THE AMERICAN BOARD OF PEDIATRICS®

CONTENT OUTLINE

Neonatal-Perinatal Medicine

Subspecialty In-Training, Certification
and
Maintenance of Certification (MOC)
Examinations
INTRODUCTION

This document was prepared by the American Board of Pediatrics Subboard of Neonatal-Perinatal Medicine for the purpose of developing in-training, certification, and maintenance of certification examinations. The outline defines the body of knowledge from which the Subboard samples to prepare its examinations. The content specification statements located under each category of the outline are used by item writers to develop questions for the examinations; they broadly address the specific elements of knowledge within each section of the outline.
EXAM BLUEPRINT
Neonatal-Perinatal Medicine

Each Neonatal-Perinatal Medicine exam is built to the same specifications, also known as the blueprint. This blueprint is used to ensure that, for the initial certification and in-training exams, each exam measures the same depth and breadth of content knowledge. Similarly, the blueprint ensures that the same is true for each Maintenance of Certification exam form. The table below shows the percentage of questions from each of the content domains that will appear on an exam. Please note that the percentages are approximate; actual content may vary.

<table>
<thead>
<tr>
<th>Content Categories</th>
<th>Initial Certification and In-Training</th>
<th>Maintenance of Certification (MOC)</th>
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<tbody>
<tr>
<td>1. Maternal-Fetal Medicine</td>
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<td>2. Asphyxia and Resuscitation</td>
<td>4%</td>
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<td>3. Cardiovascular</td>
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<td>4. Respiratory</td>
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<td>5. Genetics/Dysmorphism</td>
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<td>6. Nutrition</td>
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<td>7. Water/Salt/Renal</td>
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<td>8. Endocrine/Metabolic/Thermal</td>
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<td>9. Immunology</td>
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<td>10. Infectious Diseases</td>
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<td>11. Gastroenterology</td>
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<td>12. Bilirubin</td>
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<td>13. Skin Disorders</td>
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<td>14. Hematology/Oncology</td>
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<td>15. Neurology</td>
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<td>16. Neurodevelopmental Outcomes</td>
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<td>17. Eyes, Ears, Nose, Mouth, Throat, and Neck</td>
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<td>18. Basic Principles of Pharmacology</td>
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<td>19. Health Services Delivery, Ethical Issues, and Family Counseling</td>
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<tr>
<td>20. Core Knowledge in Scholarly Activities</td>
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1. **Maternal-Fetal Medicine**
   A. Pregnancy (For Reproductive genetics, see Section V)
      1. Factors of pregnancy (see also VI.A.1.b. and c.)
         a. Know the physiology of maternal adaptation to pregnancy and know the normal changes in maternal physiologic variables and in laboratory values that occur during pregnancy
         b. Know the essentials of prenatal care, including risk assessment, perinatal referral, screening, and standard monitoring
         c. Know the types of multiple gestation
         d. Know the normal morphologic development of the placenta
         e. Know the role of the placenta in gas exchange and oxygenation of the fetus
         f. Know the role of the placenta in the energy metabolism of the fetus, including the transfer of glucose, electrolytes, and amino acids to the fetus
         g. Know the components of pre- and periconceptional health care (including nutritional requirements during pregnancy) that influence pregnancy outcomes
         h. Know the types of assisted reproductive technologies and how they may influence pregnancy outcome
         i. Know how maternal obesity may influence pregnancy and pregnancy outcome
         j. Know the types of abnormal placentation, such as placenta previa and placenta accreta, and the potential influence on both maternal and fetal health and labor and delivery management
   2. Maternal medical disorders affecting the fetus and/or newborn infant (see also IX.B.1.a)
      a. Know the effects on the fetus and/or newborn infant of maternal immunologic diseases and their management
      b. Know the effects on the fetus and/or newborn infant of acute and chronic maternal renal diseases and their management
      c. Know the effects on the fetus and/or newborn infant of maternal or placental malignancy and its management
      d. Know the effects on the fetus and/or newborn infant of maternal diabetes mellitus (including gestational diabetes) and their management
      e. Know the effects on the fetus and/or newborn infant of maternal hematologic disorders and their management
      f. Know the effects on the fetus and/or newborn infant of maternal cardiac disease and its management
      g. Know the effects on the fetus and/or newborn infant of maternal pulmonary disease and its management
      h. Know the effects on the fetus and/or newborn infant of maternal central and peripheral nervous system and neuromuscular diseases and their management
      i. Know the effects on the fetus and/or newborn infant of maternal seizure disorders and their management
      j. Know the maternal and fetal risks and the management of a traumatic injury in a pregnant woman
k. Know the effects on the fetus and/or newborn infant of maternal connective tissue disorders and their treatment
l. Know the effects on the fetus and/or newborn infant of maternal chronic hypertension and its management
m. Know the effects on the fetus and/or newborn infant of mild preeclampsia and its management
n. Know the effects on the fetus and/or newborn infant of severe preeclampsia, including HELLP syndrome, and its management
o. Know the effects on the fetus and/or newborn infant of maternal thromboembolic, or potential thromboembolic (eg artificial valve), disorders and of their management, including the use of anticoagulants
p. Know the effects on the fetus and/or newborn infant of maternal metabolic disorders, including PKU, and their management
q. Know the effects on the fetus and/or newborn infant of maternal surgical and anesthesia (eg appendectomy)
r. Know the effects on the fetus and/or newborn infant of maternal HIV infection and its management and know the strategies employed to decrease fetal and neonatal HIV infection
s. Know the effects on the fetus and/or newborn infant of maternal psychiatric disorders and their treatment
t. Know the effects on the fetus and/or newborn infant of other maternal infections (eg malaria) and their management

