.

A. Carbohydrate source	iii. Glucose polymers
B. Protein source	vii. Free amino acids
C. Fat source	viii. Long-chain triglycerides
D. Iron fortification	xi. High dose

Tables 1 to 3 summarize the type of carbohydrate, fat, and protein that are contained in different formulas.

TABLE 1. Carbohydrates

Type of Carbohydrate	Formula Name
Lactose	Enfamil (standard, AR, Lipil, Enfacare, and Premature) Neosure (also contains glucose polymers) Similac (standard, 60/40, and Special Care)
Sucrose and glucose polymers	Alimentum Isomil Portagen, Monogen
Glucose polymers	Enfamil Lactofree Neocate Neosure (also contains lactose) Nutramigen Pregestimil ProSobee Similac Lactose Free

Obtained from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:306. Modified from: Gunn VL, Nechyba C, eds. *The Harriet Lane Handbook: A Manual for Pediatric House Officers*. 16th ed. Philadelphia, PA: Mosby; 2002:467

TABLE 2. Proteins

Type of Protein	Formula Name
Cow's milk protein	Enfamil (standard, AR, Enfacare, Lipil, Premature) Portagen Similac (standard, Lactose Free, 60/40, Neosure, and Special Care)
Soy protein	Isomil ProSobee
Hydrolysate	Alimentum Nutramigen Pregestimil
Free amino acids	Neocate

Obtained from: Brodsky D, Martin, C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:307. Modified from: Gunn VL, Nechyba C, eds. *The Harriet Lane Handbook: A Manual for Pediatric House Officers*. 16th ed. Philadelphia, PA: Mosby; 2002:470–471

TABLE 3. Fats

Type of Fat	Formula Name
Long-chain triglycerides	Enfamil (standard, AR, Lipil, Lactofree) Isomil Neocate Nutramigen ProSobee Similac (standard, 60/40, and Lactose Free)
Medium and long-chain triglycerides	Enfamil (Enfacare and Premature) Neosure Portagen Pregestimil Similac (Special Care)

Obtained from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:307. Modified from: Gunn VL, Nechyba C, eds. *The Harriet Lane Handbook: A Manual for Pediatric House Officers*. 16th ed. Philadelphia, PA: Mosby; 2002:472

The quality of fat content in preterm and full-term infant formula is important to recognize. Formulas are designed to attempt to mimic the fat content in gestationally appropriate breast milk. There are greater amounts of long-chain unsaturated fatty acids in breast milk compared with cow's milk. In addition, there are increased amounts of arachidonic acid and docosahexaenoic acid in breast milk; infant formulas now also contain arachidonic acids. The minimum fat content of infant formulas is 3.4g/100 kcal. Most infant formulas contain at least 10% of their total fatty acids as linoleic acid.

The American Academy of Pediatrics recommends iron supplementation in breast-fed infants and the use of iron-fortified infant formula when a mother chooses not to breast-feed. The rate of iron-deficiency anemia in infancy has decreased to a great extent as a result of iron fortification. Low-iron formulas should not be used, since they do not provide enough iron to provide optimal support to the growing infant.

3. A i True
B i True
C i True
D ii False
E ii False
F ii False
G ii False
H i True

MPA is a problem in infancy that may affect up to 15% of newborns. MPA manifests as an immunologic reaction to dietary proteins via IgE-mediated and non–IgE-mediated pathways. The IgE-mediated pathway is also known as a type I hypersensitivity reaction occurring when an antigen binds to mast cells. Non–IgE-mediated MPA is likely multifactorial and involves immune complexes (IgA or IgG antibodies) and T cells. The distinction is important because IgE-mediated MPA is associated with multiple food allergies and atopic conditions. Skin prick testing and in vitro immunoassays are not recommended in infants as this testing will fail to diagnose the infants with non–IgE-mediated immunologic reaction and testing is usually negative in protein-induced proctitis/proctocolitis.

An infant with MPA may appear healthy but have a history of fussiness, regurgitation, increased frequency of stools, and presence of blood-tinged and/or mucous stools. However, some infants demonstrate extreme irritability as the only symptom of MPA. An elevated serum eosinophil count as well as presence of eosinophils in stool may be detected. Protein hydrolysate formula or strict diet modification in mothers who continue to breast-feed is recommended for infants with MPA. If the infant continues to have signs and symptoms of MPA, an amino acid-based formula may be trialed. In the setting of cow's MPA, soy protein-based formulas are generally not recommended as there is a 10% or greater allergen cross-reactivity. However, almost all infants will be able to tolerate cow's milk and soy products by1 year of age.

Lactose intolerance is a separate entity from MPA, as the later involves the immune system and causes intestinal mucosal injury. Lactose is a disaccharide comprised of glucose and galactose. Lactose requires lactase to be absorbed in the small intestine. Lactose intolerance most often presents with abdominal pain, diarrhea, gas, and bloating. Milk intolerance may be attributed to lactose or protein components.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Formula feeding

Content

- Recognize that infants fed with goat milk exclusively are prone to megaloblastic anemia due to folate deficiency
- Know which infant formulas contain lactose
- Know the indications for the use of protein hydrolysate formulas
- Know the indications for the use of soy formula
- Recognize the importance of the quality of fat content in preterm and full-term infants formulas
- Understand the rationales for the use of iron-fortified formulas and recognize the misuse of low-iron formulas

Allergy

- Recognize the signs and symptoms of milk protein allergy
- Understand the difference between milk protein allergy and lactose intolerance
- Recognize soy as a potential allergen in gastrointestinal protein allergy

SUGGESTED READINGS

Basnet S, Schneider M, Gazit A, et al. Fresh goat's milk for infants: Myths and realities—a review. *Pediatrics*. 2010;125:e973–e977.

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Committee on Nutrition, American Academy of Pediatrics. Hypoallergenic infant formulas. *Pediatrics.* 2000;106:346–348.

Heyman MB. Lactose intolerance in infants, children, and adolescents. *Pediatrics*. 2006;18:1279–1286.

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SECTION IX

Renal System

CASE 1

Anuria in a newborn

A nurse in the Newborn Nursery pages the pediatric resident because she is concerned that an 18-hour-old term newborn has not voided.

1. Of the following, the most appropriate initial response to this nurse's concern is to:

   A. Meet with the baby's parents and obtain a family history
   B. Obtain a blood sample to test the baby's serum creatinine concentration
   C. Recommend continued observation and an evaluation if the baby does not void by 24 hours of age
   D. Review the baby's prenatal ultrasonographic findings

The newborn is admitted to the Neonatal Intensive Care Unit at 48 hours of age with the following data:

- Benign family history, normal prenatal ultrasonography, normal prenatal course, and normal physical examination
- Rising serum creatinine concentration with most recent measurement at 48 hours of age of 2.0 mg/dL (177 μmol/L)
- Urine output = 0.4 mL/kg/hr

The neonatologist suspects that this infant has acute renal failure.

2. Of the following, the most helpful noninvasive test to diagnose the cause of this baby's renal failure is:

   A. Complete blood cell count
   B. Urinalysis
   C. Urinary biomarkers
   D. Urine specific gravity

The neonatologist discontinues potassium in the baby's intravenous fluids and orders several blood tests, urine tests, and an imaging study. While waiting for the results of these initial studies, the neonatologist speaks with the pediatric interns to review the potential etiology of the baby's renal failure, dividing the cause into three possible categories:

- Prerenal failure as a result of decreased renal perfusion
- Intrinsic renal disease, such as renal vascular thrombosis or congenital renal disorders
- Postrenal failure as a result of an obstructive uropathy

3. Of the following, the finding that is most consistent with intrinsic renal disease is:

   A. Fractional excretion of sodium (FENa) = 6%
   B. High urine osmolality
   C. Lack of urination following a fluid challenge of 5 mL/kg
   D. Presence of a metabolic acidosis

CASE 2

Multicystic dysplastic kidney

A pregnant woman undergoes routine fetal ultrasonography at 17 weeks' gestation. The study reveals an abnormal left kidney (see Figure 1) with cysts and abnormal renal parenchyma. The fetal right kidney, pancreas, and liver appear normal.

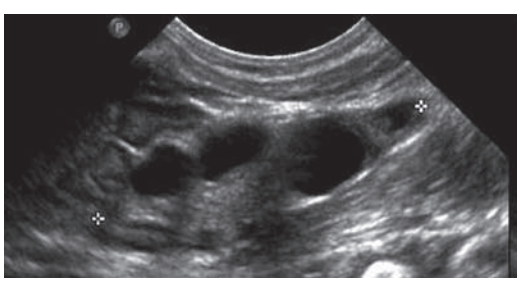

FIGURE 1. Reproduced with permission from: 2011 *NeoReviewsPlus*: March: Question 10 by the American Academy of Pediatrics

The woman's obstetrician reviews the possible causes of cystic renal disease, including the following:

- Autosomal dominant polycystic kidney disease
- Autosomal recessive polycystic kidney disease
- Medullary cystic kidney disease
- Multicystic dysplastic kidney (MCDK)

On the basis of the current information, the obstetrician believes that MCDK (also known as multicystic renal dysplasia) is the most likely etiology for this renal abnormality.

1. Of the following, the characteristic(s) most consistent with MCDK is:

   A. Abnormal renal parenchyma of the involved kidney
   B. Early intrauterine detection of cysts
   C. Isolated, unilateral renal involvement
   D. All of the above

The rest of the pregnancy is uncomplicated, and the woman delivers the baby at 39 weeks' gestation. A neonatologist examines the newborn soon after birth.

2. Of the following, the most likely clinical finding in this newborn is:

   A. Costovertebral angle tenderness
   B. Distended abdomen
   C. Hematuria
   D. Unilateral flank mass

The neonate is transferred to the Newborn Nursery and discharged at 2 days of life with a follow-up nephrology appointment.

3. Of the following, possible outcome(s) in this neonate with MCDK is:

   A. Compensatory growth of the unaffected kidney
   B. Involution of the affected kidney
   C. Vesicoureteral reflux in the unaffected kidney
   D. All of the above

CASE 3

Autosomal dominant polycystic kidney disease

A 15-year-old girl has an elevated blood pressure on routine examination. Her father reports that he has "cysts in his kidneys" that have not impacted his health. The pediatrician orders some laboratory and radiographic tests.

1. Of the following, the preferred diagnostic procedure in children suspected of having a cystic renal disease is:

   A. Magnetic resonance imaging
   B. Radionuclide scintigraphy
   C. Ultrasonography
   D. Voiding cystourethrogram

The pediatrician also reviews the child's fetal records and finds a late second-trimester fetal ultrasound that had noted some echogenicity of the renal cortices but no evidence of renal cysts.

2. Of the following, the most likely etiology for this child's cystic renal disease is:

   A. Autosomal dominant polycystic kidney disease (ADPKD)
   B. Autosomal recessive polycystic kidney disease (ARPKD)
   C. Medullary cystic kidney disease
   D. Multicystic dysplastic kidney (MCDK)

After obtaining the laboratory and radiographic results, the pediatrician meets with the girl and her parents to discuss the outcome of her renal disease.

3. Of the following, possible extrarenal manifestation(s) for the child in this vignette is:

   A. Cyst formations in the liver, spleen, and/or pancreas
   B. Intracranial aneurysms
   C. Mitral valve ballooning
   D. All of the above

CASE 4

Autosomal recessive polycystic kidney disease

A 36-year-old pregnant woman with diabetes mellitus is monitored closely by her obstetrician. She has a first-trimester fetal ultrasonography and a second-trimester fetal echocardiography that are normal. Because the woman has a uterine size that is greater than anticipated by dating, she has a second fetal ultrasound at 29 weeks' gestation. This fetal ultrasound reveals the following:

- Multiple small cysts in both kidneys that are confined to the collecting ducts
- Enlarged kidneys with increased echogenicity
- Decreased corticomedullary differentiation

The obstetrician is concerned about autosomal recessive polycystic kidney disease (ARPKD).

1. Of the following, the renal finding(s) consistent with ARPKD in a fetus is:

   A. Renal cysts visible by fetal ultrasonography before 20 weeks' gestation
   B. Small cysts that are usually confined to the collecting ducts
   C. Unilateral renal involvement
   D. All of the above

The neonate is born at 39 weeks' gestation by cesarean delivery. The neonatology team is present in the delivery room to assess the baby.

2. Of the following, the most likely associated clinical abnormality in this neonate is/are:

   A. Congenital hepatic fibrosis
   B. Hemolytic anemia
   C. Tracheoesophageal abnormalities
   D. Vertebral anomalies

A neonatologist discusses possible outcomes of ARPKD.

3. Of the following, the most likely outcome in this neonate is:

   A. Absence of clinical manifestations in the neonatal period
   B. Development of renal vein thromboses in the neonatal period
   C. Early renal failure with hypertension in the neonatal period
   D. Resolution of renal abnormalities by the second decade of life

CASE 5

Renal agenesis

A 28-year-old gravida 6 para 0 woman is now pregnant. Because of her prior pregnancy complications, she is being monitored extremely closely by her obstetrician with frequent fetal ultrasounds. A fetal ultrasound at 26 weeks' gestation reveals severe oligohydramnios.

1. Of the following, a possible mechanism of severe oligohydramnios is:

   A. A complete intestinal obstruction
   B. Continuous leakage of amniotic fluid
   C. Deep implantation of the placenta
   D. Poor fetal swallowing of amniotic fluid

The woman is admitted to the hospital for close observation. A high-risk obstetrician meets with the couple and discusses possible pregnancy outcomes. Specifically, the obstetrician is concerned that the woman is at higher risk of acquiring chorioamnionitis, which would prompt immediate delivery of the baby. The couple also meets with a neonatologist who reviews the potential associated complications after birth.

2. Of the following, a potential complication for this fetus with severe oligohydramnios is:

   A. Esophageal atresia
   B. Pulmonary hypoplasia
   C. Severe hearing loss
   D. Visual deficits

Follow-up fetal ultrasounds show that the severe oligohydramnios persists. However, the fetus remains active with appropriate growth and the woman does not have any signs of labor. At 35 weeks' gestation, the woman develops a high fever, abdominal tenderness, and an elevated white blood cell count. Because of the concern for chorioamnionitis, the high-risk obstetrician delivers the infant by cesarean. The neonatology team is present at the delivery. The infant requires initial resuscitation with bag-mask ventilation and then needs an endotracheal tube because of persistent severe respiratory distress. A thorough examination reveals the following:

- Clubbed feet
- Distinctive facial features: flattened facies, parrot-beak nose, skin fold of tissue from medial canthus across the cheek
- Multiple flexion contractures of the hands, feet, arms, and legs
- Severe respiratory distress

3. Identify the two renal disorders that can be associated with this infant's physical examination findings:

   A. Bilateral renal agenesis
   B. Bilateral multicystic dysplastic kidneys
   C. Medullary cystic renal disease
   D. Unilateral renal agenesis

Postnatal ultrasounds reveal that the infant has normal kidneys, and laboratory findings show that the infant has normal renal function. The neonatologist is uncertain about the cause of the prenatal oligohydramnios but focuses on managing the infant's lung disease.

CASE 6

Abnormalities of the collecting system, kidney, and bladder

At 20 weeks' gestation, a pregnant woman has an ultrasound that reveals fetal hydronephrosis and oligohydramnios. There are no other fetal abnormalities. The obstetrician discusses these findings with the expectant parents.

1. Of the following, the current approach to characterizing fetal hydronephrosis is based on the:

   A. Appearance of the intrarenal collecting system
   B. Degree of oligohydramnios
   C. Gestational age at which the hydronephrosis is initially observed radiographically
   D. Underlying cause of the hydronephrosis

Because the findings are consistent with severe hydronephrosis, the obstetrician refers the expectant parents to a pediatric urologist. The urologist reviews the potential causes of the hydronephrosis with the parents.

2. Match the potential causes of prenatal hydronephrosis with the prenatal ultrasonographic findings:

   A. Isolated mild hydronephrosis
   B. Posterior urethral valves
   C. Ureterocele
   D. Ureteropelvic junction obstruction
   E. Ureterovesical junction obstruction

   i. Cystic mass in the bladder with hydroureteronephrosis
   ii. Hydronephrosis and dilated ureter to the level of the bladder
   iii. Moderately or severely dilated renal pelvis without dilation of ureter or bladder
   iv. Physiologic, transient finding
   v. Posterior urethral dilation, a full bladder with thickened wall, decreased amniotic fluid

Follow-up fetal ultrasounds reveal the following:

- Bilateral hydroureter and hydronephrosis
- Distended, thin-walled bladder
- Severe oligohydramnios

Because of the concern for renal injury, the urologists decompress the fetal urinary system by inserting a vesicoamniotic shunt. This procedure was successful and the oligohydramnios improved. The male infant is born by cesarean delivery at 35 weeks' gestation. His abdominal findings are shown in Figure 1.

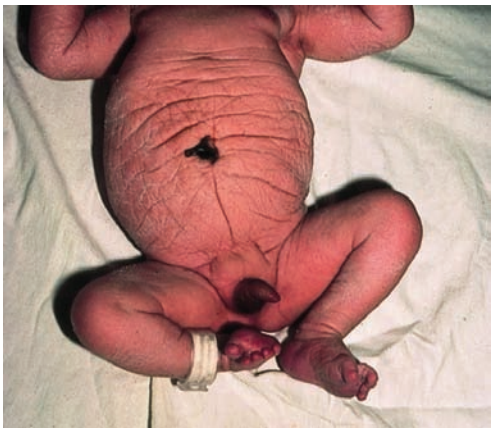

FIGURE 1. Photo courtesy of Karen M. Polise, MSN, RN, Division of Nephrology, The Children's Hospital of Philadelphia.

3. Of the following, the most likely additional finding in this infant is:

   A. Bilateral cryptorchidism
   B. Choanal atresia
   C. Hypertonia
   D. Neural tube defect

CASE 7

Posterior urethral valves

A 28-year-old pregnant woman with chronic hypertension has a fetal ultrasound performed at 32 weeks' gestation to monitor fetal growth. The radiologist is concerned about a new diagnosis of posterior urethral valves (PUV). A neonatologist and urologist then meet with the family to discuss this diagnosis.

1. Of the following, the ultrasonographic finding(s) most consistent with PUV is (are):

   A. Unilateral hydroureteronephrosis
   B. Polyhydramnios
   C. Thickened bladder wall
   D. All of the above

The rest of the prenatal course is stable, and the baby boy is born at term gestational age. He is then evaluated by the neonatology team soon after birth.

2. Of the following, the most likely clinical symptom(s) in this newborn is (are) (a):

   A. Palpable midline bladder
   B. Straining during urination
   C. Weak urinary stream
   D. All of the above

The neonatology team then contacts the consulting urologist to establish a plan.

3. Of the following, the most definitive test to diagnose PUV postnatally is:

   A. Abdominal radiography
   B. Magnetic resonance imaging
   C. Renal ultrasonography
   D. Voiding cystourethrography (VCUG)

After confirming the diagnosis of PUV, the urologist places a catheter into the neonate's bladder to relieve the urinary tract obstruction and decrease pressure on the proximal urinary tract. The neonatology team closely monitors the baby's serum electrolytes and renal function. The baby is also given antibiotics to prevent of a urinary tract infection. By day of life 5, the infant's creatinine concentration and degree of hydronephrosis has decreased and the baby undergoes transurethral ablation of the valves.

SECTION IX

Answers

CASE 1 ANSWERS

1. C. Recommend continued observation and an evaluation if the baby does not void by 24 hours of age

The first void in a newborn is highly variable. More than half of newborns void by 8 hours of age, and almost all babies urinate by 24 hours of age. An evaluation is recommended in newborns without a documented void by 24 hours of age.

Although the serum creatinine concentration is helpful to estimate renal function, measurement of this protein at this baby's age would reflect the mother's serum creatinine. Thus, the serum creatinine concentration should be measured in a newborn after the first 24 hours of age to avoid a falsely elevated result. Because absence of a void at 18 hours of age is still within normal, it is not necessary to meet with the baby's parents or review the prenatal ultrasonographic findings.

2. B. Urinalysis

Clinicians should suspect a diagnosis of acute renal failure in a newborn with the following:

- Lack of urine output by 48 hours of age or decreased urine output (<1 mL/kg/hr)
- Rising, abnormal serum creatinine concentration

The diagnosis of acute renal failure is confirmed if the baby's serum creatinine concentration is greater than 1.5 mg/dL (133 µmol/L) or increasing by >0.2 mg/dL to 0.3 mg/dL (17–267 µmol/L) per day. Although serum creatinine concentrations estimate the glomerular filtration rate and can help determine the extent and progression of renal disease, an elevated value is not helpful in diagnosing the cause of the renal failure.

A urinalysis is the most helpful noninvasive test to diagnose the cause of this baby's renal failure because there may be specific microscopic findings in the urine sediment that correlate with a specific diagnosis. The urinalysis is usually normal in infants with prerenal disease and the majority of cases of urinary tract obstruction. If an infant has acute tubular necrosis, muddy brown granular and epithelial casts are usually visible. If there are red blood cells, tubular cells, and proteinuria, the infant may have intrinsic renal disease.

While a complete blood cell count result may be abnormal, the results are not specific nor helpful in determining the etiology of the renal injury. Urine specific gravity is extremely variable, altered by protein and glucose concentrations and does not correlate with urine osmolality in the newborn. Measurement of urinary biomarkers of renal injury to diagnose acute renal failure is investigational.

Additional studies that might be useful in the evaluation of an infant with acute renal failure are:

- Urine sodium excretion and calculation of FENa to distinguish between prerenal and intrinsic renal disease
- Urine osmolality with a concentrated urine in a hypovolemic infant correlating with prerenal disease and a diluted urine in a hypovolemic infant suggesting intrinsic renal disease.
- Renal ultrasonography to determine presence/absence of kidneys, assess renal size and shape, assess renal parenchyma and presence/absence of echogenicity and/or cysts, and identify urinary tract obstruction; simultaneous Doppler examination can be helpful to assess for renal vessel occlusion
- Voiding cystourethrography to diagnose obstructive uropathy and/or vesicoureteral reflux
- Radionuclide scintigraphy to determine renal structure and function

3. A. Fractional excretion of sodium (FENa) = 6%

The FENa can be calculated as follows:

$$\text{FENa}(\%) = \frac{\text{Urine Na concentration} \times \text{Plasma creatinine}}{\text{Plasma Na concentration} \times \text{Urine creatinine}}$$

If an infant's FENa is less than 2%, the diagnosis is most likely prerenal disease because the reabsorption of most of the filter sodium is an appropriate renal response to a decrease in renal perfusion. When the FENa is above 2.5% to 3%, the infant most likely has intrinsic renal disease.

A high urine osmolality often corresponds to prerenal disease. If an infant voids after a fluid challenge, prerenal failure is a likely etiology of the renal failure. However, the volume of the fluid challenge needs to be at least 10 to 20 mL/kg. The presence of a metabolic acidosis is an abnormality found in infants with both prerenal failure and intrinsic renal disease.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that a newborn who does not urinate by 24 hours of age warrants evaluation
- Plan the evaluation of an anuric infant

SUGGESTED READINGS

Mattoo TK. Acute kidney injury (acute renal failure) in the newborn. UpToDate (Subscription required). http://www.uptodate.com/contents/acute-kidney-injury-acute-renal-failure-in-the-newborn. Accessed June 25, 2013.

CASE 2 ANSWERS

1. D. All of the above

MCDK occurs in 0.3 to 1 in 1,000 live births, with more than 50% of cases being diagnosed prenatally by early fetal ultrasonography. Although autosomal dominant polycystic kidney disease is the most common cystic renal disease in all age groups, MCDK is the most common cystic renal disorder of infancy. This disorder involves a large number of noncommunicating cysts that are surrounded by dysplastic renal tissue. Although bilateral involvement can occur, most affected individuals have unilateral involvement. Cysts are typically isolated to the involved kidney without involvement of the contralateral kidney, pancreas, or liver.

A comparison of renal cystic diseases is shown in Table 1.

TABLE 1. Comparison of Renal Cystic Diseases

Type of Renal Disease	Epidemiology	Timing of Diagnosis	Renal Findings	Clinical Findings	Prognosis
Autosomal Dominant Polycystic Kidney Disease	• Most common cystic renal disease in all age groups • 1 in 800 to 1,000 live births • Autosomal dominant	• Second decade of life	• Bilateral involvement • Large cysts • Cysts increase in size and number over time	• Abdominal mass • Flank pain • Hematuria • Hypertension • Extra renal manifestations—cysts in liver, spleen, pancreas, hepatic fibrosis, intracranial aneurysm, mitral valve ballooning • Of note, varied clinical findings because of genetic, environmental, and hormonal modifiers	• Most have worsening renal disease with advancing age
Autosomal Recessive Polycystic Kidney Disease	• Autosomal recessive • 1 in 20,000 to 40,000 live births	• After 20 weeks' gestation	• Bilateral involvement • Small cysts confined to collecting ducts	• Abdominal mass • High risk of congenital hepatic fibrosis • Renal failure, hypertension, esophageal varices	• Broad range of outcomes, including intrauterine fetal demise, Potter syndrome, early renal failure with hypertension • If survive neonatal period, 40% with renal disease and poor growth • Majority require renal transplant prior to 2nd decade of life
Medullary Cystic Kidney Disease	• Autosomal dominant • Rare	• Adulthood	• Cystic dilation of medullary part of collecting ducts	• Gout • Hyperuricemia • Renal failure	• Most with end-stage renal disease
MCDK	• Most common cystic renal disease of infancy • 0.3 to 1 in 1,000 live births • No familial recurrence	• Cysts are visible by ultrasound prior to 20 weeks' gestation (>50%)	• Noncommunicating large cysts • Dysplastic renal tissue • Most are unilateral • Usually no involvement of contralateral kidney, pancreas, or liver	• Palpable flank mass	• Unilateral—very good prognosis with affected kidney involuting months to years, some contralateral changes can occur (reflux, obstruction, compensatory growth)

2. D. Unilateral flank mass

A physical examination of a neonate or infant with unilateral MCDK will reveal a palpable flank mass. The affected individual will not have a distended abdomen, abdominal tenderness or costovertebral angle tenderness, or hematuria. Complications are rare.

3. D. All of the above

Although newborns with bilateral MCDK typically have a poor prognosis because of the associated pulmonary hypoplasia, neonates with unilateral MCDK have a very good prognosis. In most cases, the affected kidney involutes over a period of months to years. Contralateral renal changes have been observed, including compensatory growth, vesicoureteral reflux, and ureteropelvic junction obstruction in the unaffected kidney. While some studies suggest an increased risk for hypertension, other reports are inconclusive. Some patients develop renal impairment.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize that multicystic dysplastic kidney frequently presents as a unilateral flank mass in neonates or infants

SUGGESTED READINGS

American Academy of Pediatrics. Renal cystic disorders. *NeoReviews-Plus*. March 2011, Question 10.
Niaudet P. Autosomal recessive and dominant polycystic kidney disease in children. UpToDate (Subscription required). http://www.uptodate.com/contents/autosomal-recessive-polycystic-kidney-disease-in-children. Accessed May 18, 2013.
Wiener JS. Multicystic dysplastic kidney. In: Belman AB, King LR, Kramer SA, eds. *Clinical Pediatric Urology*. 4th ed. London: Martin Dunitz; 2002.

CASE 3 ANSWERS

1. C. Ultrasonography

Abdominal ultrasonography is the preferred diagnostic procedure in children suspected of having cystic renal disease.

Although magnetic resonance imaging will be able to identify renal cysts, it is a more expensive test that is unnecessary for initial diagnosis. Radionuclide scintigraphy is helpful to measure renal function and blood flow. A voiding cystourethrography can assess for an obstructive uropathy or vesicoureteral reflux.

2. A. Autosomal dominant polycystic kidney disease (ADPKD)

ADPKD is the most common cystic renal disease, occurring in 1 in 800 to 1 in 1,000 live births. This autosomal dominant disorder is caused by mutations in polycystin, resulting in renal tubular epithelium abnormalities. Although there may be some subtle renal abnormalities detected prenatally (e.g., increased echogenicity of the renal cortex, increased corticomedullary differentiation), affected individuals typically develop bilateral renal cysts during or after the second decade of life. These renal cysts increase in both number and size with advancing age, resulting in hypertension and/or renal failure.

The child in this vignette is unlikely to have multicystic dysplastic kidney because in this disorder, cysts are usually identified by 20 weeks' gestation and there is no familial occurrence. Individuals with autosomal recessive polycystic kidney disease have an autosomal recessive inheritance pattern with cysts that are evident after 20 weeks' gestation by fetal ultrasonography. Medullary cystic kidney disease has an autosomal dominant pattern of inheritance, but affected individuals present during adulthood with gout and renal failure.

3. D. All of the above

Patients with ADPKD typically present later in childhood or adolescence. Symptoms can include one or more of the following:

- Abdominal mass
- Flank pain
- Hematuria
- Hypertension

Extra renal manifestations can also occur, including:

- Cyst formation in the liver, spleen, or pancreas
- Hepatic fibrosis
- Intracranial aneurysm
- Mitral valve ballooning

Clinical manifestations vary among affected individuals because there can be genetic, environmental, and/or hormonal modifiers. Thus, the child in this vignette may have different clinical manifestations compared with her father. Many affected individuals are asymptomatic during childhood but have worsening renal disease with age.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that abdominal ultrasonography is the preferred diagnostic procedure in children suspected of having autosomal dominant polycystic kidney disease
- Know that children with autosomal dominant polycystic kidney disease may have hypertension
- Know that autosomal dominant polycystic kidney disease may be associated with intracranial aneurysms

SUGGESTED READINGS

American Academy of Pediatrics. Renal cystic disorders. *NeoReviews-Plus*. March 2011, Question 10.
Cohen JN, Ringer SA. Congenital kidney abnormalities: Diagnosis, management, and palliative care. *NeoReviews*. 2010;11:e226–e235.
Niaudet P. Autosomal recessive and dominant polycystic kidney disease in children. UpToDate (Subscription required). http://www.uptodate.com/contents/autosomal-recessive-polycystic-kidney-disease-in-children. Accessed May 18, 2013.

CASE 4 ANSWERS

1. B. Small cysts that are usually confined to the collecting ducts

ARKPD is an uncommon cystic renal disease with an incidence of 1 in 20,000 to 40,000 live births. It is caused by abnormalities in the fibrocystin protein, leading to abnormalities of tubular cilia formation in the collecting tubules and biliary tree. Findings consistent with ARKPD include the following:

- Bilateral renal involvement
- Renal cysts visible radiographically *after* 20 weeks' gestation
- Small cysts that are usually confined to the collecting ducts

2. A. Congenital hepatic fibrosis

Many infants with ARKPD also have congenital hepatic fibrosis, which can lead to portal hypertension. The degree of liver disease has an indirect correlation with the severity of renal disease; individuals with severe kidney disease tend to have a milder amount of liver involvement. Affected patients also are at high risk for developing hypertension and esophageal varices.

3. C. Early renal failure with hypertension in the neonatal period

There is a broad range of outcomes for individuals with ARPKD, including intrauterine fetal demise, Potter syndrome, and early renal failure with hypertension. Early mortality from respiratory failure and/or sepsis occurs in more than one-fourth of affected patients. Approximately 40% of infants with ARPKD develop chronic renal disease and delayed growth in infancy and early childhood. For those individuals who survive infancy, the majority require renal transplantation before their second decade of life. A small number of children with ARPKD initially have normal renal function with progressive hepatic fibrosis in adulthood.

Affected individuals are not at increased risk for renal vein thrombosis. Clinical manifestations are typically apparent during infancy, and renal abnormalities are not reversible.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the clinical presentation of autosomal recessive polycystic kidney disease in neonates, infants, and children
- Know the association of autosomal recessive polycystic kidney disease with congenital hepatic fibrosis

SUGGESTED READINGS

American Academy of Pediatrics. Renal cystic disorders. *NeoReviews-Plus*. March 2011, Question 10.

Cohen JN, Ringer SA. Congenital kidney abnormalities: Diagnosis, management, and palliative care. *NeoReviews*. 2010;11:e226–e235.

Niaudet P. Autosomal recessive and dominant polycystic kidney disease in children. UpToDate (Subscription required). http://www.uptodate.com/contents/autosomal-recessive-polycystic-kidney-disease-in-children. Accessed May 18, 2013.

CASE 5 ANSWERS

1. B. Continuous leakage of amniotic fluid

Fetal urine becomes the major component of amniotic fluid at the beginning of the second trimester, with fetal urine accounting for more than 90% of amniotic fluid content by 20 weeks' gestation. The amniotic fluid then gets swallowed by the fetus. Following, the fluid is absorbed in the gastrointestinal tract and then reintroduced into the amniotic fluid with urination. Thus, a constant amount of amniotic fluid volume is maintained.

Severe oligohydramnios can occur in the following scenarios:

- Amniotic fluid leakage
- Bilateral severe renal disease
- Urinary tract obstruction
- Severe placental insufficiency

A fetus with a complete intestinal obstruction may develop *poly*hydramnios because the fetus will be unable to adequately absorb amniotic fluid. Similarly, a fetus with a poor ability to swallow amniotic fluid, as occurs in severe neurologic disorders, can develop excessive amounts of amniotic fluid. Although shallow placental implantation is associated with placental insufficiency and pregnancy-induced hypertension, deep placental implantation does not impact amniotic fluid production.

2. B. Pulmonary hypoplasia

With loss of amniotic fluid, fluid within the fetal lungs will preferentially egress from the trachea and airways into the amniotic sac. Because fetal lung growth requires an adequate amount of fetal lung fluid, pulmonary development is limited in fetuses with severe oligohydramnios, and after birth, the infant is at risk for pulmonary hypoplasia. This risk is greatest if the oligohydramnios is severe, long-standing, and occurs early in gestation.

Esophageal atresia, severe hearing loss, and visual deficits are not directly associated with severe oligohydramnios.

3. A and B

The clinical findings of the infant in this vignette (clubbed feet; distinctive facies; multiple flexion contractures of the hands, feet, arms and legs; and severe respiratory distress as a result of pulmonary hypoplasia) are most consistent with Potter sequence (see Figure 1).

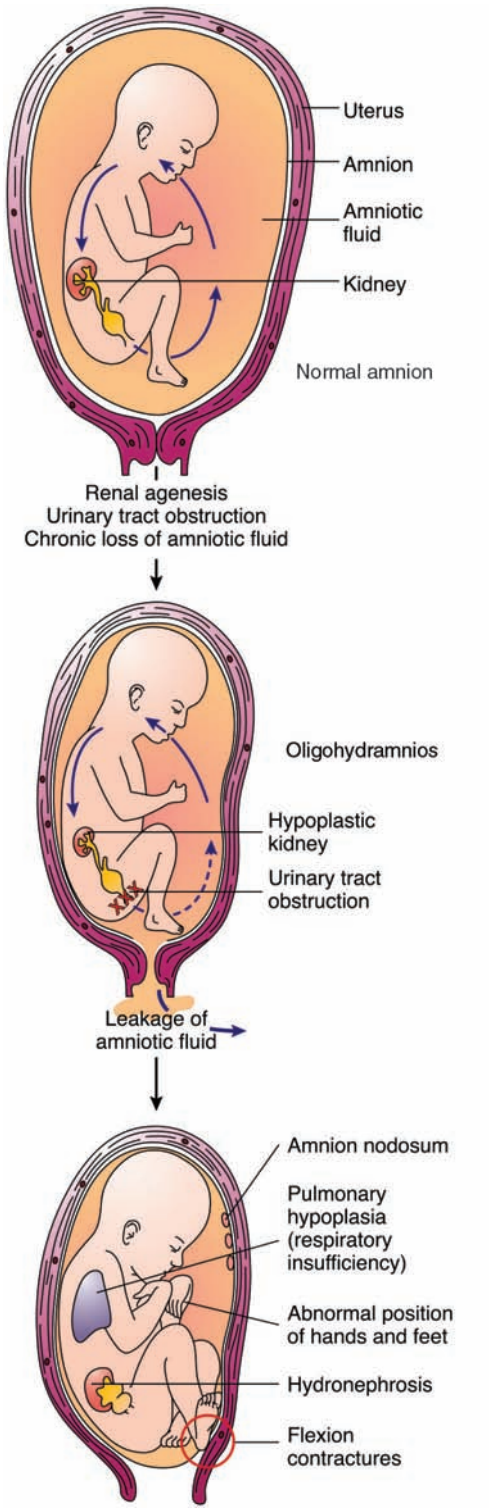

FIGURE 1. Image from: Rubin E, Farber JL. *Pathology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999. Figure 6.04

Potter sequence occurs in a fetus with severe, prolonged oligohydramnios. Possible reasons for this extreme degree of oligohydramnios include:

- Autosomal polycystic kidney disease (recessive type more often than dominant type)
- Bilateral renal agenesis
- Bilateral multicystic dysplastic kidneys
- Complete ureteral obstruction

The majority of infants with unilateral renal agenesis have normal renal function; oligohydramnios is not an associated finding with this abnormality because the other kidney can produce adequate amounts of urine prenatally.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize the association of bilateral renal aplasia or severe dysplasia with pulmonary hypoplasia (Potter syndrome)

SUGGESTED READINGS

American Academy of Pediatrics. Renal cystic disorders. *NeoReviewsPlus*. March 2011, Question 10.

Waters AM, Rosenblum ND. Evaluation of congenital anomalies of the kidney and urinary tract. UpToDate (Subscription required). http://www.uptodate.com/contents/evaluation-of-congenital-anomalies-of-the-kidney-and-urinary-tract-cakut. Accessed May 18, 2013.

CASE 6 ANSWERS

1. A. Appearance of the intrarenal collecting system

Although an infant with hydronephrosis can present with an abdominal mass on postnatal examination, most affected infants are diagnosed prenatally by fetal ultrasonography. Indeed, fetal hydronephrosis is the most common abnormality detected by routine fetal ultrasonography. Currently, the challenge for clinicians is to determine which infants have clinically significant fetal hydronephrosis that could impair renal function. At present, there are two main approaches used to standardize the severity of fetal hydronephrosis:

1. Measurement of the anterior–posterior (AP) diameter of the renal pelvis by fetal ultrasonography:
   In this method, the size of the renal pelvis is considered clinically significant (moderate or severe) if the AP diameter is greater than 8 mm in the second trimester and above 10 mm in the third trimester.
2. Appearance of the intrarenal collecting system:
   This method was described by the Society for Fetal Urology in 1993, and it classifies the severity of fetal hydronephrosis based on the degree of collecting system dilation and renal parenchymal findings. Figure 2 summarizes this classification system.