3. Obstetric conditions and complications (fetus/newborn)
   a. Know the definition, risks to the fetus and/or newborn infant, and management of post-term pregnancy
   b. Know the differential diagnosis and potential risks to the fetus and/or newborn infant of first, second, and third trimester vaginal bleeding

4. Effect of drugs and environmental agents (fetus/newborn) (see also I.B.5.)
   a. Know the gestational age at which teratogenic exposure (eg rubella, alcohol, retinoic acid) will be most likely to produce fetal anomalies
   b. Know the effects on the fetus and/or newborn infant of tocolytic agents used during pregnancy
   c. Know the effects on the fetus and/or newborn infant of maternal substance abuse (eg heroin, cocaine, cannabis, methamphetamines, tobacco)
   d. Know the effects on the fetus and/or newborn infant of maternal alcohol use
   e. Know the effects on the fetus and/or newborn infant of exposure to ionizing radiation, including x-rays and radioactive substances used for diagnosis and/or treatment of maternal disorders
   f. Know the pulmonary and non-pulmonary effects on the fetus and/or newborn infant of maternally administered steroids (including betamethasone, dexamethasone, and prednisone)
   g. Know the effects on the fetus and/or newborn infant of exposure during pregnancy to environmental agents (eg, mercury, pesticides, etc)

B. Fetal assessment and treatment modalities during pregnancy
   1. Screening
a. Know the indications for and complications of methods of direct assessment of the fetus, including chorionic villus sampling, amniotic fluid sampling, and fetal blood sampling
b. Know the rationale for, and approaches to, screening for maternal Group B Streptococcal colonization during pregnancy
c. Know the rationale, methods, and interpretation of results of screening for maternal infections such as rubella, CMV, viral hepatitis, HIV, and syphilis
d. Know the rationale, methods, and interpretation of results of first and second trimester screening for aneuploidy (e.g., nuchal translucency, choroid plexus cysts) and neural tube defects
e. Know the rationale, methods, and interpretation of results of screening for carrier status of genetic diseases such as cystic fibrosis, Tay Sachs, and hemoglobinopathies

2. Ultrasonography and imaging
   a. Know the general principles, applications, and limitations of ultrasonography, including Doppler blood flow measurements, in assessment of fetal conditions and well-being
   b. Know how to use obstetric and ultrasonographic data to determine gestational age, and know their limitations
c. Know the importance and limitations of ultrasonographic findings of common fetal anomalies including congenital heart disease
d. Know the role and risks of magnetic resonance imaging, as well as other non-ultrasonographic imaging techniques in assessing fetal anatomy

3. Assessment of fetal status
   a. Understand the rationale, interpretation, and limitations of maternal detection of fetal movement, of the biophysical profile, the non-stress test, and the contraction stress test as means of assessing fetal well-being

4. Fetal conditions that jeopardize the fetus during pregnancy (see also I.A.1.)
   a. Know the potential fetal complications of multiple gestation such as cord problems, twin-twin transfusion, "stuck twin," conjoined twins, etc.
b. Know the diagnostic evaluation and perinatal management of fetal-maternal blood group incompatibility
c. Know the differential diagnosis and the plan of evaluation and management of a fetus with non-immune hydrops
d. Know the limitations in diagnosis and implications of fetal macrosomia
e. Know how to evaluate fetal growth rate and fetal growth restriction and the management of fetal growth restriction
f. Know the significance of oligohydramnios and the management of pregnancy when it is diagnosed
g. Know the significance of polyhydramnios and the management of pregnancy when it is diagnosed
h. Know the implications and treatment options for the surviving fetus when its twin dies in utero
i. Know how specific fetal diagnoses, such as airway abnormalities, abdominal wall defects, myelomeningocele, or severe hydrocephalus might alter prenatal care and intrapartum management (e.g., fetal intervention "Exit" strategy)
5. Evaluation of fetal lung maturity (See also I.A.4. and IV.B.1)
   a. Know the indications for and interpretation of tests of fetal lung maturity

C. Labor
1. Factors of labor (See also I.B.3.)
   a. Know how to assess fetal well-being during labor
   b. Know the physiologic characteristics of normal labor and parturition
   c. Know the effects of normal labor on uteroplacental physiology and its effects on the fetus
   d. Know the risk factors, including the effects of choriodecidual infection and inflammation as contributing factors, for preterm labor
2. Complications of labor that affect the fetus (see also II.B.)
   a. Know the diagnosis and management of maternal/fetal blood loss such as placenta previa, placenta abruption, vasa previa, and maternal-fetal hemorrhage
   b. Know the significance and obstetrical management of meconium-stained amniotic fluid
   c. Know the differential diagnosis and management of maternal hypotension in labor, and its effect on the fetus
   d. Know the significance, interpretation, and management of abnormalities or changes in fetal heart rate patterns during labor including reassuring and nonreassuring and indeterminate patterns
   e. Know the effects on the fetus and/or newborn infant of analgesics and anesthetics administered to the mother during labor
3. Other (see also I.C.1.)
   a. Know the significance of a maternal temperature increase during labor
   b. Know the complications and effects of chorioamnionitis in the mother and the fetus
   c. Know the causes, complications, and management of preterm premature rupture of membranes

D. Delivery
1. Know how to recognize and differentiate complications of soft tissue injury to an infant's scalp, like caput and subgaleal bleed
2. Know the clinical features and prognosis of birth injuries, such as fractures, lacerations, and facial palsies
3. Know the neonatal complications of abnormal presentations (breech, shoulder dystocia, etc)
4. Know the indications for and fetal/newborn complications of cesarean delivery
5. Know the indications for and perinatal complications of operative vaginal delivery (forceps, vacuum extraction, etc) and of vaginal delivery after cesarean delivery
6. Know the rationale, risks, and benefits of delayed cord clamping

E. Breast feeding (See Section VI.C.1.)
2. Asphyxia and Resuscitation
   A. Pathophysiology of acute and chronic asphyxia syndromes
      1. General
         a. Know the incidence, causes and pathophysiology, including cellular abnormalities, of acute perinatal asphyxia
         b. Know the causes and pathophysiology, including cellular abnormalities, of chronic asphyxia syndromes (eg, chronic fetal hypoxia and placental insufficiency)
c. Know the clinical features, diagnosis, and management of perinatal hypoxic ischemic encephalopathy

2. Organ effects
   a. Recognize the neonatal systemic complications and vascular redistribution of blood flow caused by perinatal hypoxia or asphyxia
   b. Understand reperfusion injury

3. Biochemistry
   a. Know the biochemical responses to and consequences of asphyxia

B. Diagnosis and management of asphyxia

1. Diagnosis
   a. Differentiate asphyxia from other causes of depression at birth, including drug effects and hypovolemia
   b. Understand the significance, limitations, and causes of low Apgar scores, including the relationship between Apgar scores and later outcomes in preterm and full-term infants
   c. Know the interpretation of umbilical cord blood gas and pH values

2. Management
   a. Airway (See also I.C.2 and IV.C.2)
      1. Know the proper approach to airway management in the delivery room
      2. Know the potential complications of airway management in the delivery room and know their management
      3. Know the current recommendations regarding suctioning meconium from the airway during and following delivery
   b. Ventilation and oxygenation
      1. Know the indications for assisted ventilation, including continuous positive airway pressure, immediately after birth and how to assess its effectiveness
      2. Understand how to use self-inflating and flow-inflating bags or T-piece resuscitators to provide assisted ventilation immediately after birth
      3. Know indications for and proper administration of supplemental oxygen immediately after birth
   c. Circulatory support
      1. Know the indications for, techniques, and potential complications of chest compression immediately after birth
      2. Know the indications for and management of intravascular fluid volume replacement immediately after birth
   d. Pharmacologic management
      1. Know the indications, contraindications, and methods of administration of drugs used for neonatal resuscitation

3. Cardiovascular
   A. Normal and abnormal cardiac morphogenesis and development
      1. Know normal and abnormal morphogenesis and development of the heart and great arteries and the local regulatory factors involved
      2. Know the neonatal developmental cardiac manifestations of maternal diseases and maternal drug and environmental exposures
      3. Know the genetic and developmental mediators of heart and vascular development
4. Know the neonatal developmental cardiac manifestations of common perinatal syndromes (e.g., congenital rubella)

B. Cardiovascular physiology
   1. Know the factors affecting and regulating myocardial performance and function in the fetus and newborn infant and during the perinatal transitional period
   2. Know the factors affecting and regulating the systemic circulation in the fetus (including umbilical vessels) and newborn infant during the perinatal transitional period
   3. Understand the factors affecting and regulating the pulmonary circulation in the fetus and newborn infant and during the perinatal transitional period
   4. Know the appropriate techniques to assess cardiovascular function in the fetus and newborn infant
   5. Know the physiology of the ductus arteriosus and understand the factors affecting and regulating the ductus arteriosus in the fetus and newborn infant during the perinatal transitional period

C. Congenital heart disease
   1. Cyanotic heart defects
      a. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a cyanotic neonate
      b. Know the anatomy and pathophysiology (including genetics) of a cyanotic neonate
      c. Recognize the clinical features and possible associated defects of a cyanotic neonate
      d. Recognize the laboratory, imaging, and other diagnostic features of a cyanotic neonate
      e. Formulate a differential diagnosis for a cyanotic neonate
   2. Left-to-right shunt lesions (see also XV.H.3.)
      a. Know the anatomy and pathophysiology (including genetics) of a neonate with a left-to-right shunt lesion
      b. Recognize the clinical features of a neonate with a left-to-right shunt lesion
      c. Recognize the laboratory, imaging, and other diagnostic features of a neonate with a left-to-right shunt lesion
      d. Formulate a differential diagnosis for a neonate with a left-to-right shunt lesion
      e. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a neonate with a left-to-right shunt lesion
      f. Know the anatomy and pathophysiology of a preterm neonate with a patent ductus arteriosus
      g. Recognize the clinical features of a preterm neonate with a patent ductus arteriosus
      h. Recognize the laboratory, imaging, and other diagnostic features of a preterm neonate with a patent ductus arteriosus
      i. Formulate a differential diagnosis of a preterm neonate with a patent ductus arteriosus
      j. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a preterm neonate with a patent ductus arteriosus
3. Left-sided obstructive lesions
   a. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a neonate with a left-sided cardiac obstructive lesion
   b. Know the anatomy and pathophysiology, including genetics, of a neonate with a left-sided cardiac obstructive lesion
   c. Recognize the clinical features of a neonate with a left-sided cardiac obstructive lesion
   d. Recognize the laboratory, imaging, and other diagnostic features of a neonate with a left-sided cardiac obstructive lesion
   e. Formulate a differential diagnosis of a neonate with a left-sided cardiac obstructive lesion

4. Right-sided lesions (cyanotic or acyanotic)
   a. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a neonate with a right-sided cardiac lesion
   b. Know the anatomy and pathophysiology (including genetics) of a neonate with a right-sided cardiac lesion
   c. Recognize the clinical features of a neonate with a right-sided cardiac lesion
   d. Recognize the laboratory, imaging, and other diagnostic features of a neonate with a right-sided cardiac lesion
   e. Formulate a differential diagnosis for a neonate with a right-sided cardiac lesion

5. Mixing lesions (bidirectional shunting)
   a. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a neonate with a mixing cardiac lesion
   b. Know the anatomy and pathophysiology (including genetics) of a neonate with a mixing cardiac lesion
   c. Recognize the clinical features of a neonate with a mixing cardiac lesion
   d. Recognize the laboratory, imaging, and other diagnostic features of a neonate with a mixing cardiac lesion
   e. Formulate a differential diagnosis of a neonate with a mixing cardiac lesion