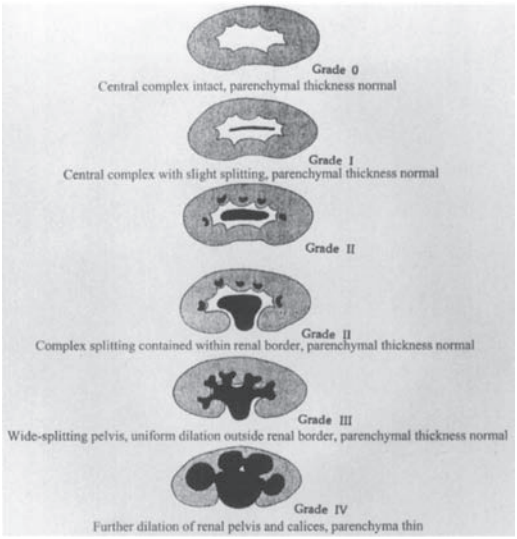

FIGURE 2. From MacDonald MG, Mullett MD, Seshia MM, eds. *Avery's Neonatology: Pathophysiology & Management of the Newborn*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 43.13

In both the approaches described earlier, there is a correlation between the degree of prenatal involvement and the risk of persistent postnatal uropathy. Although the earlier in gestation that the hydronephrosis is found has been shown to correlate with clinically significant postnatal pathology, the gestational age at the time of diagnosis is not used to determine the severity of fetal hydronephrosis.

2.

A. Isolated mild hydronephrosis	iv. Physiologic, transient finding
B. Posterior urethral valves	v. Posterior urethral dilation, a full bladder with thickened wall, decreased amniotic fluid
C. Ureterocele	i. Cystic mass in the bladder with hydroureteronephrosis
D. Ureteropelvic junction obstruction	iii. Moderately or severely dilated renal pelvis without dilation of ureter or bladder
E. Ureterovesical junction obstruction	ii. Hydronephrosis and dilated ureter to the level of the bladder

Fetal hydronephrosis is most often a result of a physiologic, transient finding, accounting for 50% to 70% of cases. An ureteropelvic junction obstruction, caused by an adynamic segment, polyp, or crossing of lower pole vessels, is found in 10% to 30% of patients with fetal hydronephrosis. Approximately 10% to 40% of cases are attributable to primary vesicoureteral reflux. Less-common causes of antenatal hydronephrosis include ureterovesical junction obstruction (5%–15%), multicystic dysplastic kidney disease (2%–5%), posterior urethral valves (1%–5%), and ureterocele (1%–3%). Less than 1% of cases result from an ectopic ureter, urethral atresia, prune belly syndrome, polycystic kidney disease, and renal cysts.

3. A. Bilateral cryptorchidism

The abdominal findings shown in the figure are consistent with Eagle–Barrett syndrome, also known as prune belly syndrome. Antenatal findings in this rare syndrome include:

- Bilateral hydroureter and hydronephrosis
- Distended, thin-walled bladder
- Severe oligohydramnios

After birth, affected infants typically have a low-pressure dilated urinary tract from the renal pelvis to the urethra. The ureters are often elongated and tortuous because smooth muscle has been replaced by collagen and fibrous tissue. Most affected infants also have vesicoureteral reflux.

Affected individuals also have the following clinical findings:

- Bilateral cryptorchidism
- Deficient or absent abdominal wall musculature
- Hypotonia

Less commonly, patients can have pulmonary hypoplasia (60%), structural heart disease (25%), gastrointestinal abnormalities (25%), and/or musculoskeletal findings (25%). The neurologic system is typically not impacted in patients with prune belly syndrome.

The pathogenesis of prune belly syndrome is uncertain. One possible theory is that prune belly syndrome results from urethral obstruction, leading to bladder distention and urinary tract dilation. This distention may then prevent appropriate muscularization of the abdominal wall and lead to inadequate testicular descent. However, because infants with posterior urethral valves have a normal abdominal wall musculature, other theories have been suggested. It is possible that prune belly syndrome results from a failure of mesodermal development, although only some mesodermal tissues are affected.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that hydronephrosis is one of the causes of abdominal masses in infants
- Know the ultrasonographic findings of fetal hydronephrosis
- Know the differential diagnosis of urinary tract obstruction
- Know that a ureterocele may lead to urinary tract obstruction
- Know the urologic findings associated with prune belly (Eagle–Barrett) syndrome

SUGGESTED READINGS

Hassett S, Smith GHH, Holland AJA. Prune belly syndrome. *Pediatr Surg Int*. 2012;28:219–228.
Kennedy WA. Assessment and management of fetal hydronephrosis. *NeoReviews*. 2002;3:e214–e219.
Yamacake KGR, Nguyen HT. Current management of antenatal hydronephrosis. *Pediatr Nephrol*. 2013;28:237–243.

CASE 7 ANSWERS

1. C. Thickened bladder wall

PUV are the most common cause of lower-tract urinary obstruction in males, affecting 1 in 2,000 to 4,000 male infants. A diagnosis of PUV is typically made during routine prenatal ultrasonography with the following findings:

- Bilateral hydroureteronephrosis
- Oligohydramnios
- Thickened bladder wall

If these ultrasonographic findings are evident prior to 20 weeks' gestation and the upper-tract dilation is moderate or severe, the fetus may develop dysplastic kidneys with limited renal function. If the diagnosis is made after 24 weeks' gestation, the renal function outcome is usually good.

2. D. All of the above

Between 50% and 70% of children with PUV are diagnosed in the first year of life, with 25% to 50% noted during the neonatal period. The most common clinical symptoms of PUV in the newborn period are associated with urinary obstruction, including:

- Palpable midline bladder
- Straining during urination
- Weak urinary stream

Some affected individuals may present later in childhood with urinary tract infections and failure to thrive.

3. D. Voiding cystourethrography (VCUG)

Although postnatal renal ultrasonography is helpful in the diagnosis of PUV with findings of hydronephrosis and bladder wall thickening, the VCUG is the most definitive diagnostic tool. In neonates with PUV, a VCUG will reveal a dilated posterior urethra, a trabeculated bladder, vesicoureteral reflux (in some cases), and valve leaflets (in some cases). Figure 1 shows the spinnaker-sail sign of the valve (*arrow*), consistent with PUV.

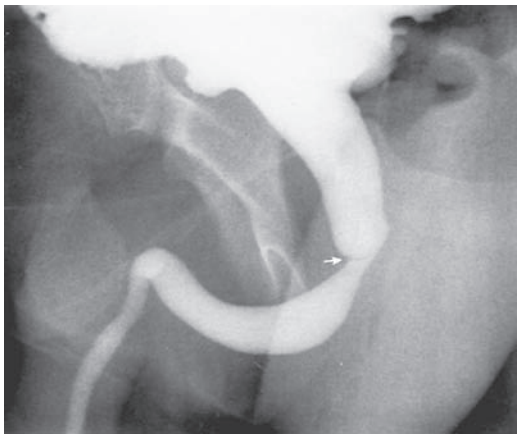

FIGURE 1. Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 26.01

Abdominal radiography and magnetic resonance imaging are not helpful in the diagnosis of PUV in a neonate.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize that a palpably distended bladder and a weak urinary stream in a male newborn are suggestive of posterior urethral valves

SUGGESTED READINGS

Hodges SJ, Patel B, McLorie G, et al. Posterior urethral valves. *ScientificWorldJournal*. 2009;9:1119–1126.
Joseph VT. The management of renal conditions in the perinatal period. *Early Hum Dev*. 2006;82:313–324.

SECTION X

Gastroenterology

CASE 1

Stooling pattern in neonates

A pediatric resident is asked by a nurse in the Newborn Nursery to examine a 24-hour-old term female infant because she has not yet had a stool. That baby has been breast-feeding exclusively. The resident reviews the normal stooling pattern of newborns with the medical students rotating in the Nursery.

1. Of the following, early passage of stool is associated with:

   A. Birth by vaginal delivery
   B. First feeding consisting of breast milk
   C. Passage of meconium in utero
   D. Younger birth gestational age

2. Match the stool color, consistency, and frequency in neonates receiving breast milk vs. formula:

   A. Green-colored stools more frequent than yellow-colored stools
   B. Larger stools in the first week of life
   C. More frequent stools in the first week of life
   D. More pronounced decrease in stool frequency after 3 weeks of age

   i. Breast-feeding neonates
   ii. Formula-fed neonates

At 48 hours of age, the baby has still not had a bowel movement and her abdomen is now distended.

3. Of the following, a possible cause(s) of this newborn's delay in stooling is (are):

   A. Hirschsprung disease
   B. Intestinal atresia
   C. Meconium plug
   D. All of the above

Diagnostic studies, including a contrast enema and rectal biopsy, reveal aganglionosis in the distal intestine. The neonatologist meets with the parents to discuss the management.

4. Of the following, the most appropriate management of this infant is:

   A. Anorectal manometry
   B. Dilation of the anal sphincter
   C. Multiple hypertonic contrast enemas
   D. Resection of the aganglionic segment and pull-through of the ganglionic bowel to the anus

CASE 2

Scaphoid abdomen

The neonatology team is asked to attend a delivery of a term infant because of fetal distress and meconium-stained amniotic fluid. The infant cries immediately after birth and is brought to the warmer. The team dries the baby and then observes that the infant has significant respiratory distress with moderate to severe intercostal retractions, tachypnea, and cyanosis. The team begins bag-mask ventilation with minimal improvement. The amount of oxygen supplementation is increased, but the infant remains cyanotic. The rest of the infant's physical examination reveals a scaphoid abdomen, barrel-shaped chest, and decreased breath sounds appreciated over the left chest. The heart sounds are loudest over the right side of the chest.

1. Of the following, the most likely diagnosis in this infant is:

   A. Congenital diaphragmatic hernia (CDH), left-sided
   B. Meconium aspiration syndrome
   C. Pneumothorax, left-sided
   D. Structural cyanotic heart disease

The neonatology fellow then places an endotracheal tube and provides positive pressure ventilation.

2. Of the following, the resuscitation step that retrospectively should have been avoided in this infant is:

   A. Bag-mask ventilation
   B. Endotracheal intubation
   C. Use of supplemental oxygen
   D. All of the above steps were appropriate in this infant

The infant is then brought to the Neonatal Intensive Care Unit for further management.

3. Of the following, the most appropriate next step in the management of this infant is to:

   A. Administer intratracheal surfactant
   B. Avoid use of high-frequency ventilation
   C. Minimize infant movements by using paralytic agents and maximal sedation
   D. Use lowest possible peak inspiratory pressure

After being treated in the hospital, the baby is ready for discharge to home. The family meets with the neonatal team to discuss monitoring for potential long-term outcomes.

4. Of the following, a possible long-term outcome(s) in this infant is:

   A. Developmental delay
   B. Poor growth
   C. Sensorineural hearing loss
   D. All of the above

CASE 3

Necrotizing enterocolitis

A nurse in the Neonatal Intensive Care Unit asks the neonatology fellow to evaluate an infant because she is concerned about a new diagnosis of necrotizing enterocolitis (NEC). The male patient was born at 26 weeks' gestational age and is now 2 weeks of age. His clinical course has been complicated by:

- Surfactant deficiency treated with intubation and surfactant administration
- A large patent ductus arteriosus with left atrial dilation treated with three doses of indomethacin
- Mild intestinal dysmotility leading to slow advancement of nasogastric feedings
- Apnea of prematurity treated with caffeine
- Sepsis evaluation with antibiotic therapy for 2 days and negative blood culture results

The baby is currently on continuous positive airway pressure with a positive end-expiratory pressure of 6-cm H_2O. He is being fed 50 mL/kg/day of his mother's pumped breast milk without additives. He is receiving the remainder of his maintenance fluid requirement in the form of total parenteral nutrition. After reviewing the infant's new clinical symptoms with the nurse and examining the baby, the fellow is also concerned about a diagnosis of NEC in this baby.

1. Of the following, early clinical finding(s) consistent with a diagnosis of NEC is (are):

   A. Abdominal distention
   B. Grossly bloody stools
   C. Increased gastric residuals
   D. All of the above

An anteroposterior abdominal radiograph shown in Figure 1 confirms the diagnosis of NEC.

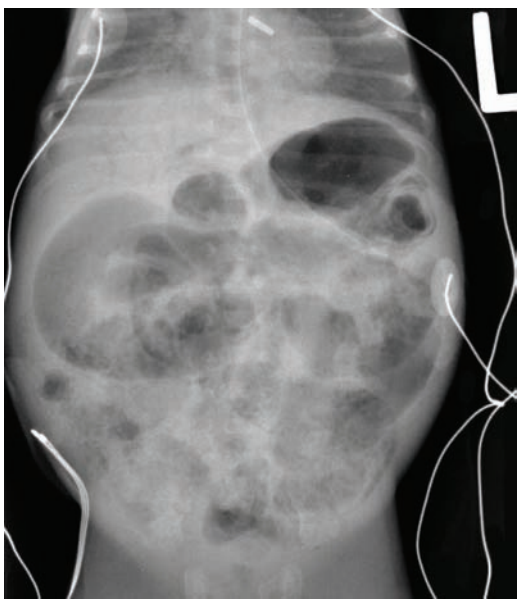

FIGURE 1. Courtesy of Dmitry Dukhovny, MD

2. Of the following, the radiographic finding in this film most consistent with the diagnosis of NEC is:

   A. Ascites
   B. Fixed dilated loop of bowel
   C. Pneumoperitoneum
   D. Portal venous air

The neonatology fellow then contacts the family about the infant's critical status and discusses the initial management.

3. Of the following, the most appropriate next steps in the management of this infant are:

   A. Monitor for apneic spells and try to avoid intubation by giving additional caffeine boluses
   B. Start intravenous antibiotics if the infant's white blood cell or platelet counts are low
   C. Stop enteral feedings and place an orogastric or nasogastric replogle catheter connected to continuous suction
   D. All of the above

The infant remains stable and the family is relieved that his medical NEC does not progress to surgical NEC. Feedings are slowly restarted 2 weeks after the initial presentation. After 5 days of refeeding, the infant's nurse asks the neonatology fellow to again evaluate the infant because of feeding intolerance. The nurse relays that the infant has slowly advanced to 60 mL/kg/day of expressed breast milk and has been having gastric residuals with a recent bilious spit. The infant has not had any spells in the past 12 hours. On examination, the infant appears well with normal vital signs. The fellow examines the infant's abdomen and appreciates normal bowel sounds, but the abdomen is distended.

4. Of the following, the diagnosis most likely in this infant is:

   A. Isolated malrotation
   B. Recurrent NEC
   C. Stricture
   D. Volvulus

CASE 4

Intestinal obstruction

A nurse in the Newborn Nursery asks a pediatric resident to evaluate a term infant with bilious emesis. The 12-hour-old infant was born by vaginal delivery and has been breastfeeding every 3 hours. The baby has voided but has not yet passed any stool. On physical examination, the resident finds that the infant is active but has an extremely distended abdomen with infrequent bowel sounds. The blanket next to the baby has a large amount of green-colored fluid. The pediatric resident is concerned about an intestinal obstruction and discusses the possible locations of an obstruction with the infant's parents.

1. Match the specific finding (A–D) with the location of the intestinal obstruction (i–iv):

   A. Abdominal radiograph with double bubble
   B. Abdominal radiograph with more than five large dilated loops
   C. Bilious emesis
   D. Distended abdomen

   i. High-intestinal obstruction (up to proximal ileum) only
   ii. Low-intestinal obstruction (distal ileum and colon) only
   iii. Both high- and low-intestinal obstruction
   iv. Neither high- nor low-intestinal obstruction

The pediatric resident then brings the baby to the Neonatal Intensive Care Unit for evaluation and management.

2. Of the following, the most appropriate initial radiographic study to obtain in this infant is a(n):

   A. Abdominal radiography, anterior–posterior view
   B. Abdominal ultrasound
   C. Contrast enema
   D. Upper gastrointestinal series

The infant has several radiographic tests, and one of the images is shown in Figure 1.

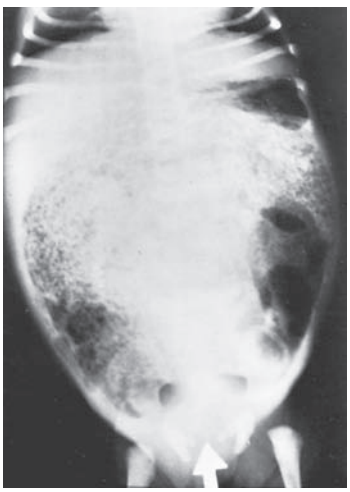

FIGURE 1. From Eisenberg RL. *An Atlas of Differential Diagnosis*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Figure 23.6

3. Of the following, the most likely diagnosis in this infant is:

   A. Duodenal atresia
   B. Gastric atresia
   C. Hirschsprung disease
   D. Meconium ileus

The neonatal nurse inserts an orogastric replogle connected to continuous suction. Following, she places an intravenous line and administers continuous intravenous fluid.

4. Of the following, the most appropriate next step(s) in the management of this infant is to:

   A. Consult with a pediatric surgeon
   B. Evaluate for cystic fibrosis
   C. Perform a Gastrografin enema
   D. All of the above

CASE 5

Anterior abdominal wall defects

A 25-year-old pregnant woman from Ghana is visiting her relatives in the United States. At 34 weeks' gestation, she develops severe back pain and goes to the local hospital. The obstetric evaluation reveals that the woman is in preterm labor. Despite tocolysis, labor progresses and the infant is born. In the delivery room, the neonatology team observes that the infant has an abdominal mass that is consistent with a gastroschisis.

1. Of the following, the characteristic most often found in an infant with a gastroschisis is:

   A. Additional anomalies, such as structural heart disease
   B. A defect that is located adjacent to the umbilical cord
   C. Presence of a sac
   D. None of the above

The neonatology fellow discusses the differences between an omphalocele and a gastroschisis with the rest of the team.

2. Match the specific finding(s) (i–vii) with the abdominal wall defect:

   A. Gastroschisis alone
   B. Omphalocele alone
   C. Both gastroschisis and omphalocele
   D. Neither gastroschisis nor omphalocele

   i. Associated with an elevation of maternal serum α-fetoprotein
   ii. Caused by failure of intestines to return to the abdominal cavity after herniation
   iii. Delivery by cesarean has been shown to be beneficial
   iv. Higher incidence in adolescent mothers
   v. Intestinal atresia is the most common anomaly
   vi. Planned preterm delivery is advantageous
   vii. Prognosis dependent on intestinal damage during fetal life

The neonatology fellow focuses on several issues in the initial management of this infant.

3. Of the following, a potential complication that is *least* likely to occur in this infant is:

   A. Fluid loss
   B. Hyperthermia
   C. Infection
   C. Injury to the exposed bowel

CASE 6

Biliary atresia

A term male infant is born by vaginal delivery and appears well. His bilirubin at 40 hours of age is normal. His parents visit the pediatrician for a routine appointment 2 days after discharge and the mother reports that he is breast-feeding well. His examination is normal. At 16 days of age, the infant has another pediatric appointment. Although the baby appears well, he is jaundiced. The mother recalls that the infant's urine has become dark in color. The infant passes a stool during the visit, and this stool is shown in Figure 1.

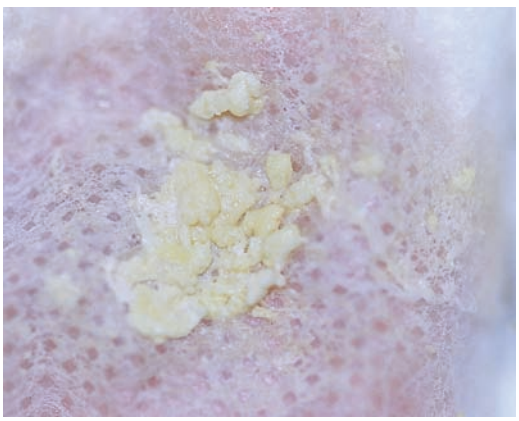

FIGURE 1. From Fleisher GR, Ludwig S, Baskin MN. *Atlas of Pediatric Emergency Medicine*. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. Figure 8.29

The pediatrician orders a bilirubin test, and the infant's total bilirubin concentration is 6.8 mg/dL (116 µmol/L) with a direct component of 2.6 mg/dL (44.4 µmol/L).

1. Of the following, the most appropriate radiographic study in the initial evaluation of this infant is:

   A. Abdominal ultrasonography
   B. Computed tomography scan of the abdomen
   C. Hepatobiliary scintigraphy
   D. Magnetic resonance imaging of the abdomen

The pediatrician is concerned about a possible diagnosis of biliary atresia and consults with a pediatric surgeon. The surgeon performs a percutaneous liver biopsy that confirms this diagnosis. The surgeon then meets with the family to discuss this disease.

2. Of the following, the most accurate statement about biliary atresia is:

   A. Biliary atresia is an uncommon cause of cholestasis in neonates.
   B. Biliary atresia is the most common reason for a liver transplant in children.
   C. The majority of infants with biliary atresia appear unhealthy, with poor growth at 3 to 6 weeks of age.
   D. The majority of infants with biliary atresia have other congenital malformations.

The surgeon then performs the Kasai portoenterostomy procedure to reestablish bile flow when the infant is 28 days old.

3. Of the following, the outcome of an infant with biliary atresia depends on:

   A. Degree of liver damage
   B. Resolution of jaundice after the Kasai portoenterostomy procedure
   C. Timing of the Kasai portoenterostomy procedure
   D. All of the above

SECTION X

Answers

CASE 1 ANSWERS

1. C. Passage of meconium in utero

Ninety-nine percent of term infants have a bowel movement within the first 48 hours after birth, with 94% passing stools within the first 24 hours of life. Newborns who have passed meconium in utero are significantly more likely to pass the first postnatal stool earlier than those newborns who did not pass meconium in utero (3 hours vs. 8 hours). The time to the first bowel movement in a newborn is independent of the mode of delivery. The initial type of feeding (i.e., breast milk vs. formula) also does not impact the timing of the first stool. On average, preterm infants pass their first stool later than term infants. Some early gestational age infants may have a delay in passing their first meconium of more than 10 days after birth.

2.

A	ii
B	i
C	i
D	i

The first few stools in a newborn are usually meconium, and after a baby begins to drink milk, the infant's stool color, frequency, and consistency vary based on the type of diet. Breast-feeding infants typically have yellow-colored stools, while formula-fed infants are more likely to have green-colored stools. Breast-fed infants have more frequent and larger stools in the first week of life. However, after 3 weeks of age, breast-fed babies have a more pronounced decrease in stool frequency compared with formula-fed infants.

3. D. All of the above

If a term infant has not passed stools by 48 hours of age, further evaluation is warranted to assess for a distal intestinal obstruction, even if the infant is asymptomatic. Potential causes of a delay in stooling include the following:

- Anorectal malformations including anal atresia and anal stenosis
- Meconium ileus
- Meconium plug
- Left small colon syndrome
- Small bowel and colonic atresia
- Hirschsprung disease
- Visceral neuropathy or myopathy

Although an infant's physical examination can help to exclude an external anorectal malformation, most infants with a distal bowel obstruction will require a contrast enema to determine the precise cause of the obstruction.

4. D. Resection of the aganglionic segment and pull-through of the ganglionic bowel to the anus

Hirschsprung disease is caused by aganglionosis in the distal intestine, which is limited to the rectum and sigmoid in 75% of affected patients. Approximately 75% of neonates with Hirschsprung disease will have a transition zone between the normal and aganglionic bowel evident by contrast enema. A rectal suction biopsy is necessary to confirm the absence of ganglion cells in the abnormal bowel segment. If this biopsy is equivocal, a full thickness rectal wall biopsy may be needed. Surgical management involves resection of the aganglionic segment and pull-through of the ganglionic bowel to the anus.

Anorectal manometry can be helpful in the diagnosis of Hirschsprung disease by showing the absence of a rectoanal inhibitory reflex. However, the infant in this vignette does not require further diagnostic confirmation. Dilation of the anal sphincter will not be helpful in the management of an infant with Hirschsprung disease. Multiple hypertonic contrast enemas are useful in infants with a meconium ileus or meconium plug to remove the thick, tenacious meconium.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the difference between bottle-fed infants and breast-fed infants as related to stool frequency, consistency, and color
- Recognize that the delayed or absent passage of meconium is associated with colonic obstruction (e.g., meconium plug syndrome, Hirschsprung disease, imperforate anus)

SUGGESTED READING

Nurko S. Motility of the colon and anorectum. *NeoReviews*. 2006;7:e34–e47.

CASE 2 ANSWERS

1. A. Congenital diaphragmatic hernia (CDH), left-sided

The infant in this vignette has physical examination findings that are consistent with a diagnosis of CDH, including:

- Cyanosis
- Displaced heart sounds to the side of unaffected lung
- Barrel-shaped chest
- Respiratory distress with decreased breath sounds over the affected lung
- Scaphoid abdomen

In addition, bowel sounds are often heard in the chest of the affected lung. Figure 1 shows the radiographic findings of an infant with CDH: multiple gas-filled bowel loops in the left thorax, shift of mediastinal structures to the contralateral side, and a nasogastric tube with the distal tip in the stomach within the chest.

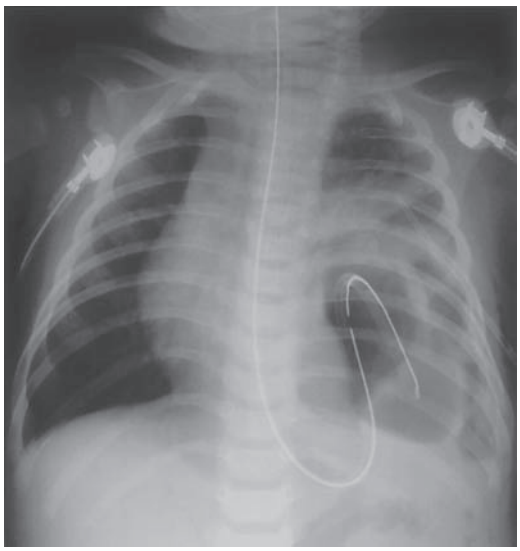

FIGURE 1. From Mulholland MW, Maier RV, et al. *Greenfield's Surgery: Scientific Principles and Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. Figure 109.22A

An infant with meconium aspiration syndrome may have severe respiratory distress and cyanosis but typically has a symmetric respiratory exam and heart sounds that are not displaced. An infant with a left-sided pneumothorax will have decreased breath sounds in the affected lung with possible shift in heart sounds to the contralateral lung and might have a barrel-shaped chest. However, the infant's abdominal examination should be normal. An infant with structural cyanotic heart disease will have cyanosis and may have respiratory distress, but the lung examination should be symmetric and the abdominal examination should be normal.

2. A. Bag-mask ventilation

In most cases, the diagnosis of a left-sided CDH is made prenatally with fetal ultrasonography demonstrating a fluid-filled stomach within the thorax. A right-sided CDH is more difficult to diagnose prenatally because the herniated portion typically involves the right lobe of the liver, which has an echogenicity similar to the fetal lung. The approach to delivery room management of an infant with CDH includes:

- Avoidance of bag-mask ventilation to minimize intestinal distention
- Immediate postnatal endotracheal intubation to minimize intestinal distention
- Placement of an orogastric or nasogastric tube to decompress bowel air
- Supplemental oxygen, as needed, to avoid hypoxemia and minimize pulmonary vasoconstriction

3. D. Use lowest possible peak inspiratory pressure

Infants with CDH may have the following immediate postnatal issues:

- Impaired systemic venous return as a result of mediastinal compression
- Pulmonary hypoplasia from inadequate lung development on the side of the CDH
- Pulmonary hypertension

Postnatal management strategies focus on these issues. In addition, postnatal management involves preventing further lung injury by decreasing barotrauma. This approach involves:

- Tolerating higher levels of $Paco_2$ (i.e., permissive hypercapnia)
- Using the lowest possible peak inspiratory pressures
- Having a lower threshold for the use of high-frequency ventilation

Most centers also focus on minimizing use of sedation. The use of paralytic agents is controversial as some clinicians feel that paralysis increases the ventilation–perfusion mismatch by increasing the chance of atelectasis and leads to edema with decreased chest wall compliance. In contrast, other clinicians postulate that paralytic agents help to improve oxygenation and ventilation.

Administration of surfactant to term infants with CDH is controversial. Although studies reveal surfactant deficiency in animals with CDH, studies in humans have not demonstrated that surfactant improves outcomes in affected infants.

Infants with CDH and severe pulmonary hypoplasia and pulmonary hypertension who do not respond to medical management may require extracorporeal membrane oxygenation (ECMO). All infants with CDH require surgical repair, usually performed 7 to 10 days after birth when pulmonary vascular resistances are lower.

4. D. All of the above

As the mortality rate of CDH has declined, the risk of long-term morbidities has become more evident. Potential long-term outcomes include:

- Chronic pulmonary hypertension
- Developmental delay

- Gastroesophageal reflux, feeding difficulties, and failure to thrive
- Pulmonary sequelae, such as chronic lung disease, reactive airway disease, recurrent respiratory infections
- Tracheomalacia or bronchomalacia
- Sensorineural hearing loss

Infants are also at greater risk for reherniation months to years after the initial repair. Affected infants can present with an intestinal obstruction as a result of a midgut volvulus or adhesions. Chest wall and spinal deformities are also common in survivors of CDH. As a result of these potential long-term morbidities, close follow-up by a multidisciplinary team is required after the infant is discharged from the hospital.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical manifestations of a newborn with diaphragmatic hernia
- Know the initial stabilization maneuvers for a newborn with a diaphragmatic hernia
- Know the appropriate initial therapy for a diaphragmatic hernia
- Know that diaphragmatic hernia is associated with persistent pulmonary hypertension and subsequent abnormalities including poor growth, tracheomalacia, and developmental delay

SUGGESTED READINGS

Benjamin JR, Bizzarro MJ, Cotton CM. Congenital diaphragmatic hernia: Updates and outcomes. *NeoReviews*. 2011;12:e439–e451.
Kays DW. Congenital diaphragmatic hernia: Real improvements in survival. *NeoReviews*. 2006;7:e428–e439.

CASE 3 ANSWERS

1. D. All of the above

NEC impacts 5% to 10% of premature infants born less than 1,500 g. There are four major risk factors that are currently believed to lead to the development of NEC:

1. Prematurity
2. Formula feeding
3. Intestinal ischemia
4. Bacterial colonization

Although the precise pathophysiologic pathway of NEC has not yet been clearly delineated, these risk factors all lead to stimulation of the inflammatory cascade.

Infants with NEC usually present with gastrointestinal symptoms. Early signs include:

- Abdominal distention (70%–98%)
- Feeding intolerance with increased gastric residuals (>70%)
- Emesis (>70%)
- Grossly bloody stools (25%–63%)
- Occult bloody stools (22%–59%)
- Diarrhea (4%–26%)

With advancing disease, patients develop abdominal distention, ascites, and/or abdominal wall erythema. In severe cases, infants may have an intestinal perforation, leading to a bluish or purplish hue to the abdominal wall.

Nonspecific signs include lethargy, increased number of apneic episodes, temperature instability, and hypotension. Laboratory findings include:

- Coagulopathy
- Electrolyte abnormalities
- Elevated or extremely low white blood cell count
- Hypoglycemia or hyperglycemia
- Metabolic acidosis
- Thrombocytopenia

2. D. Portal venous air

The anteroposterior abdominal radiograph of the infant in this vignette reveals multiple areas of pneumatosis intestinalis. Pneumatosis is the pathognomonic radiographic finding in an infant with NEC. It represents gas between subserosal and muscularis layers of the bowel wall and results from hydrogen produced by pathogenic bacteria.

This radiograph also demonstrates portal venous gas in the right upper-abdominal quadrant evident by thin, linear areas in the region of the liver. This is caused by intramural air that gets absorbed into the mesenteric venous system.

Although there are several large dilated loops in the abdominal radiograph, additional films are needed to assess if these loops are fixed. If a loop of bowel is unchanged over a period of 24 to 36 hours, this may result from transmural necrosis. Many infants with NEC have ascites, but this is best diagnosed by ultrasonography instead of an abdominal radiography. Pneumoperitoneum is a serious complication in patients with NEC and can best be visualized with a lateral decubitus film with the infant placed left side down (i.e., left lateral decubitus). When the infant is in this position, perforated air will be visible between the body wall and the liver, as shown in the Figure 2.

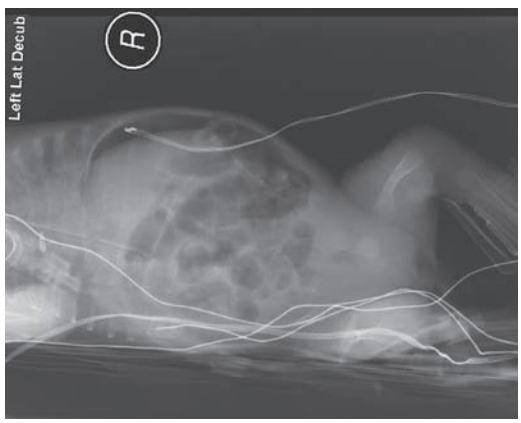

FIGURE 2. Courtesy of Dmitry Dukhovny, MD

A pneumoperitoneum may sometimes be visible on an anteroposterior radiograph as a large central collection of air, known as the "football" sign. In the abdominal radiograph of this infant, a pneumoperitoneum is not evident.

3. C. Stop enteral feedings and place an orogastric or nasogastric replogle catheter connected to continuous suction

After an infant is diagnosed with medical NEC, the following steps should be taken:

- Assess the infant's blood pressure, monitor the infant's acid–base balance, and provide fluid boluses/inotropic support as needed
- Examine the infant's abdomen frequently
- Monitor for apneic spells with a low threshold for intubation to minimize intestinal air entry
- Obtain a complete blood cell count and transfuse with platelets if infant has thrombocytopenia
- Order abdominal radiographs every few hours and obtain additional radiographs if there is a change in the infant's clinical examination
- Start intravenous antibiotics after a blood culture is obtained (regardless of the infant's white blood cell or platelet count)
- Stop enteral feedings and place an orogastric or nasogastric replogle catheter connected to continuous suction
- Test the infant for a coagulopathy and treat as appropriate

The surgical team should be consulted if the infant develops a pneumoperitoneum or worsening clinical status. If the infant remains stable, most clinicians would hold off on enteral feedings and continue the antibiotic regimen for a 2-week period.

4. C. Stricture

The infant in this vignette most likely has an intestinal stricture. After an infant has NEC, areas of intestinal ischemia heal by scarring, and if these scars contract, a stricture will form. Although strictures can be found anywhere within the small and large bowels, the most common site is the junction of the descending and sigmoid colon. Clinical findings that are consistent with a stricture include:

- Abdominal distention
- Bilious emesis
- Gastric residuals

Infants usually appear well and have a normal physical examination and laboratory findings. Abdominal radiographs may reveal dilated bowel loops proximal to the stricture. A contrast enema is required to confirm the diagnosis, and if a stricture is found, surgery is warranted.

An infant with an isolated malrotation typically is asymptomatic unless a volvulus occurs. An infant with a volvulus or recurrent NEC will present with bilious emesis and usually will appear ill.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the usual presentation of necrotizing enterocolitis, and plan initial management
- Know that the radiographic finding of pneumatosis intestinalis is the hallmark of necrotizing enterocolitis
- Recognize that intestinal stricture formation is a late complication of necrotizing enterocolitis

SUGGESTED READINGS

Caplan MS, Jilling T. The pathophysiology of necrotizing enterocolitis. *NeoReviews*. 2001;2:e103–e109.

Dimmitt RA, Moss RL. Clinical management of necrotizing enterocolitis. *NeoReviews*. 2001;2:e110–e116.

CASE 4 ANSWERS

1.	A	i
	B	ii
	C	iii
	D	iii

An intestinal obstruction in a newborn can be characterized into a high (i.e., proximal) or low (i.e., distal) obstruction. A high-intestinal obstruction occurs proximal to the ileum and a low-intestinal obstruction involves the distal ileum or colon. Causes of high-intestinal obstruction include:

- Gastric atresia
- Duodenal atresia
- Duodenal stenosis with annular pancreas
- Duodenal web
- Malrotation with volvulus
- Jejunal atresia
- Jejunal stenosis

Causes of low intestinal obstructions include:

- Ileal atresia
- Meconium ileus
- Functional immaturity of the colon
- Hirschsprung disease
- Colonic atresia
- Anal atresia and anorectal malformations

While a newborn with gastric atresia will have nonbilious emesis, any obstruction below the pylorus will lead to bilious emesis. Regardless of the location of the obstruction, neonates can have a distended abdomen because of increased amount of air within the bowel. Radiographically, infants with high-intestinal obstructions typically have three or fewer dilated

bowel loops, while newborns with low-intestinal obstructions have multiple diffusely dilated loops of bowel. A neonate with gastric atresia will have a markedly distended stomach bubble without distal intestinal air, leading to the "single-bubble sign." Newborns with duodenal atresia have a dilated stomach and dilated duodenal bulb, leading to the classic "double-bubble sign." Dilation of the stomach, duodenum, and proximal jejunum leads to the "triple-bubble sign" in patients with jejunal atresia.

2. A. Abdominal radiograph, anterior–posterior view

A newborn with bilious emesis, with or without abdominal distention, warrants immediate evaluation. An anterior–posterior abdominal radiography is the most appropriate initial radiographic study in an infant with bilious emesis and abdominal distention. In most cases, an upper gastrointestinal series is then obtained to evaluate for a malrotation and volvulus. If the radiograph shows a double bubble consistent with duodenal atresia, a pediatric surgeon might recommend surgery without the need for further imaging. A contrast enema is recommended in an infant with signs of a low-intestinal obstruction. An abdominal ultrasound is helpful in the diagnosis of pyloric stenosis when a newborn presents with projectile nonbilious emesis.

3. D. Meconium ileus

The radiograph reveals a "ground-glass" appearance of gas (i.e., swallowed air) mixed with meconium, which is consistent with meconium ileus. Other radiographic findings of meconium ileus include:

- Multiple dilated loops of bowel
- Lack of air–fluid levels within the dilated loops because of the abnormally thick intraluminal meconium
- Contrast enema with an unused narrow colon, known as a microcolon (shown in the enema in Figure 2), with filling defects representing meconium concretions

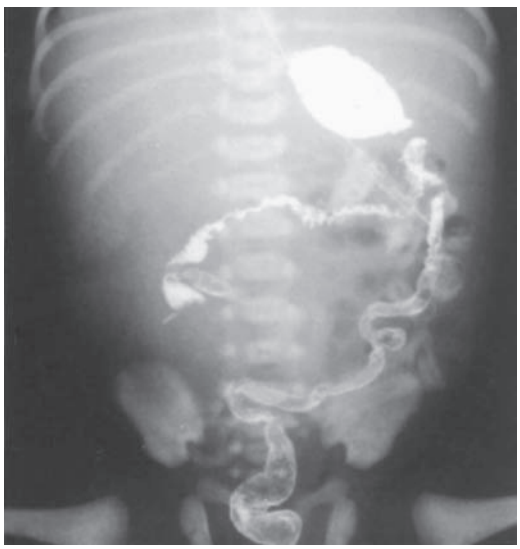

FIGURE 2. From Mulholland MW, Maier RV, et al. *Greenfield's Surgery: Scientific Principles and Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. Figure 110.24B

Duodenal atresia results from failure of recanalization of the duodenal region at 9 to 11 weeks' gestational age. An infant with a duodenal atresia will have a "double-bubble sign" on abdominal radiograph that consists of a gas-filled dilated stomach and the duodenal bulb, as shown in Figure 3. With complete duodenal obstruction, there is no bowel gas distal to the proximal duodenum.