6. Arterial vascular lesions
   a. Know the anatomy and pathophysiology (including genetics) of a neonate with an arterial vascular abnormality
   b. Recognize the clinical features of a neonate with an arterial vascular abnormality
   c. Recognize the laboratory, imaging, and other diagnostic features of a neonate with an arterial vascular abnormality
   d. Formulate a differential diagnosis for a neonate with an arterial vascular abnormality
   e. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for a neonate with an arterial vascular abnormality

D. Cardiopulmonary dysfunction in the absence of congenital heart disease
   1. Myocardial disorders (eg, cardiomyopathy, myocarditis, and tumors)
a. Know the anatomy and pathophysiology (including genetics) of an infant with a condition affecting myocardial performance
b. Recognize the clinical features in an infant with a condition affecting myocardial performance
c. Recognize the laboratory, imaging, and other diagnostic features of an infant with a condition affecting myocardial performance
d. Formulate a differential diagnosis of an infant with a condition affecting myocardial performance
e. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for an infant with a condition affecting myocardial performance

2. Systemic blood pressure regulation (see VII.B.3.b)
   a. Know the pathophysiology of a term or preterm infant with a condition affecting the systemic blood pressure, such as hypotension or hypertension
   b. Recognize the clinical features of an infant with systemic hypotension
   c. Recognize the laboratory and imaging features of an infant with systemic hypotension
   d. Formulate a differential diagnosis for an infant with systemic hypotension
   e. Know the management of an infant with systemic hypotension and the adverse effects of such management
   f. Formulate a differential diagnosis for an infant with systemic hypertension in early infancy
   g. Know the management of an infant with systemic hypertension, including adverse effects of management
   h. Know the factors which regulate systemic blood pressure in term and preterm infants and know the normal range of pressures and pressure patterns
   i. Know the clinical and diagnostic features of an infant with systemic hypertension, including laboratory and imaging studies

3. Cardiovascular effects of birth
   a. Know the pathophysiology of an infant with cardiac manifestations produced by perinatal events such as asphyxia, hypovolemia, or hypervolemia
   b. Recognize the clinical features of an infant with cardiac manifestations produced by perinatal events such as asphyxia hypovolemia or hypervolemia
   c. Recognize the laboratory, imaging, and other diagnostic features of an infant with cardiac manifestations produced by perinatal events such as asphyxia, hypovolemia, or hypervolemia
   d. Formulate a differential diagnosis of an infant with cardiac manifestations produced by perinatal events such as asphyxia, hypovolemia, or hypervolemia
   e. Know the evaluation and medical and/or surgical management and associated potential complications or adverse effects of such management for an infant with cardiac manifestations produced by perinatal events such as asphyxia, hypovolemia, or hypervolemia

E. Electrocardiography, electrophysiology, and dysrhythmias
   1. Differentiate normal from common abnormal electrocardiographic patterns and rhythms in the fetus and newborn infant
   2. Know the physiologic consequences of an arrhythmia in a fetus or newborn infant
3. Know appropriate management of common arrhythmias in the fetus and newborn infant, and understand the potential complications or adverse effects of approaches and drugs used

F. Pharmacologic therapy of heart disease
   1. Vasopressor and inotropic drugs
      a. Know the mechanism of action of commonly used adrenergic vasopressor and/or inotropic drugs (eg dopamine, dobutamine, epinephrine)
      b. Know the therapeutic indications for, and toxicity of, commonly used adrenergic drugs
      c. Know the mechanisms of action, therapeutic indications for, and toxicity of chronotropic drugs
      d. Know the mechanisms of action, therapeutic indications for, and toxicity of inotropic drugs
   2. Diuretics
      a. Know the therapeutic indications for, and toxicity of, commonly used diuretic drugs in preterm and term infants with cardiovascular disease
   3. Pharmacologic management of the ductus arteriosus
      a. Know the indications, application, and complications of the use of prostaglandin E1 to maintain patency of the ductus arteriosus in neonates
   4. Nitric oxide (see IV.F.1.)

G. Neurodevelopmental outcome of infants with congenital heart disease
   1. Know the long-term prognosis and outcome, including neurodevelopmental outcome, of infants with cyanotic or acyanotic congenital heart disease

4. Respiratory
   A. Embryology and physiology
      1. Morphologic development of the lung - normal and abnormal
         a. Know the stages and mediators of normal and abnormal cellular and structural development of all components of the lung
      2. Fetal respiration
         a. Know the mechanism of production and factors affecting the clearance of fetal lung liquid, its contribution to amniotic fluid, and its importance to fetal lung development
      3. Control of Breathing - normal and abnormal
         a. Know the effects of pulmonary reflexes and oxygen, carbon dioxide, and hydrogen ion concentrations on control of neonatal breathing
      4. Pulmonary surfactant
         a. Know the effects of surface tension on alveolar and airway stability and lung mechanics (LaPlace law)
         b. Know the timing of the biochemical maturation of the lung and the physiological and biochemical factors affecting this timing
      5. Pulmonary function - normal and abnormal
         a. Ventilation/perfusion
            1. Know the concepts of anatomic and physiologic dead space
            2. Know the causes of and the effects of ventilation/perfusion mismatching
            3. Know the determinants of gas exchange
4. Know the causes of and how to evaluate arterial hypoxemia in an infant with a structurally normal heart
5. Know the effects of changes in altitude on oxygenation
6. Know how to calculate an alveolar-arterial oxygen gradient

b. Respiratory mechanics - normal and abnormal
1. General
   a. Distinguish the differences in pulmonary mechanics between the neonate and the adult
   b. Know the basic gas laws and their clinical applications
2. Lung volume
   a. Know factors that determine residual lung volume, functional residual capacity, and tidal volume, and how they change with various pulmonary disorders
3. Lung and chest wall compliance
   a. Recognize the factors (including pressure-volume and flow-volume relationships) that alter lung compliance and chest wall compliance and how they change with various pulmonary disorders and with gestational age
4. Airway resistance
   a. Know the factors that affect airway resistance and how resistance changes with various lung disorders
5. Respiratory muscles
   a. Know the factors that influence upper airway patency
   b. Know the developmental characteristics of respiratory muscle function
6. Dynamic interactions
   a. Know the physical principles governing gas flow, including airway diameter, turbulence, and time constants
   b. Know the causes of pulmonary edema and its effects on lung function
   c. Know how intrapleural pressure affects cardiovascular function
   d. Know how acute and chronic lung disease affects cardiovascular function
7. Oxygen transport and delivery
   a. Know the various factors affecting oxygen uptake, transport, and delivery, including the blood and circulation

7. Pulmonary function testing
   a. Know how to interpret arterial blood gas measurements and noninvasive methods for estimating arterial oxygenation
   b. Know the interpretation and limitations of methods for measuring pulmonary function

B. Respiratory distress syndrome (RDS)/Transient tachypnea
1. RDS
   a. Know the pathophysiology and risk factors for RDS
   b. Recognize the clinical, imaging, and laboratory features of RDS
   c. Recognize the pathologic features of RDS
   d. Know the clinical strategies and therapies used to decrease the risk and severity of RDS
   e. Know the management of RDS, including surfactant replacement
2. Transient tachypnea
a. Know the pathogenesis, pathophysiology, and risk factors of transient tachypnea of the newborn infant
b. Know the clinical, laboratory, and imaging features of transient tachypnea of the newborn infant and formulate a differential diagnosis
c. Know the prevention and management of transient tachypnea of the newborn infant

C. Pneumonias, meconium aspiration, and persistent pulmonary hypertension
1. Pneumonias
   a. Know the pathogenesis and causative agents in an infant in whom neonatal pneumonia is suspected
   b. Know the clinical, imaging, and laboratory features and plan the management of an infant in whom neonatal pneumonia is suspected
2. Meconium aspiration syndrome (See also I.C.2 and II.B.2.a)
   a. Know the pathogenesis, pathophysiology, pathologic features, and risk factors of meconium aspiration syndrome
   b. Know how to manage meconium aspiration syndrome
   c. Know the clinical, laboratory, and imaging features of meconium aspiration syndrome
3. Persistent pulmonary hypertension
   a. Know the pathogenesis, pathophysiology, pathologic features, and risk factors for persistent pulmonary hypertension
   b. Recognize the clinical features and differential diagnosis of persistent pulmonary hypertension
   c. Recognize the laboratory, imaging, and other diagnostic features of persistent pulmonary hypertension
   d. Know the management of persistent pulmonary hypertension including assisted ventilation, pharmacologic approaches, and ECMO

D. Other causes of respiratory distress
1. Extrapulmonary (eg, diaphragmatic hernia, cord transection, etc.)
   a. Plan appropriate therapy for an infant with extrapulmonary causes of respiratory distress
   b. Recognize the clinical features of extrapulmonary causes of respiratory distress
   c. Recognize the imaging features of extrapulmonary causes of respiratory distress
2. Airway obstruction (eg, vascular rings, choanal atresia, etc.)
   a. Know the clinical features of an infant with airway obstruction
   b. Plan appropriate diagnostic evaluation and management for an infant with airway obstruction
3. Miscellaneous
   a. Recognize the clinical and imaging features of congenital malformations of the lung, including congenital pulmonary lymphangiectasia, the cystic lung diseases, such as congenital lobar emphysema, cystic adenomatoid malformation, and mediastinal tumors
   b. Know the appropriate management for an infant with congenital malformations of the lung, including congenital pulmonary lymphangiectasia, and the cystic lung diseases, such as congenital lobar emphysema, cystic adenomatoid malformation, and mediastinal tumors
4. Pleural disorders (effusion, chylothorax)
a. Know the pathophysiology and recognize the clinical, radiographic, and laboratory manifestations of hydrothorax/chylothorax
b. Plan the therapeutic management of hydrothorax/chylothorax

E. Apnea of prematurity and neonatal respiratory depression
1. Know the pathophysiology of apnea of prematurity
2. Know the management of apnea of prematurity

F. Treatment
1. Assisted ventilation
   a. Plan the ventilatory therapy for infants with respiratory failure of different etiologies
   b. Know the indications for and techniques of continuous positive airway pressure (CPAP)
   c. Know the effects and risks of CPAP
   d. Know the indications for and techniques of high-frequency ventilation
   e. Know the effects and risks of high-frequency ventilation
   f. Know the indications for and techniques of positive-pressure ventilation (PPV), including volume and pressure-targeted ventilator modes
   g. Know the effects and risks of PPV
2. ECMO
   a. Know the indications, techniques, effects, and risks of extra-corporeal membrane oxygenation (ECMO)
3. Pharmacologic agents
   a. Know the mechanism of action, indications, techniques of administration, effects, and risks of inhaled pulmonary vasodilators such as nitric oxide

G. Air leaks
1. Know the pathophysiology of air leaks
2. Recognize the clinical, laboratory, and imaging features of air leaks
3. Know how to prevent and manage air leaks