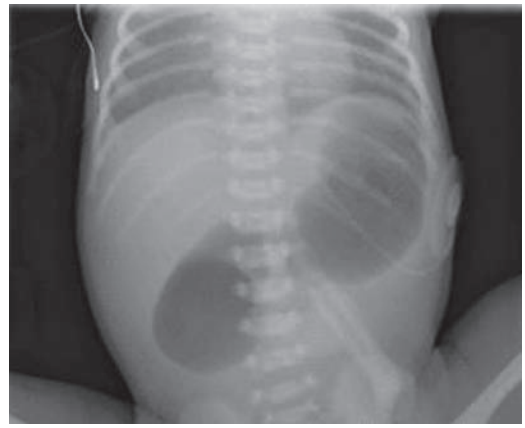

FIGURE 3. Courtesy of Dmitry Dukhovny, MD

Complete gastric atresia is extremely rare, likely caused by a local intrauterine vascular occlusion. Affected neonates present with nonbilious vomiting and abdominal distention soon after birth. Abdominal radiographs will demonstrate a large stomach bubble with an absence of distal intestinal air, as shown in Figure 4.

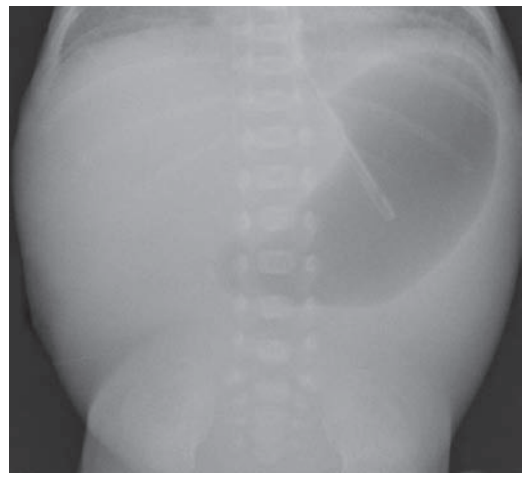

FIGURE 4. Courtesy of Dara Brodsky, MD

Hirschsprung disease results from an arrest of ganglion cell migration to the distal bowel, typically involving the rectum and a portion of the sigmoid colon. Neonates with Hirschsprung disease have radiographic findings of a low-intestinal obstruction. A contrast enema study reveals a small rectosigmoid ratio and a transition zone. Contrast is often retained within the bowel on follow-up films. The radiograph

below shows the results of a contrast enema in an infant with Hirschsprung disease. A dilated colon ending in a small, tapered atonic segment at the rectum (*black arrow*) is evident in Figure 5.

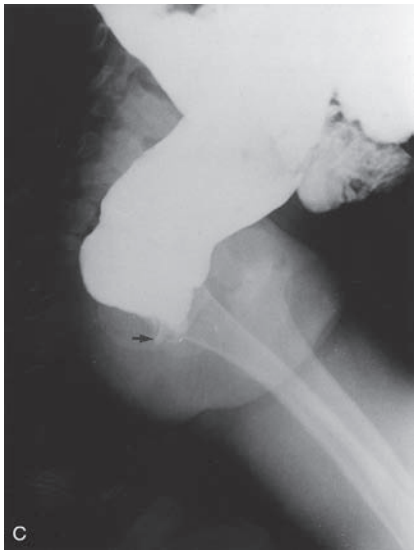

FIGURE 5. From Daffner RH. *Clinical Radiology: The Essentials*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. Figure 8.71

4. D. All of the above

Meconium ileus results from retention of thick meconium in the ileum, jejunum, and/or colon that leads to a low-bowel obstruction. Infants may develop complications, such as volvulus, bowel perforation, or meconium peritonitis. Initial management of an infant with meconium ileus includes placement of an orogastric or nasogastric replogle connected to continuous suction. In patients with uncomplicated meconium ileus, an enema using a hypertonic solution, typically Gastrografin, can be performed to help draw fluid into the bowel to facilitate expulsion of the meconium. If the hypertonic enema is unsuccessful, additional enemas might be required. If the meconium is still unable to be removed, surgery is necessary to disimpact the meconium. Because meconium ileus occurs in 15% of newborns with cystic fibrosis and only 5% to 10% of newborns with meconium ileus do not have cystic fibrosis, testing for cystic fibrosis is necessary in all affected patients.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the differences in clinical presentation of upper and lower congenital bowel obstruction
- Know the management of a newborn with bilious vomiting
- Know the treatment of abdominal distention caused by a congenital small bowel obstruction
- Know the etiology, diagnostic evaluation, and treatment of meconium ileus

SUGGESTED READINGS

Carlyle BE, Borowitz DS, Glick PL. A review of pathophysiology and management of fetuses and neonates with meconium ileus for the pediatric surgeon. *J Pediatr Surg*. 2012;47:772–781.

Kimura K, Loening-Baucke V. Bilious vomiting in the newborn: Rapid diagnosis of intestinal obstruction. *Am Fam Physician*. 2000;61:2791–2798.

Vinocur DN, Lee EY, Eisenberg RL. Neonatal intestinal obstruction. *Am J Roentgenol*. 2012;198:W1–W10.

CASE 5 ANSWERS

1. B. A defect that is located adjacent to the umbilical cord

The two most common anterior abdominal wall defects are gastroschisis and omphalocele. These masses are typically detected prenatally by fetal ultrasonography. The characteristics consistent with a gastroschisis are:

- Absence of a sac
- A defect that is located adjacent to the umbilical cord (usually to the right of the umbilicus)
- Rare to have additional anomalies

An example of a gastroschisis is shown in Figure 1.

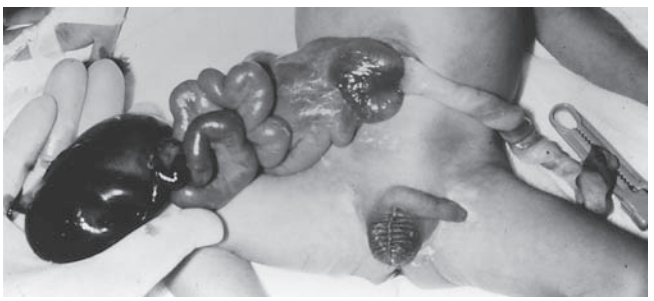

FIGURE 1. Courtesy of Dr. S. Lacey, Department of Surgery, University of North Carolina

In contrast, an omphalocele is typically covered by a membranous sac (consists of amnion, Wharton jelly, and peritoneum), and the umbilical cord inserts into the sac. In some cases, the covering sac might rupture and the contents of the omphalocele are then exposed. An example of an unruptured omphalocele is shown in Figure 2.

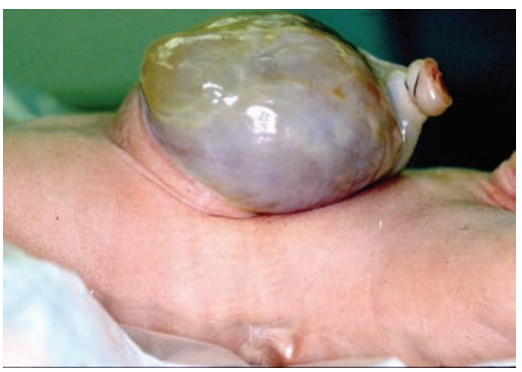

FIGURE 2. Courtesy of Douglas Katz, MD

More than 50% of infants with an omphalocele are at risk for anomalies, including congenital heart defects, holoprosencephaly, and VACTERL defect. Chromosomal abnormalities, such as trisomies 13, 18, and 21, and Beckwith–Wiedemann syndrome may be found in many infants with an omphalocele. A large omphalocele has also been associated with pulmonary hypoplasia. Thus, after a fetus is diagnosed with an omphalocele, further evaluations with fetal echocardiography and chromosomal assessment are recommended. The presence of the liver within the sac of infants with an omphalocele has been associated with a lower risk of chromosomal anomalies.

2. A iv, v, vii
B ii
C i
D iii, vi

The vast majority of pregnancies complicated by a gastroschisis or omphalocele are diagnosed prenatally. An early indicator of a gastroschisis is an elevated maternal serum α-fetoprotein. Less commonly, a fetus with an omphalocele may also be associated with a maternal serum α-fetoprotein. Late first-trimester or early second-trimester fetal ultrasonography will identify both abdominal wall abnormalities.

An omphalocele is caused by failure of the intestines to return to the abdominal cavity after herniation. It is believed that this results from a folding defect in the abdominal wall instead of a disruption of genes important for intestinal rotation. The pathogenesis of a gastroschisis is still uncertain but is likely attributable to an intrauterine vascular accident.

The optimal mode of delivery for a fetus with gastroschisis or omphalocele is controversial. Although some clinicians are proponents of elective cesarean delivery to avoid bowel injury during a vaginal delivery, studies have failed to demonstrate a difference in benefit of cesarean delivery. Thus, the mode of delivery is typically decided by the obstetrician in discussion with the family.

Pregnant women younger than 20 years of age are at higher risk of having a fetus with a gastroschisis. Maternal age does not impact the risk of having a fetus with an omphalocele. For unknown reasons, there has been a 10- to 20-fold increase in the incidence of gastroschisis in all age groups over the past 20 years.

Although more than half of infants with an omphalocele will have an associated anomaly, anomalies are uncommon in infants with gastroschisis. However, ~10% of infants with a gastroschisis are at risk of an intestinal atresia.

Although preterm delivery is more frequent in infants with gastroschisis (50%–60%) or omphalocele (10%–20%), there is no advantage to deliver an infant with a gastroschisis or omphalocele prior to term gestational age. Some clinicians advocate selective preterm delivery in fetuses with gastroschisis if fetal ultrasonography demonstrates intestinal compromise, such as increased bowel wall thickness and/or significant bowel distention.

The long-term prognosis in an infant with an omphalocele depends on the infant's associated anomalies. In contrast, the prognosis of an infant with a gastroschisis is determined by the degree of intrauterine intestinal injury and presence/absence of an intestinal atresia.

3. B. Hyperthermia

Infants with gastroschisis are at risk for the following:

- Fluid loss
- Hypothermia
- Infection
- Injury to the exposed bowel (of note, this injury can occur in utero as well)

As a result of these potential complications, initial management focuses on prompt intravenous fluid administration, placement of the bowel contents in a plastic bag to help retain heat and protect the bowel, prophylactic antibiotic administration, and nasogastric tube placement to decompress the bowel. Pediatric surgeons need to assess the bowel for atresia, necrosis, and/or perforation and, based on these findings, determine the approach and timing of the repair.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Know the difference between gastroschisis vs omphalocele

SUGGESTED READINGS

Christison-Lagay ER, Kelleher CM, Langer JC. Neonatal abdominal wall defects. *Semin Fetal Neonatal Med*. 2011;16:164–172.
Davis AS, Blumenfeld Y, Rubesova E, et al. Challenges of giant omphalocele: from fetal diagnosis to follow-up. *NeoReviews*. 2008;9:e338–e347.
Waldhausen JHT. Surgical management of gastroschisis. *NeoReviews*. 2005;6:e500–e507.

CASE 6 ANSWERS

1. A. Abdominal ultrasonography

The infant in this vignette appears healthy but has conjugated jaundice beyond 14 days of age, acholic stool, and dark urine. Any infant with these findings requires immediate evaluation to assess for biliary atresia because infants with biliary atresia have better outcomes if surgery is performed prior to 45 days of life. An abdominal ultrasound is the most appropriate next step in the evaluation of this infant to exclude other possible reasons for the cholestasis. During this study, radiologists will assess the following:

- Presence or absence of an extrahepatic obstruction lesion, such as a choledochal cyst, mass, inspissated bile, gallstones
- Liver structure, size, and composition
- Presence or absence of ascites

Patients with biliary atresia may have the following ultrasonographic findings:

- "Triangular cord sign," which is a solid biliary remnant in front of the bifurcation of the portal vein
- Absent or atrophic gallbladder
- Polysplenia or asplenia
- Interrupted inferior vena cava
- Preduodenal portal vein
- Situs inversus

However, while these findings may be present in infants with biliary atresia, they are neither sensitive nor specific in the diagnosis of biliary atresia.

Following an abdominal ultrasound study, most centers rely on a percutaneous liver biopsy to diagnose biliary atresia. However, the interpretation of the results may be challenging. The best predictors of biliary atresia include the following:

- Bile duct proliferation
- Portal fibrosis
- Absence of sinusoidal fibrosis

If the biopsy is not diagnostic, some infants may require cholangiography by endoscopic retrograde cholangiopancreatography or laparoscopy and possibly a hepatobiliary scan.

2. B. Biliary atresia is the most common reason for a liver transplant in children.

Biliary atresia is the most common cause of neonatal cholestasis. Most clinicians categorize biliary atresia into two types—the acquired form and the embryonic form. The acquired form is more common (~85%) and is associated with a significant inflammatory response involving the intra- and extrahepatic bile ducts, resulting in replacement of the ducts with fibrous scar tissue and eventual obliteration of the bile duct lumen. Affected infants with this form typically appear healthy with a normal growth pattern and present in the first few weeks of life with jaundice, acholic stool, and dark urine. The embryonic form is less common (~15%) and is associated with other congenital malformations, such as heterotaxy syndrome and polysplenia. This group of neonates typically appears jaundiced soon after birth.

Affected infants require a Kasai portoenterostomy procedure to reestablish bile flow. If this procedure is performed prior to 45 days of age, it is more likely to be successful. Most patients with biliary atresia have progressive disease. Indeed, biliary atresia is the most common reason for a pediatric liver transplant, accounting for ~50% of pediatric liver transplant recipients.

3. D. All of the above

Studies have shown that if the Kasai portoenterostomy procedure is performed in neonates with biliary atresia at less than age 45 days, there is an 80% rate of success in achieving bile drainage. In contrast, if the procedure is performed in infants older than 90 days, bile flow can be established only in less than 20% of patients. If the surgery is effective and the infant's jaundice resolves, then the 10-year transplant-free survival rate has been reported at 75% to 90%. However, if jaundice is still present after the procedure, the 3-year transplant-free survival rate is 20%. The degree of liver damage also impacts the outcome in infants with biliary atresia, and thus, early recognition and timely surgery, followed by appropriate medical management post-surgery, are critical.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the signs and symptoms of biliary atresia
- Know the diagnostic tests for biliary atresia
- Know the management of biliary atresia

SUGGESTED READINGS

Brumbaugh D, Mack C. Conjugated hyperbilirubinemia in children. *Peds Rev*. 2012;33:291–302.

Davenport M. Biliary atresia: Clinical aspects. *Sem Ped Surg*. 2012; 21:175–184.

Feldman AG, Sokol RJ. Neonatal cholestasis. *NeoReviews*. 2013; 14:e63–e73.

SECTION XI

Hematology

CASE 1

Hematocrit and anemia of prematurity

A nurse is caring for two infants admitted to the Neonatal Intensive Care Unit (NICU). The pediatric resident orders a complete blood count (CBC) with differential and a blood culture on both the babies. After the nurse receives the results, she pages the resident.

1. Match the findings below (A–D) with the appropriate gestational age (i–ii):

   A. Hematocrit at birth typically ranges between 45% to 55%
   B. Hematocrit at birth usually is lower than described in A
   C. Physiologic nadir of hematocrit occurs around 8 weeks of life
   D. Physiologic nadir of hematocrit occurs around 10 to 12 weeks of life

   i. 25 weeks' gestation at birth
   ii. 40 weeks' gestation at birth

2. Match the following red blood cell (RBC) indices (A–E) with the appropriate response (i–iii):

   A. RBC number
   B. Hematocrit
   C. Mean corpuscular volume
   D. Nucleated RBCs
   E. Reticulocytes

   i. Decreases with increasing birth gestational age
   ii. Increases with increasing birth gestational age
   iii. Peaks at 26 to 27 weeks' gestation, then declines

CASE 2

Polycythemia

A large-for-gestational-age (LGA) male infant born at 41 $\frac{3}{7}$ weeks' gestation is brought to the Neonatal Intensive Care Unit (NICU) because the infant's mother had a fever of 100.6 °F (38.1 °C) during labor. Following the Group B *Streptococcus* sepsis algorithm, the nurse sends a complete blood count (CBC) with differential and blood culture. Other than LGA status and a ruddy complexion, the infant's examination is unremarkable. His laboratory values are notable only for a hematocrit of 72%.

1. Of the following, the risk(s) associated with polycythemia in a newborn is:

   A. Hypoglycemia
   B. Indirect hyperbilirubinemia
   C. Respiratory distress
   D. All of the above

The infant in this vignette develops clinical symptoms consistent with polycythemia. The neonatology fellow reviews the management of an infant with symptomatic polycythemia and calculates the blood volume for a partial exchange transfusion.

2. Given the following values, select the appropriate blood volume for an exchange transfusion:

   Birth weight = 4 kg
   Observed hematocrit = 72%
   Desired hematocrit = 55%
   Infant blood volume:
   Full-term infant, 80 mL/kg
   Preterm infant, 100 mL/kg

   A. 30 mL
   B. 75 mL
   C. 100 mL
   D. 750 mL

The neonatal fellow then teaches a group of medical students about polycythemia in a newborn. He presents a case of an infant with trisomy 21, polycythemia, and cyanotic congenital heart disease (CCHD).

3. Select True or False (i–ii) for the following statements (A–D) about CCHD and polycythemia:

   i. True
   ii. False

   A. Chronic arterial hypoxemia stimulates erythropoietin secretion, leading to polycythemia.
   B. Polycythemia increases viscosity in the blood, which may lead to thromboembolic events.
   C. To prevent complications, a partial exchange transfusion to maintain the hematocrit at ~60% should be considered in infants with CCHD and polycythemia.
   D. All infants with CCHD will have polycythemia.

CASE 3

Bilirubin metabolism

A term female infant is born via repeat cesarean delivery and appears well. She has a picture taken at 48 hours of age, which is shown in Figure 1.

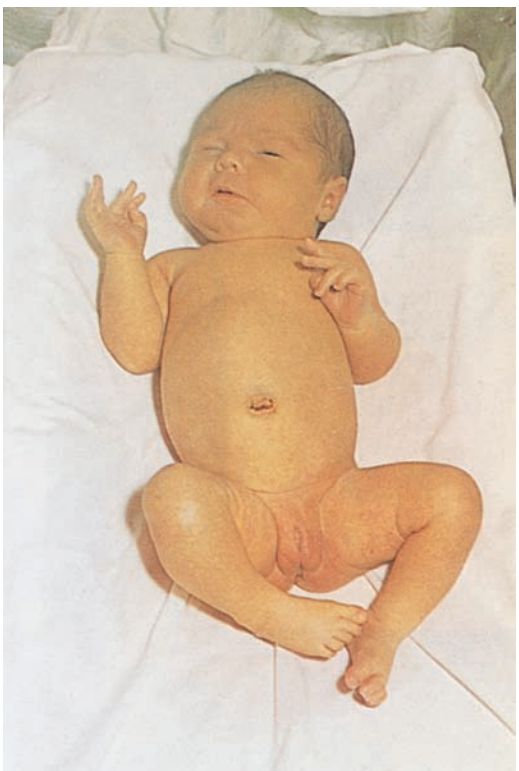

FIGURE 1. From O'Doherty N. Atlas of the Newborn. Philadelphia, PA: JB Lippincott; 1979

Her total bilirubin concentration is 10 mg/dL with a direct component of 0.4 mg/dL

1. Of the following, the most common factor(s) contributing to indirect hyperbilirubinemia in the newborn is:

   A. Decreased glucuronyl transferase activity
   B. Increased enterohepatic circulation
   C. Increased red blood cell (RBC) volume and turnover
   D. All of the above

The Chief Pediatric Resident gives a short lecture on bilirubin metabolism to the medical students rotating through the Newborn Nursery.

2. Match the choices (i–v) to the proper label (A–E) in the pathway shown in Figure 2:

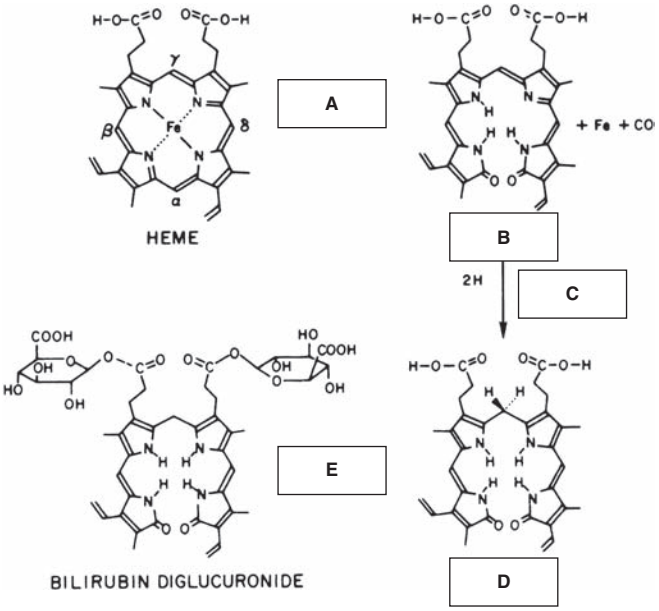

FIGURE 2. From MacDonald MG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 35.1

A. ____
B. ____
C. ____
D. ____
E. ____

i. Bilirubin
ii. Biliverdin
iii. Biliverdin reductase
iv. Glucuronyl transferase
v. Heme oxygenase

One of the medical students asks if there is a difference between bilirubin metabolism in the fetus versus the neonate. The Chief Pediatric Resident concludes his lecture by describing the mechanism for clearance of bilirubin in the fetus.

3. Select True or False (i–ii) for the following statements regarding fetal bilirubin metabolism:

i. True
ii. False

A. Can be conjugated by maternal exposure to sunlight
B. Can be removed by transfer across the placenta into the maternal circulation
C. Can be transferred into and removed from the amniotic fluid
D. Can pass through the fetal liver and be excreted into fetal bile

CASE 4

Physiologic jaundice

A nurse in the Neonatal Intensive Care Unit (NICU) reviews the bilirubin results of two infants. One infant is male and born at 40 weeks' gestation, while the other infant is female and born at 34 weeks' gestation.

1. Select the correct statement(s) about physiologic jaundice in the newborn. More than one selection may be correct:

A. Clinical jaundice develops in 10% of all newborns.
B. Direct hyperbilirubinemia reflects a neonatal adaptation to bilirubin metabolism and is termed physiologic jaundice.
C. Peak bilirubin occurs around 3 days old at a value of 6 to 8 mg/dL in the term infant.
D. Peak bilirubin occurs around 5 days old at a value of 10 to 12 mg/dL in the preterm infant.

On day three of life, the bilirubin values for the term infant are 10 mg/dL (total bilirubin) and 0.4 mg/dL (direct bilirubin), and the preterm infant has a total bilirubin concentration of 6 mg/dL and a direct bilirubin concentration of 0.3 mg/dL.

2. Select the one strategy below that is *not consistent* with the recommendations by the American Academy of Pediatrics (AAP) for the prevention and management of indirect hyperbilirubinemia in newborns of 35 or more weeks' gestation:

A. Early and focused follow-up based on the risk assessment
B. Promotion and support of successful breast-feeding
C. Serum bilirubin testing only for infants who appear jaundiced
D. Utilization of phototherapy or exchange transfusion, when indicated, to prevent severe hyperbilirubinemia

By day of life 5, the term infant is breast-feeding well and his weight is 3% below his birth weight. His total bilirubin value is 8 mg/dL. However, the preterm infant is not latching well; her mother's breast milk is not "in" yet; and the baby's weight is 10% below birth weight. The infant's total bilirubin value is 12 mg/dL with a direct bilirubin concentration of 0.4 mg/dL, and the pediatrician begins phototherapy.

3. Select additional step(s) appropriate for the management of this preterm infant's indirect hyperbilirubinemia. More than one answer may be selected:

   A. Continue breast-feeding and supplement with formula
   B. Continue with exclusive breast-feeding as mother's milk should "come in" soon
   C. Discontinue breast-feeding and give only formula
   D. Discontinue breast-feeding and start intravenous fluids

The term infant is now 2 weeks old. He returns to the pediatrician because his mother thinks he looks yellow. He is breast-feeding exclusively and is above his birth weight. Overall, he is doing well. The pediatrician checks his bilirubin level, which is 15 mg/dL (total) and 0.6 mg/dL (direct). The pediatrician suspects breast milk jaundice.

4. Select appropriate step(s) for the management of this infant's breast milk jaundice. More than one answer may be selected:

   A. Avoid interruption of breast-feeding
   B. Monitor the bilirubin and if the value is >20 mg/dL, consider phototherapy
   C. Rule out other causes of prolonged jaundice
   D. Supplement with formula as a routine, even if the infant is taking in adequate breast milk volumes

CASE 5

Nonphysiologic jaundice

A male infant is born via spontaneous vaginal delivery to a 27-year-old woman with prenatal screens as follows: blood type—O positive, Antibody—negative, Hepatitis B surface antigen—negative, Rubella—immune, RPR—nonreactive, HIV—negative, and Group B *Streptococcus*—negative. When the baby is 12 hours old, the nurse notices that he is significantly jaundiced. He is otherwise well-appearing. The pediatrician agrees with the nurse's assessment and orders a bilirubin level, which is 11 mg/dL (total) and 0.5 mg/dL (direct).

1. Select the appropriate study (or studies) in the evaluation of this infant. More than one answer may be selected:

   A. Blood type and Coombs test
   B. Complete blood count (CBC) with differential, reticulocyte count, and peripheral smear
   C. Lumbar puncture to assess for meningitis
   D. No studies required as ~60% of all newborn will develop jaundice

The infant's laboratory results are as follows:

- Blood type: B positive with direct Coombs test positive
- Hematocrit: 37%
- Reticulocyte count: 13%

2. Select the most appropriate step(s) in the management of the infant in this vignette:

   A. Immediately start intensive phototherapy and provide adequate hydration
   B. Prepare for potential use of intravenous immunoglobulin (IVIG)
   C. If phototherapy fails to prevent rise in bilirubin to toxic levels, prepare for exchange transfusion
   D. All of the above

The infant was managed appropriately, and the jaundice improved. Prior to his discharge from the hospital at 1 week of age, the pediatrician reviews potential future symptoms with the family.

3. Of the following, possible symptom(s) that the infant in this vignette may develop is:

   A. Cyanosis and sweating during feedings
   B. Extreme pallor, tachycardia, and decreased activity
   C. Light-colored stools
   D. Recurrence of jaundice

CASE 6

Kernicterus

A 3-kg male infant is born at 37 weeks' gestation via uncomplicated spontaneous vaginal delivery. His Apgar scores are 8 and 9 at 1 and 5 minutes, respectively. His mother's blood type is O positive and the infant's blood type is A positive, Coombs negative. He is discharged home at age 2 days after an uncomplicated course in the Newborn Nursery.

At 11 days old, his family brings him to the pediatrician's office because they are concerned by the yellow color to his skin and his extreme sleepiness. The pediatrician finds that he has a "glowing" orange color to his skin, a weight loss of 18% from birth, and has opisthotonus. Figure 1 depicts an infant with this diagnosis.

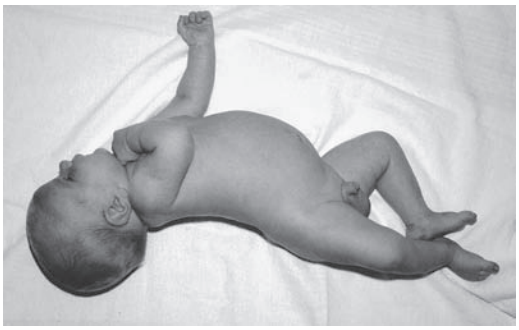

FIGURE 1. From MacDonald MG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 35.10

The baby's admission bilirubin level is 38 mg/dL. The pediatrician emergently admits the infant to the hospital for further care, including intensive phototherapy, intravenous hydration, and a double volume exchange transfusion. The pediatrician reviews the distinction between acute bilirubin encephalopathy and kernicterus.

1. Select the statement(s) that describe(s) the appropriate use of the terms acute bilirubin encephalopathy and kernicterus:

   A. Acute bilirubin encephalopathy is seen in the first few weeks of life.
   B. Acute bilirubin encephalopathy represents acute manifestations of bilirubin toxicity.
   C. Kernicterus is a term that describes the chronic and permanent clinical sequelae of bilirubin toxicity.
   D. All of the above

The pediatrician discusses potential long-term complications with the family.

2. Of the following, potential long-term sequelae for this infant is.

   A. Dental dysplasia
   B. Hearing loss
   C. High-pitched cry
   D. All of the above

CASE 7

Thrombocytopenia

A 1.9-kg female infant is born at 39 weeks' gestation by cesarean delivery because of fetal distress. Her mother is a 42-year-old woman with unremarkable prenatal screens aside from positive Group B *Streptococcus* status. Spontaneous rupture of membranes occurred 24 hours prior to delivery, and the maximum maternal temperature was 100.6°F (38.1°C). The baby's Apgar scores are 7 and 8 at 1 and 5 minutes, respectively. She is small for gestational age (SGA) for an unknown reason and otherwise appears well and has no additional findings.

1. Select all of the appropriate laboratory studies that should be requested with the admission orders. More than one answer may be selected:

   A. Chest radiograph
   B. Complete blood count (CBC) with differential and blood culture
   C. Urine for cytomegalovirus (CMV) early antigen
   D. None

Appropriate testing is obtained, and the infant is found to have a platelet count of 60,000/μL.

2. Of the following, a possible etiology/etiologies of this infant's thrombocytopenia is (are):

   A. Bacterial sepsis
   B. Congenital CMV
   C. Maternal idiopathic thrombocytopenic purpura (ITP)
   D. All of the above

CASE 8

Coagulation disorders

A well-appearing full-term male infant has a circumcision at 36 hours of age. Immediately after the procedure, the newborn has an excessive amount of bleeding. The obstetrician is able to stop the bleeding and then consults with the baby's pediatrician because she is concerned that the infant might have a hematologic disorder.

1. Of the following, the most likely hematologic cause of this infant's excessive bleeding is:

   A. Disseminated intravascular coagulation
   B. Factor XII deficiency
   C. Hemophilia A
   D. Von Willebrand disease

The pediatrician orders several preliminary laboratory tests to help identify the cause of this neonate's bleeding.

2. Match the following laboratory findings (A–D) with the hematologic disorder (i–iv):

   A. Both partial thromboplastin time (PTT) and prothrombin time (PT) are normal
   B. Isolated prolonged PT
   C. Isolated prolonged PTT
   D. Prolonged PT and prolonged PTT

   i. Hemophilia A
   ii. Hereditary factor VII deficiency
   iii. Platelet dysfunction
   iv. Severe liver dysfunction

The infant's laboratory findings suggest the possibility of hemophilia A.

3. Based on the inheritance of hemophilia A, which of the following statements is true?

   A. An affected father cannot transmit the disease to a son but can transmit the carrier state to a son.
   B. An affected father will transmit the carrier state to 50% of his daughters.
   C. A heterozygote mother who is phenotypically normal has a 50% chance of transmitting the disease to a son.
   D. A heterozygote mother has a 50% chance of transmitting the disease to a daughter.

CASE 9

Hemorrhagic disease of the newborn

A full-term male infant is born by vaginal delivery after an uncomplicated intrauterine course. The mother is concerned that her baby might be at risk for early hemorrhagic disease of the newborn because of intrauterine exposure to her medications. Although she is planning on breast-feeding, she asks the nurse in the Labor & Delivery Room to first administer vitamin K to the baby.

1. Of the following, the maternal medication that may affect coagulation in a newborn is:

   A. Heparin
   B. Levothyroxine
   C. Phenytoin
   D. Vancomycin

The nurse administers a dose of intramuscular vitamin K to the baby.

2. Of the following, the most accurate statement about prophylactic administration of vitamin K is:

   A. Breast-feeding newborns are less likely to need vitamin K prophylaxis compared with formula-fed newborns.
   B. One intramuscular dose of vitamin K provides almost complete protection against hemorrhagic disease of the newborn.
   C. Oral and intramuscular routes of vitamin K administration are equally effective.
   D. All of the above are true

The mother is still concerned that her infant might develop hemorrhagic disease of the newborn and asks the pediatrician about clinical signs and symptoms of this disease.

3. Of the following, the most accurate statement about the clinical presentation of hemorrhagic disease of the newborn is:

   A. Classic hemorrhagic disease of the newborn most commonly presents between 2 and 3 weeks of age.
   B. More than 50% of infants with late vitamin K deficiency present with an intracranial hemorrhage.
   C. Preterm infants receiving total parenteral nutrition have low serum vitamin K concentrations.
   D. Late hemorrhagic disease of the newborn occurs equally in males and females.

SECTION XI

Answers

CASE 1 ANSWERS

1. A ii
   B i
   C i
   D ii

The typical hematocrit in a full-term infant after birth ranges from 45% to 55%. The birth hematocrit in very-low-birth-weight (VLBW) infants usually ranges between 41% and 45%. Preterm infants are at increased risk for anemia in the first few weeks of life for the following reasons:

- Deprivation of third-trimester hematopoiesis and iron transport
- Shorter life span of RBCs
- Hemodilution caused by rapidly increasing body mass
- Phlebotomy (as preterm infants are more likely to require frequent blood draws)

Both term and preterm infants experience a progressive decline in hemoglobin concentration over time. This normal decline in hemoglobin is referred to as physiologic anemia. However, the expected postnatal decline in hemoglobin for preterm infants is more pronounced than for term infants. Table 1 shows the physiologic hemoglobin nadir in preterm versus term newborns.

TABLE 1. Physiologic Hemoglobin Nadir in Preterm vs. Term Newborns

	Nadir Hemoglobin Level (mg/dL)	Postnatal Age
Term	9	10 to 12 weeks
Preterm	7 if <1 kg 8 if 1 to 1.5 kg	Earlier, age 8 weeks

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2. A ii
   B ii
   C i
   D i
   E iii

Table 2 depicts the changes in RBC indices as birth gestational age increases.

TABLE 2. Changes in RBC Indices

	RBC Indices	Change with Increasing Gestational Age
A	RBC number ($\times 10^6$)	Increases
B	Hematocrit (%)	Increases
C	Mean corpuscular volume (MCV) (μm^3)	Decreases
D	Nucleated RBC	Decreases
E	Reticulocytes (%)	Peaks at 26 to 27 weeks, then declines

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Normal levels of RBCs at birth are higher in term infants compared to preterm infants. Nucleated RBCs are immature erythrocytes that are rarely found in the circulating blood of an adult but common in a newborn because of stress of delivery or elevated erythropoietin levels in the presence of the relatively hypoxemic intrauterine environment. Nucleated RBC counts decrease with increasing gestational age. The reticulocyte count at birth peaks at 26 to 27 weeks' gestation when in utero erythropoiesis is most active and then declines as gestation progresses.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the normal range of the hematocrit value for a newborn infant
- Recognize that preterm infants have lower hematocrit values than full-term infants
- Distinguish between the timing of physiologic anemia of the full-term infant and of the preterm infant

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Obladen M, Diepold K, Maier RF. Venous and arterial hematologic profiles of very low birth weight infants. *Pediatrics*. 2000; 106(4):707–711.
Widness J. Pathophysiology of anemia during the neonatal period, including anemia of prematurity. *NeoReviews*. 2008;9(11):e520–e525.

CASE 2 ANSWERS

1. D. All of the above

Polycythemia is an abnormal elevation of the circulating red blood cell (RBC) mass and is defined as a hemoglobin >20 g/dL or hematocrit >65% from a peripheral venous sample. Using this definition, the incidence of polycythemia in healthy newborns is reported to be 0.4% to 5%. The pathophysiology has two components:

- Primary—caused by increased fetal production of erythropoietin
- Secondary—caused by transfer of RBC mass to the fetus

Polycythemia may affect the viscosity of blood and blood flow properties in the microcirculation. Viscosity refers to the "thickness" of a fluid and is a measure of a fluid's resistance to flow. Viscosity (h) is expressed in the following equation and is proportional to resistance to flow (R):

$R = 8hL/\pi r^4$

R = Resistance to flow
h = Viscosity
L = Length of the vessel
r = Radius of the vessel

At high hematocrit levels (usually >70%), plasma viscosity is increased and infants may become symptomatic. Symptoms secondary to polycythemia and hyperviscosity include:

- Plethora
- Lethargy
- Hypoglycemia
- Hypocalcemia
- Thrombocytopenia
- Indirect hyperbilirubinemia
- Poor feeding

2. B. 75 mL

The formula used to calculate blood volume for partial exchange transfusion is:

$$BVE = \frac{(OBS\ HCT - DES\ HCT) \times infant's\ blood\ volume}{OBS\ HCT}$$

BVE = blood volume exchanged
OBS HCT = observed hematocrit
DES HCT = desired hematocrit

The blood volume required for a partial exchange transfusion in the infant in this vignette is 75 mL. Normal saline is the preferred fluid used in the exchange. The extent of short-term and long-term outcomes adversely affected by polycythemia remains controversial.

3. A i True
B i True
C i True
D ii False

The first three statements (A–C) are true. Statement D is false, as not all infants with CCHD will have polycythemia.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that newborns with polycythemia are at risk for hypoglycemia and hyperbilirubinemia, and manage appropriately
- Know that the treatment for symptomatic polycythemia is a partial exchange transfusion
- Know the complications of polycythemia in a patient with cyanotic congenital heart disease

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Remon J, Raghavan A, Maheshwari A. Polycythemia in the newborn. *NeoReviews*. 2011;17: e20–e28.

CASE 3 ANSWERS

1. D. All of the above

Indirect hyperbilirubinemia, clinically known as jaundice, is one of the most frequent problems in the neonatal period, affecting up to 60% of all term infants and most preterm infants. Causes of physiologic jaundice include the following:

- Defective conjugation caused by decreased glucuronyl transferase activity
- Decreased gut motility with poor evacuation of bilirubin-laden meconium
- Decreased hepatic excretion of bilirubin
- Increased enterohepatic circulation caused by high levels of intestinal β-glucuronidase
- Increased RBC volume and decreased RBC survival in infants (90 days) compared to adults (120 days)
- Ineffective erythropoiesis

2. A v Heme oxygenase
B ii Biliverdin
C iii Biliverdin reductase
D i Bilirubin
E iv Glucuronyl transferase

Figure 3 represents the enzymatic pathway of the breakdown of heme to bilirubin. This breakdown occurs in the macrophages of the reticuloendothelial system (macrophages, spleen, and liver).

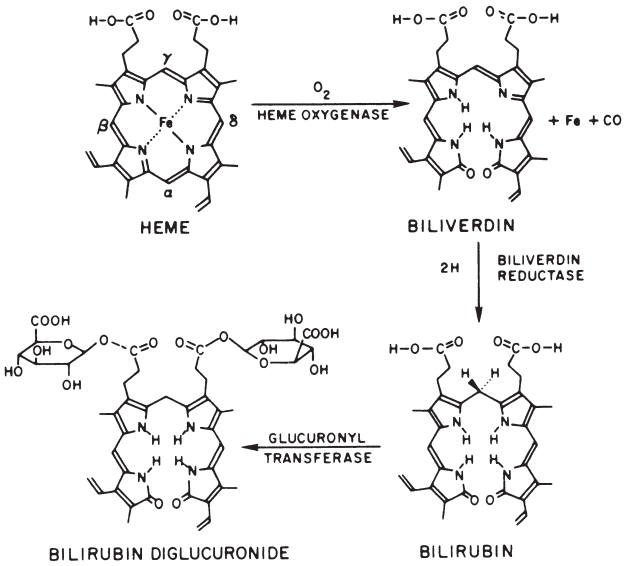


FIGURE 3. From MacDonald MG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 35.1

Most of the bilirubin is then transported in the serum bound to albumin, while a minor fraction is "free" or unbound. The "free" bilirubin can cross the blood-brain barrier of the neonate.