H. Chronic lung disease, bronchopulmonary dysplasia
1. Know the pathogenesis, pathophysiology, and pathologic features of bronchopulmonary dysplasia/chronic lung disease
2. Know the prenatal and postnatal risk factors for bronchopulmonary dysplasia/chronic lung disease and be aware of various preventive strategies
3. Recognize the clinical features of bronchopulmonary dysplasia/chronic lung disease
4. Recognize the laboratory, radiographic, and other imaging features of bronchopulmonary dysplasia/chronic lung disease
5. Know the management of bronchopulmonary dysplasia/chronic lung disease
6. Know the prognosis, long-term complications, and permanent sequelae of bronchopulmonary dysplasia

5. Genetics/Dysmorphism
A. Basic understanding of molecular genetics (see also V.B.3.)
1. Know the functions of messenger, ribosomal, and transfer RNA
2. Know concept of DNA and mRNA sequence encoding amino acid structure of proteins
3. Know the function of DNA polymerase, RNA polymerase, and reverse transcriptase enzymes
4. Know the concepts of insertion, deletion, inversion, and translocation
5. Know the principles and clinical implications of anticipation and amplification in trinucleotide repeat syndromes
6. Know the significance of DNA methylation and epigenetics

B. Specific patterns of congenital disorders

1. Chromosomal disorders
   a. Types of chromosomal abnormalities
      1. Aneuploidy
         a. Autosomal
            1. Recognize the physical findings and chromosomal pattern and know the prognosis in trisomy 13
            2. Identify the physical characteristics and chromosomal pattern and know the prognosis in trisomy 18
            3. Be aware of the maternal factors, incidence, and clinical manifestations, including common complications and prognosis, of Down syndrome
         b. Sex chromosome
            1. Know the physical characteristics, chromosomal pattern, and long-term outcomes of sex chromosome aneuploidies
         c. Polyploidy
            1. Know fetal and placental manifestations of triploidy
         d. Mosaicism
            1. Know how mosaicism modifies clinical presentation
   b. Sex chromosome
      1. Know the physical characteristics, chromosomal pattern, and long-term outcomes of sex chromosome aneuploidies
   c. Polyploidy
      1. Know fetal and placental manifestations of triploidy
   d. Mosaicism
      1. Know how mosaicism modifies clinical presentation

2. Structural chromosomal abnormalities
   a. Balanced translocations
      1. Know the difference between balanced and unbalanced chromosome translocation
      2. Know the appropriate cytogenetic evaluation of the family and infant with a structural chromosome abnormality
   b. Deletion syndromes (eg, cri du chat, DiGeorge, etc)
      a. Recognize the clinical manifestations and laboratory methods for diagnosis of the common deletion syndromes
      b. Recognize clinical manifestations and laboratory methods for diagnosis of the microdeletion syndromes
      c. Recognize clinical manifestations and laboratory methods for diagnosis of the contiguous gene disorders

2. Single-gene (Mendelian) disorders
   a. Types
      1. Differentiate between homozygous and heterozygous
      2. Recognize specific patterns of Mendelian inheritance
   b. Clinical features
      1. Autosomal dominant disorders
         a. Demonstrate understanding of inheritance patterns and recurrence risks for autosomal dominant disorders
      2. Autosomal recessive disorders
         a. Demonstrate understanding of inheritance patterns and recurrence risks for autosomal recessive disorders
3. X-linked disorders
   a. Know the clinical features and diagnosis of fragile X syndrome
   b. Know the inheritance patterns and recurrence risks for X-linked dominant or recessive disorders
4. Mitochondrial disorders
5. Know the maternal/paternal and mitochondrial/chromosomal contributions to inheritance of mitochondrial disorders
6. Recognize the clinical features associated with mitochondrial disorders

3. Non-Mendelian inheritance
   a. Genomic imprinting and parent of origin effects
      1. Know the etiology, molecular phenotype, and clinical manifestations of disorders associated with genetic imprinting, such as Prader-Willi syndrome
      2. Know the etiology, molecular phenotype, and clinical manifestations of disorders associated with uniparental disomy
   b. Genetic anticipation (eg, congenital myotonic dystrophy)
      1. Recognize the DNA findings, clinical manifestations, and inheritance of trinucleotide repeat syndromes, such as myotonic dystrophy

4. Multifactorial disorders
   a. Differentiate between multifactorial and Mendelian inheritance
   b. Know the recurrence risks and factors of multifactorial disorders

C. Non-genetic etiologies for congenital defects
   1. Environmental factors (See I.A.4)
   2. Maternal metabolic disorders (See 1.A.2)
   3. Deformations/disruptions
      a. Differentiate between a malformation, a deformation, and a disruption
      b. Recognize the characteristics of the amniotic band syndrome and know its consequences
   4. Infections
      a. Maternal infections (See I.A.2 and X.B)
   5. Birth defects associated with assisted reproductive technology
      a. Know the risk of congenital anomalies and chromosomal or genetic abnormalities associated with assisted reproductive technology

D. Evaluation of infants with congenital anomalies (See also I.B.1)
   1. Diagnostic approach
      a. History
         1. Know the components of a complete family history for genetic disorders
         2. Know how age at presentation (in utero, neonate, infancy or later) affects the differential diagnosis of the clinical presentation of genetic disorders
         3. Know the relationship between ethnic origin of the parents and risk for specific genetic conditions
      b. Physical evaluation
         1. Recognize the diagnostic implications of single vs. multiple anomalies
         2. Know the frequency of minor congenital anomalies
         3. Know the frequency of major congenital malformations
         4. Recognize the clinical features and know how to diagnose craniofacial anomalies
5. Recognize the clinical features and know how to diagnose and manage congenital anomalies of the upper extremities, such as syndactyly, polydactyly, absent clavicles, absent radius, Sprengel deformity, limb reduction
6. Recognize the clinical features and know how to diagnose and manage congenital anomalies of the lower extremities, such as metatarsus adductus, talipes equinovarus, syndactyly, polydactyly, limb reduction
7. Recognize the clinical features and know how to diagnose and manage skeletal dysplasias, such as achondrogenesis, achondroplasia, chondrodermal dysplasia, epiphyseal dysostosis, osteogenesis imperfecta, hypophosphatasia, etc
8. Know the clinical features and inheritance patterns of common syndromes or associations that can be recognized in the newborn period (eg, VATER association and DiGeorge syndrome)
c. Cytogenetic studies
   1. Know when to obtain karyotypes on the subject, parents, or other family members
   2. Know the indications and limitations of molecular cytogenetic studies (eg FISH), in the diagnosis of aneuploidy and microdeletion
   3. Know the indications for and utility of comparative genomic hybridization studies
d. DNA diagnostic studies
   1. Know the disorders for which molecular genetic studies are clinically indicated, such as cystic fibrosis, and how to interpret test results
e. Other diagnostic studies
   1. Know the indications, limitations, and techniques for newborn screening for genetic disorders

6. Nutrition
   A. Nutrition and growth
      1. The fetus
         a. Changes in body composition
            1. Know how body composition changes during fetal growth
         b. Nutrient requirements (See also I.A.1)
            1. Determine the nutrients and the relative amounts required for normal fetal growth
         c. Factors that influence intrauterine growth (See also i.A.1)
            1. Know the hormonal factors that affect intrauterine fetal growth
            2. Know the maternal, placental, and fetal factors that affect intra-uterine fetal growth
      2. Newborn infants
         a. Changes in body composition
            1. Know how body composition changes during postnatal growth and development and understand the effect of prematurity
         b. Energy requirements kcal/kg/day
            1. Know the caloric requirements for optimal postnatal growth of preterm and term infants, accounting for caloric expenditures needed for physical activity and maintenance of body temperature
         c. Protein requirements
1. Distinguish between indispensable, essential, and non-essential amino acids
2. Know the protein requirements of preterm and full-term infants
3. Know the consequences of feeding preterm infants too little or too much protein
4. Know the physiology of protein/amino acid digestion (absorption and metabolism) in newborn infants
d. Fat requirements
   1. Know the clinical and laboratory features of essential fatty acid deficiency and how to prevent it
   2. Distinguish between essential and nonessential fatty acids
   3. Know the fat requirements of preterm and full-term infants
   4. Know the physiology of fat digestion, absorption, and metabolism in newborn infants
e. Carbohydrate requirements
   1. Know the physiology of carbohydrate digestion, absorption, and metabolism in newborn infants
3. Large- and small-for-gestational age (LGA - SGA) infants
   a. Know the postnatal growth patterns of SGA infants
   b. Recognize the effects of fetal programming and nutrition on the prevalence and types of adult onset disorders
   c. Know the definitions, causes, clinical features, differential diagnosis, and typical laboratory findings of SGA and LGA infants
B. Minerals, vitamins, and trace elements
   1. Minerals (for calcium, phosphorus, and magnesium see Section VIII.A.5)
      a. Know the changing requirements of sodium, potassium, and chloride by the neonate at various gestational ages
      b. Know the changing requirements of calcium and phosphorous by the neonate at various gestational ages
   2. Vitamins
      a. Know the requirements for vitamins in newborn infants, and the differences between preterm and full-term infants
      b. Know the clinical and laboratory manifestations of deficiencies of water soluble vitamins
      c. Know the clinical and laboratory manifestations of deficiencies of fat soluble vitamins
      d. Know the potential adverse effects of pharmacologic use of fat soluble vitamins
   3. Trace elements
      a. Iron (see XIV.A.3.b.)
      b. Other
         1. Know the clinical manifestations, diagnosis, management, and prevention of zinc, copper, selenium, manganese, and chromium deficiency
         2. Know the potential toxicities of trace element supplementation in neonatal conditions such as cholestasis and renal insufficiency
C. Enteral nutrition
   1. Human milk
      a. Know the differences between the composition of breast milk of the mother of a preterm infant and that of a full-term infant
b. Know the differences in the nutritional composition of human milk and infant formula
c. Know the immunologic and anti-infective constituents in human milk and their physiologic effects
d. Recognize the effects of different methods of processing of human milk, such as freezing, pasteurization, sterilization, and microwaving
e. Know that human milk needs to be fortified in order to meet the nutritional needs of preterm infants
f. Know the physiology and pathophysiology of human milk production and secretion
g. Realize common problems associated with breast milk production in the NICU, and their management
h. Know the advantages and disadvantages of the use of donor human milk

2. Formulas
   a. Know the distribution of nutrients (protein, fat, and carbohydrates) in infant formulas
   b. Know the mineral and vitamin content of infant formulas
   c. Know the benefits and risks of formulae that contain non-standard soy proteins
   d. Know the medical indications for the use of non-standard infant formulas to meet the needs of infants with special health problems
   e. Know how standard infant formulas are modified in order to meet the needs of preterm infants

D. Parenteral nutrition
   1. Indications
      a. Know the indications and advantages of total parenteral nutrition (TPN) and combined enteral and parenteral nutrition
   2. Composition and energy content
      a. Know the nutritional composition of parenteral solutions
      b. Know the importance of protein and non-protein nutrients in achieving optimal utilization of energy and nitrogen
      c. Know how to calculate the caloric content of parenteral nutrition solutions
   3. Complications of parenteral nutrition (See also XI.D.2)
      a. Recognize the relationship between the calcium and phosphorus content of parenteral nutrition solutions and osteopenia
      b. Recognize the association of cholestasis with total parenteral nutrition, know how to manage this, and understand how to diagnose other possible causes
      c. Recognize the causes and clinical manifestations of catheter complications of parenteral nutrition
      d. Recognize the causes and clinical manifestations of metabolic complications of parenteral nutrition
      e. Recognize the potential toxicities associated with the use of parenteral nutrition