Figure 4 is a schematic representation of the metabolism, transport, and eventual excretion of bilirubin. Steps 5–10 describe the transport of bilirubin once it has been conjugated with glucuronic acid.

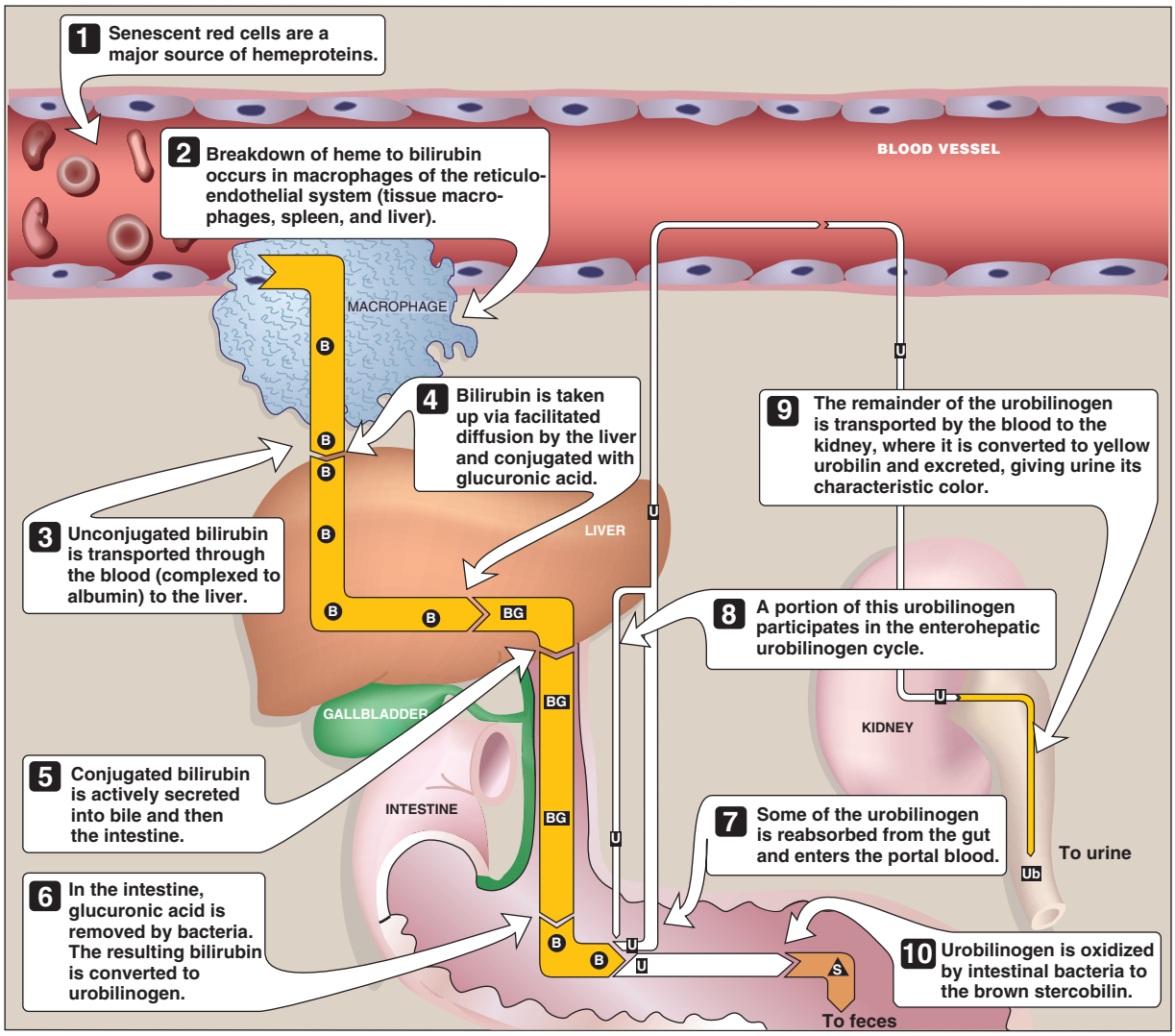


FIGURE 4. Harvey R, Ferrier D. Lippincott's Illustrated Reviews: Biochemistry. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010. Figure 21.10

3. A ii False
   B i True
   C i True
   D i True

Bilirubin first appears in the fetal circulation at 14 weeks' gestation, and by 38 weeks' gestation, the primary isomer is bilirubin-IX-α (Z,Z), the predominant isomer in humans. Most of the unconjugated bilirubin in the fetus is cleared by the placenta and enters the maternal circulation. Fetal bilirubin may also pass though the fetal liver and be excreted into fetal bile. This protein can also be transferred quickly into and removed from the amniotic fluid.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Understand the age-related differences in bilirubin metabolism (increased erythrocyte turnover and decreased intracellular metabolism and excretion in the newborn infant)
- Understand bilirubin synthesis, transport, and metabolism

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Hansen T. Core concepts: Bilirubin metabolism. *NeoReviews*. 2010;11:e316–e321.
Harvey R, Ferrier D. *Lippincott's Illustrated Reviews: Biochemistry*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010.

CASE 4 ANSWERS

1. C. Peak bilirubin occurs around 3 days old at a value of 6 to 8 mg/dL in the term infant.
D. Peak bilirubin occurs around 5 days old at a value of 10 to 12 mg/dL in the preterm infant.

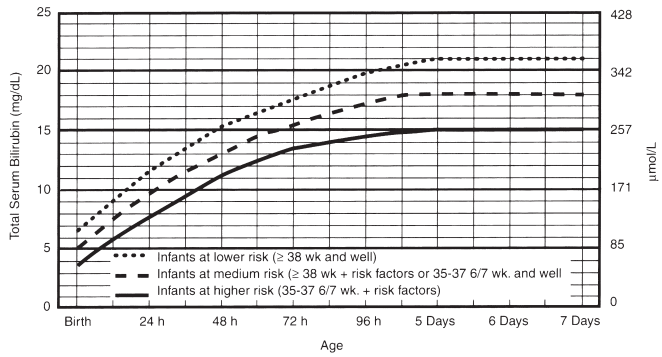
Bilirubin peaks later and at a higher value in preterm infants than in term infants. *Indirect* hyperbilirubinemia reflects a neonatal adaptation to bilirubin metabolism and is termed physiologic jaundice. Clinical jaundice develops in up to 60% of all term infants and almost all preterm infants.

2. C. Serum bilirubin testing only for infants who appear jaundiced

The recommendations by the AAP for the prevention and management of indirect hyperbilirubinemia in newborns of 35 or more weeks' gestation include serum bilirubin testing of all newborns. Statements A, B, and D are correct. In addition, the AAP recommends that the pediatrician perform a systematic assessment before discharge to determine the risk of severe indirect hyperbilirubinemia. The AAP has published a Clinical Practice Guideline for the management of hyperbilirubinemia in the healthy newborn infant born at 35 weeks or more of gestation. Management is dictated by risk factors and bilirubin values as reflected on the hour-specific nomogram. Figure 1 represents the AAP hour-specific bilirubin nomogram.

Guidelines for Phototherapy in Hospitalized Infants ≥35 Weeks

Note: These guidelines are based on limited evidence and the levels shown are approximations. The guidelines refer to the use of intensive phototherapy which should be used when the TSB exceeds the line indicated for each category.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin <3.0g/dL (if measured)
- For well infants 35–37 6/7 can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2–3mg/dL (35–50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

FIGURE 1. From MacDonald MG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 35.22

3. A. Continue breast-feeding and supplement with formula

The infant in this vignette was born at 34 weeks' gestation. She is not latching well and may be demonstrating immature feeding skills. Her weight loss of 10% is significant and her mother's milk is not "in" yet. This infant requires additional intake; thus, supplementation with pumped breast milk or formula is warranted. In addition, close attention to hydration status is needed, as phototherapy may contribute to further dehydration.

Jaundice related to breast-feeding is the most common cause of exaggerated unconjugated hyperbilirubinemia in the newborn period. It occurs because of lack of breast milk intake, resulting in dehydration in the infant; it is often referred to as "breast nonfeeding jaundice." Although breast-feeding can be linked with unconjugated hyperbilirubinemia, it does not contribute to conjugated jaundice.

4. A. Avoid interruption of breast-feeding
B. Monitor the bilirubin and if the value is >20 mg/dL, consider phototherapy
C. Rule out other causes of prolonged jaundice

The infant in this vignette most likely has "breast-feeding jaundice," which is thought to be related to a component in the breast milk itself. Although levels fall rapidly with cessation of breast-feeding, routine cessation of breast-feeding is not indicated in a healthy infant with a mild to moderately increased bilirubin level. However, if the bilirubin level is excessive, cessation of breast milk may help to decrease the degree of jaundice. In this type of breast milk jaundice, higher bilirubin levels are reached for a longer period of time. The levels can reach 20 to30 mg/dL by age 2 weeks and then normalize over 4 to 12 weeks.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Distinguish between physiologic jaundice in a full-term infant and physiologic jaundice in a preterm infant
- Understand the strategies for prevention of severe hyperbilirubinemia in newborns (e.g., increasing frequency of breast-feeding, screening prior to hospital discharge)
- Recognize that breast-feeding is the most frequent cause of exaggerated unconjugated hyperbilirubinemia in the neonatal period
- Know that breast-feeding does not cause conjugated hyperbilirubinemia
- Know the management of the infant with breast milk jaundice

SUGGESTED READINGS

Almeida M, Draque C. Neonatal jaundice and breastfeeding. *NeoReviews*. 2007;7:e282–e288.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, Stark AR (eds): *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

Subcommittee on Hyperbilirubinemia, American Academy of Pediatrics. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114(1): 297–316.

CASE 5 ANSWERS

1. A. Blood type and Coombs test
B. Complete blood count (CBC) with differential, reticulocyte count, and peripheral smear

Pathologic jaundice is defined as jaundice within the first 24 hours of an infant's life or a rapid rate of bilirubin rise. Tables 1 and 2 represent characteristics of nonphysiologic or pathologic jaundice in the newborn.

TABLE 1. Basic Characteristics of Nonphysiologic or Pathologic Jaundice

1. Onset before age 24 hours
2. Rate of increase > 0.5 mg/dL/hour
3. Evidence of underlying illness (gastrointestinal [GI], hematologic, infectious)
4. Jaundice that persists >8 days in terms infants and >14 days in preterm infants

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:364

TABLE 2. Broad Diagnostic Categories of Nonphysiologic or Pathologic Jaundice

Increased "load" of bilirubin	• Hemolytic disease: ABO, Rh incompatibility, minor group incompatibility, nonimmune • Enzyme deficiencies: glucose-6-phosphatase deficiency, pyruvate kinase deficiency • Membrane defects: spherocytosis, elliptocytosis, pyknocytosis • Other: cephalohematoma, polycythemia
Decreased hepatic ligandin	
Decreased activity of glucuronyl transferase	Gilbert's, Crigler–Najjar
Increased enterohepatic circulation	GI obstruction: intestinal atresia, meconium ileus, Hirschsprung disease
Multifactorial	Congenital hypothyroidism, hypopituitarism, metabolic disorder (e.g. tyrosinemia), liver failure, sepsis

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:364

In a well-appearing jaundiced infant less than 24 hours of age born to a mother with blood type O, checking the infant's blood type and Coombs test are essential. Obtaining a CBC with differential and a reticulocyte count is important to evaluate for infection, hemolysis, and initial polycythemia. The peripheral smear can be helpful to detect Coombs negative hemolytic disease (e.g. spherocytosis). Less-common minor antigens may also be implicated in hemolytic disease of the newborn.

Performing a lumbar puncture at 12 hours of life in a well-appearing jaundiced infant would not be one of the first steps in the evaluation. If the suspicion for sepsis becomes greater (e.g., if the infant becomes hypotensive, hypothermic, or develops a fever), a lumbar puncture could be considered. The differential diagnosis for infectious causes of jaundice in the newborn includes Hepatitis B and the TORCH infections:

- T—Toxoplasmosis/*Toxoplasma gondii*
- O—Other (coxsackievirus, human immunodeficiency virus, parvovirus B19, syphilis, varicella zoster virus)
- R—Rubella
- C—Cytomegalovirus
- H—Herpes simplex virus-2

2. D. All of the above

The infant in this vignette has ABO incompatibility with resultant hemolytic anemia and indirect hyperbilirubinemia. Figure 1 describes Coombs testing for anti-red cell antibodies. In the direct Coombs test, the infant's red blood cells are tested for presence of antibodies on the red cell membranes. In the indirect Coombs test, antibody content is tested in the patient's blood sample.

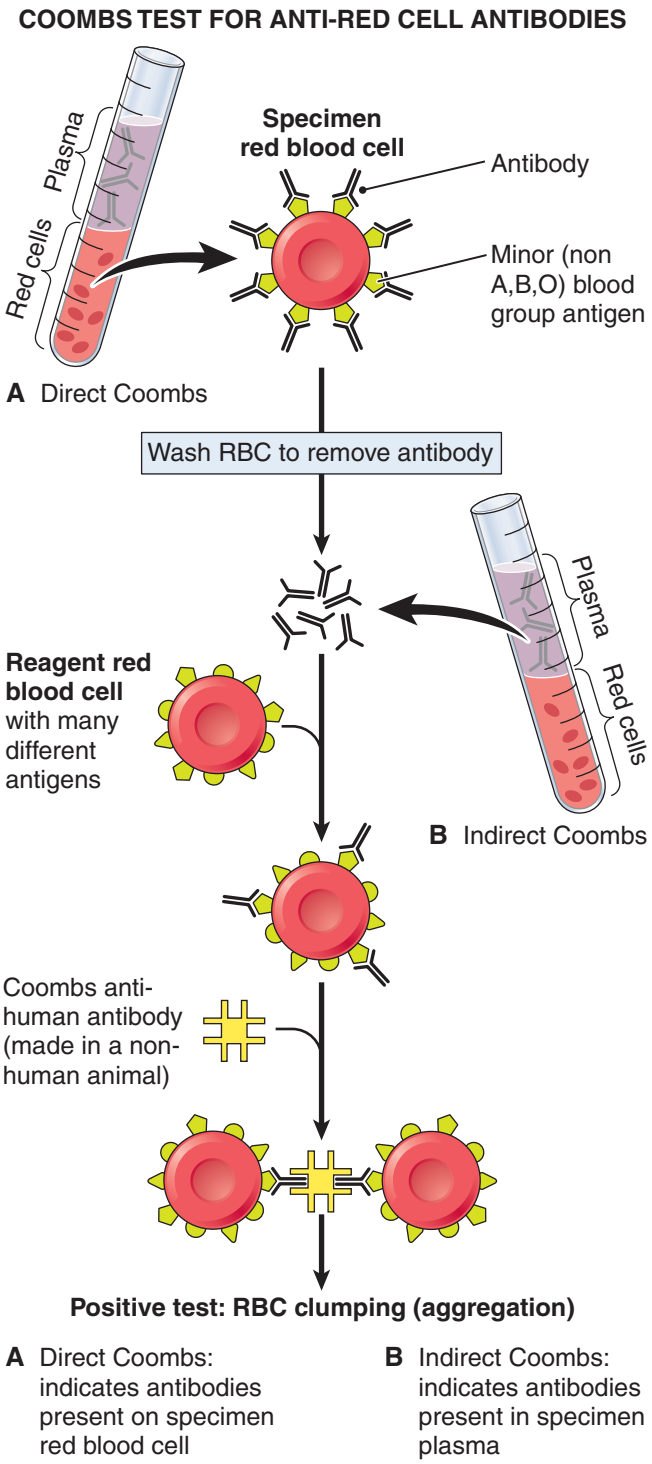


FIGURE 1. McConnell TH. Nature of Disease: Pathology for the Health Professions. 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. Figure 8.2

In addition to close monitoring of this infant's bilirubin levels, additional potential management includes:

- Intensive phototherapy
- Adequate hydration (also be aware that hydration itself does not decrease serum bilirubin concentrations)
- IVIG
- Exchange transfusion

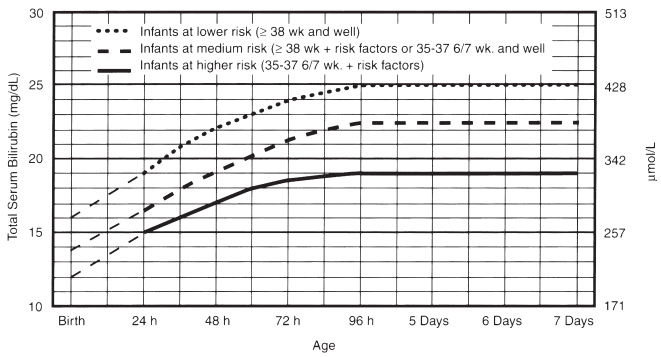
IVIG is thought to act by binding to the Fc receptor on reticuloendothelial cells so that destruction of red cells cannot occur. Studies have shown a significant reduction in exchange transfusions in infants with ABO incompatibility and hemolytic anemia who received IVIG.

Double volume exchange transfusion is performed less commonly now that Rhogam is routinely utilized. During this procedure, bilirubin and antibodies are removed from the infant's blood and replaced with fresh irradiated whole blood or reconstituted packed red blood cells with fresh frozen plasma. The hematocrit of the replacement blood should equal 40% to 55%. Close monitoring of the infant's heart rate, blood pressure, pH, serum potassium, glucose, calcium, and magnesium is necessary during the procedure. This exchange removes and replaces ~87% of the infant's blood volume.

The American Academy of Pediatrics provides guidelines for bilirubin values reaching threshold for performing an exchange transfusion (see Figure 2).

Guidelines for Exchange Transfusion in Infants ≥35 Weeks

Note: These guidelines are based on limited evidence and the levels shown are approximations. During birth hospitalization exchange transfusion is recommended if TSB rises to these levels despite intensive phototherapy. For readmitted infants, if TSB is above levels indicated after intensive phototherapy for 6 hours.



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shoes sign of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB≥5mg/dL (85μmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis
- Measure serum albumin and calculate B/A ratio (See legend)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35–37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

FIGURE 2. From MacDonaldMG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 35.23

3. B. Extreme pallor, tachycardia, and decreased activity

Infants with ABO or Rh incompatibility may have progressive and severe anemia at 4 to 8 weeks of age. Affected infants may present with extreme pallor, tachycardia, and decreased activity. With increased age of life, liver and intestinal processes are more mature and will be able to help infants excrete bilirubin and the risk for late-onset jaundice is low. An infant with cholestasis may present with light-colored stools, but this is not a common finding in an infant with ABO incompatibility. An infant with congenital heart disease may present with sweating during feedings and/or cyanosis at 1 to 3 months of age.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that diagnostic studies to detect hemolytic diseases are necessary in a full-term infant who becomes clinically icteric during the first day after birth
- Know the appropriate diagnostic tests to establish the cause of unconjugated hyperbilirubinemia
- Review diagnosis and management of ABO and Rh incompatibility (direct vs. indirect Coombs test)
- Know other causes of isoimmunization, such as minor antigens
- Formulate a differential diagnosis of infectious causes of jaundice in an infant
- Plan the management of a patient with hyperbilirubinemia
- Know that progressive and severe anemia may occur at 4 to 8 weeks of age in infants with ABO or Rh incompatibility

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Subcommittee on Hyperbilirubinemia, American Academy of Pediatrics. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114:297–316.

CASE 6 ANSWERS

1. D. All of the above

The infant in this vignette has acute bilirubin encephalopathy. This disorder represents acute manifestations of bilirubin toxicity within the first weeks of life. There are three phases to this disease:

- Phase 1: Occurs in the first few days of life; newborn has decreased activity, hypotonia, poor feeding
- Phase 2: Variable onset and duration; infant with hypertonia, retrocollis (arching of neck backwards), and/or opisthotonus (arching of back)
- Phase 3: Occurs in newborns over age 1 week—Hypotonia

Emergent management of an infant with acute bilirubin toxicity is essential because it may evolve into chronic bilirubin toxicity or kernicterus.

Kernicterus describes the chronic and permanent clinical sequelae that might occur in an infant with bilirubin toxicity.

2. D. All of the above

The infant in the vignette is at risk for developing kernicterus in the first several years of life. Fortunately, this disease is far less common than centuries ago. Johannes Orth was the first to describe the pathologic findings of this disease in 1975. He observed anatomic deposition of bilirubin in brain tissue with yellow staining found in the basal ganglia and hippocampus.

Classic findings of kernicterus or chronic and permanent sequelae of bilirubin toxicity are:

- Abnormal motor control, movements, and muscle tone
- An auditory processing disturbance and potential hearing loss
- Oculomotor impairments, most commonly an upward vertical gaze impairment
- Dysplasia of the enamel of deciduous teeth

Cognitive function is usually spared in children with kernicterus.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the clinical manifestations of acute bilirubin encephalopathy
- Recognize the permanent clinical sequelae of bilirubin toxicity (kernicterus)

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Brown A. Kernicterus: Past, present, and future. *NeoReviews*. 2003; 4:e33–e39.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 7 ANSWERS

1. B. Complete blood count (CBC) with differential and blood culture
C. Urine for cytomegalovirus (CMV) early antigen

A CBC with differential and blood culture is warranted based on the most recent Group B *Streptococcus* prevention guidelines, because of the maternal GBS positive status, prolonged rupture of membranes >18 hours, and maternal fever. Based on current guidelines, this infant also requires a minimum of 48 hours of antibiotic administration, regardless of the results of the CBC. The infant's symmetric SGA status (i.e., microcephaly) may be due to congenital infections, including TORCH infections: *t*oxoplasmosis, *o*ther (syphilis), *r*ubella, *c*ytomegalovirus, or *h*erpes simplex virus. It is appropriate to send a urine sample for CMV early antigen (i.e., shell vial assay) or CMV culture. A chest radiograph is not indicated at this time in this infant without respiratory or cardiac symptoms.

2. D. All of the above

Thrombocytopenia in a newborn may be a sign of bacterial sepsis. This infant should be started on antibiotics for a minimum of 48 hours pending the clinical course and blood culture results. Congenital CMV in addition to other TORCH infections may lead to neonatal thrombocytopenia. Maternal history, including platelet count trends and any maternal medications, should be reviewed as part of the evaluation of neonatal thrombocytopenia.

An infant born to a mother with ITP may have severe thrombocytopenia because of maternal antiplatelet antibodies passing across the placenta to the fetus. Neonatal management may include platelet transfusion, intravenous immunoglobulin, and/or corticosteroids. Thrombocytopenia due to maternal ITP usually resolves by 6 to 12 weeks of life.

Table 1 shows the differential diagnosis of an infant with thrombocytopenia.

TABLE 1. Differential Diagnosis in Infant with Thrombocytopenia

Infant with Thrombocytopenia	Maternal Platelet Count	Differential Diagnosis
Well	Normal	• Neonatal alloimmune thrombocytopenia • Neonatal drug exposure • Hemangioma • Congenital thrombocytopenia • Maternal ITP in remission
	Decreased	• Maternal ITP—autoimmune thrombocytopenia, increased platelet-associated IgG levels • Maternal drug exposure • Pregnancy-induced hypertension • Familial
Sick	Normal	• Disseminated intravascular coagulation • Sepsis

Modified from: Cloherty JP, Stark AR, eds. *Manual of Neonatal Care*. 4th ed. Philadelphia, PA: Lippincott-Raven; 1998:471 and Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:355

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that thrombocytopenia in a newborn may be a sign of bacterial sepsis and, in an ill child, should lead to appropriate culture and antibiotic therapy
- Recognize that a history of medications should be part of the evaluation of a child with thrombocytopenia
- Recognize that the presence of thrombocytopenia in a newborn with microcephaly or other congenital abnormalities may be due to a congenital viral infection such as cytomegalovirus
- Know that a mother with idiopathic thrombocytopenic purpura may have an infant with thrombocytopenia, and know how to manage the infant

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 8 ANSWERS

1. C. Hemophilia A

Causes of bleeding in the newborn period can be categorized based on the overall health of the neonate. Potential causes of bleeding in a well-appearing neonate include the following:

- Immune thrombocytopenia (alloimmune or autoimmune)
- Inherited coagulation factor deficiencies, such as hemophilia A
- Vitamin K deficiency

Potential causes of bleeding in an ill neonate include the following:

- Disseminated intravascular coagulation, which is often associated with sepsis
- Liver failure
- Platelet consumption from an infectious etiology

Excessive bleeding after circumcision may be the first sign of a congenital coagulation factor deficiency. Neonates with bleeding disorders can also present with prolonged bleeding from the umbilical stump, after blood drawing, or following placement of an intravenous catheter.

Because the infant in this vignette is well appearing, factor VIII deficiency, also known as Hemophilia A, is one potential cause of bleeding postcircumcision. A neonate with disseminated intravascular coagulation is usually ill appearing. Patients affected by factor XII deficiency are usually asymptomatic while individuals with von Willebrand disease rarely have symptoms in the newborn period.

2. A iii
   B ii
   C i
   D iv

Clotting factors are produced by the fetus beginning in the first trimester, with increased production as gestation advances. Because maternal clotting factors are unable to cross the placenta, a neonate's factor levels depend on endogenous production. At ~ age 6 months, most neonates attain factor levels similar to adult levels. The factors involved in the coagulation pathway are shown in Figure 1.

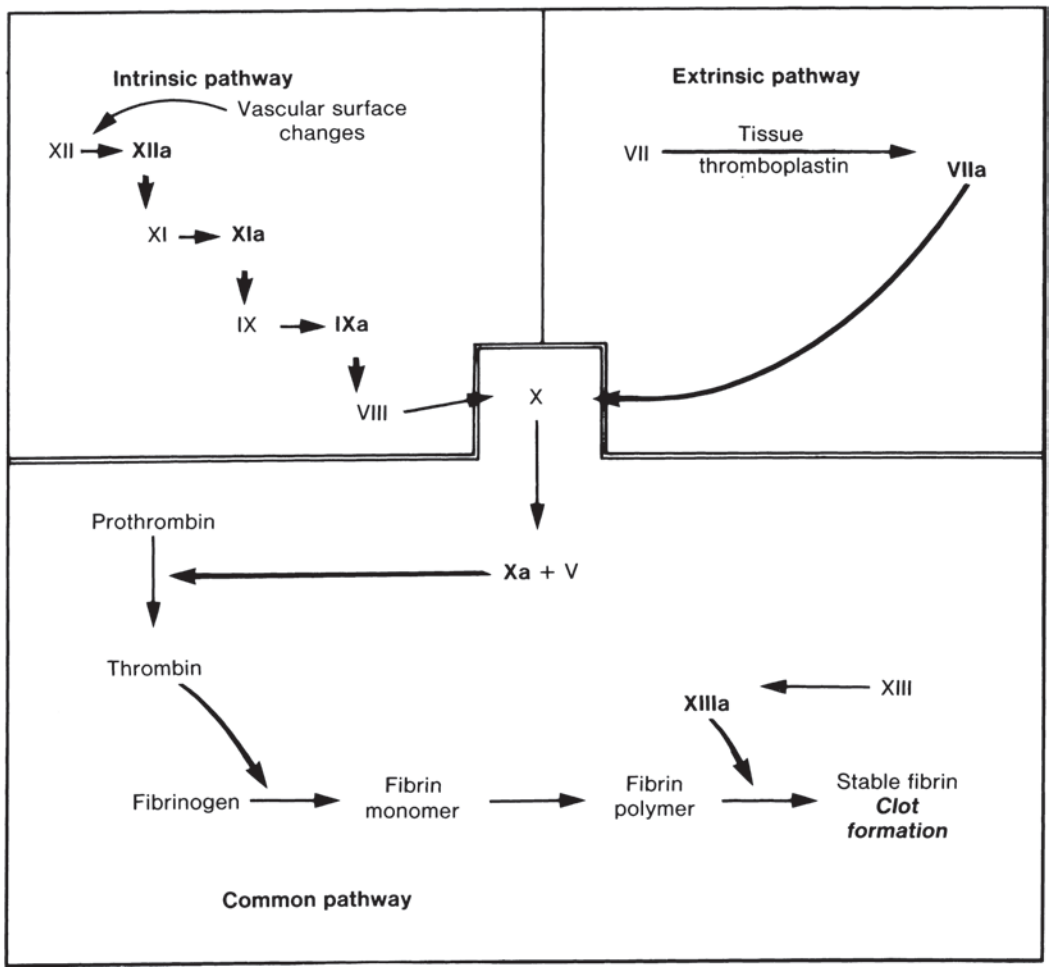


FIGURE 1. Fleisher GR, Ludwig S, Henretig FM, et al. Textbook of Pediatric Emergency Medicine. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 65.1

Measurement of a newborn's PT and PTT are helpful in the evaluation of an infant with bleeding and/or increased bruising. An abnormality within the extrinsic pathway leads to a prolonged PT, while an abnormality within the intrinsic pathway correlates with a prolonged PTT. Any abnormality within the common pathway is associated with a prolonged PT and PTT. An infant with a bleeding disorder and a normal PTT and PT may have factor XIII deficiency, platelet dysfunction, or plasminogen activation inhibitor-1 deficiency. An isolated prolonged PT is found in infants with hereditary factor VII deficiency. Infants with an isolated prolonged PTT may have hemophilia A (i.e., factor VIII deficiency), hemophilia B (i.e., factor IX deficiency), factor XI deficiency, or factor XII deficiency. Prolongation of both PT and PTT can be observed in infants with severe liver dysfunction, disseminated intravascular coagulation, vitamin K deficiency, and prothrombin deficiency.

3. C. A heterozygote mother who is phenotypically normal has a 50% chance of transmitting the disease to a son.

Hemophilia A is caused by factor VIII deficiency and is the most common cause of hemophilia. Clinical symptoms vary based on the degree of factor VIII deficiency. Because this disorder has an X-linked recessive inheritance pattern, the following transmission characteristics will be observed:

- Clinical evidence in affected males
- Because X-inactivation is random, heterozygote females may be phenotypically abnormal if the majority of active X chromosomes are abnormal.
- A heterozygote mother who is phenotypically normal has a 50% chance of transmitting the disease to a son and a 50% chance of transmitting the carrier state to a daughter.
- An affected father will transmit the carrier state to *all* his daughters but cannot transmit the disease or carrier state to his sons.

Figure 2 shows a family pedigree of hemophilia with carrier females shown in the pale yellow circles and an affected male in the green rectangles.

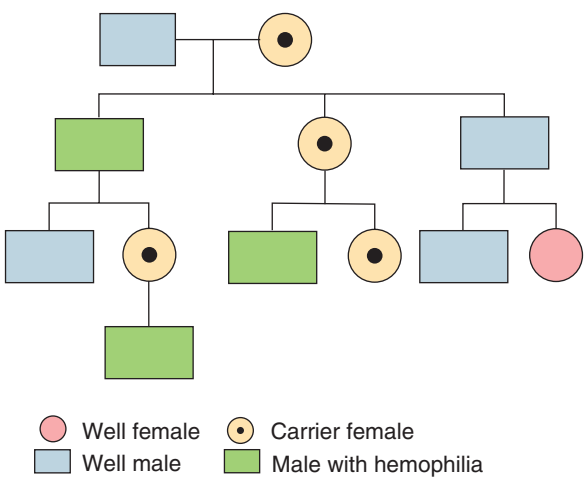


FIGURE 2. LifeART © 2014 Lippincott Williams & Wilkins. All rights reserved

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that excessive bleeding after circumcision may be the first sign of a congenital coagulation factor deficiency
- Identify prothrombin time and partial thromboplastin time as important parts of the evaluation of a patient with increased bruising
- Know that for a woman who is a carrier of hemophilia, there is a 50% chance that a male offspring will have that bleeding disorder

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Manco-Johnson MJ. Bleeding disorders in the neonate. *NeoReviews*. 2008;9:e162–e169.

CASE 9 ANSWERS

1. C. Phenytoin

Hemorrhagic disease of the newborn, also known as vitamin K deficiency bleeding, is one of the most common causes of bleeding in well term infants. Vitamin K deficiency leads to decreased production of factors II (i.e., prothrombin), VII, IX, and X. Although the coagulation pathway can function with low factor concentrations, as vitamin K deficiency worsens, procoagulatory mechanisms will fail and bleeding can occur.

There are three types of vitamin K deficiency: early (rare), classic, and late hemorrhagic disease of the newborn. Early disease occurs in newborns less than 24 hours of age and is caused by exposure to maternal medications, including:

- Antituberculosis medications, such as rifampin and isoniazid
- Barbiturates
- Carbamazepine
- Cephalosporins
- Phenytoin
- Warfarin

2. B. One intramuscular dose of vitamin K provides almost complete protection against hemorrhagic disease of the newborn.

One dose of intramuscular vitamin K soon after birth has been shown to provide almost complete protection against the development of hemorrhagic disease of the newborn. Studies have shown that the oral route is less effective and multiple doses are required to improve efficacy. Infants with cholestasis (e.g., biliary atresia, α1-antitrypsin deficiency, or cystic fibrosis) are at highest risk of ineffective oral vitamin K prophylaxis because of malabsorption of vitamin K.

Breast-feeding infants who receive low amounts of milk in the first few days of life are at greater risk of developing

vitamin K deficiency compared with formula-fed infants. Thus, vitamin K prophylaxis is extremely important in the prevention of classic hemorrhagic disease of the newborn in breast-feeding newborns.

3. B. More than 50% of infants with late vitamin K deficiency present with an intracranial hemorrhage.

Table 1 compares the timing, etiology, and clinical findings of early, classic, and late hemorrhagic disease of the newborn.

Infants with late hemorrhagic disease of the newborn have a much higher prevalence of intracranial hemorrhage compared with infants with early or classical vitamin K deficiency. If an infant has late vitamin K deficiency, more than 50% of infants will present with an intracranial hemorrhage, regardless of birth gestational age.

As noted in the Table 1, the onset of early disease typically occurs within the first 24 hours of age, while the onset of classic disease occurs between age 2 and 7 days old, and the late form presents between 2 weeks and 6 months of age, with the peak occurring between age 3 and 8 weeks.

Preterm infants receiving formula or human milk supplemented with fortifiers have vitamin K concentrations comparable to term infants receiving formulas. Preterm infants who require total parenteral nutrition tend to have higher vitamin K concentrations, correlating with the high amount of vitamin K in the parenteral preparation.

TABLE 1. Comparison of Diseases in the Newborn

Type	Features
Early	• Onset within first 24 hours of life • Secondary to placental transferred maternal drugs affecting vitamin K production (e.g., carbamazepine, phenytoin, barbiturates, cephalosporins, rifampin, isoniazid, and warfarin) • Scalp subperiosteal, intracranial, intrathoracic, or intra-abdominal bleeding
Classic	• Onset between 2 and 7 days old • Inadequate vitamin K (increased risk in breast-fed infants taking inadequate amounts) • Gastrointestinal bleeding (most common), umbilical cord bleeding, intracranial hemorrhage, prolonged bleeding after phlebotomy and circumcisions
Late	• Onset between 2 weeks and 6 months of life (peak 3 to 8 weeks) • Caused by inadequate intake or hepatobiliary disease • High risk for intracranial hemorrhages and death • More common in boys, more common in summer

Modified from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:360

Population studies have found that the late form of vitamin K deficiency is approximately twice as likely to occur in male infants compared with female infants. The reason for this discrepancy is unknown.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize that maternal exposure to drugs that may affect coagulation can result in early hemorrhagic disease of the newborn
- Know that prophylactic administration of vitamin K will prevent classic hemorrhagic disease of the newborn
- Understand that the low vitamin K content of human milk may contribute to hemorrhagic disease of the newborn
- Recognize the presenting signs and symptoms of classic hemorrhagic disease of the newborn

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Greer FR. Vitamin K the basics—What's new? *Early Hum Dev*. 2010;86:S43–S47.

Shearer MJ. Vitamin K deficiency bleeding (VKDB) in early infancy. *Blood Rev*. 2009;23:49–59.

SECTION XII

Endocrinology

CASE 1

Hypothyroidism

A pediatrician receives a call from the newborn state laboratory about a full-term infant with an elevated thyroid-stimulating hormone (TSH) concentration. The pediatrician wonders if the value could be falsely elevated.

1. A falsely elevated TSH concentration is most likely in the following scenario:

   A. The blood sample was obtained when the newborn was less than 24 hours of age.
   B. The newborn does not have any symptoms consistent with hypothyroidism.
   C. The newborn's mother has been taking supplemental thyroid hormone during the pregnancy.
   D. The state laboratory ran the test 12 hours after the sample was drawn.

Repeat testing confirms that the infant's TSH level is elevated. The state laboratory performs additional testing on the infant's blood sample.

2. Of the following, the most likely additional state newborn screening test is:

   A. Thyroxine (T4)
   B. T4-binding globulin
   C. Triiodothyronine (T3)
   D. T3 resin uptake

The pediatrician contacts the family with these laboratory results and asks the family to come to the office. When the family arrives, the pediatrician examines the baby and does not find any findings consistent with congenital hypothyroidism. The pediatrician informs the family that newborns with congenital hypothyroidism are usually asymptomatic. However, symptoms may appear later if newborns with congenital hypothyroidism are not treated.

3. Of the following, a clinical finding of an infant with untreated congenital hypothyroidism is:

   A. Diarrhea
   B. Enlarged posterior fontanel
   C. Hyperthermia
   D. Hypertonia

The pediatrician then consults with an endocrinologist, and further blood testing reveals that the infant has congenital hypothyroidism. The infant's thyroid gland is not visible by ultrasonography, and the endocrinologist suspects that the infant has thyroid dysgenesis, the most common cause of congenital hypothyroidism. The endocrinologist meets with the family to review the diagnosis. He discusses that thyroid dysgenesis is attributable to thyroid aplasia, hypoplasia, or ectopy, and he recommends starting Synthroid supplementation.

4. Synthroid supplementation in an infant with congenital hypothyroidism has been shown to decrease the incidence and severity of:

   A. Cognitive deficits
   B. Delays in motor development
   C. Poor growth
   D. All of the above

The parents recognize the importance of hormonal treatment and want to know how the endocrinologist will determine the appropriate dosage.

5. Of the following, the most helpful approach to guide hormonal treatment in this infant is to:

   A. Measure the size of the thyroid gland by ultrasonography
   B. Monitor for clinical signs/symptoms of hypothyroidism
   C. Obtain serial TSH concentrations
   D. All of the above

The endocrinologist reviews the approach to guide treatment and discusses the importance of follow-up into adulthood.

CASE 2

Congenital adrenal hyperplasia

A Labor & Delivery Room nurse pages the pediatric resident because she is uncertain about the sex of a newborn. The newborn's genitalia are shown in Figure 1.

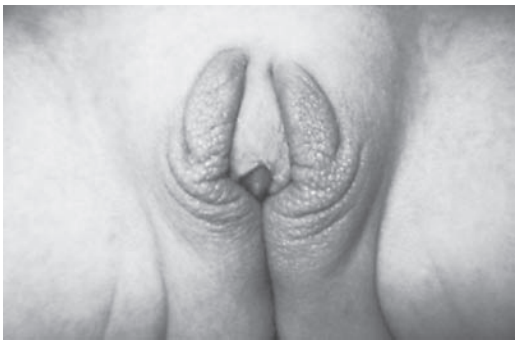


FIGURE 1. From Becker KL, Bilezikian JP, Brenner WJ, et al. Principles and Practice of Endocrinology and Metabolism. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:808, with permission

The resident notes that the baby has clitoromegaly, labial enlargement, and a scrotal appearance to the labia. The resident is unable to palpate gonads.

1. Of the following, the most likely cause(s) of ambiguous genitalia in this newborn is:

   A. Undervirilization of a genetic female
   B. Virilization of a genetic female
   C. Virilization of a genetic male
   D. Any of the above

The resident recognizes the need for urgency and sensitivity in the evaluation and management of this newborn. He speaks with the baby's parents and obtains a detailed history. He learns that the family history is noncontributory and the pregnancy had been uncomplicated. He then consults with his attending and contacts an endocrinologist. Based on their recommendations, the resident orders several laboratory tests.

2. The laboratory testing that should be obtained urgently in this newborn is:

   A. Electrolytes
   B. Karyotype
   C. Testosterone
   D. All of the above

The resident also orders a pelvic ultrasound, which reveals that the newborn has a uterus. The consultants are concerned that the baby has classical congenital adrenal hyperplasia (CAH) and suggest sending a state newborn screen.

3. Which of the following hormones is tested on the state newborn screen to assess for classical CAH?

   A. Cortisol
   B. 11-deoxycortisol
   C. 11-deoxycorticosterone
   D. 17-hydroxyprogesterone

The newborn state screening test and additional hormonal tests confirm the diagnosis of 21-hydroxylase deficiency in a virilized female. The endocrinologist recommends hormonal supplementation to prevent the baby from having an adrenal crisis.

4. Of the following, the most appropriate management of an adrenal crisis in an infant with 21-hydroxylase deficiency is:

   A. Electrolyte replacement
   B. Glucocorticoids
   C. Hydration
   D. All of the above

The baby does well with hormonal supplementation and does not have any adrenal crises. When the child is 2 years old, her parents meet with the endocrinologist because they are interested in having another child. Specifically, they want to know the risk of having another child with this disorder, whether prenatal testing is available, and if prenatal treatments are available if this recurs.

5. Of the following, the most likely statement by the endocrinologist to this family is:

   A. CAH from 21-hydroxylase deficiency is an X-linked recessive disorder.
   B. High-dose prenatal dexamethasone to the pregnant woman during the last trimester might decrease a female fetus's degree of virilization.
   C. Prenatal diagnosis of 21-hydroxylase deficiency is currently not possible.
   D. Prenatal therapy with dexamethasone can improve outcomes only in female fetuses with 21-hydroxylase deficiency.

CASE 3

Abnormal male genitalia

A term infant is born by vaginal delivery after an uncomplicated prenatal course. After the baby is held by his mother and father, the obstetrical nurse places the infant on the radiant warmer. She places identification bands on the infant and mother. She then applies erythromycin ophthalmic ointment and gives the infant a vitamin K injection. As she is placing a diaper on the baby, she notices that the baby's genitalia have not formed appropriately. She contacts the covering pediatrician who examines the infant's genitalia. The ventral side of the infant's genitalia is shown in Figure 1.

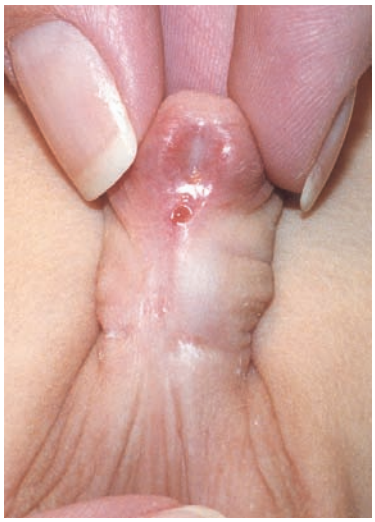


FIGURE 1. Courtesy of Warren Snodgrass, MD, UT—Southwestern Medical Center at Dallas

1. Of the following, the most likely diagnosis in this infant is:

   A. Ambiguous genitalia
   B. Chordee
   C. Epispadias
   D. Hypospadias

The pediatrician discusses the genital findings with the baby's parents. The family has a lot of questions about the approach to treatment.

2. Of the following, the most appropriate management of this infant is to:

   A. Consult with a urologist for surgery prior to discharge
   B. Ensure that the family postpones the planned circumcision
   C. Order an abdominal ultrasound because of the high risk of associated renal anomalies
   D. All of the above

On the day of this infant's discharge, the pediatrician examines another term male infant and is unable to palpate the right testicle.

3. Of the following, the most accurate statement(s) about cryptorchidism is:

   A. Cryptorchidism is thought to have a multifactorial etiology
   B. Neural tube defects may be associated with cryptorchidism.
   C. Pathologic bladder enlargement may be associated with cryptorchidism.
   D. All of the above

The pediatrician performs a complete physical examination to evaluate the infant for a possible genetic syndrome, hypospadias, or genital ambiguity. The pediatrician finds that the infant does not have any dysmorphic features and the urethral opening is in the appropriate location. Continuing with the examination, the pediatrician then places one hand over the right scrotal region while moving the other hand along the inguinal canal, starting from the superolateral portion of the inguinal canal.

4. The purpose of the two-handed technique performed on this infant is to evaluate for a(n):

   A. Abdominal testicle
   B. Hydrocele
   C. Inguinal hernia
   D. Retractile testicle

The pediatrician is unable to palpate any structure using this technique.

5. Of the following, the most appropriate management of this infant with unilateral cryptorchidism is to:

   A. Evaluate for intersex disorders
   B. Refer the infant to a urologist by 6 months of age
   C. Postpone the planned circumcision
   D. Wait for the child to reach puberty to allow testosterone to have an effect

The infant is managed appropriately. However, the family is aware that their child might still have long-term complications.

6. Of the following, potential long-term complication(s) in an infant with cryptorchidism is:

   A. Increased incidence of testicular tumors
   B. Infertility
   C. Inguinal hernia
   D. All of the above

Later in the week, a pediatric resident rotating in the Newborn Nursery asks this pediatrician to evaluate an infant who appears to have a small-sized penile length (see Figure 2).

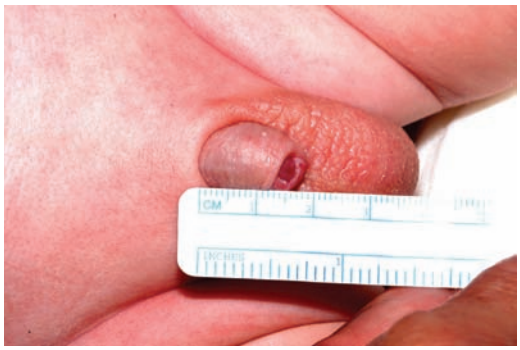


FIGURE 2. Courtesy of T. Ernesto Figueroa

7. Of the following, the most appropriate approach in the diagnosis of a micropenis is to:

   A. Avoid compressing any suprapubic fat pad
   B. Calculate the penile circumference-to-length ratio
   C. Compare the penile length with the scrotal length
   D. Use the stretched penile length

The infant meets the criteria for a diagnosis of micropenis.

8. Of the following, the most appropriate study/studies in this infant is (are):

   A. Brain magnetic resonance imaging
   B. Karyotype
   C. Thyroid-stimulating hormone concentration
   D. All of the above

The pediatrician and resident meet with the infant's parents to discuss the finding of micropenis and necessary evaluation. The family is appropriately concerned and reports that their first son had a mass in the inguinal area. The pediatrician discusses with the resident that the differential diagnosis of a mass in the inguinal area in an infant can be caused by a hydrocele, inguinal hernia, trauma, or a tumor.

9. A communicating hydrocele, noncommunicating hydrocele, and an inguinal hernia all result from various degrees of obliteration of the:

   A. Epididymis
   B. Processus vaginalis
   C. Vas deferens
   D. None of the above

CASE 4

Female genital findings

A medical student is performing the initial examination on a female baby who is 2 hours old. During his assessment, he astutely notes an abnormality on the vaginal exam, as shown in Figure 1.

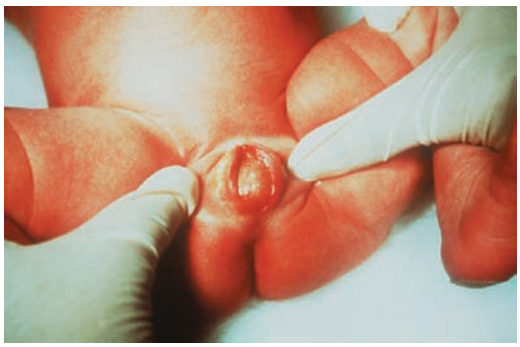


FIGURE 1. Used with permission from: Emans SJ, Laufer MR, Goldstein DP, eds. Pediatric and Adolescent Gynecology. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:plate 21

1. Of the following, the most likely clinical finding in this newborn is:

   A. Absence of symptoms
   B. Hematuria
   C. Leukorrhea
   D. Menstrual bleeding

The student shows this clinical finding to his supervising pediatrician. The pediatrician is concerned because she is also able to palpate a pelvic mass. Prior to speaking with the parents, the pediatrician and student review the fetal radiographic findings and find a T2-weighted fetal magnetic resonance imaging (MRI) that reveals two masses (identified by the *dotted pink line* and the *solid green line* in Figure 2).

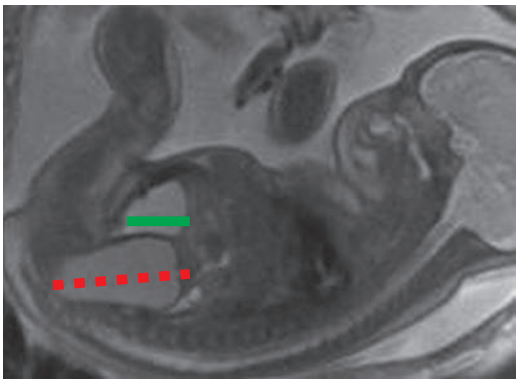


FIGURE 2. Courtesy of Dara Brodsky, MD

2. Of the following, the most likely complication associated with this infant's pelvic mass is:

   A. Adjacent venous obstruction
   B. Intestinal venous obstruction
   C. Urinary tract obstruction
   D. All of the above

The pediatrician then reviews other potential vaginal abnormalities that present during infancy. She shows the student Figure 3 of a 3-month-old infant and asks the student to discuss the appropriate management.

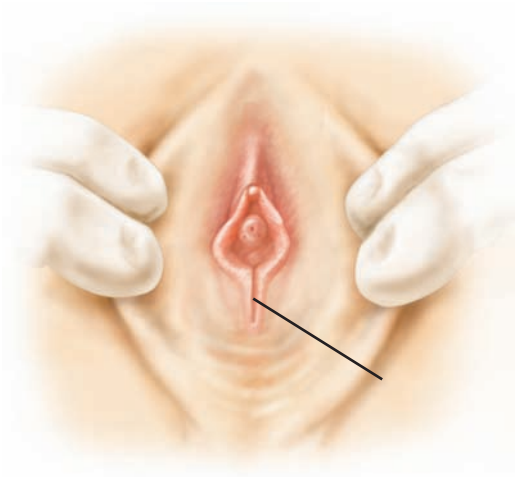


FIGURE 3. From Bickley LS, Szilagyi P. Bates' Guide to Physical Examination and History Taking. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003

3. Of the following, the most appropriate management of this infant is:

   A. Application of cream to involved area
   B. Limited bathing
   C. Oral estrogen supplementation
   D. Surgery

SECTION XII

Answers

CASE 1 ANSWERS

1. A. The blood sample was obtained when the newborn was less than 24 hours of age.

Newborns in the United States all have a newborn screening blood test at 36 to 72 hours of age to assess for various diseases. To screen for congenital hypothyroidism, state screening programs measure the amount of TSH or thyroxine (T4) in the blood sample. Reference values for TSH and T4 vary by gestational age and chronological age. Full-term infants have a rapid increase in TSH levels within the first 24 hours of age, resulting in an increase in T4 production. Thus, if a blood sample is obtained in a full-term infant who is less than 24 hours of age, the TSH concentration will be falsely elevated. Premature infants often have a delayed rise in TSH.

Most newborns with congenital hypothyroidism are asymptomatic, and thus, newborn state screening is critical for early diagnosis.

Although a pregnant woman's antithyroid treatment may impact the infant's thyroid function, maternal thyroid hormone supplementation should not impact the infant.

After a blood sample is obtained from a newborn and placed on filter paper, the sample is sent to the state newborn screening program for testing. If a baby's blood was drawn in the late evening, the state laboratory will usually run the sample the following day. This delay does not impact the test results.

2. A. Thyroxine (T4)

State newborn programs test for congenital hypothyroidism by measuring a TSH concentration or by testing the amount of T4. If this initial test is abnormal, the laboratory will need to repeat the test. If repeat testing confirms the abnormal value, then the laboratory measures the other thyroid study to narrow the potential cause. Thus, after the newborn in this vignette had an elevated TSH concentration, the laboratory confirmed this finding and then tested for T4. Potential etiologies of an abnormal newborn screen are shown in Table 1.

TABLE 1. Potential Etiologies of an Abnormal Newborn Screen

Newborn Screening Results	Possible Etiologies
Low T4 and high TSH	• Congenital hypothyroidism, usually resulting from thyroid dysgenesis (due to developmental defect of the thyroid gland) or dyshormonogenesis (due to disruptions in thyroid hormone synthesis) • Transient hypothyroidism (low endogenous iodine stores, increased exogenous iodine exposure, maternal antithyroid medications)
Low T4 and normal TSH	• Transient hypothyroxinemia of prematurity • Sick euthyroid syndrome (i.e., thyroid suppression from an acute illness) • Thyroid-binding globulin (TBG) deficiency as occurs in an infant with malnutrition or liver immaturity • TSH deficiency • Congenital hypothyroidism with a delayed rise in TSH (possibly up to 8 weeks later), as occurs in premature infants or full-term infants with congenital heart disease or trisomy 21
Normal T4 and high TSH	• Transient hypothyroidism • Compensated congenital hypothyroidism

Modified from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu Press; 2010:373

Although measurements of an infant's T3, T3 resin uptake, and T4-binding globulin are helpful in establishing the type of thyroid disorder, these tests are not obtained by newborn state screening programs.

3. B. Enlarged posterior fontanel

A newborn with congenital hypothyroidism typically is often asymptomatic. Subtle, nonspecific signs may include:

- Constipation
- Distended abdomen
- Dry, mottled skin
- Enlarged posterior fontanel (>1 cm diameter)
- Feeding difficulty
- Hoarse cry
- Hypothermia
- Lethargy
- Macroglossia
- Prolonged jaundice (>7 days)
- Umbilical hernia

If a newborn has hypothyroidism as a result of an iodide transport defect, organification defect, thyroglobulin abnormalities, or deiodinase deficiency, the clinician may be able to palpate a goiter.

4. D. All of the above

Congenital hypothyroidism occurs in ~1 in 3,500 live births. The causes of this disease are summarized below:

1. Primary congenital hypothyroidism
   a. Thyroid dysgenesis (75%) as a result of developmental defects of the thyroid gland
   b. Thyroid dyshormonogenesis (10%) as a result of disruptions in thyroid hormone synthesis
2. Secondary congenital hypothyroidism as a result of a hypothalamic–pituitary abnormality (5%)
3. Transient congenital hypothyroidism (10%) as a result of maternal antithyroid medications, maternal antibodies, or neonatal iodine exposure

Possible long-term effects of an infant with untreated congenital hypothyroidism include:

- Cognitive deficits
- Delay in motor development
- Poor growth

Early diagnosis and hormonal treatment has been shown to decrease the risk of these long-term complications. At present, there is a lack of follow-up data of adults with congenital hypothyroidism. Most adults are reported to lead normal lives. Studies from Italy and Switzerland have found that young adults with congenital hypothyroidism are at greater risk for obesity, impaired diastolic function, and increased intima–media thickness, but the impact and significance of these findings are unknown.

5. C. Obtain serial TSH concentrations

After hormonal therapy is initiated, most endocrinologists monitor the infant's TSH and T4 levels weekly for the first month to ensure that TSH levels decrease to normal. After the TSH normalizes, serial TSH and T4 monitoring at longer intervals is recommended. Because most newborns with congenital hypothyroidism are asymptomatic, clinical signs/symptoms of hypothyroidism are not helpful to guide hormonal treatment. Ultrasonographic size of the thyroid gland in an infant with congenital hypothyroidism is also not helpful for guiding hormonal therapy.

For infants with transient hypothyroidism, endocrinologists may recommend discontinuing hormonal therapy after age 3 years and monitor thyroid studies to determine if treatment is still warranted. Infants with a diagnosis of permanent congenital hypothyroidism will require hormonal treatment for life.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the possible causes of a decreased serum thyroxine concentration in a term and preterm neonate with or without illness
- Know the varying causes of congenital and acquired hypothyroidism
- Recognize the signs and symptoms of congenital and acquired hypothyroidism
- Know how to manage and treat congenital and acquired hypothyroidism and the use of thyroid-stimulating hormone to guide treatment
- Know the consequences of untreated hypothyroidism in the neonate
- Know the prognosis for a patient with congenital or acquired hypothyroidism

SUGGESTED READINGS

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CASE 2 ANSWERS

1. B. Virilization of a genetic female

Ambiguous genitalia are usually caused by virilization of a genetic female or undervirilization of a genetic male. Clinical findings in a virilized female vary from mild clitoromegaly to complete labial fusion and depend on differences in timing, amount, and duration of testosterone exposure. Etiologies of virilization in a female infant include:

- Increased androgen production caused by congenital adrenal hyperplasia (CAH), which results from 21-hydroxylase deficiency, 11β-hydroxylase deficiency, or 3β-hydroxysteroid dehydrogenase deficiency
- Abnormal androgen metabolism as a result of placental aromatase deficiency
- Excessive maternal androgen exposure as occurs with increased production from a luteoma, adrenal tumor, or untreated CAH

Because the resident was unable to palpate gonads in this newborn, the diagnosis of a virilized female is most likely.

Incomplete masculinization of a genetic male can be caused by:

- Abnormal testosterone production from Leydig cell abnormalities or defects in testicular and adrenal steroidogenesis such as 3β-hydroxysteroid dehydrogenase deficiency, 17α-hydroxylase deficiency, 17,20-lyase deficiency, or 17β-hydroxysteroid dehydrogenase deficiency
- Abnormal testosterone metabolism as a result of 5α-reductase deficiency
- Defect of testosterone action due to androgen insensitivity syndrome
- Exogenous estrogen or progestin exposure

Ambiguous genitalia can also result from genetic disorders of sexual differentiation, such as gonadal dysgenesis, true hermaphroditism, or Smith–Lemli–Opitz syndrome.

2. D. All of the above

As recognized by the resident, urgency and sensitivity are necessary in the evaluation and management of a newborn with ambiguous genitalia. The pediatric team should consult with an endocrinologist and a geneticist to assist with the evaluation. The following laboratory tests should be obtained urgently in a newborn with ambiguous genitalia:

- Electrolytes to assess for mineralocorticoid deficiency
- Karyotype
- Testosterone concentration

Additional testing can include measurements of renin, 17-hydroxyprogesterone, 17-hydroxypregnenolone, progesterone, androstenedione, dehydroepiandrosterone, deoxycorticosterone, 11-deoxycortisol, testosterone, and cortisol, as well as an adrenocorticotrophic hormone (ACTH) stimulation test.

3. D. 17-hydroxyprogesterone

The most common type of CAH is 21-hydroxylase deficiency, which is associated with two forms:

1. Classical CAH
   - Incidence is ~1 in 15,000 to 20,000
   - Categorized into two types based on degree of aldosterone deficiency:
     a. Salt-wasting (67% of classical CAH)
     b. Non-salt-wasting or simple virilizing (33% of CAH)
   - Females typically present in the newborn period with ambiguous genitalia because of excessive androgen exposure prenatally
   - Affected males have normal genitalia except for hyperpigmentation and are usually diagnosed by the newborn screening test
2. Nonclassical CAH
   - Lower incidence than classical CAH
   - Milder virilization
   - Late onset
   - Affected males and females present with premature pubarche prior to age 8 and tall stature
   - Some patients are asymptomatic
   - Not usually detected by the newborn screening test

Approximately 75% of patients with classical salt-wasting CAH have 0% 21-hydroxylase activity. Patients with classical simple virilizing CAH have ~1% enzymatic activity. In contrast, children with later-onset nonclassical CAH have 20% to 50% enzymatic activity.

Deficiency of 21-hydroxylase leads to:

- Decreased mineralocorticoids, including 11-deoxycorticosterone, corticosterone, and aldosterone
- Decreased glucocorticoids, including 11-deoxycortisol and cortisol
- Increased sex steroids, such as testosterone, androstenedione, and dehydroepiandrosterone
- Increased anterior pituitary hormones, such as hypothalamic corticotropic releasing hormone and pituitary ACTH (this occurs because low cortisol amounts decrease the negative feedback on corticotroph cells)

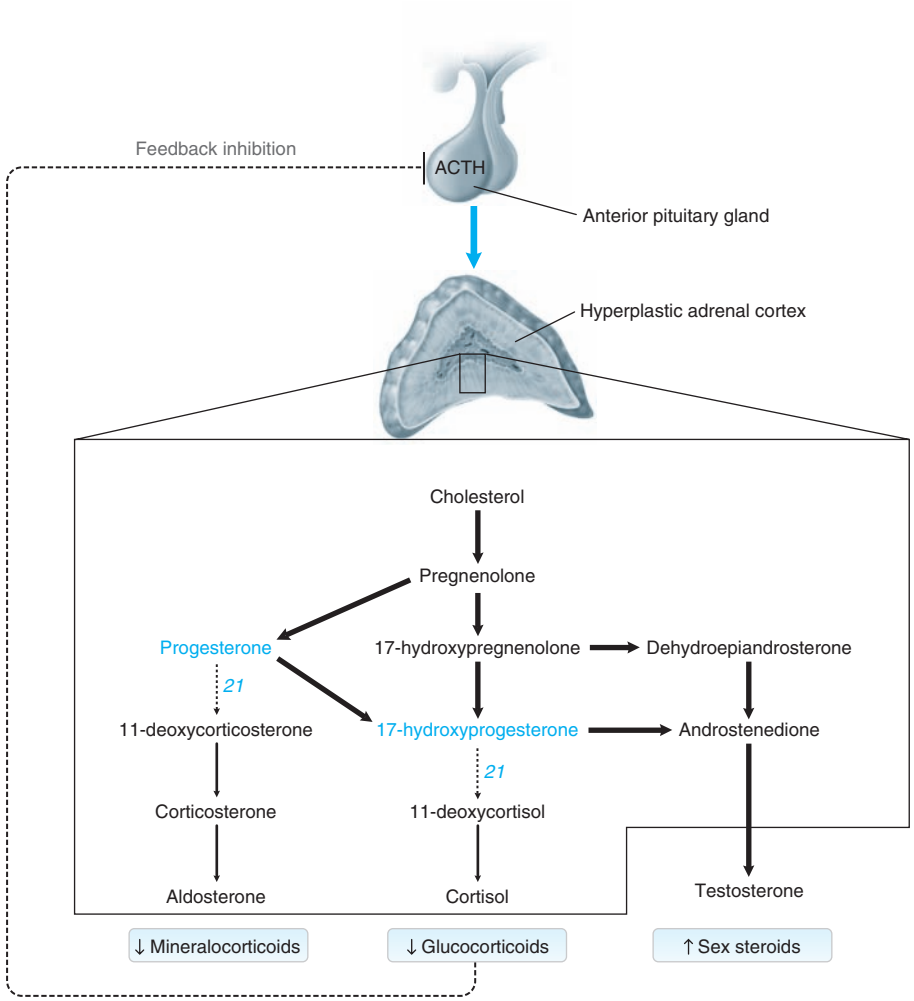

FIGURE 2. Congenital adrenal hyperplasia. Steroid 21-hydroxylase deficiency, the most common cause of CAH, results in impaired biosynthesis of aldosterone and cortisol (dashed lines). Therefore, steroid hormone synthesis in the adrenal cortex is shunted toward increased production of sex steroids (thick lines). The lack of cortisol production decreases the negative feedback on corticotroph cells of the anterior pituitary gland (dashed line), causing increased ACTH release (thick blue arrow). Increased levels of ACTH induce adrenal hyperplasia and further stimulate the synthesis of sex steroids. This pathway can be interrupted by administering exogenous cortisol. The deficient enzyme is shown as a number: 21, steroid 21-hydroxylase. Adapted from: Cotran RS, Kumar V, Collins T, eds. Robbins Pathologic Basis of Disease, 6th ed. Philadelphia, PA: WB Saunders, 1999. Figure 26.27, with permission from Elsevier

Figure 2 shows the 21-hydroxlase pathway (*dotted arrow*).

All newborn screening programs in the United States measure 17-hydroxyprogesterone from whole blood collected on filter paper. Newborns with classical 21-hydroxylase deficiency will have elevated 17-hydroxyprogesterone concentrations. While females with classical 21-hydroxylase deficiency usually present with ambiguous genitalia, males with classical 21-hydroxylase deficiency are usually identified by newborn state screening. Prior to this newborn screening testing, affected males typically presented with an adrenal crisis in the first few weeks of life. Males with a milder form of classical 21-hydroxylase deficiency may present with symptoms during their toddler years.

Newborns with nonclassical 21-hydroxylase deficiency are not usually diagnosed by the newborn state screening test because their 17-hydroxyprogesterone concentrations are closer to normal.

4. D. All of the above

Untreated newborns with classical 21-hydroxylase deficiency can present in an adrenal crisis with the following findings:

- Hypoglycemia
- Hyponatremia
- Hyperkalemia
- Hypotension
- Lethargy
- Vomiting

Treatment focuses on electrolyte replacement, glucocorticoid administration, and hydration.

To prevent adrenal crises, newborns with classical salt-wasting CAH require supplementation of mineralocorticoids (fludrocortisone tablets), glucocorticoids (crushed hydrocortisone tablet), and sodium chloride. During times of increased stress (e.g., febrile illness, gastroenteritis with dehydration,

surgery, major trauma), infants should receive a higher amount of glucocorticoids. Depending on the degree of virilization, some affected females may require feminizing surgery.

Newborns with nonclassical CAH are treated based on clinical symptoms. Affected children with premature pubarche and rapid growth should receive low-dose hydrocortisone. Females with hirsutism can be given an oral contraceptive or antiandrogen medication. Most affected patients do not exhibit clinical signs of adrenal insufficiency.

5. D. Prenatal therapy with dexamethasone will improve outcomes only in female fetuses with 21-hydroxylase deficiency.

Because 21-hydroxylase deficiency is an autosomal recessive disorder, parents with a previous child affected by this disorder have a 25% chance of having a fetus with CAH. To date, more than 170 mutations of the affected gene have been identified, and a diagnosis can be made prenatally. High-dose dexamethasone administered to a pregnant woman can improve outcomes in female fetuses with 21-hydroxylase deficiency by decreasing the degree of virilization. However, prenatal therapy does not obviate the long-term need for glucocorticoid and mineralocorticoid replacement.

It is important that prenatal dexamethasone treatment occurs during the first trimester, as androgens can virilize fetal genitalia 6 to 7 weeks after conception. Unfortunately, at present, the prenatal diagnosis by chorionic villus biopsy occurs at 10 to 12 weeks' gestation. Thus, for the treatment to be effective, dexamethasone needs to be initiated prior to having a prenatal diagnosis. Prenatal therapy with dexamethasone is controversial and considered experimental, as treatment would unnecessarily expose all fetuses to this hormone, even though only one of four fetuses who have a sibling with CAH will have 21-hydroxylase deficiency. Furthermore, because only females will benefit from dexamethasone exposure, only one in eight fetuses will ultimately benefit from prenatal treatment. Families with a previous child with CAH need to receive genetic counseling to determine whether they want to initiate fetal therapy. If the family decides in favor of high-dose dexamethasone, preconception diagnosis of the gene mutations is important to increase the speed of prenatal diagnosis, potentially reducing the amount of time that unaffected fetuses are treated.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the signs and symptoms of congenital adrenal hyperplasia
- Know the laboratory evaluation of congenital adrenal hyperplasia
- Understand the value of neonatal screening for salt-losing congenital adrenal hyperplasia in male infants with normal genitalia
- Plan the treatment for an adrenal crisis in a patient with congenital adrenal hyperplasia
- Know that congenital adrenal hyperplasia can be diagnosed prenatally

SUGGESTED READINGS

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CASE 3 ANSWERS

1. D. Hypospadias

The figure shows an infant with hypospadias, the most common type of penile abnormality. In this abnormality, the urethral meatus is located on the ventral side of the infant's penis. This infant has a mild hypospadias, while infants with more severe forms have a meatal opening that is lower on the penile shaft.

Figure 3A–C shows the various types of urethral defects. Figure 3A shows a mild hypospadias, Figure 3B reveals an epispadias (meatal opening on the dorsal surface of the penile shaft), and Figure 3C shows hypospadias with a chordee.

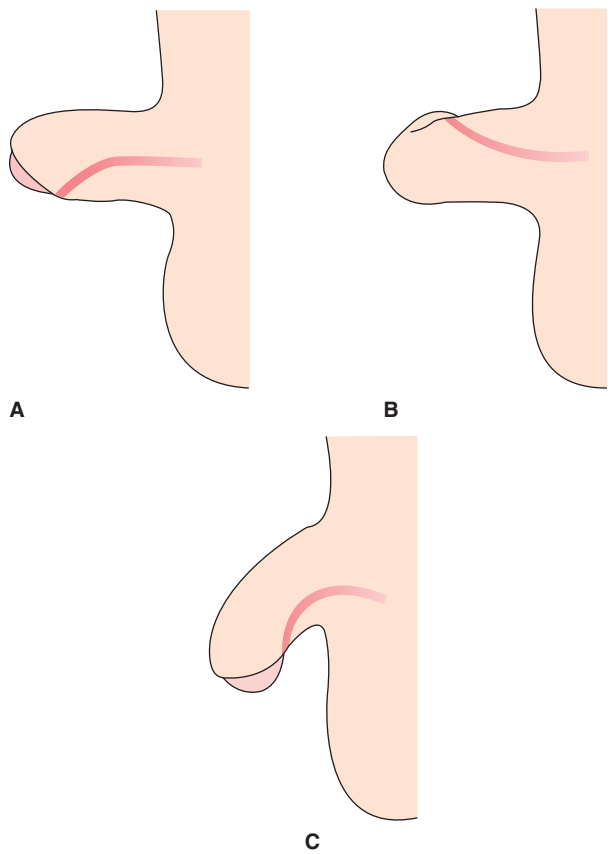

FIGURE 3A–C. LifeART © 2014 Lippincott Williams & Wilkins. All rights reserved

2. B. Ensure that the family postpones the planned circumcision

After an infant is diagnosed with hypospadias, it is important to defer a planned circumcision because some of the foreskin can be used during the repair. There is no need to obtain an abdominal ultrasound as hypospadias is rarely associated with renal anomalies. However, because hypospadias may be associated with a genetic syndrome, further studies are warranted if the infant has additional abnormalities. If an infant has hypospadias, the diagnosis of an endocrinopathy should be considered if the infant also has micropenis, cryptorchidism (unilateral or bilateral), or scrotal abnormalities. Surgery to repair the hypospadias is recommended within the first year of life.

3. D. All of the above

An undescended testis, or cryptorchidism, is caused by a defect in the regulation or anatomical blockage of the normal descent of the testis from the abdominal cavity into the scrotum. Cryptorchidism is found in 3% to 5% of term male infants and in as many as 30% of preterm infants. The precise etiology of cryptorchidism is unknown but is believed to be multifactorial. Infants with neural-tube defects are at increased risk of having cryptorchidism, possibly because of disruption of the thoracolumbar nerve. In addition, cryptorchidism is more common in infants with extremely large bladders (e.g., prune belly syndrome, posterior urethral valves), possibly because of interference of the inguinal ring or altered intra-abdominal pressure.

4. D. Retractile testicle

When a clinician is unable to palpate an infant's testicle, it is important to examine the inguinal region closely. An undescended testicle may be located high in the scrotum (60%), in the inguinal canal (25%), or within the abdominal cavity (15%), as shown in Figure 4.

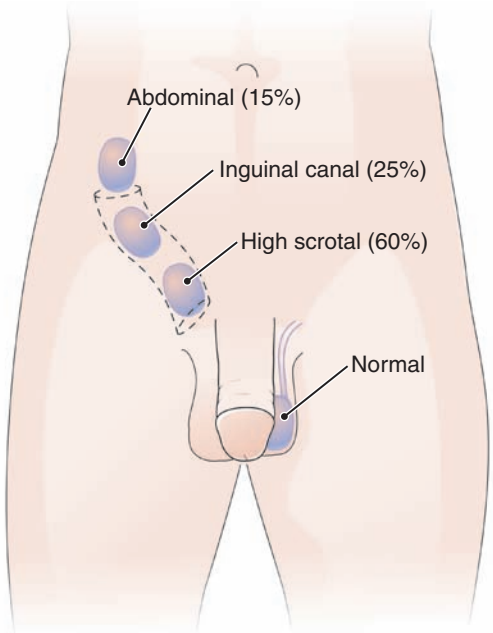

FIGURE 4. McConnell TH. The Nature of Disease: Pathology for the Health Professions. 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007. Figure 20.8

The pediatrician in this vignette placed one hand over the affected scrotal region and moved the other hand along the inguinal canal, starting at the superolateral region of the canal. This technique will help to determine if the infant has a retractile testicle, evident by palpation of the moveable testicle into the scrotum. Sometimes, it is difficult to distinguish between an undescended and a retractile testicle, and a consultation with a urologist may be warranted.

5. B. Refer the infant to a urologist by 6 months of age

If an infant has isolated unilateral cryptorchidism, the pediatrician should refer the infant to a urologist by 6 months of age for evaluation and management. Some affected infants may respond to hormonal therapy. If the infant has persistent cryptorchidism, surgical repair is warranted by age 1 year. Delay in surgical repair beyond age 1 year may lower the surgical success rate and may impair spermatogenesis. A urologist should evaluate the infant prior to age 6 months if the infant has bilateral cryptorchidism or if the infant also has hypospadias.

Evaluation for intersex disorders is indicated if an infant has either of the following:

- Bilateral cryptorchidism
- Unilateral cryptorchidism with hypospadias

An infant with unilateral or bilateral cryptorchidism in the absence of hypospadias can still have a circumcision prior to discharge home.

6. All of the above

Men who are born with cryptorchidism are at greater risk of infertility. Earlier orchiopexy prior to age 1 year has been shown to lower the risk of infertility. Male adults with a history of an undescended testicle are at greater risk of developing testicular germ-cell cancers. Although orchiopexy does not decrease this incidence, placement of the intra-abdominal testicle into the scrotum allows for earlier detection of abnormal changes. Infants with cryptorchidism also have a higher incidence of both testicular torsion and inguinal hernia.

7. D. Use the stretched penile length

An accurate diagnosis of a micropenis in a newborn requires the following:

- Normally formed penis
- Complete compression of any suprapubic fat
- Measurement from the pubic symphysis to the tip of the glans
- Measurement of the stretched penis

A micropenis measures 2.5 standard deviations less than the mean length for age using published standards of penile length. A full-term newborn male's penile length should be at least 1.9 cm.

Typically, the ratio of penile length with the penile circumference is normal in infants with a micropenis. The scrotal sac of an infant with micropenis usually is small, and cryptorchidism is frequently present. The relationship between the penile length and scrotal length is irrelevant when evaluating the size of an infant's penis.

8. D. All of the above

An infant with a true micropenis most likely has some type of hormonal abnormality that occurred after 14 weeks' gestation. The most common causes of micropenis include the following:

- Deficient testosterone secretion
  - Hypogonadotropic hypogonadism
  - Primary hypogonadism
- Defect in testicular function
- Developmental anomalies
- Idiopathic

The infant's pediatrician should consult an endocrinologist to help identify the level of the hypothalamic–pituitary–testicular axis that is involved. Because an infant with hypogonadotropic hypogonadism is at high risk for growth hormone or adrenocorticotropic hormone deficiency, measuring the infant's serum glucose, electrolytes, and cortisol concentrations are necessary. The following hormone levels are also typically measured:

- Growth hormone
- Prolactin
- Thyroid-stimulating hormone
- Adrenocorticotropic hormone

A brain magnetic resonance imaging can help to assess midline structural abnormalities.

The infant's testicular function can be determined by measuring testosterone concentrations before and after human chorionic gonadotropic administration. Because micropenis is often associated with chromosomal abnormalities, testing the newborn's karyotype may sometimes be indicated.

An infant with micropenis is usually treated with androgen therapy, and if this is unsuccessful, reconstructive surgery may be needed.

9. B. Processus vaginalis

During normal male development, the testes descend between 25 and 35 weeks' gestation from the retroperitoneal intra-abdominal space through the inguinal canal. As the testes descend, they bring an extension of the peritoneal lining, which is the processus vaginalis. This structure then involutes so that there is no communication between the peritoneal cavity and the inguinal canal and scrotum. If the processus vaginalis remains patent, this can lead to a communicating hydrocele, noncommunicating hydrocele, or an inguinal hernia.

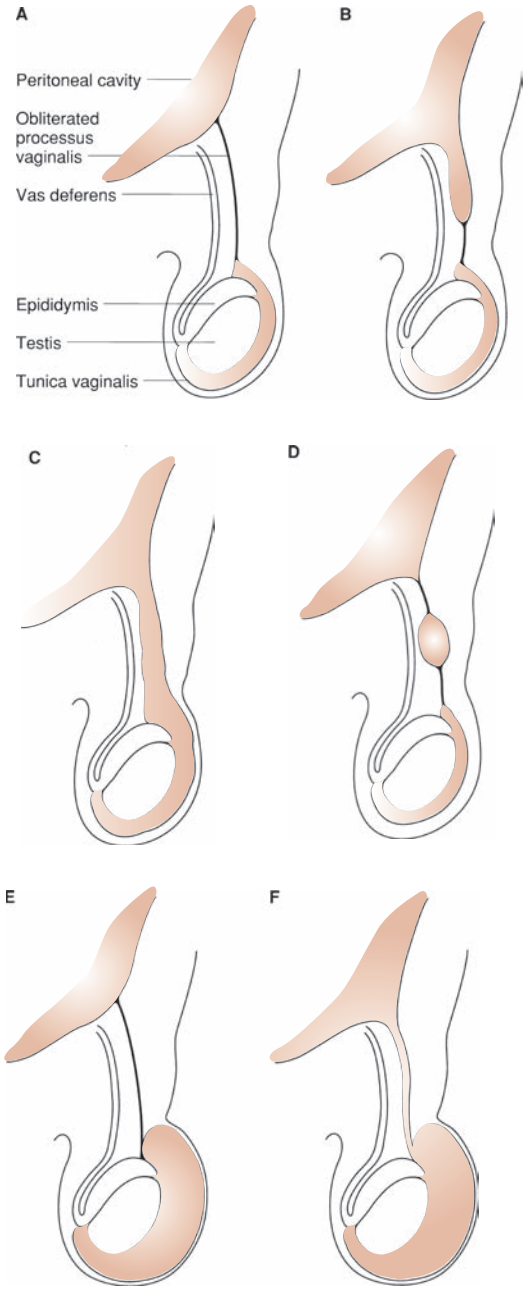

FIGURE 5. Mulholland MW, Maier RV, et al. Greenfield's Surgery: Scientific Principles and Practice. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006. Figure 110.6

Figure 5 shows the result of different degrees of obliteration of the processus vaginalis. Figure 5A indicates normal with complete involution of the processus vaginalis. Figure 5B shows a proximal hernia with distal obliteration of the processus vaginalis. Figure 5C illustrates a hernia extending into the scrotum with complete patency of the processus vaginalis. Figure 5D shows proximal and distal obliteration of the processus vaginalis with a hydrocele of the cord. Figure 5E represents a noncommunicating hydrocele with an obliterated processus vaginalis. Figure 5F shows a communicating hydrocele with a patent processus vaginalis.

An infant with bilateral hydroceles is shown in Figure 6.

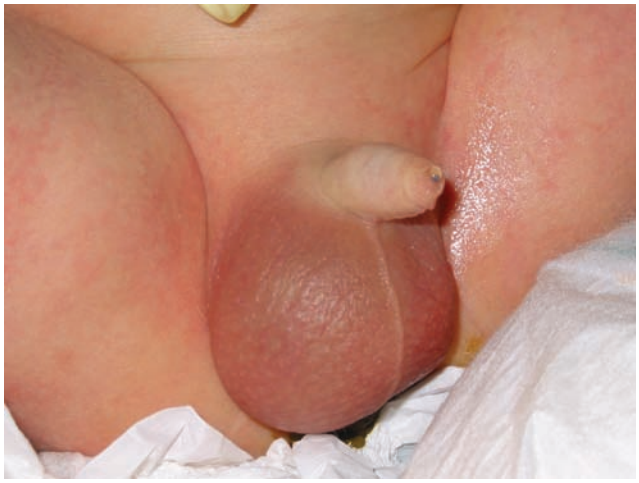

FIGURE 6. Courtesy of T. Ernesto Figueroa

If an infant has a communicating hydrocele, the processus vaginalis is small and fluid from the peritoneal cavity enters into the scrotal space. This sac will transilluminate. The size of this hydrocele may increase when the infant's intra-abdominal pressure is higher, such as occurs with crying or coughing. The communicating hydrocele is often larger when the infant is in the vertical position as gravity leads to greater passage of intraperitoneal fluid into the scrotum. In contrast, an infant with a noncommunicating hydrocele will not have variability in the size of the fluid collection.

A wide opening of the processus vaginalis allows bowel and intraperitoneal fluid to enter the area, leading to an inguinal hernia. The scrotal sac of an infant with an inguinal hernia does not transilluminate unless there are herniated loops of thin-walled bowel. When an affected infant's abdominal pressure increases, the amount of herniated contents may increase. In contrast to an infant with an inguinal hernia, an infant with a hydrocele will have a narrowing at the external inguinal ring without entry into the inguinal ring. Sometimes, an ultrasound may be needed to help distinguish between a hydrocele and an inguinal hernia.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Hypospadias

- Recognize that first-degree hypospadias is rarely associated with renal anomalies
- Know that circumcision should be delayed in patients with hypospadias
- Know that surgical correction should be done within the first year after birth for patients with first-degree hypospadias

Cryptorchidism

- Know the pathophysiology and natural history of cryptorchidism
- Distinguish between undescended testes and retractile testes
- Know that hypospadias with bilateral cryptorchidism is an indication to evaluate for intersex disorders
- Plan the appropriate management of a patient with undescended testes
- Know the complications of undescended testes: infertility and increased incidence of testicular tumors

Micropenis

- Understand the significance of the suprapubic fat pad in evaluating penile size
- Know how to diagnose micropenis by measurement in a newborn boy
- Know the significance of hypoglycemia in a patient with micropenis

Hydrocele and Inguinal Hernia

- Know the differential diagnosis of a mass in the inguinal area in an infant: hydrocele, inguinal hernia, trauma, tumor
- Know how to diagnose a hydrocele
- Know how to diagnose an inguinal hernia

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CASE 4 ANSWERS

1. A. Absence of symptoms

The newborn in this vignette appears to have an imperforate hymen on physical examination. This occurs in 0.1% of newborn girls. Neonates affected with an imperforate anus are usually asymptomatic with clinical symptoms, such as abdominal pain and amenorrhea, typically occurring during puberty.

If a newborn with an imperforate hymen has an associated urinary obstruction, urine output will be altered; typically, hematuria is not an associated clinical finding in affected newborns. Vaginal discharge (i.e., leukorrhea) and menstrual bleeding are not possible in a newborn with an imperforate hymen.

2. D. All of the above

A newborn can develop a hydrometrocolpos if a vaginal blockage, such as an imperforate hymen, high vaginal septum, vaginal atresia, or urogenital sinus, coexists with an excessive amount of vaginal fluid production (caused by maternal estrogen stimulation). The name "hydrometrocolpos" describes a fluid collection (hydro) located in the uterus (metro) and vagina (colpos). The fetal MRI in this vignette reveals a hydrometrocolpos (mass surrounding the *dotted pink line*).

If a newborn has a large hydrometrocolpos, this can lead to obstruction of the adjacent veins, intestines, and/or urinary tract. The *solid green line* of the fetal MRI reveals a large bladder with fluid of a different consistency than the fluid inside the pelvic mass. Depending on the size of the pelvic mass and the degree of local obstruction, neonates with a hydrometrocolpos can have one or more of the following findings:

- Pelvic mass
- Translucent bulge from an imperforate hymen
- Acute renal failure and/or urinary ascites

Some newborns may develop a secondary infection within the vagina or uterus and have signs of sepsis.

The management of hydrometrocolpos focuses on vaginal drainage and relief of the vaginal obstruction, typically with bedside incision and drainage. In some cases, a laparotomy may be needed.

3. A. Application of cream to involved area

This 3-month-old infant most likely has labial adhesions (identified by the *black line* on the figure). These usually occur in females between age 3 months and 6 years. The development of labial adhesions may be associated with lower estrogen concentrations and vulvar irritation. Because of intrauterine passage of maternal estrogens to fetuses, newborns are protected and typically do not develop labial adhesions.

Most adhesions will resolve spontaneously. Some studies have shown that application of a cream to the involved area can be helpful. A mild emollient can be used if the adhesions are small, or for larger lesions, an estrogen-containing cream may be warranted. For the rare situations in which labial adhesions persist, surgery may be indicated. Limited bathing has not been shown to impact the clinical course of infants with labial adhesions.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

Imperforate hymen

- Know the signs and symptoms of an imperforate hymen
- Recognize the clinical manifestations of hydrometrocolpos

Labial adhesions

- Recognize labial adhesions
- Know the natural history of labial adhesions and the appropriate therapy

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SECTION XIII

Inborn Errors of Metabolism

CASE 1

Newborn screening

The nurse caring for a term infant tells the covering pediatric resident that the parents have questions about metabolic screening. The resident reviews the expanded metabolic screening offered to families.

1. Select True or False (i–ii) for the following statements (A–D) regarding metabolic screening:

   A. A venipuncture is done to obtain 2 ml of blood for the expanded metabolic screening.
   B. If diagnosed early, these disorders can often be treated to prevent severe developmental delay, intellectual and physical disabilities, and death.
   C. The expanded newborn screening uses technology such as tandem mass spectrometry to screen babies for >24 rare metabolic and genetic disorders.
   D. The goal of newborn screening is to identify infants with treatable congenital conditions before they become symptomatic.

   i. True
   ii. False

The infant's screen comes back at day 4 of life with an out-of-range result for 17-hydroxyprogesterone. The infant was discharged home from the hospital at day 3 of life and has not yet been seen in follow-up.

2. Select the appropriate initial response to a positive neonatal screening test for metabolic diseases:

   A. Call the parents and tell them to go the emergency room (ER) immediately
   B. Consult the ACT sheet and the Newborn Screening Program
   C. Do nothing as there are many false-positive results
   D. Have the administrative assistant call the family to arrange for an appointment in 2 weeks

CASE 2

Phenylketonuria

A 3,600-g female is born by spontaneous vaginal delivery to a 39-year-old gravida 4 para 3 now 4 Caucasian woman with normal prenatal screens. The infant and mother are initially doing well. The mother requests early discharge at 16 hours as all of her prior deliveries were home births and she prefers being home as soon as possible.

Soon after discharge, the infant develops frequent vomiting and has a peculiar smell to her urine. In response, her mother changes her diet thinking that her breast milk was not agreeing with her infant. On her third day of life, the infant has a 3-minute generalized seizure and is brought via ambulance to the emergency room (ER). The infant is stable upon arrival to the ER.

A pediatric resident obtains the history and performs a physical exam. He notes that the infant has blond hair, a head circumference that only measures 10%, fair skin, and blue eyes. After a lengthy workup, the baby is diagnosed with phenylketonuria (PKU).

1. Select the limitations recognized in the newborn screening for PKU:

   A. Accurate testing needs to be done after feedings have been established (i.e., not within the first 24 hours of life).
   B. The screening will determine elevated phenylalanine levels but does not distinguish between potential prematurity (immature enzymes), laboratory error, or actual disease.
   C. The type of PKU cannot be determined by the screening.
   D. All of the above

The parents are extremely anxious about this new diagnosis and ask many questions about the management and expected outcome of infants with PKU.

2. Select True or False (i–ii) for the following statements regarding treatment and sequelae of PKU:

A. Infants with blood phenylalanine levels greater than 10 mg/dL should be started on a specific dietary regimen as soon as possible, ideally by the time the infant is 7 to 10 days old. Most of these infant will be able to lead full lives.

B. Treatment is futile. All patents with PKU will succumb to seizures, developmental delays, severe intellectual disability, and behavior problems.

C. With early dietary restrictions, about 50% of patient will be able to lead productive lives.

D. With early dietary regimen, several hundred of babies each year are growing up normally and leading productive lives. Without treatment, severe mental deficiency and seizures are likely to ensue.

i. True

ii. False

SECTION XIII

Answers

CASE 1 ANSWERS

1. A ii False
B i True
C i True
D i True

Newborn screening first became a public health program in the United States in the early 1960s with the purpose of identifying infants with treatable congenital conditions before they become symptomatic. Initially, this screening tested for only a few disorders. Now with evolving technological advances, more conditions are being screened in the newborn period than ever before. Tandem mass spectrometry is an efficient means of screening many metabolic conditions simultaneously, as opposed to the previous method of analyzing for each condition individually. The testing merely requires a blood draw by heel stick, and the drops of whole blood are then placed on a filter paper. The disorders that are tested are determined by each state with some states screening for more than 30 disorders. If diagnosed early, affected infants can often be treated to prevent severe developmental delay, intellectual and physical disabilities, and death.

2. B. Consult the ACT Sheet and the Newborn Screening Program

The Newborn Screening Committee, in collaboration with the American Academy of Pediatrics (AAP) and the American College of Medical Genetics (ACMG), provides recommendations for pediatric providers in the setting of positive newborn screening results. The ACMG has developed and maintains Web-based resources, called action (ACT) sheets, which contain algorithms to guide the pediatrician through preliminary responses to out-of-range newborn screening results. The infant in this vignette may potentially have congenital adrenal hyperplasia (CAH). Figures 1 and 2 represent (1) the steroid pathway showing that 21-hydroxylase deficiency leads to increased 17-hydroxyprogesterone and androgen production and (2) the genitalia of an infant with CAH.

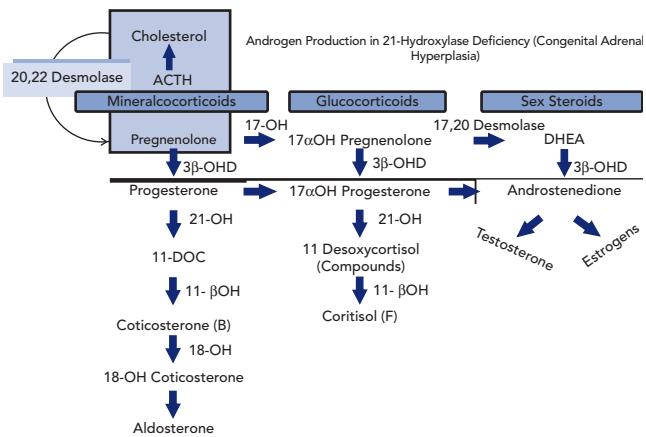


FIGURE 1. From MacDonald MG, Seshia MK, et al. Avery's Neonatology: Pathophysiology & Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. Figure 13.6

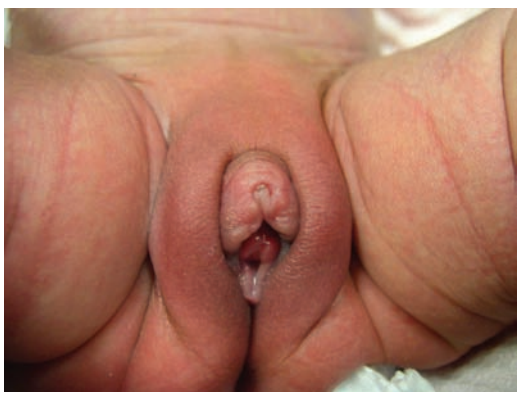


FIGURE 2. Courtesy of Philip Siu, MD

For the infant described in the vignette, the recommendations, per the ACT sheet, are to:

- Contact the family to inform them of the newborn screening result and ascertain clinical status
- Consult with a pediatric endocrinologist, having the following information available (sex, age at sampling, birth weight) and refer, if needed
- Examine the newborn (assess for ambiguous genitalia or nonpalpable testes, lethargy, vomiting, poor feeding)
- Initiate timely confirmatory/diagnostic testing as recommended by the specialist
- Emergency treatment as indicated (e.g. intravenous fluids, hydrocortisone)
- Educate the family about signs, symptoms, and need for urgent treatment of adrenal crisis
- Report findings to newborn screening program

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Review expanded metabolic screening
- Plan the appropriate initial response to a positive neonatal screening test for metabolic diseases

SUGGESTED READINGS

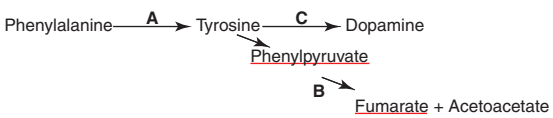
ACT resource: http://www.ncbi.nlm.nih.gov/books/NBK55827/.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Newborn Screening Authoring Committee, American Academy of Pediatrics. Newborn screening expands: Recommendations for pediatrician and medical homes—Implications for the system. *Pediatrics*. 2008;121:192–210.

CASE 2 ANSWERS

1. D. All of the above

Newborn screening for PKU relies on the detection of elevated levels of PKU. During pregnancy, the pregnant woman is able to metabolize fetal phenylalanine; therefore, a newborn will not have elevated phenylalanine levels until protein feedings are established. Newborn screening is not recommended prior to 24 hours; if the testing is done prior to 24 hours, a repeat sample must be obtained.

Figure 1 shows the pathway for the breakdown of phenylalanine.



A Phenylalanine hydroxylase: produced in liver, requires tetrahydrobiopterin (BH_4)

B Fumarylacetoacetate hydrolase; if deficiency → tyrosinemia

C Tyrosine hydroxylase, requires BH_4

FIGURE 1. Printed with permission from: Brodsky D, Martin C. Neonatology Review. 2nd ed. Raleigh, NC: Lulu; 2010:402

The specific enzymatic defect determines the clinical effect on the infant. Table 1 describes the three types of PKU.

TABLE 1. Types of PKU

Classic	More common, secondary to complete phenylalanine hydroxylase deficiency, elevated phenylalanine with normal or low tyrosine; requires low phenylalanine diet	Urine detection of phenylpyruvic acid (add 10% ferric chloride to urine; if positive, urine will turn blue-green)
Allelic variants of phenylalanine hydroxylase	May require dietary restriction	
Pterin defect	Defect of tetrahydrobiopterin (important for phenylalanine, tyrosine, and tryptophan hydroxylase reactions); requires low phenylalanine diet and must replace tetrahydrobiopterin; less successful therapy than classic form	Measure dihydrobiopterin reductase in red blood cells and in urine

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:402

2. A i True
B ii False
C ii False
D i True

Early diagnosis and treatment is essential for patients with PKU. Most patients will be able to lead productive lives.

The graph (Figure 2) represents the typical intellectual ability in untreated patients with PKU at different ages.

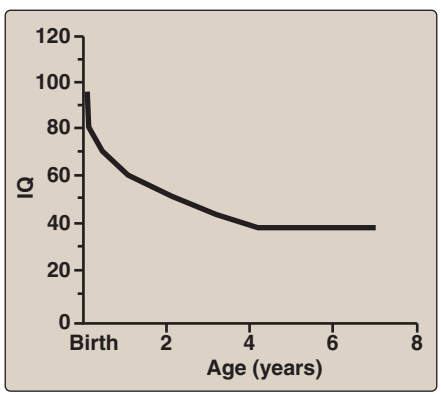


FIGURE 2. From Harvey RA, Ferrier DR. Lippincott's Illustrated Reviews: Biochemistry. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2011

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the utility and limitations of PKU screening
- Know the natural history of treated and untreated phenylketonuria

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Brosco J, Sander L, Seider M, et al. Adverse medical outcomes of early newborn screening programs for phenylketonuria. *NeoReviews*. 2008;121:192–197.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

SECTION XIV

Ophthalmology and Audiology

CASE 1

Ophthalmologic prophylaxis

A term female infant is born to a mother who does not want vitamin K and ophthalmologic prophylaxis to be administered to her newborn. The infant's nurse pages the pediatric resident to discuss the importance of these routine newborn therapies.

After explaining that vitamin K prevents hemorrhagic disease of the newborn (HDN), the mother agrees to vitamin K administration. Next, the resident explains the importance of ophthalmologic prophylaxis.

1. Select True or False (i–ii) for the following statements (A–D):

   i. True
   ii. False

   A. Multiuse tubes of ophthalmic ointment containing erythromycin or tetracycline may be used.
   B. Ophthalmologic prophylaxis is given to newborns to prevent ocular gonorrheal infection and chlamydial conjunctivitis.
   C. Silver nitrate solution may be used as an option to prevent ocular gonorrheal infection and chlamydial conjunctivitis.
   D. The risk of not providing ophthalmologic prophylaxis can be devastating and may lead to blindness.

CASE 2

Congenital glaucoma and cataracts

Vignette A: A 37-week-gestation male infant is born to a primiparous woman with normal prenatal screens. The infant appears well and is admitted to the Newborn Nursery. He later develops photophobia, increased lacrimation, and excessive rubbing of his right eye. The ophthalmologic exam is abnormal. Figures 1 and 2 represent findings consistent with the infant in this vignette.

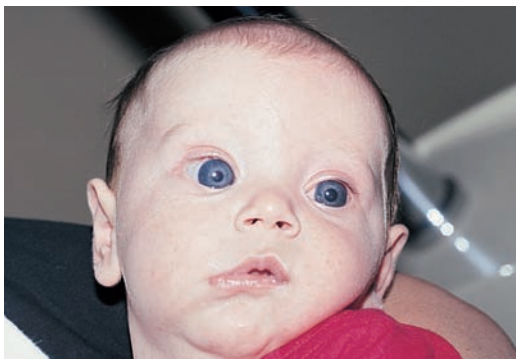


FIGURE 1. From Tasman W, Jaeger E. The Wills Eye Hospital Atlas of Clinical Ophthalmology. 2nd ed. Lippincott Williams & Wilkins; 2001. Figure 11.43

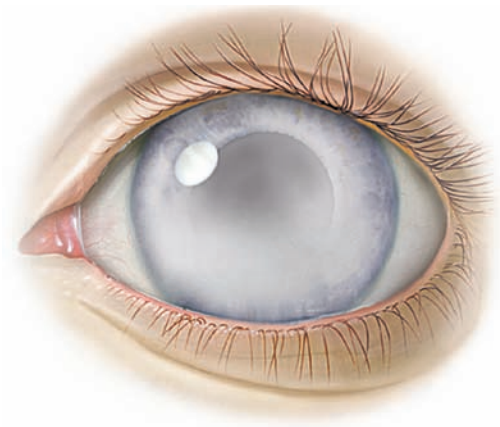


FIGURE 2. Anatomical Chart Company © 2014 Lippincott Williams & Wilkins. All rights reserved

Vignette B: Another infant is born the same night, also at 37 weeks' gestation. Labor was complicated by prolonged rupture of membranes and intermittent fetal tachycardia. A fetal scalp electrode was placed for closer monitoring. At birth, the infant is noted to be severely growth-restricted, weighing

1,700 g. He is admitted to the Neonatal Intensive Care Unit (NICU) for further care. On day of life 4, he becomes lethargic, febrile, and irritable. His skin examination now shows papulovesicular lesions. The ophthalmologic exam is abnormal. Figure 3 represents findings consistent with the infant in this vignette.

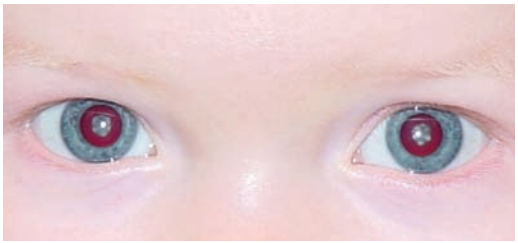


FIGURE 3. Courtesy of Brian Forbes, MD

1. Select the most likely diagnosis for the infant in vignette A and for the infant in vignette B, respectively:

   A. Congenital cataracts; congenital glaucoma
   B. Congenital glaucoma; congenital cataracts
   C. Congenital glaucoma; exophthalmos
   D. Retinoblastoma; congenital cataracts

2. From the list below, select a physical finding that may be associated with congenital glaucoma:

   A. Cleft lip
   B. Congenital heart disease
   C. Erythema toxicum neonatorum
   D. Port-wine stains involving the upper and lower eyelids

The infant in vignette B starts to seize, and the papulovesicular skin lesions spread throughout his mucous membranes and areas of friction.

3. From the list below, select the most likely infectious organism leading to the congenital ocular condition in the infant in vignette B:

   A. Herpes simplex virus (HSV)
   B. Rubella
   C. Varicella
   D. None of the above

The pediatric resident obtains an infectious disease history from the mother. In addition, he asks about a family history of congenital eye abnormalities.

4. Which of the following are most likely associated with congenital cataracts? (Note: there may be more than one correct answer.)

   A. An X-linked dominant inheritance pattern
   B. In utero radiation exposure
   C. Genetic syndromes, including Smith–Lemli–Opitz syndrome, Stickler syndrome, trisomy 21, and WAGR syndrome
   D. Phenylketonuria

CASE 3

Retinoblastoma

A term male infant is born by vaginal delivery to a 37-year-old gravida 1 para 0 woman with normal prenatal screens. The infant's Apgar scores are 8 and 9 at 1 and 5 minutes, respectively. The infant is discharged to home on day 3 of life with a normal physical examination. At a few months of life, he presents with an abnormal eye finding. Figure 1 is a photograph of his eyes.

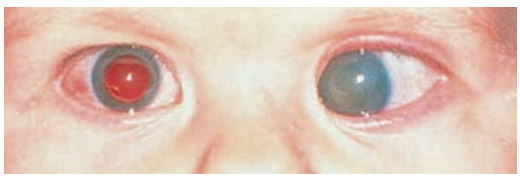


FIGURE 1. From Tasman W, Jaeger E. The Wills Eye Hospital Atlas of Clinical Ophthalmology. 2nd ed. Lippincott Williams & Wilkins; 2001. Figure 7.2

The pediatrician is concerned and obtains a more detailed family history. There is no reported family history of congenital abnormalities of the eye on either the maternal or paternal side.

1. Although not definitive, *based on the information from this vignette*, select the Inheritance Pattern (A or B) (Figure 2) that would be most representative of this infant's inheritance pattern and why:

   A. Inherited form (Pattern A); presented at birth
   B. Inherited form (Pattern A); presented after birth, no family history
   C. Sporadic form (Pattern B); presented at birth
   D. Sporadic form (Pattern B); presented after birth, no family history

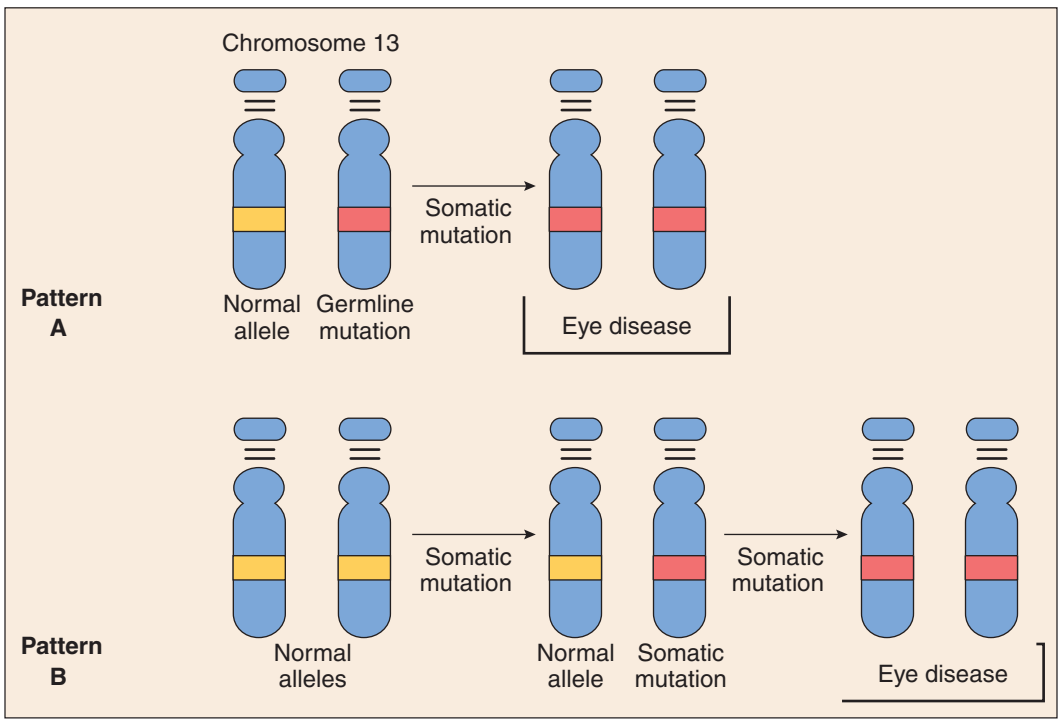


FIGURE 2. From Rubin E, Rubin R, Aaronson S. Neoplasia. In: Rubin E, Gorstein F, Rubin R, et al., eds. Rubin's Pathology: Clinicopathologic Foundations of Medicine. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins: 2005:171

CASE 4

Retinopathy of prematurity

The Resource Nurse in the Neonatal Intensive Care Unit (NICU) receives a phone call from the office of a Pediatric Ophthalmologist who is available to perform ophthalmologic examinations the following day. The nurse then asks the pediatric resident to prepare a list of infants who need initial eye examinations for evaluation for retinopathy of prematurity (ROP).

1. Which of the following neonates require an ophthalmologic examination to screen for ROP? More than one answer may be appropriate:

   A. Neonate born at 26 weeks' gestation
   B. Neonate born at 29 weeks' gestation with a birth weight of 1,000 g
   C. Neonate born at 36 weeks' gestation with a birth weight of 1,499 g
   D. Neonate born at 40 weeks' gestation with hypoxic–ischemic encephalopathy

The pediatric resident recognizes that the current American Academy of Pediatric guidelines for ROP screening recommend that ophthalmologic examinations be performed based on postmenstrual age (i.e., gestational age [GA] at birth plus chronologic age).

2. Match the following neonates (A–D) with the timing of their first ophthalmologic examination to screen for ROP (i–iii):

A. Neonate born at 25 weeks' gestation	i. 4 weeks of life
B. Neonate born at 29 weeks' gestation	ii. 6 weeks of life
C. Neonate born at 30 weeks' gestation with a birth weight of 1,200 g	iii. Does not meet criteria for a screening ophthalmologic examination for ROP
D. Neonate born at 33 weeks' gestation with significant cardiorespiratory compromise	

The neonate born at 29 weeks' gestation is now 2 months old and has ROP. He has "threshold disease."

3. Select the description that is an accurate statement about "threshold disease":

A. Defined by ROP in zone I with five contiguous clock hours accompanied by plus disease
B. Defined by ROP in zone II with eight total clock hours accompanied by plus disease
C. 50% of infants with threshold disease progress to stage 5
D. All of the above

CASE 5

Hearing screening

Vignette A: A term male infant is admitted to the Neonatal Intensive Care Unit (NICU) with lethargy and poor perfusion at 12 hours of life. He then has a seizure and is subsequently diagnosed with *Escherichia coli* (*E. coli*) sepsis and meningitis.

Vignette B: A preterm female infant with a postmenstrual age (i.e., birth gestational age plus chronologic age) of 36 weeks' gestation fails the otoacoustic (OAE) neonatal hearing screen.

Vignette C: A 37-week-gestation male infant is readmitted to the hospital with an indirect bilirubin of 25 mg/dL for severe hyperbilirubinemia and receives prolonged phototherapy.

Vignette D: A 30-week-gestation male is status-post surfactant administration for respiratory distress syndrome.

Vignette E: A 38-week-gestation female infant is born to a father with hearing loss.

1. Select the correct statement regarding the risks for hearing loss in the above vignettes (A–E):

A. All have increased risk for hearing loss
B. All but D have increased risk for hearing loss
C. B and E have increased risk for hearing loss
D. A, B, and C have increased risk for hearing loss

The infant in vignette B fails the OAE but passes the automated brainstem response (ABR) neonatal hearing screen.

2. Match the findings below (A–D) with the type of neonatal hearing screen (i–iii):

A. Acceptable for newborn screening	i. OAE
B. Measures acoustic feedback from the cochlea	ii. ABR
C. Measures EEG waves generated by the infant's auditory system in response to clicks	iii. Both OAE and ABR
D. Takes longer time to complete	

SECTION XIV

Answers

CASE 1 ANSWERS

1.	A	ii	False
	B	i	True
	C	ii	False
	D	i	True

Ophthalmologic prophylaxis is given to newborns to prevent ocular gonorrheal infection and chlamydial conjunctivitis. Single-dose tubes of ophthalmic ointment containing erythromycin or tetracycline may be used. Single-dose ampules of silver nitrate can be used to prevent ocular gonorrheal infections, but these are inadequate for prophylaxis of neonatal chlamydial conjunctivitis. Last, the risk of not providing prophylaxis can be devastating and may lead to blindness.

The photograph (Figure 1) depicts a child with ocular gonorrheal infection. Note the purulent material at the lid margins.

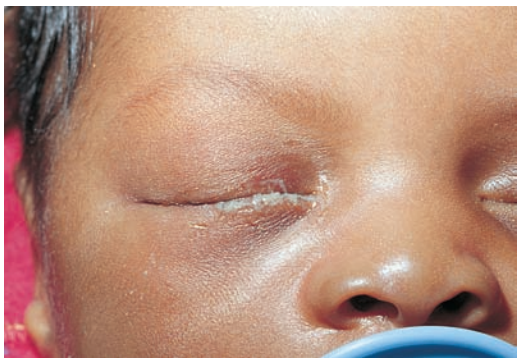


FIGURE 1. From Tasman W, Jaeger E. The Wills Eye Hospital Atlas of Clinical Ophthalmology. 2nd ed. Lippincott Williams & Wilkins; 2001. Figure 11.37

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that prophylaxis of ocular gonorrheal infection in a newborn should include silver nitrate solution in single-dose ampules or single-use tubes of ophthalmic ointment containing erythromycin or tetracycline
- Recognize that silver nitrate solution is not adequate prophylaxis for neonatal chlamydial conjunctivitis

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 2 ANSWERS

1. B. Congenital glaucoma; congenital cataracts

The infant in vignette A most likely has congenital glaucoma, with the first figure showing that the right cornea is larger than the left cornea. Congenital glaucoma is characterized by the classic triad:

- Epiphora (excessive lacrimation)
- Photophobia
- Blepharospam (involuntary eyelid closure/spasm)

Additional clinical findings include buphthalmos (enlargement of the globe) and eye rubbing.

Congenital glaucoma may be categorized into two groups:

- Primary—incidence of 1/10,000 births, autosomal recessive, males>female, presents at birth
- Secondary—may be caused by homocystinuria, congenital rubella syndrome, retinopathy of prematurity, and other syndromes (e.g., Sturge–Weber syndrome [30%], Stickler syndrome); presents after the neonatal period

The majority of cases of congenital glaucoma are caused by obstruction of aqueous humor flow, leading to increased intraocular pressure, breaks in the Descemet membrane, and subsequent corneal clouding. The increased intraocular pressure also causes damage to the optic nerve and enlargement of the cornea. Urgent consultation with an ophthalmologist is needed.

The infant in vignette B most likely has congenital cataracts, defined as a nonspecific reaction to a change in lens metabolism leading to opacification. Congenital cataracts can be diagnosed by the finding of leukocoria (white papillary reflex).

Congenital cataracts may be associated with:

- Congenital infections—HSV, varicella syndrome, rubella syndrome (50%), toxoplasmosis
- Metabolic disorders—galactosemia, galactokinase deficiency, mevalonic aciduria, some mucolipidoses, hypocalcemia, vitamin A or D deficiency
- Specific syndromes—Smith–Lemli–Opitz syndrome, Stickler syndrome, trisomy 21, WAGR syndrome (predisposition to *W*ilms tumor, *a*niridia, *g*enitourinary anomalies, and mental *r*etardation)
- In utero radiation exposure

Surgery is considered for cataracts >3mm in diameter or in the setting of strabismus or nystagmus. Urgent consultation with an ophthalmologist is needed as the timing of surgery may be critical.

2. D. Port-wine stains involving the upper and lower eyelids

Congenital glaucoma may be associated with Sturge–Weber syndrome, evident by port-wine stains on the newborn's face, possibly involving the upper and lower eyelids. None of the other choices (A–C) are associated with congenital glaucoma.

3. A. Herpes simplex virus (HSV)

The infant in this vignette may have congenital HSV with eye manifestations that include microphthalmia, chorioretinitis, *cataracts*, and visual loss. Congenital rubella and varicella may also lead to congenital cataracts, but the infant in this vignette has papulovesicular skin lesions that spread throughout his mucous membranes and areas of friction. The skin lesions in this vignette are consistent with HSV. The characteristic cicatricial skin lesions found in congenital varicella may be depressed and pigmented in a dermatomal distribution, while the classic cutaneous rash in rubella is described as a *blueberry muffin rash* (resulting from dermal extramedullary hematopoiesis).

4. B. In utero radiation exposure
C. Genetic syndromes, including Smith–Lemli–Opitz syndrome, Stickler syndrome, trisomy 21, and WAGR syndrome

Hereditary forms of congenital cataracts have an isolated autosomal dominant pattern in 25% of cases. Affected patients with an X-linked or autosomal recessive inheritance pattern have also been described. Congenital cataracts are associated with metabolic conditions, including galactosemia, galactokinase deficiency, mevalonic aciduria, mucolipidoses, hypocalcemia, and vitamin A or D deficiency. Phenylketonuria is not associated with congenital cataracts.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize the signs and symptoms of congenital glaucoma
- Know that congenital glaucoma may be associated with port-wine stains involving the upper and lower eyelids
- Know that congenital cataracts may be associated with congenital infections, inherited conditions, and radiation
- Understand the risk factors for the development of cataracts
- Understand that an abnormal pupil may be a sign of congenital cataract

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Ramasubramanian A, Johnston S. Neonatal eye disorders requiring ophthalmology consultation. *NeoReviews*. 2011;12:e216–e222.

CASE 3 ANSWERS

1. D. Sporadic form (Pattern B); presented after birth, no family history

The photograph of the dilated eyes of the infant in this vignette reveals a left eye with leukocoria (white pupillary reflex), esotropia, cloudy cornea, and unilateral involvement. These findings are consistent with retinoblastoma (RB). This disorder is the most common malignant ocular tumor of childhood, with an incidence of 1 in 20,000 to 1 in 30,000 births. In half of affected patients, leukocoria is the presenting sign; however, leukocoria can be missed in the undilated ophthalmic examination. Strabismus (esotropia or exotropia) is the first sign of RB in 25% of cases. Other less-common signs of RB are vitreous hemorrhage, hyphema, ocular inflammation, glaucoma, and proptosis.

There are two types of RB:

1. Sporadic (60%): no familial inheritance pattern, present after birth, unilateral involvement
2. Inherited (40%): autosomal dominant inheritance pattern, present at birth, may be difficult to detect by an undilated pupillary examination, bilateral involvement

Based on these distinctions, the infant in this vignette most likely has the sporadic form of RB. Infants with the inherited form of RB are at risk for secondary malignancies, including osteosarcoma and pinealoblastoma.

Figure 3 depicts the inheritance patterns of RB.

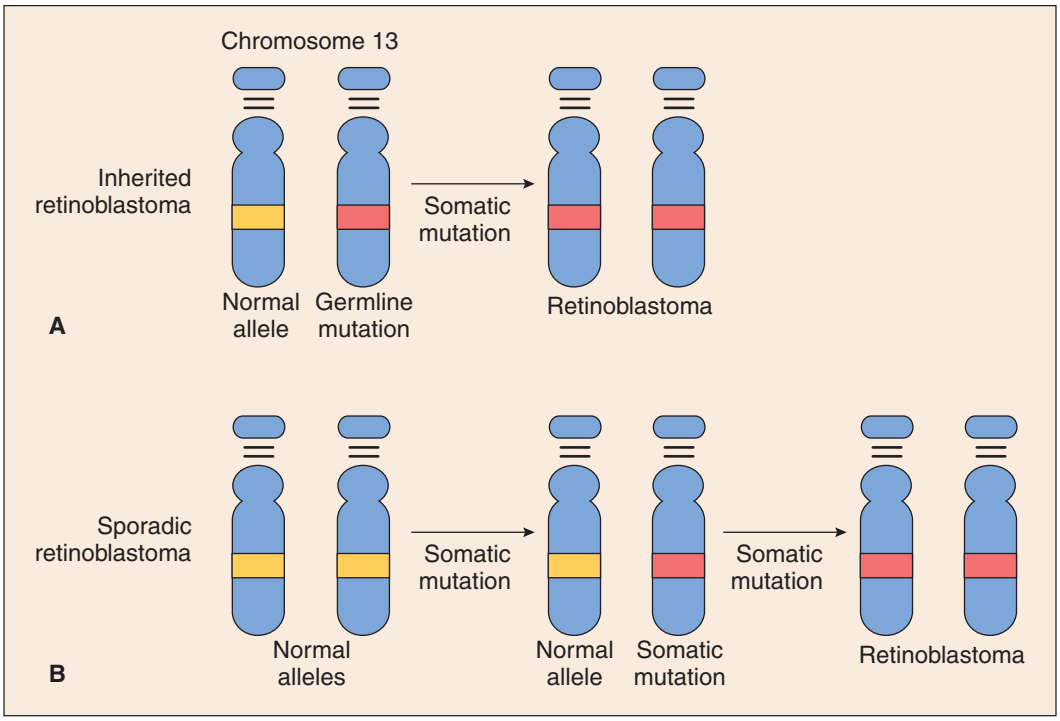


FIGURE 3. The "two-hit" origin of RB. (A) A child with an inherited form of RB is born with a germline mutation in one allele of the RB gene located on the long arm of chromosome 13. A second somatic mutation in the retina leads to inactivation of the normally functioning RB allele and subsequent development of RB. (B) In sporadic (noninherited) cases of RB, the child is born with two normal RB alleles. It requires two independent somatic mutations to inactivate RB gene function and allow for appearance of a neoplastic clone. (From Rubin E, Rubin R, Aaronson S. Neoplasia. In: Rubin E, Gorstein F, Rubin R, et al., eds. Rubin's Pathology: Clinicopathologic Foundations of Medicine. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:171)

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that retinoblastoma may be inherited
- Recognize the presenting signs of retinoblastoma

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Canzano J, Handa J. Utility of papillary dilation for detecting leukocoria in patients with retinoblastoma. *NeoReviews*. 1999;104(4):e44.

CASE 4 ANSWERS

1. A. Neonate born at 26 weeks' gestation
B. Neonate born at 29 weeks' gestation with a birth weight of 1,000 g
C. Neonate born at 36 weeks' gestation with a birth weight of 1,499 g

The risk and severity of ROP increase with decreasing GA. The American Academy of Pediatrics section on Ophthalmology published updated guidelines for ROP screening in the following populations:

- All infants born at 30 weeks' GA or less
- All infants with a birth weight ≤1,500 g, regardless of GA
- Selected infants with a birth weight between 1,500 g and 2,000 g or GA >30 weeks with an unstable clinical course at high risk for ROP

A term infant with hypoxic–ischemic encephalopathy is not at risk for ROP.

2. A ii 6 weeks of life
B i 4 weeks of life
C i 4 weeks of life
D i 4 weeks of life

Risk factors for ROP include:

- Low GA
- Low birth weight
- Prolonged oxygen exposure

Timing for the initial ophthalmologic examination to screen for ROP is based on postmenstrual age with preterm infants of lower GA taking a longer time to develop significant ROP. The American Academy of Pediatrics section on Ophthalmology published updated guidelines regarding timing for ROP screening, which is summarized in Table 1.

TABLE 1. Guidelines on Timing for ROP Screening

GA at Birth (Weeks)	Chronologic Age at First Examination (Weeks)
23	8
24	7
25	6
26	5
27–30	4
>30 with BW < 1,500 g or risk factors	4

Based on: American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2013;131:190

Follow-up after this initial screening examination is based on the infant's specific retinal findings, with more significant disease requiring closer follow-up.

3. D. All of the above

The classification of ROP includes:

- Zone—location where the abnormal retinal vessels end (I, II, III; from most posterior part of the retina to most anterior part of the retina)
- Clock hours—extent (See Figure 1 that illustrates clock hours)

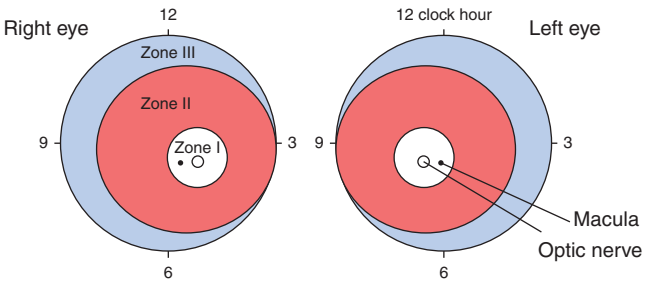


FIGURE 1. Modified from: American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2013;131:191

- Stage—severity of transition site of the vascularized and avascular retina
- Other descriptive terms of ROP disease are provided in Table 2.

TABLE 2. Other Descriptive Terms of ROP disease

"Plus disease"	• Findings of dilated, tortuous vessels that demonstrate advanced vascular disease • Always evident before retinal detachment • May also have iris vascular engorgement, papillary rigidity, vitreous haze or hemorrhage
"Threshold disease"	• ROP in zone I or II with at least five contiguous clock hours or eight total clock hours; must be accompanied by plus disease • 50% progress to stage 5
"Prethreshold disease"	• Any ROP in zone I that is not threshold • ROP in zone II, stage 2 with plus disease • ROP in zone II, stage 3 without plus disease • ROP in zone II, stage 3 and plus disease but inadequate clock hours to meet threshold disease

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:450

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the groups of infants who should be screened for retinopathy of prematurity
- Recognize that preterm infants who have been treated with oxygen require a first retinal examination at 4 to 6 weeks of age to identify those who have retinopathy of prematurity

SUGGESTED READINGS

American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2013;131:189–195.

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 5 ANSWERS

1. B. All but D have increased risk for hearing loss.

The etiology of hearing loss includes genetic (50%), acquired (25%), and unknown (25%) reasons. Table 1 summarizes the etiologies of hearing loss.

TABLE 1. Etiologies of Hearing Loss

Genetic	• 70% autosomal recessive; 15% autosomal dominant; 15% associated with other types of genetic transmission • Connexin 26 causes 20% to 30% of congenital hearing loss • Syndrome association includes Alport syndrome, Pierre Robin syndrome, Usher syndrome, Pendred syndrome, Waardenburg syndrome, Treacher Collins syndrome, CHARGE syndrome, Klippel–Feil sequence, trisomy 8, Stickler syndrome, trisomy 21
Acquired	• Develops secondary to injury to the developing auditory system in the intrapartum or perinatal period • Secondary to hypoxia, infections (particularly meningitis), ischemia, severe hyperbilirubinemia, complications of prematurity, ototoxic medications (e.g., gentamicin, vancomycin, furosemide) • Congenital cytomegalovirus infection is the most common cause of nonhereditary sensorineural hearing loss
Unknown	

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:183

The infants in the vignettes, who have meningitis, a failed OAE screen, an indirect hyperbilirubinemia over 20 mg/dL, and a family history of hearing loss, are all at increased risk for hearing loss.

2. A iii Both OAE and ABR
B i OAE
C ii ABR
D ii ABR

Table 2 provides a comparison of the two newborn hearing screen methods.

TABLE 2. Newborn Hearing Screening Methods

	ABR	Evoked Otoacoustic Emissions (EOAE)
Newborn Screening	• Acceptable for newborn screening • Threshold of ≥35 db suggests abnormal screen	• Acceptable for newborn screening • Threshold of ≥35 db suggests abnormal screen
Measurement	• Measures EEG waves generated by the infant's auditory system in response to clicks via three electrodes placed on infant's scalp	• Measures acoustic "feedback" from the cochlea through the ossicles to the tympanic membrane and ear canal after a click stimulus given to infant
Reliability	• After 34 weeks' postmenstrual age	
Advantages	• Automated version enables test to be done quickly and by trained staff • At present, preferred initial screening method for NICU graduate because of ability to detect auditory dyssynchrony	• Quicker than ABR
Disadvantages	• Longer time than EOAE	• More likely to be affected by debris or fluid in external and/or middle ear and thus, higher referral rates • Unable to detect some forms of sensorineural hearing loss

Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:184

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Understand the use of otoacoustic emission (OAE) devices for neonatal hearing screening

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
Cunningham M, Cox E. Hearing assessment in infants and children: Recommendations beyond neonatal screening. *Pediatrics*. 2003; 111:436–439.

SECTION XV

Dermatology

CASE 1

Pigmentary and vascular lesions

A term female infant is born by spontaneous vaginal delivery. The infant's Apgar scores are 8 and 9 at 1 and 5 minutes, respectively. The mother's prenatal course was uncomplicated, and her family history is unremarkable.

Figure 1 is a photograph of the infant shortly after birth.

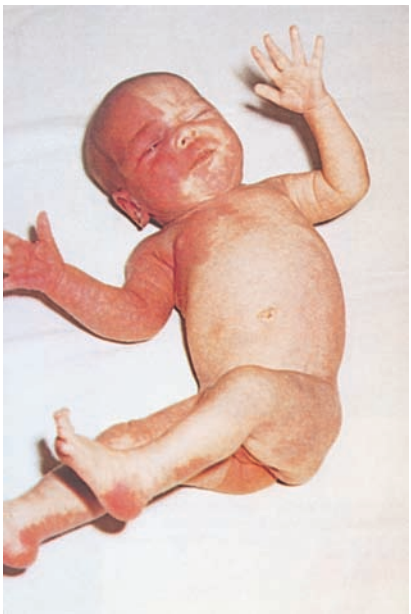


FIGURE 1. From O'Doherty N. Atlas of the Newborn. Philadelphia, PA: JB Lippincott; 1979

1. Select the term that describes this baby's vascular skin lesion:

   A. Infantile hemangioma
   B. Port-wine stain
   C. Salmon patch
   D. Venous malformation

This infant's pediatrician is considering the possible diagnosis of Sturge–Weber syndrome.

2. Refer to Figure 2. Select the dermatologic distribution that is most consistent with Sturge–Weber syndrome:

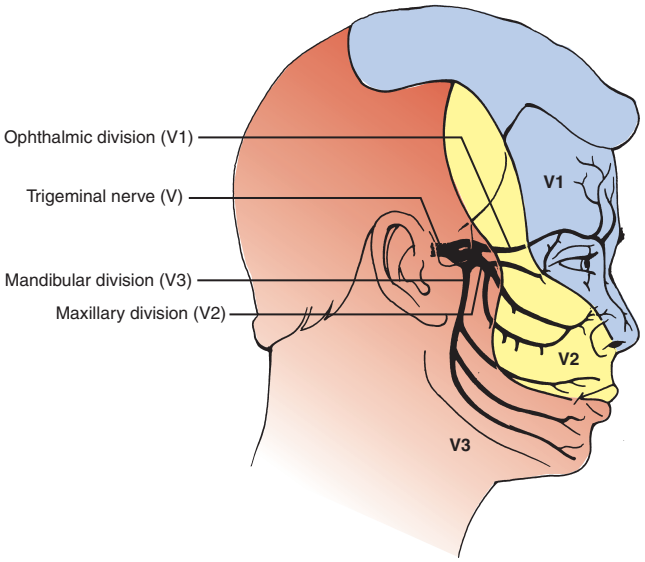


FIGURE 2. Smeltzer SC, Bare BG, Hinkle JL, et al. Brunner & Suddarth's Textbook of Medical Surgical Nursing. 11th ed. Lippincott Williams & Wilkins; 2008. Figure 64.7

   A. V1
   B. V2
   C. V3
   D. V2 and V3 but not V1

The infant in this vignette undergoes treatment for cosmetic palliation.

3. Select the treatment below that offers effective cosmetic palliation for this infant's skin lesion:

   A. Compression
   B. Excision
   C. Pulsed dye laser
   D. There are no current effective treatments for port-wine stains

CASE 2

Benign pustular lesions

A term male infant is born by uncomplicated vaginal delivery to a mother with normal prenatal screens. The mother has no history of sexually transmitted diseases. On day of life 2, the infant develops the most common pustular rash of infancy with lesions distributed over his trunk and proximal extremities. His palms and soles are not involved.

1. Select the photograph (see Figures 1 A–D) that best represents the rash of the infant in this vignette:

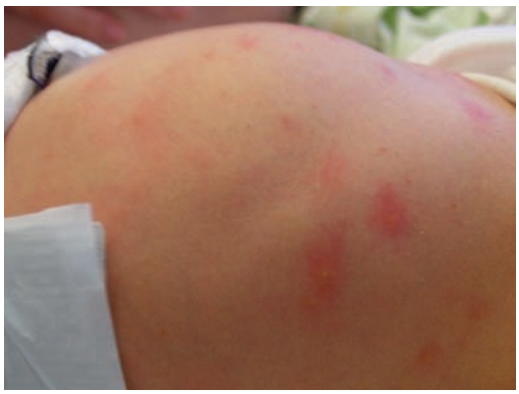


FIGURE 1A. Courtesy of Esther K. Chung, MD

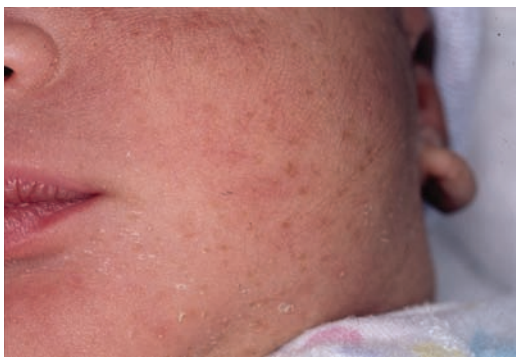


FIGURE 1B. Courtesy of Paul S. Matz, MD

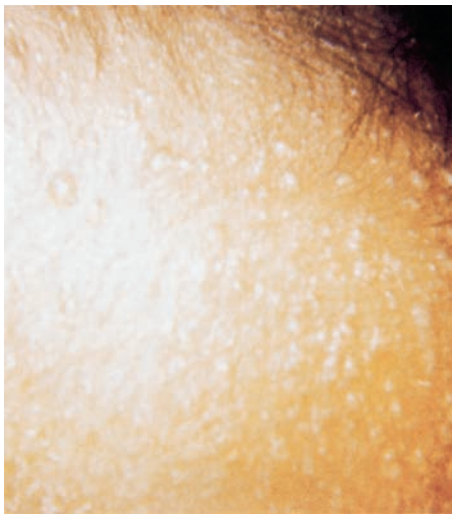


FIGURE 1C. Used with permission from: Fletcher MA. Physical Diagnosis in Neonatology. Philadelphia, PA: Lippincott Williams & Wilkins; 1998:124

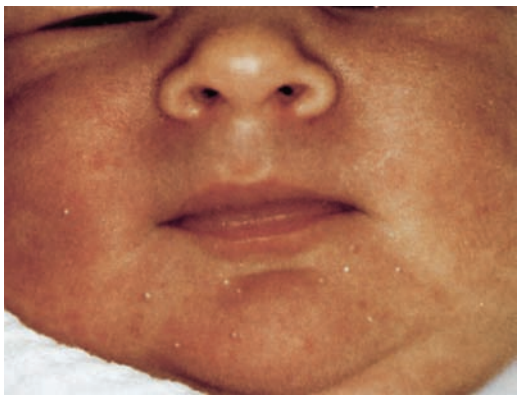


FIGURE 1D. Used with permission from: Fletcher MA. Physical Diagnosis in Neonatology. Philadelphia, PA: Lippincott Williams & Wilkins; 1998:124

2. Select the investigative study that can be used to confirm the diagnosis chosen above in question 1. More than one answer may be selected:

   A. If necessary, confirmation by presence of numerous eosinophils by Wright stain of the pustule
   B. If necessary, confirmation by presence of numerous neutrophils by Wright stain of the pustule
   C. If necessary, confirmation by presence of sparse squamous cells and lymphocytes by Wright stain of the lesion
   D. Usually diagnosed by clinical features

Another infant in the Newborn Nursery has a rash. She is born at term to a woman with normal prenatal screens. At birth, she is noted to have a rash as depicted in Figure 2.

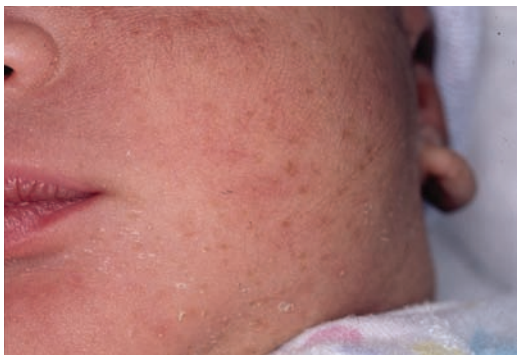


FIGURE 2. Courtesy of Paul S. Matz, MD

The pediatric resident rotating in the Newborn Nursery discusses the clinical differences between transient neonatal pustular melanosis and staphylococcal skin infection with the medical students.

3. Select True or False (i–ii) for the following statements (A–D) about staphylococcal skin infections and transient neonatal pustular melanosis:

   i. True
   ii. False

   A. Staphylococcal skin infections are characterized by pustules, erythematous papules, and honey-crusted lesions.
   B. Staphylococcal skin infections can be confirmed by gram-positive cocci in clusters and neutrophils on gram stain of vesicular fluid; transient neonatal pustular melanosis can be confirmed by the presence of numerous neutrophils by Wright stain or gram stain, but there is no presence of bacteria.
   C. Staphylococcal skin infections can be found in the diaper area and the axilla.
   D. Transient neonatal pustular melanosis is more common in dark-skinned infants.

SECTION XV

Answers

CASE 1 ANSWERS

1. B. Port-wine stain

Vascular anomalies are disorders of blood vessels with the majority being congenital and present at birth. This vascular skin lesion of the infant in this vignette is a port-wine stain (also known as nevus flammeus) with a sharp demarcation and unilateral distribution. This infant's vascular anomaly is not consistent with infantile hemangioma, salmon patch, or venous malformation. Table 1 provides a summary of port-wine stains.

TABLE 1. Port-Wine Stain

Etiology	• Also known as nevus flammeus • Secondary to capillary malformation, permanent developmental defect
Clinical	• Present at birth, remain the same size, may become darker in color during adolescence • Majority located in head or neck • 85% unilateral • Sharp demarcation, flat in infancy and pebbly surface later in life • May cause soft-tissue or bony overgrowth • Observed in patients with: o Sturge–Weber syndrome—unknown inheritance pattern; facial port-wine stain in first or second division of trigeminal nerve distribution; intellectual deficiency; seizures; hemiparesis contralateral to facial lesion; ipsilateral "tramline" intracortical calcifications, often with ipsilateral eye abnormalities such as glaucoma, optic atrophy, buphthalmos o Klippel–Trénaunay–Weber syndrome—superficial vascular abnormalities that are present at birth with underlying hypertrophy of bones or soft tissue, some with venous or lymphatic malformations o Beckwith–Weidemann syndrome and Cobb syndrome (cutaneous meningospinal angiomatosis)
Management	• Treat with pulsed dye laser, often yields very good outcome • Requires neurological and ophthalmologic evaluations if periorbital or forehead involvement exists

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:434

Figure 3 is of an infant with infantile hemangiomas located in the right upper abdominal and groin regions.

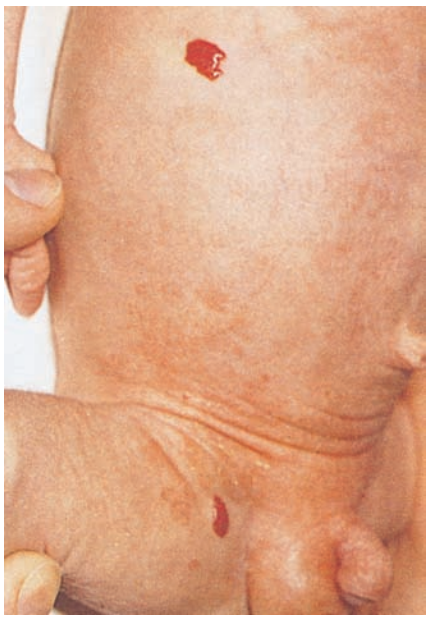


FIGURE 3. From O'Doherty N. Atlas of the Newborn. Philadelphia, PA: JB Lippincott; 1979

Table 2 describes the epidemiology, clinical findings, complications, and management of infantile hemangiomas.

TABLE 2. Infantile Hemangioma

Epidemiology	• 1% to 2% of all newborns • Females > males in term infants • Occurs more often in premature infants (male = female in this group)
Clinical	• 90% observed by second month of age • Face is most common location; initially appear as small telangiectasias or red macules that increase in size and color intensity • All increase during 6 to 8 months of age because of rapid endothelial cell proliferation • 40% to 50% disappear by 5 years of age • 60% to 75% disappear by 7 year of age

(continued)

TABLE 2. Infantile Hemangioma *(Continued)*

Complications	• Scarring may occur • May have multiple hemangiomas that involve internal organs • Found in infants with Kasabach–Merritt syndrome—multiple lesions that resemble hemangiomas or a single, large, rapidly growing hemangioma-like lesion; these lesions may lead to high-output heart failure, disseminated intravascular coagulation, and thrombocytopenia • Some hemangiomas may be associated with underlying abnormalities
Management	• If internal and/or systemic effects, treat with corticosteroids or propranolol; interferon if life-threatening (not first-line because of association with spastic diplegia)

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:433

Two infants with salmon patches (also known as nevi simplex or nevi flammeus simplex) are shown in Figures 4 and 5, and Table 3 provides an explanation of this skin lesion.

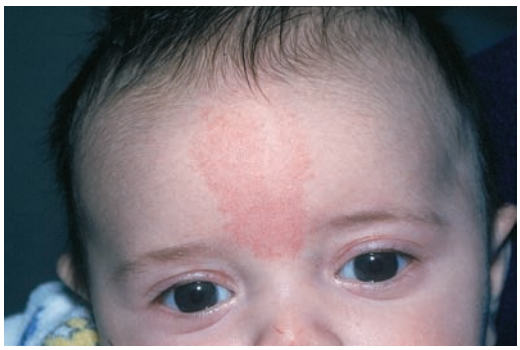


FIGURE 4. Used with permission from: Goodheart HP. Goodheart's Photoguide to Common Skin Disorders. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003:1

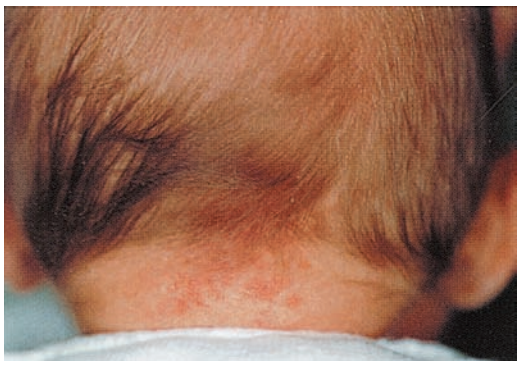


FIGURE 5. Fletcher M. Physical Diagnosis in Neonatology. Philadelphia, PA: Lippincott-Raven Publishers; 1998

TABLE 3. Salmon Patch

Etiology	• Also known as nevus flammeus simplex • Vascular malformation resulting from capillary malformation
Clinical	• Present in 40% to 50% of neonates • Usually on neck ("stork bite") or forehead ("angel kiss"), upper eyelids • Pink color, may darken with crying or activity • Irregular borders, blanches • Usually fade within first year of life
Management	• None needed

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:433

A venous malformation is described as a soft, compressible, purple tissue mass most often located over the head or neck region. Table 4 outlines the details of this vascular skin lesion.

TABLE 4. Venous Malformation

Etiology	• Compressible tissue mass, purple, soft
Clinical	• Often visible at birth • Located in head, neck (may cause significant airway compromise or distortion), or intestines (may cause gastrointestinal bleeding) • Does not change significantly over time • If multiple lesions, consider blue-rubber bleb syndrome • A large lesion can lead to pulmonary embolism • Stagnation within the lesion causes a localized intravascular coagulopathy
Evaluation and Management	• Low-flow Doppler ultrasonography, enhancement with contrast MRI • Treatment with compression, aspirin to prevent thromboses, sclerotherapy, excision

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:434

2. A. V1

Sturge–Weber syndrome is a leptomeningeal angiomatosis that is characterized by the classic triad:

- Facial port-wine stain in the ophthalmic (V1) distribution of the trigeminal nerve
- Eye abnormalities
- Leptomeningeal and brain abnormalities

The V2 and V3 distribution may also be seen in port-wine stains associated with Sturge–Weber syndrome, but patients with V2 and V3 *without V1* involvement are *not* at risk for Sturge–Weber syndrome.

Figure 6 is a brain MRI of an infant with Sturge–Weber syndrome. This infant has central nervous system (CNS) involvement with extensive enhancement of the leptomeningeal angioma in the right occipital lobe.

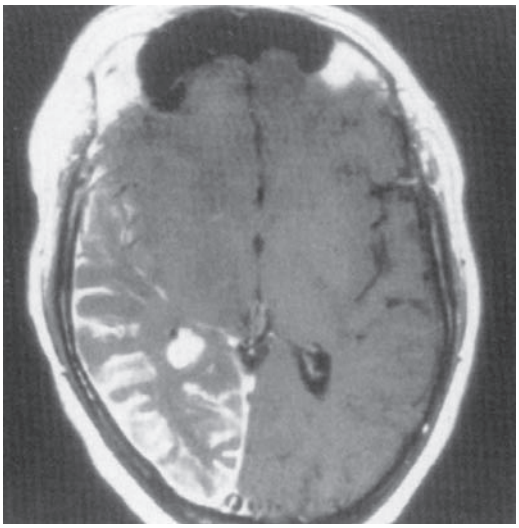


FIGURE 6. Eisenberg L. An Atlas of Differential Diagnosis. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. Original: Reprinted with permission from: Castillo M. *Neuroradiology Companion: Methods, Guidelines, and Imaging Fundamentals*. Philadelphia, PA: Lippincott-Raven; 1999

3. C. Pulsed dye laser

Tunable pulsed dye laser offers effective cosmetic palliation of port-wine stains. The other selections are incorrect in the management of port-wine stains. However, treatment of symptomatic venous malformation includes compression, aspirin, sclerotherapy, and excision.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that the distribution of a port-wine stain is important in determining whether it will be associated with a leptomeningeal angiomatosis (Sturge–Weber syndrome)
- Know that a tunable dye laser offers effective cosmetic palliation of port-wine stains

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

CASE 2 ANSWERS

1. A.

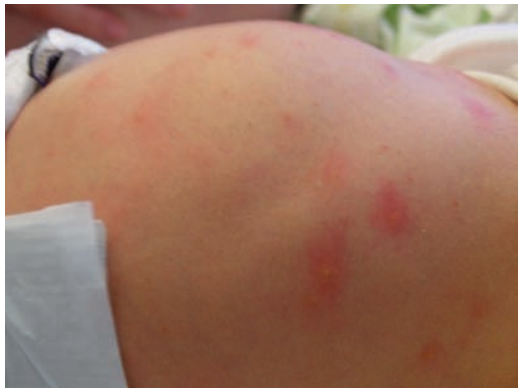


FIGURE 1A. Courtesy of Esther K. Chung, MD

All the options in this question are benign pustular lesions of infancy. The first figure describes an infant with erythema toxicum neonatorum, and Table 1 summarizes this lesion.

TABLE 1. Erythema Toxicum Neonatorum

Epidemiology	• Most common pustular rash, occurs in 30% to 70% of full-term infants • Less common with decreasing birth weight and gestational age
Etiology	• Unknown • May be related to immaturity of sebaceous gland and hair follicles
Clinical	• Benign, may be present at birth but typical onset second to third day of life (can occur up to 2–3 weeks of age) • 1- to 3-mm erythematous macules and papules that may evolve into pustules on an erythematous base • Isolated or clustered; fades over 5 to 7 days, may recur
Diagnosis	• Usually diagnosed by clinical features • If necessary, confirmation by presence of eosinophils by Wright-staining of the pustule • Minority of infants with peripheral eosinophilia

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:429

Option B shows an infant with transient neonatal pustular melanosis with the findings noted in Table 2.

TABLE 2. Transient Neonatal Pustular Melanosis

Epidemiology	• Greater in dark-skinned infants • Males = Females
Three Stages	• Small, noninflammatory pustules without erythematous base, usually present at birth • Ruptured pustules with scale • Hyperpigmented macules (can last up to 3 months)
Clinical	• Benign, usually present at birth (at any of the three stages) • Clusters under the chin, forehead, neck or lower back; occasionally involving cheeks, trunk, extremities, and palms/soles • Pustules are fragile and can be wiped off easily • No treatment
Diagnosis	• Usually diagnosed by clinical features • If necessary, confirmation by presence of numerous neutrophils by Wright-staining of the pustule

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:429–430

The infant in option C has miliaria; characteristics of this lesion are described in Table 3.

TABLE 3. Miliaria

Etiology	• Secondary to obstruction of sweat glands, leading to sweat retention
Clinical	• Rarely present at birth • Intertriginous areas, face, scalp, and trunk • Worse in humid environment, improves when placed in a cooler environment
Types	• Miliaria crystalline—superficial, thin-walled, 1- to 2-mm vesicles, no inflammation • Miliaria rubra—obstructed sweat leaks into the debris and causes a local inflammatory reaction; small groups of red papules and pustules; known as "prickly heat" • Miliaria pustulosa—results from localized inflammation; pustules with an erythematous base • Miliaria profunda—rare, deeper blockage; nonerythematous pustules; skin-colored
Diagnosis	• Usually diagnosed by clinical features • If necessary, confirmation by presence of sparse squamous cells and lymphocytes by Wright-staining of the vesicle

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:430

The image in option D reveals an infant with milia, and Table 4 summarizes the characteristics of this lesion.

TABLE 4. Milia

Etiology	• Secondary to small epidermal inclusion cysts with retention of keratin and sebaceous material in the follicles
Clinical	• Pearly nonerythematous yellow or white papules over face, shin, and forehead • Cannot be removed easily • Resolve by 1 to 3 months of age (usually within the first few weeks of life)
Pearls	• Large (usually single) milia located on genitalia, areola, mouth (= Epstein pearls)

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:430

2. A. If necessary, confirmation by presence of numerous eosinophils by Wright stain of the pustule
D. Usually diagnosed by clinical features

Erythema toxicum is typically diagnosed by clinical exam. If necessary, confirmation using Wright staining is possible with the finding of eosinophils within the pustule. Options B and C are incorrect, as they represent transient neonatal pustular melanosis and miliaria, respectively.

3. A i
B i
C i
D i

All of the statements are true.

Staphylococcal skin infections are not benign, while transient neonatal pustular melanosis is benign. At times, these diagnoses may have similar skin findings. However, infants with staphylococcal infections can be distinguished by the presence of bacteria on gram stain or culture. Figure 3 shows gram-positive cocci in clusters, representing *Staphylococcus*.

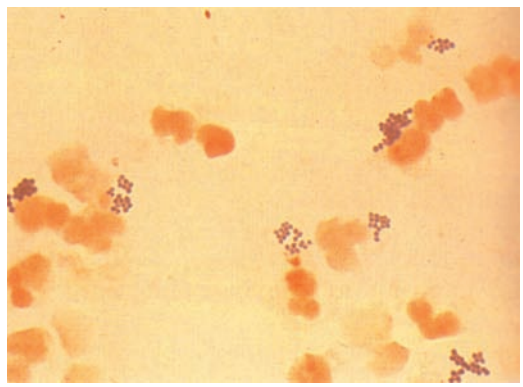


FIGURE 3. From Koneman EW et al. Diagnostic Microbiology. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins; 1997:color plate 11.1C

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Recognize erythema toxicum
- Know that the lesions of erythema toxicum are filled with eosinophils
- Recognize the lesions of transient neonatal pustular melanosis
- Know that a Gram stain will help distinguish between transient neonatal pustular melanosis and staphylococcal pustules

SUGGESTED READINGS

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

Cloherty J, Eichenwald EC, Hansen A, et al., eds. *Manual of Neonatal Care*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

SECTION XVI

Thermoregulation

CASE 1

Temperature control

A 600-g male infant is born at 25 weeks' gestation by vaginal delivery after unstoppable preterm labor. He cries immediately and appears vigorous. The neonatal team is particularly focused on preventing hypothermia. Thus, he is placed on a radiant warmer and his body is wrapped in a plastic material. He requires intubation at 2 minutes of life because of moderate respiratory distress and intermittent apnea.

1. Select the reason(s) why newborns are more likely to have heat loss:

   A. Decreased epidermal and dermal thickness leading to increased radiant and conductive heat loss
   B. Immature nervous system leading to decreased response to cooling
   C. Increased surface area to body weight ratio (three times greater than adult ratio)
   D. Minimal subcutaneous fat causing decreased response to cooling

After the parents meet their baby, the team places him in a transport isolette. Upon admission to the Neonatal Intensive Care Unit (NICU), he is again placed on a radiant warmer.

2. Match the statements (A–E) with the type of warmer (i–iii):

   i. Convective incubator
   ii. Radiant warmer
   iii. Both

   A. Higher evaporative heat loss because of insensible water loss with greater skin–air temperature differences
   B. Leads to a large difference in skin temperature between exposed and unexposed areas
   C. Servocontrol of forced air by using skin or air temperature as a temperature control
   D. Servocontrol of skin temperature by using infrared radiant warming
   E. Still has evaporative heat loss

The pediatric resident leads a discussion with the medical students about four types of heat loss in the neonate.

3. Match the type of heat loss (A–D) with the appropriate row (i–iv) as shown in Table 1:

   A. Conductive
   B. Convective
   C. Evaporative
   D. Radiant

Another infant is admitted to the NICU soon after the 25-week-gestational-age infant admission. This new admission is a term female born to a mother with diabetes mellitus. The baby is large for gestational age (LGA) who presents to the NICU with hypoglycemia after her first bath.

4. Select all of the potential etiologies of this infant's hypoglycemia:

   A. Cold stress
   B. Infant of a diabetic mother (IDM)
   C. LGA
   D. Sepsis

TABLE 1. Match Type of Heat Loss

	Definition	Examples	Prevention
i	Transfer of heat from neonate to a contacting solid object	Cold blanket or mattress	Place infant on warm blanket or mattress
ii	Transfer of heat from neonate to surrounding gas The heated air expands and then travels upwards	Cool air Air currents will lead to more turbulence and displacement of heated gas ~40% to 50% of nonevaporative neonatal heat loss	Limit air currents, plastic cover May require environmental temperature to be greater than skin temperature to maintain a normal core temperature
iii	Transfer of heat from skin and respiratory tract to a drier environment	Prematurity leading to immature stratum corneum and poor epidermal barrier function Younger postnatal age High velocity of surrounding air	Plastic cover Increase incubator humidity
iv	Transfer of heat between neonate and surface that is *not* in contact with neonate Heat loss is in the form of electromagnetic waves	Incubator walls, windows, chairs, light bulbs, other people	Protect incubator walls from excess cooling Double-walled isolette Plastic cover

SECTION XVI

Answers

CASE 1 ANSWERS

1. A, B, C, D

All of the statements are correct.

Regulation of body temperature is a critical component in caring for newborns. Preterm infants have an even greater risk of heat loss compared to full-term infants. Even back in 1907, a French obstetrician, Pierre Budin, noted that without the use of heating devices, infants weighing <1,500 g have a mortality approaching 100%, especially if their core temperature dropped below 89.6°F (32°C). Even in the present day, the EPICure study of extremely-low-birth-weight (<1,000 g) infants in the United Kingdom identified hypothermia as an independent risk factor for mortality. The risk factors for hypothermia (as stated in A–D) are exacerbated by prematurity and low birth weight.

2.

A	ii	Radiant warmer
B	ii	Radiant warmer
C	i	Convective incubator
D	ii	Radiant warmer
E	iii	Both

Table 2 shows the features of convective incubators and radiant warmers.

TABLE 2. Incubators

Convective incubators	• Servocontrol of forced air by using skin or air temperature as a temperature control • If infant placed inside, still has a large amount of radiant heat loss and some evaporative heat loss • If *increase humidity* or swaddle infant, will *decrease evaporative* heat loss • If *double-walled* incubator instead of single-walled incubator, will *decrease radiant* heat loss • If add *plastic heat shields*, will *decrease radiant* heat loss • If utilize *portholes* during care of neonate, will *decrease convective* heat loss • If use *rubber foam mattress*, will *decrease conductive* heat loss
Radiant warmers	• Servocontrol of skin temperature by using infrared radiant warming • Leads to a large difference in skin temperature between exposed and unexposed areas • If infant placed inside, still has significant convective and evaporative heat losses • Higher evaporative heat loss compared to convective incubators due to insensible water loss with greater skin–air temperature differences and lower relative humidity compared with convective incubators • If cover with *plastic film*, will decrease convective and evaporative heat losses • Heat loss in the delivery room can be reduced by the use of a *radiant warmer*, drying, and swaddling

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:425

3.

A	i	Conductive
B	ii	Convective
C	iii	Evaporative
D	iv	Radiant

TABLE 3. Matched Types of Neonatal Heat Loss

Types of Neonatal Heat Loss	Definition	Examples	Prevention
Conductive	Transfer of heat from neonate to a contacting solid object	Cold blanket or mattress	Place infant on warm blanket or mattress
Convective	Transfer of heat from neonate to surrounding gas The heated air expands and then travels upwards	Cool air Air currents will lead to more turbulence and displacement of heated gas ~40% to 50% of nonevaporative neonatal heat loss	Limit air currents, plastic cover May require environmental temperature to be greater than skin temperature to maintain a normal core temperature
Evaporative	Transfer of heat from skin and respiratory tract to a drier environment	Prematurity leading to immature stratum corneum and poor epidermal barrier function Younger postnatal age High velocity of surrounding air	Plastic cover Increase incubator humidity
Radiant	Transfer of heat between neonate and surface that is *not* in contact with neonate Heat loss is in the form of electromagnetic waves	Incubator walls, windows, chairs, light bulbs, other people	Protect incubator walls from excess cooling Double-walled isolette Plastic cover

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4. A, B, C, D

All of the selections are possible etiologies for this infant's hypoglycemia. A baby can develop cold stress after a bath and rapidly deplete essential stores of fat and glycogen. The selections IDM and LGA are both risk factors for hypoglycemia as a result of hyperinsulinism. In addition to infants with IDM and/or LGA, hyperinsulinism can also develop in neonates with perinatal depression, Beckwith–Wiedemann syndrome, pancreatic islet adenoma, and erythroblastosis fetalis. Sepsis is another risk factor for hypoglycemia as a result of increased metabolic demand.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that a newborn is prone to heat loss because of a high surface area-to-body mass ratio
- Know that heat loss in the delivery room can be reduced by the use of a radiant warmer, drying, and swaddling
- Recognize the hazards and benefits associated with the use of radiant warmers for neonates
- Know that a newborn who is cold stressed rapidly depletes essential stores of fat and glycogen

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SECTION XVII

Pharmacology

CASE 1

Aminoglycosides

A 29-week-gestation male infant is born by vaginal delivery to a 32-year-old gravida 1 para 0 woman with normal prenatal screens. The pregnancy was complicated by unstoppable preterm labor and spontaneous rupture of membranes. The infant is critically ill with severe respiratory distress requiring high ventilator settings and inotropic support for hypotension. His initial complete blood count (CBC) is as follows:

- White blood cell count = $3.2 \times 10^3/\mu L$ ($3.2 \times 10^9/L$)
- Differential = 57% neutrophils, 32% bands
- Hematocrit = 51% (0.51)
- Platelets = $87 \times 10^3/\mu L$ ($87 \times 10^9/L$)

1. Select the most appropriate choice of antibiotic coverage:

   A. Ampicillin and gentamicin
   B. Ceftriaxone
   C. Clindamycin and cefotaxime
   D. Vancomycin and fluconazole

A urine culture from the infant's mother, which had been collected upon this admission, is positive for gram-negative rods within 12 hours. The Microbiology Laboratory contacts the pediatric resident when the infant is 18 hours old because the infant's blood culture is also growing gram-negative rods. The pediatric resident orders gentamicin levels to be drawn 30 minutes before and 30 minutes after the infant's third gentamicin dose.

The father of the infant asks why gentamicin levels need to be ordered. The attending neonatologist discusses the toxicities of aminoglycosides and why it is important to monitor gentamicin levels.

2. Select the major toxicity (toxicities) of aminoglycoside use in neonates. More than one answer may be selected:

   A. Auditory/vestibular damage
   B. Cardiotoxicity
   C. Nephrotoxicity
   D. Reproductive organ toxicity

The infant's laboratory results are as follows:

- Gentamicin peak: 14.7 mg/L
- Gentamicin trough: 1 mg/L
- Final blood culture: *Escherichia coli* (*E. coli*)

3. Select the appropriate management for this infant's gentamicin dosing:

   A. Change the interval of dosing from every 24 hours to every 18 hours
   B. Change the interval of dosing from every 24 hours to every 36 hours
   C. Decrease the gentamicin dose by 10%
   D. Increase the gentamicin dose by 10%

The pediatric resident decides to review the pharmacokinetics of various medications.

4. Of the following, the term that best describes a drug that has an elimination rate directly proportional to the serum drug concentration and has a half-life that is independent of drug dosage is:

   A. First-order kinetics
   B. Zero-order kinetics
   C. Two compartment model
   D. One compartment model

CASE 2

β-Lactam antibiotics

Four infants in the Neonatal Intensive Care Unit (NICU) are being treated for different infections, as described below:

i. 32-week-gestation female 6-hour-old newborn with Group B *Streptococcus* (GBS) sepsis
ii. 24-week-gestation male 6-hour-old newborn with gram-negative sepsis
iii. Former 25-week-gestation male infant now at 30 weeks' postmenstrual age with a methicillin-resistant *Staphylococcus aureus* (MRSA) central-line infection
iv. Former 23-week-gestation male infant now at 29 weeks' postmenstrual age requiring mechanical ventilation with a tracheal culture positive for *Pseudomonas*

1. Although many infections may benefit from double coverage for synergism (i.e., not just a single antibiotic agent), match the above vignettes (i–iv) with the single most appropriate antibiotic selection below. Each antibiotic can only be used once:

   A. Ampicillin ___
   B. Ceftazidime ___
   C. Gentamicin ___
   D. Vancomycin ___

2. Match the mechanisms of action (i–iv) with the antibiotic types listed below (A–D):

   i. Binds to 30S subunit of bacterial ribosomes and inhibits protein synthesis
   ii. Binds to penicillin-binding proteins and inhibits bacterial cell wall synthesis
   iii. Inhibits bactericidal enzymes necessary for the synthesis of peptidoglycan (important component of cell wall)
   iv. Inhibits peptidoglycan synthesis in bacteria cell wall

   A. Aminoglycoside family
   B. Cephalosporin family
   C. Penicillin family
   D. Vancomycin

Vignette ii in question 1 describes an infant born at 24 weeks' gestation with *Escherichia coli* sepsis. When the infant is able to tolerate a lumbar puncture, the pediatric resident describes the procedure to the parents and obtains consent. The infant's cerebrospinal fluid (CSF) is grossly abnormal with >300 white blood cells per millimeter and a low glucose value, indicative of meningitis (presumably *E. coli* meningitis). Because of the potential for gentamicin-resistant *E. coli* organisms, the NICU fellow discusses broadening the antibiotic coverage until antibiotic sensitivities are reported.

3. Select the most appropriate additional antibiotic to treat this infant's meningitis:

   A. First-generation cephalosporin
   B. Second-generation cephalosporin
   C. Third-generation cephalosporin
   D. None of the above

CASE 3

Diuretics

Twins born at 24 weeks' gestation are approaching their day of discharge from the Neonatal Intensive Care Unit (NICU). They are now ~4 months old and are at term postmenstrual age. They both have chronic lung disease.

- Twin 1 is receiving furosemide.
- Twin 2 is receiving acetazolamide.

1. Fill in the mode of action (i–iv) corresponding to the drugs listed (A–D):

   i. Blocks active chloride transport
   ii. Carbonic anhydrase inhibitor that inhibits sodium bicarbonate ($NaHCO_3$) reabsorption
   iii. Competitive antagonist of aldosterone
   iv. Inhibits sodium chloride (NaCl) reabsorption

   A. Acetazolamide (Diamox)
   B. Chlorothiazide (Diuril)
   C. Furosemide (Lasix)
   D. Spironolactone (Aldactone)

2. Select the drug below that can lead to a hyperchloremic metabolic acidosis:

   A. Acetazolamide (Diamox)
   B. Chlorothiazide (Diuril)
   C. Furosemide (Lasix)
   D. Spironolactone (Aldactone)

Twin 1 is also receiving supplements due to electrolyte abnormalities associated with furosemide.

3. Select the oral supplements commonly needed when an infant is receiving chronic furosemide. Only one answer may be selected:

   A. Bicarbonate
   B. Calcium
   C. NaCl and potassium chloride
   D. Magnesium

Ototoxicity and nephrotoxicity are potential adverse effects of chronic furosemide administration.

4. Select additional possible long-term adverse effects of chronic furosemide therapy. More than one answer may be selected:

   A. Cardiotoxicity
   B. Liver toxicity
   C. Metabolic bone disease
   D. Renal calcifications

SECTION XVII

Answers

CASE 1 ANSWERS

1. A. Ampicillin and gentamicin

For a newborn with suspected sepsis, the appropriate antibiotic regimen should provide broad coverage of gram-negative and gram-positive organisms that are present in the maternal genital tract. These organisms include the following:

- Group B *Streptococcus* (GBS)
- *Escherichia coli (E. coli)*
- *Listeria monocytogenes*
- Nontypeable *Haemophilis influenza*
- *Enterococcus*

Because *L. monocytogenes* is a possible cause of neonatal sepsis, coverage with ampicillin is important. Administration of gentamicin is important to provide coverage for gram-negative enteric bacilli and many staphylococcal species. Gentamicin also provides synergy with ampicillin for *Listeria*, GBS, and *Enterococcus* organisms.

2. A. Auditory/vestibular toxicity
C. Nephrotoxicity

At toxic levels, gentamicin may lead to:

- Auditory/vestibular toxicity
- Nephrotoxicity
- Neuromuscular blockage (worse if hypermagnesemia)

Options B and D are incorrect as cardiotoxicity and reproductive organ toxicity are not associated with excessive amounts of gentamicin.

3. C. Decrease the gentamicin dose by 10%

The infant in this vignette has a gentamicin peak that is too high and a gentamicin trough that is within normal limits. Therefore, the infant's dose needs to be decreased by 10%, and the gentamicin levels need to be rechecked when the drug reaches steady state (estimated to be around the time of the third new dose).

Options A, B, and D are incorrect. Decreasing the interval of dosing from every 24 hours to every 18 hours would be appropriate if the gentamicin trough was low. Increasing the interval of dosing from every 24 hours to every 36 hours would be appropriate if the gentamicin trough was high. Increasing the dose by 10% would be correct if the peak was low. Gentamicin provides coverage for aerobic gram-negative infections, including *E. coli*. However, because of recent concerns about gentamicin-resistant organisms, some clinicians would also consider adding another antibiotic to provide additional gram-negative coverage, particularly if the infant remains ill. The results of the antibiotic sensitivities of this infant's *E. coli* organism will then help determine the most appropriate antibiotic coverage.

4. A. First-order kinetics

Medications can have zero- or first-order kinetics. These pharmacokinetics are described in Table 1.

TABLE 1. Pharmacokinetics Characteristics

Pharmacokinetics	Characteristics
Zero-order kinetics	• Excrete a constant amount of drug per unit time regardless of the serum drug concentration • There is a linear decrease of serum concentration over time • The half-life is dependent on drug dosage (larger doses are cleared more slowly, so they have longer half-lives) • The fraction of the drug that is eliminated (i.e., elimination rate constant) is not constant
First-order kinetics	• Excrete a certain percentage of drug per unit time so that the rate of drug elimination is directly proportional to the serum drug concentration • There is an exponential decrease of serum concentration over time • The half-life is independent of drug dosage • The fraction of drug that is eliminated (i.e., elimination rate) is constant • Most drugs have this type of kinetics, including gentamicin phenobarbital and theophylline

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:458–459

Drug equilibration into the tissues also plays an important role in pharmacokinetics and can be described as one or two compartment models. The comparisons of these models are described in Table 2.

TABLE 2. Model Compartment Comparisons

Type of Compartment Model	Characteristics
One-compartment model	• Assumes that a drug distributes equally to all areas of the body • Assumes that a drug rapidly equilibrates with the peripheral tissues • Assumes first-order kinetics (linear if log drug concentration plotted vs. time) • Aminoglycosides rapidly equilibrate with tissues so that the one-compartment model can be used
Two-compartment model	• Assumes that a drug initially rapidly equilibrates with the central compartment and then more slowly equilibrates with the peripheral compartment • Vancomycin slowly equilibrates with tissues so that the two-compartment model can be used • Biphasic line if log drug concentration is plotted over time with the initial phase = distribution phase (half-life = t½) and the second phase = elimination phase (half-life = βt½)

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:460

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the appropriate use of aminoglycosides (i.e., serious aerobic gram-negative infections)
- Be aware of the major toxicity of aminoglycosides (auditory/vestibular damage, nephrotoxicity)
- Know how to modify aminoglycoside doses when peak or trough concentrations are too high

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 2 ANSWERS

1. A i
B iv
C ii
D iii

Ampicillin is a β-lactam antibiotic that covers most gram-positive organisms except for *Staphylococcus*. It is often used in the treatment for GBS and *Listeria* infections. Penicillin G covers the majority of *Streptococcus* (pneumococcus coverage is variable), *Treponema pallidum*, *Bacteroides* (except *B. fragilis*), *Neisseria meningitides*, and some *Staphylococcus* infections. A third-generation cephalosporin, such as ceftazidime, is an ideal antibiotic choice for *Pseudomonas* (in combination with an aminoglycoside). Gentamicin is an aminoglycoside that provides coverage for most gram-negative enteric bacilli. Third-generation cephalosporins, such as cefotaxime and ceftriaxone, also provide excellent coverage for gram-negative organisms. Vancomycin is used to treat coagulase-negative *Staphylococcus* and MRSA.

2. A i
B ii
C iii
D iv

Table 1 depicts the mechanism of action for bactericidal and bacteriostatic medications.

TABLE 1. Mechanism of Action for Bactericidal and Bacteriostatic Medications

Mechanism of Action	Antibiotics
Bactericidal Completely destroy bacteria (Ideal for endocarditis, meningitis, severe *Staph* and gram-negative infection)	• Penicillins—inhibit bacterial enzymes (penicillin-binding proteins) necessary for the synthesis of peptidoglycan (important component of cell wall) • Cephalosporins—bind to penicillin-binding proteins and inhibit bacterial cell wall synthesis • Aminoglycosides—bind to 30S subunit of bacterial ribosomes and inhibit protein synthesis • Vancomycin—inhibits peptidoglycan synthesis in bacteria cell wall (note: bacteriostatic against *Enterococcus*) • Quinolones—inhibit DNA gyrase
Bacteriostatic Inhibit growth and reproduction of bacteria	• Erythromycin—binds reversibly to the 50S subunit of bacterial ribosomes and inhibit protein synthesis • Clindamycin • Chloramphenicol • Tetracycline (at therapeutic concentrations)—bind reversibly to 30S subunit of bacterial ribosome • Sulfonamides—inhibit folate synthesis

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β-Lactam antibiotics are a broad class of antibiotics with a β-lactam ring in their molecular structure. Examples of β-lactam antibiotics include penicillin and its derivatives, cephalosporins, monobactams (e.g., aztreonam), and carbapenems (e.g., imipenem and meropenem).

3. C. Third-generation cephalosporin

A third-generation cephalosporin has better penetration into the CSF than a first- or second-generation cephalosporin. Table 2 describes the differences between first-, second-, and third-generation cephalosporins.

TABLE 2. Differences Between First-, Second-, and Third-Generation Cephalosporins

Medication	Organism Coverage	Comments
Cephalosporin (β-lactam) (first generation)	• Most gram-positive cocci, *E. coli*, *Klebsiella* and *Proteus* • *None* of the cephalosporins cover *Enterococcus* or *Listeria*	• e.g., cephalexin, cefazolin • Treatment of cellulitis • Poor CSF penetration
Cephalosporin (β-lactam) (second generation)	• More gram-negative coverage compared with first-generation cephalosporin	• e.g., cefoxitin, cefuroxime, cefaclor, cefotetan
Cephalosporin (β-lactam) (third generation)	• Excellent gram-negative coverage • Cefotaxime and ceftriaxone: GBS, many gram-negative enteric bacilli; gonorrhea and *Salmonella*; some species of *Citrobacter*; no coverage for *Staph* • Ceftazidime: ideal for *Pseudomonas* (in combination with aminoglycoside)	• e.g., cefotaxime, ceftriaxone and ceftazidime • Good CSF penetration • Cefotaxime: routine use can result in resistant gram-negative organisms • Ceftriaxone: possible increased risk of bilirubin displacement from albumin • Ceftazidime: may yield false-positive Coombs reaction

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In this case, a third-generation cephalosporin is the most appropriate selection as it has good CSF penetration with excellent gram-negative coverage. Cephalosporins have a low toxicity profile when compared to the toxicity profile of Gentamicin without the need to monitor renal function and drug concentrations. Importantly, however, widespread use of cephalosporins can lead to antibiotic resistance and potential for development of Clostridium difficile enterocolitis in older children and adults.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the appropriate use of ampicillin
- Know the appropriate use of penicillinase-resistant penicillins
- Know the mechanism of action of penicillin and other beta-lactam antibiotics
- Know that third-generation cephalosporins provide a broad spectrum of coverage and have excellent penetration into the cerebrospinal fluid
- Understand the advantages of third-generation cephalosporins over aminoglycosides (e.g., greater activity in deep-tissue infections, less toxicity, avoidance of need to monitor renal function and drug concentrations)
- Know the appropriate use of second-generation cephalosporins
- Know that first-generation cephalosporins do not penetrate well into the cerebrospinal fluid
- Recognize the problems that have resulted from the widespread use of broad-spectrum cephalosporins (e.g., antibiotic resistance, Clostridium difficile enterocolitis)

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

CASE 3 ANSWERS

1. A ii
B iv
C i
D iii

Table 1 describes the mode of action, site of action, and side effects of four types of diuretics.

TABLE 1. Diuretics

Drug	Mode of Action	Site of Action	Side Effects
Acetazolamide (Diamox)	• Carbonic anhydrase inhibitor • Inhibits $NaHCO_3$ reabsorption	Proximal tubule	• Mild hyperchloremic metabolic acidosis • Hypokalemia • Other uses: can decrease progression of hydrocephalus by decreasing CSF production, anticonvulsant if refractory seizures, glaucoma
Furosemide (Lasix) Bumetanide (Bumex) 40 × more potent	• Blocks active chloride transport	Ascending loop of Henle	• Increased urine losses of K, Na, Cl, Ca, and Mg leading to serum deficiencies of these electrolytes • Hypercalciuria and nephrocalcinosis • Contraction hypochloremic metabolic alkalosis • Increased renin, hyperuricemia • Ototoxicity • Relief of symptoms sometimes precedes diuresis secondary to pulmonary venous dilation
Spironolactone (Aldactone)	• Competitive antagonist of aldosterone	Collecting system	• Decreased urinary losses of K and thus, *K-sparing* • Increased urine losses of Na, Cl, Ca, and Mg • Contraindicated if hyperkalemia or anuria
Chlorothiazide (Diuril)	• Inhibits NaCl reabsorption	Distal tubule	• Increased urinary losses of Na, K, Mg, Cl, HCO_3, and phosphate • Decreased renal excretion of Ca • Mild hypochloremic alkalosis • Inhibits pancreatic release of insulin leading to hyperglycemia • Displaces bilirubin from albumin—use cautiously if hyperbilirubinemia • Hyperuricemia

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2. A. Acetazolamide (Diamox)

Acetazolamide inhibits the reabsorption of $NaHCO_3$, leading to a potential mild metabolic acidosis. Chlorothiazide and furosemide may lead to a metabolic alkalosis. Spironolactone administration leads to decreased urinary losses of potassium, resulting in increased serum potassium and hydrogen; use of this diuretic is not typically associated with a predominant alkalosis or acidosis in neonates.

3. C. NaCl and potassium chloride

Furosemide use in neonates is often associated with urinary losses of sodium, potassium, and chloride, leading to oral supplementation of these electrolytes. Although furosemide administration may also lead to increased urinary losses of calcium and magnesium, supplements of calcium and magnesium are not commonly required. Furosemide may lead to a metabolic alkalosis, so administration of bicarbonate would not be an appropriate therapy.

4. C. Metabolic bone disease
D. Renal calcifications

Adverse effects of chronic furosemide use in neonates include the following:

- Ototoxicity
- Nephrotoxicity
- Renal calcifications
- Metabolic bone disease

Cardiotoxicity and liver toxicity are not recognized as adverse effects of chronic furosemide administration in neonates.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know that chronic diuretic therapy can produce hyponatremia
- Know which diuretics produce a metabolic alkalosis
- Know which diuretics produce a metabolic acidosis
- Recognize ototoxicity and nephrotoxicity as potential adverse dose-related effects of Furosemide
- Understand the long-term complications of Furosemide therapy

SUGGESTED READING

Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.

SECTION XVIII

Ethics

CASE 1

Maternal–fetal conflicts

A 45-year-old woman presents to her obstetrician after a positive home pregnancy test within 2 weeks of a missed menstrual cycle. Her unexpected but welcomed pregnancy occurs just days after her last Papanicolaou (PAP) test. Her PAP test shows malignant cells, and she is diagnosed with an advanced stage of invasive cervical cancer. Treatment is recommended immediately, which includes surgical resection of her cervix and uterus.

The pregnant woman refuses treatment for her cancer and wants to continue the pregnancy.

1. Select True or False (i–ii) for the statements (A–D) regarding ethical decision-making for the woman in this vignette:

   i. True
   ii. False

   A. Best medical evidence is the only factor that should be considered.
   B. Cultural and social values play no role.
   C. Gestational age bears no impact.
   D. No discussion is warranted, as the pregnant woman must undergo resection of her cervix and uterus; her pregnancy must be terminated.

The obstetrician presents the case to the hospital ethics team. Before the meeting, he reviews some important concepts of ethical decision-making.

2. Match the definitions (i–vii) with the ethical terms below (A–G):

   i. Knowledge obtained about a patient will not be revealed to others except when it will benefit the patient or if it would override social good
   ii. Obligation to help others
   iii. Obligation to keep promises and contracts
   iv. Obligation to not harm others, including not treating them cruelly
   v. Obligation to treat people fairly
   vi. Respect for individual's plan of life; thus, must allow people to make decision for themselves
   vii. Sufficient mental ability to understand the nature and consequences of one's actions and thereby, able to make a rational decision

   A. Autonomy ____
   B. Beneficence ____
   C. Competence ____
   D. Confidentiality ____
   E. Fidelity ____
   F. Justice ____
   G. Nonmaleficence ____

The obstetrician extensively reviews the risks and benefits of continuing the pregnancy with the woman. The woman decides to continue the pregnancy and forego treatment. She delivers at 32 weeks' gestation via a planned cesarean delivery after receiving antenatal steroids to mature the fetal lungs. Four days after delivery, the mother has surgery to remove her cervix and uterus. Although the plan to continue the pregnancy was a unilateral decision, the obstetrician reviewed the ethical principles of decision-making and discussed the options at length with the woman.

CASE 2

Imperiled newborns

A 19-year-old woman is rushed to the hospital with vaginal bleeding after a motor vehicle accident (MVA). Upon arrival, the fetal heart rate pattern is nonreassuring. The pregnant teenager has had only one prenatal visit, 3 days prior to the MVA, with an estimated gestational age (GA) at the time of 22 weeks. A brief discussion takes place between the pregnant teen, her mother, and the neonatologist.

The neonatologist provides the family with the best medical evidence about outcomes of infants born at the limits of viability. He informs the family that this evidence may be even more variable in the setting of an unclear estimated date of confinement. After the family is provided with more information, they decide on comfort care only unless there is a profound discrepancy in estimated GA.

After the meeting, the neonatologist leads a discussion with the pediatric residents and medical students rotating in the Neonatal Intensive Care Unit (NICU) that month. He reviews four basic ethical principles.

1. Match the basic ethical principles (A–D) with the corresponding definitions (i–iv):

   i. A group of norms for distributing benefits, risks, and costs fairly by:
      - Fair distribution process
      - Respect for people's rights
      - Respect for morally acceptable laws

   ii. A group of norms for providing benefits and balancing benefits with risks and costs

   iii. A norm of avoiding causing harm

   iv. Respect for decision-making abilities of autonomous persons/family members

   A. Nonmaleficence

   B. Respect for beneficence

   C. Respect for justice

   D. Respect for persons

When the female infant is born, her physical examination and abbreviated Ballard maturational assessment are more consistent with an infant born at 24 to 25 weeks' gestation. The infant is born vigorous and is crying with a heart rate of 150 beats per minute. With this information of potential older gestation and given the infant's clinical status, the family decides that they want resuscitation to be provided to their baby. The infant is intubated and given surfactant. There is no need for chest compressions or epinephrine administration.

At 48 hours of age, the infant sustains a massive pulmonary hemorrhage. She is placed on high-frequency oscillatory ventilation. Her head ultrasound shows large bilateral intraventricular hemorrhages with extremely dilated ventricles and large extensions of the hemorrhages into the adjacent parenchyma. The neonatologist sits down with the family to update them on the infant's status and to discuss potential options for care. After much discussion, the family decides to withdraw medical treatment and to provide only comfort care. The infant dies several hours later.

The neonatologist reviews the concept of withholding versus withdrawing medical treatment with the pediatric residents and medical students.

2. Select True or False (i–ii) for the following statements:

   i. True
   ii. False

   A. The amended Child Abuse Act in 1984 states that medical treatment could be withheld when:
      - The infant is chronically and irreversibly comatose.
      - Treatments would be both "virtually futile in terms of survival of the infant" and "inhumane."

   B. The "Born-Alive Act" (2001) states that every liveborn infant, regardless of GA, should be resuscitated.

   C. There is no ethical distinction between withholding and withdrawing medical treatment, as supported by the American Academy of Pediatrics Neonatal Resuscitation Program.

   D. Withholding medical treatment may be viewed as easier for many families compared to withdrawing medical treatment

   E. Withdrawing medical treatment often presents more barriers for clinicians and families compared to withholding medical treatment.

SECTION XVIII

Answers

CASE 1 ANSWERS

1. A ii False
B ii False
C ii False
D ii False

All of the statements offered as options in this question are false. In most cases, fetal and maternal best interests are aligned or very quickly become aligned. However, when fetal and maternal interests are not aligned, an ethical conflict may ensue. Fetal and maternal best interests must be discussed; ultimately, respect for the autonomy of the pregnant woman along with bodily integrity should prevail. Harm to the fetus as a result of the pregnant woman's decision needs to be evaluated in the context of:

- Best medical evidence
- Cultural beliefs
- Social network and values

Gestational age must be weighed in light of potential options and possible outcomes. Evidence shows that care and treatment in a supportive fashion is far beneficial to coercion. The most effective hospital guidelines support shared decision-making in the setting of fetal/maternal conflict with the goal of compassionate conflict resolution.

2. A vi
B ii
C vii
D i
E iii
F v
G iv

Table 1 provides the basic definitions for concepts in ethics.

TABLE 1. Concepts in Ethics

Autonomy	Respect for individual's plan of life; thus, must allow people to make decision for themselves
Beneficence	Obligation to help others
Competence	Sufficient mental ability to understand the nature and consequences of one's actions and thereby, able to make a rational decision
Confidentiality	Knowledge obtained about a patient will not be revealed to others except when it will benefit the patient or if it would override social good
Fidelity	Obligation to keep promises and contracts
Justice	Obligation to treat people fairly
Nonmaleficence	Obligation to not harm others, including not treat them cruelly

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:499

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Recognize and apply ethical principles when dealing with a situation that involves maternal–fetal conflicts

SUGGESTED READINGS

Boyle R. Ethical issues in the care of the neonate: Overview. *NeoReviews*. 2004;11:e471–e475.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
McHaffie H, Laing I, Parker M, et al. Deciding for imperiled newborns: Medical authority or parental autonomy? *J Med Ethics*. 2001;27:104–109.
Meadow W, Lantos J. Ethics at the limit of viability: A premie's progress. *NeoReviews*. 2003; 4:e157–e161.

CASE 2 ANSWERS

1. A iii
B ii
C i
D iv

Table 1 provides the definitions of the ethical concepts listed as options.

TABLE 1. Basic Ethical Principles

Respect for persons	A norm of respecting the decision-making abilities of autonomous persons/family members In research, this principle highlights the need for informed consent In clinical care, this principle imparts the need for maintaining confidentiality
Nonmaleficence	A norm of avoiding causing harm
Respect for beneficence	A group of norms for providing benefits and balancing benefits with risks and costs
Respect for justice	A group of norms for distributing benefits, risks, and costs fairly This principle can be divided into three categories: a. Fair distribution of scarce resources b. Respect for people's rights (despite disapproval of patient's lifestyle) c. Respect for morally acceptable laws

Adapted from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:499

2. A i True
B ii False
C i True
D i True
E i True

All of the statements are true except for B. The "Born-Alive" Act of 2001 states that infants who are born alive, at any stage in development, are persons who are entitled to the protection of the law. Every liveborn infant needs to be evaluated to determine appropriate care. The interpretation of the Act is that appropriate care can include comfort measures and explanation alone, with no additional interventions.

Table 2 identifies benefits of withholding versus withdrawing medical treatment.

TABLE 2. Withholding Versus Withdrawing Medical Treatment

Benefits of Withdrawing Medical Treatment	Benefits of Withholding Medical Treatment
Only way to know if some infants may benefit from a treatment is to initiate therapy and then withdraw if ineffective	Often easier to "do nothing" then intervene and stop
Presents more barriers for clinicians and families	May prevent infant from having pain and suffering
May increase chance of obtaining more information that could impact outcome	May be easier emotionally because family has not observed and interacted with infant
	While may gather more clinical information if withdraw medical treatment, may take long period of time; during this time, family has become more emotionally invested, making decision about stopping more difficult or there may not be any aggressive therapy to withdraw

Printed with permission from: Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010:504

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Discussions at the threshold of viability
- Recognize and apply ethical principles regarding imperiled newborns and delivery room resuscitation issues
- Recognize and apply ethical principles involved in decision-making for imperiled newborns in the Neonatal Intensive Care Unit

SUGGESTED READINGS

Boyle R. Ethical issues in the care of the neonate: Overview. *NeoReviews*. 2004;11:e471–e475.
Brodsky D, Martin C. *Neonatology Review*. 2nd ed. Raleigh, NC: Lulu; 2010.
McHaffie H, Laing I, Parker M, et al. Deciding for imperiled newborns: Medical authority or parental autonomy? *J Med Ethics*. 2001;27:104–109.
Meadow W, Lantos J. Ethics at the limit of viability: A premie's progress. *NeoReviews*. 2003; 4:e157–e161.

SECTION XIX

Discharge Planning

CASE 1

Newborn discharge from the hospital

A nurse in the postpartum unit is caring for the two patients described in the vignettes below.

Vignette A: A 39-year-old gravida 5 para 5 now 6 woman with experience breast-feeding all of her infants desires early discharge with her full-term newborn 24 hours after vaginal delivery. The neonate has been breast-feeding adequately; mother's milk is starting to "come in"; and the infant's 24-hour bilirubin value is 3 mg/dL.

Vignette B: A 23-year-old Asian-American gravida 1 para 0 now 1 woman planning to exclusively breast-feed her infant desires early discharge with her late preterm male infant 24 hours after vaginal delivery. The infant's birth weight is 2.1 kg (4 pounds 10 ounces). He is not latching well; mother's milk is not "in"; and the infant's bilirubin value is 8 mg/dL.

The nurse alerts the pediatrician rounding in the nursery that both patients are requesting early discharge.

1. Select the criteria for safe discharge to home from the list below (A–I). More than one answer may be selected:

   A. Access to health care
   B. Bilirubin less than 10 mg/dL
   C. Family readiness and competence
   D. Full-term gestation
   E. Gaining weight (from birth weight)
   F. High school diploma received by mother
   G. Physiologic stability of mother and newborn
   H. Social support network availability
   I. Weight of more than 5 pounds at discharge

2. Select True or False (i–ii) for the following statements. Refer to vignettes A and B above when appropriate:

   i. True
   ii. False

   A. *Based on the information provided*, patient A does not have risk factors to prevent early discharge.
   B. Benefits of early discharge may include facilitation and bonding, enhanced family interactions, increased family satisfaction, and increased breast-feeding.
   C. Neither patient should be granted early discharge due to the chance of readmission for hyperbilirubinemia.
   D. Risk factors for unsafe discharge for patient B and her newborn include primigravida, Asian ethnicity, late preterm status, lack of established breast-feeding, and male gender.
   E. The infant born to patient B must remain in the hospital for 1 week due to his low birth weight.
   F. The only benefit to early discharge is economic.
   G. The pediatrician must review the unique characteristics of the *infant only* prior to deeming the infant ready for discharge.
   H. The American Academy of Pediatrics (AAP) developed the *Safe and Healthy Beginnings Newborn Discharge: A Readiness Checklist* to aid clinicians with preparation of a newborn for discharge.

3. Select the potential complications of early discharge. More than one answer may be selected:

   A. Failure to detect congenital hearing loss
   B. Feeding difficulties leading to dehydration and jaundice
   C. Inability to detect some metabolic disorders on the newborn screening test
   D. Prolonged timing of umbilical cord stump adherence

CASE 2

Sudden infant death syndrome prevention

A full-term male infant is born to a 37-year-old woman by uncomplicated vaginal delivery. The mother's prenatal screens and pregnancy course were unremarkable except for daily tobacco use. The family history is significant for a prior male child who died of sudden infant death syndrome (SIDS) 2 years prior to this current pregnancy. The family is overwhelmed with anxiety that their newborn might also die of SIDS.

Before sitting down with the family, the pediatric resident reviews the current information on SIDS and the expanded American Academy of Pediatrics (AAP) recommendations for a safe sleeping environment.

The attending pediatrician supervises the pediatric resident as he leads the discussion on SIDS with the family.

1. Select the accepted definition of SIDS:

   A. A cause assigned to infant deaths that cannot be explained after a thorough review of the clinical history, case investigation, and autopsy.
   B. A cause assigned to death attributed to child abuse.
   C. A cause assigned to death attributed to a rare metabolic disorder.
   D. There is no accepted definition for SIDS.

2. Select the accepted SIDS prevention guidelines from the list below:

   A. Infants should sleep in supine or side-lying positions.
   B. Infants should only sleep in a safety-approved crib and never sleep in a portable crib, play yard, or bassinet.
   C. Infants should not sleep routinely in their car seat at home.
   D. Room-sharing and bed-sharing are recommended.
   E. Cobedding of twins is recommended.
   F. Pillows, quilts, and comforters are not recommended for infant use during sleep.
   G. Wedges and positioning devices are approved for use by all infants during sleep.
   H. Bumper pads are not recommended.
   I. Smoking during pregnancy and in the infant's environment should be avoided.
   J. Breast-feeding is recommended.
   K. Pacifier use is recommended at nap time and bedtime.
   L. The use of a hat during sleep is recommended.
   M. Infants should be immunized according to the AAP and Centers for Disease Control and Prevention.

The parents in the vignette above want to use a home monitor to prevent SIDS from happening to their baby.

3. Select True (i) or False (ii) for the following statement:

   There is no evidence that apparent life-threatening events are precursors for SIDS, and infant home monitors should not be used as a strategy for preventing SIDS.

SECTION XIX

Answers

CASE 1 ANSWERS

1. A, C, G, and H are all correct.

Safe discharge of a newborn from hospital to home requires:

- Physiologic stability
- Family preparedness and competence
- Social support network
- Access to health care

Prior to discharge to home, the bilirubin level of the newborn needs to be appropriate for the baby's age of life and gestational age using established bilirubin nomograms. Depending on a baby's risk factors, a bilirubin over 10 mg/dL may be normal and would not hold up discharge.

Late preterm infants (34 $^{0}/_{7}$ weeks' gestation to 36 $^{6}/_{7}$ weeks' gestation) who demonstrate physiologic stability may be able to be discharged from home prior to reaching term gestational age. These infants need to have evidence of the following:

- Normal respiratory pattern
- Mature feeding ability
- Maintenance of a normal temperature
- Bilirubin level that is appropriate for age of life and gestation

Prior to discharge, late preterm infants also need to have a car safety screening test to confirm cardiorespiratory stability in an upright position.

Most newborns lose weight in the first week of age and thus, are not required to be gaining weight to be discharged from the hospital. Hospital clinicians must closely review an infant's percent weight loss and more closely assess an infant with greater than 10% weight loss, as it might be a sign of dehydration and/or lack of established feeding.

Whether a mother has received a high school diploma has no impact on a newborn's discharge from the hospital. Rather, the family needs to be prepared, be competent, have access to health care, and have a good social support network prior to discharge.

There is no specific weight required of a newborn prior to discharge to home. However, babies who weigh less than 5 pounds at discharge need to demonstrate normal temperatures and normal blood glucose concentrations. Most infants will be close to 5 pounds or greater when ready for discharge.

2.

A	i	True
B	i	True
C	ii	False
D	i	True
E	ii	False
F	ii	False
G	ii	False
H	i	True

The AAP developed the *Safe and Healthy Beginnings Newborn Discharge: A Readiness Checklist* to aid clinicians with preparation of a newborn for discharge. The categories in the check list include:

- General health
- Hyperbilirubinemia assessment
- Breast-feeding assessment
- Transition to medical home
- Health and safety counseling
- Psychosocial and referral

Studies report potential risk factors for readmission of the infant as:

- Asian ethnicity
- Primiparity
- Associated maternal morbidities
- Shorter gestational age
- Low birth weight
- Instrumented vaginal delivery
- Male gender

The pediatrician must always view the infant as a maternal/infant dyad to ascertain the unit is ready for a safe discharge to home.

3. B and C

Potential complications of early discharge include:

- Lack of established feeding (poor feeding ability or lack of maternal supply)
- Dehydration
- Significant jaundice
- Inability to detect some metabolic disorders on the newborn screening test as detection of some disorders requires an infant to have established feedings

Early discharge does not lead to failure to detect hearing loss (even with early discharge, a hearing screen is required). There is no association with early discharge and prolonged umbilical stump adherence.

Failure to detect ductal-dependent cardiac lesions has been reported as a potential complication of early discharge of a newborn. The Critical Congenital Heart Disease Screening mandate should decrease this risk as all infants, even those being discharged early, will need to have an oxygen saturation screening test.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATIONS

- Know the qualifications for consideration of early discharge of a newborn
- Know the benefits and complications of early discharge of a newborn
- Know the importance of follow-up after early discharge of a newborn

SUGGESTED READINGS

AAP online resource: http://www.aap.org/en-us/professional-resources/practice-support/Vaccine-Financing-Delivery/Documents/Newborn_Discharge_SAMPLE.pdf. Accessed August 30, 2013.

Committee on Fetus and the Newborn, American Academy of Pediatrics. Policy Statement—Hospital stay for the healthy term newborn. *Pediatrics*. 2010;125(2):405–409.

Danielsen B, Castles AG, Damberg CL, et al. Newborn discharge timing and readmissions: California, 1992–1995. *Pediatrics*. 2000;106 (1, pt 1):31–39.

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Grupp-Phelan J, Taylor JA, Liu LL, et al. Early newborn hospital discharge and readmission for mild and severe jaundice. *Arch Pediatr Adolesc Med*. 1999;153(12):1283–1288.

Kotagal UR, Atherton HD, Eshett R, et al. Safety of early discharge for Medicaid newborns. *J Am Med Assoc*. 1999;282(12):1150–1156.

Paul IM, Lehman EB, Hollenbeak CS, et al. Preventable newborn readmissions since passage of the Newborns' and Mothers' Health Protection Act. *Pediatrics*. 2006;118(6):2349–2358.

CASE 2 ANSWERS

1. A. A cause assigned to infant deaths that cannot be explained after a thorough review of the clinical history, case investigation, and autopsy.

Definitions:

- **SIDS:** A cause assigned to infant deaths that cannot be explained after a thorough review of the clinical history, case investigation, and autopsy
- **SUID**, sudden unexpected infant death (or **SUDI**, sudden unexpected death of infancy): a term used to describe any sudden and unexpected death, whether explained or unexplained (including SIDS), that occurs during infancy; can be attributed to suffocation, asphyxia, entrapment, infection, ingestions, metabolic diseases, and trauma (accidental or nonaccidental)

2. The correct answers are C, F, H, I, J, K, and M.

The following statements are accepted SIDS-prevention guidelines:

- Infants should sleep supine; side-lying positions are not recommended.
- Infants should sleep in a safety-approved crib, portable crib, play yard, or bassinet.
- Infants should not sleep routinely in their car seat at home.
- Room-sharing is recommended; bed-sharing is *not* recommended.
- Cobedding of twins is *not* recommended.
- Pillows, quilts, and comforters are not recommended for infant use during sleep.
- Wedges and positioning devices are not recommended.
- Bumper pads are not recommended.
- Smoking during pregnancy and in the infant's environment should be avoided.
- Breast-feeding is recommended.
- Pacifier use is recommended at nap time and bedtime.
- Overheating and head covering of infants should be avoided.
- Infants should be immunized according to the AAP and Centers for Disease Control and Prevention.

3. i. True

The Task Force on SIDS and the AAP Committee on Fetus and Newborn agree that infant home monitors should *not* be used as a strategy to prevent SIDS, although it can be useful for some infants who have had an apparent life-threatening event.

AMERICAN BOARD OF PEDIATRICS CONTENT SPECIFICATION

- Know the SIDS-prevention guidelines and advise parents

SUGGESTED READINGS

Committee on Fetus and Newborn, American Academy of Pediatrics. Apnea, sudden infant death syndrome, and home monitoring. *Pediatrics*. 2003;111(4, pt 1):914–917.

Task Force on Sudden Infant Death Syndrome, American Academy of Pediatrics. SIDS and other sleep-related infant deaths: Expansion of recommendations for a safe infant sleeping environment. *Pediatrics*. 2011;128(5):e1341–e1387.

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