7. Water/Salt/Renal (see XIII.A.)
   A. Water and electrolyte metabolism
      1. Water metabolism
         a. Body water compartments during development
            1. Know the changes in body water distribution and body fluid composition that occur during fetal and postnatal development
b. Methods of monitoring water balance
   1. Know how to evaluate neonatal hydration
   2. Know how to evaluate and manage inadequate or excessive water intake

c. Insensible water loss (see also XIII.A.)
   1. Know physiologic, environmental, and other factors such as thermal environment and gestational age that contribute to insensible water loss (IWL)
   2. Know therapeutic interventions that can be used to decrease IWL
   3. Be able to estimate insensible water loss in infants at various gestational ages

d. Endocrine control of water metabolism
   1. Know the specific hormonal factors that influence water balance in newborn infants
   2. Know how to diagnose and treat the syndrome of inappropriate secretion of arginine vasopressin (antidiuretic hormone) and diabetes insipidus
   3. Know the effects of arginine vasopressin (antidiuretic hormone) on sodium and water balance

e. Management of water balance
   1. Know the impact of renal dysfunction on water requirements
   2. Know the impact on water requirements of renal and metabolic fluid disorders associated with endocrine dysfunction in infants

2. Electrolyte metabolism
   a. Know the etiology of electrolyte abnormalities in the neonate
   b. Recognize the clinical and laboratory manifestations of electrolyte abnormalities in the neonate
   c. Know how to manage electrolyte abnormalities in the neonate
   d. Know the causes and differential diagnosis of metabolic acidosis and metabolic alkalosis in infants
   e. Recognize the clinical and laboratory manifestations of metabolic acidosis and metabolic alkalosis in infants
   f. Know how to manage metabolic acidosis and metabolic alkalosis in infants

B. Normal and abnormal renal function in the fetus and neonate
   1. Development of renal function
      a. Glomerular and tubular function during development
         1. Know the changes in glomerular and tubular function that occur during development, including the handling of glucose, sodium, potassium, calcium, bicarbonate, and phosphate
         2. Recognize the causes, diagnosis, and treatment of renal tubular acidosis in the neonate
         3. Be able to differentiate between proximal, distal, and transient renal tubular acidosis
      b. Hormonal controls of renal function during development (see III.C.2.)
         1. Know the production sites and actions of various types of vasoactive substances that affect renal function
         2. Know the production pathway and the actions of the components of the renin-angiotensin system
3. Know the effects of drugs such as cyclo-oxygenase inhibitors, angiotensin-converting enzyme inhibitors, prostaglandins, and catecholamines on renal function (antenatal and postnatal)

c. Evaluation of renal function
   1. Know how to interpret various renal function tests (eg, urinalysis, creatinine clearance)
   2. Understand indications for and methods of antenatal assessment of renal function

2. Abnormal renal development
   a. Recognize the clinical manifestations of anatomic abnormalities of the kidneys and urinary tract in infants
   b. Know how to diagnose specific anatomic abnormalities of the kidneys and urinary tract in infants
   c. Know the recommended supportive and corrective treatment of anatomic abnormalities of the kidneys and urinary tract in infants
   d. Know how prenatal diagnosis of renal abnormalities affects postnatal management

3. Acquired renal disease
   a. Renal vascular thrombosis (see also XIV.C.2.b.)
      1. Know the etiology, clinical manifestations, laboratory features, differential diagnosis, and management of renal vein thrombosis
      2. Know the etiology, clinical manifestations, laboratory features, and management of renal artery thrombosis
   b. Hypertension (see III.D.2.)
   c. Acute renal failure
      1. Know the causes of renal failure in the neonate
      2. Know the clinical manifestations, imaging, and laboratory features of renal failure in the neonate
      3. Know the management of renal failure in the neonate, including indications for and complications of the use of hemofiltration, peritoneal dialysis, and hemodialysis
   d. Urinary tract infections (See X.A.10)
   e. Diuretics (see also III.F.2)
      1. Know the mechanism of action of commonly used diuretic drugs in infants

8. Endocrine/Metabolic/Thermal
   A. Endocrine and metabolism
      1. Normal and abnormal sexual differentiation
         a. Normal sexual differentiation
            1. Know normal fetal sexual differentiation
         b. Abnormal sexual differentiation
            1. Disorders of sexual differentiation
               a. Differentiate among disorders of testicular hormone synthesis or action
               b. Know the etiology of abnormal sexual differentiation
               c. Know the diagnostic approaches to and management of abnormal sexual differentiation
               d. Know the etiology of and diagnostic approaches to an infant with ambiguous genitalia, not including congenital adrenal hyperplasia
e. Know the clinical manifestations, laboratory features, and therapeutic management of an infant with ambiguous genitalia, not including congenital adrenal hyperplasia

2. Other disorders of sexual differentiation
   a. Know the causes of micropenis, including pituitary deficiency
   b. Know how to evaluate and manage an infant with micropenis
   c. Know how to evaluate and manage an infant with hypospadias and epispadias
   d. Know how to evaluate and manage an infant with cryptorchidism

2. Adrenal disorders
   a. Recognize the clinical manifestations and laboratory features of the various types of congenital adrenal hyperplasia
   b. Define the appropriate therapy for the various types of congenital adrenal hyperplasia
   c. Understand the basic enzymatic defects involved in the various types of congenital adrenal hyperplasia

3. Thyroid disorders
   a. Embryology and physiology
      1. Know the physiological roles of the hormones and other proteins involved in the regulation of thyroid function
      2. Know the relationship between fetal and maternal thyroid physiology
      3. Know the embryology and normal physiological function of the thyroid gland
   b. Tests of thyroid function
      1. Know the proper use of laboratory tests (including screening tests) in the diagnosis of thyroid dysfunction
   c. Congenital hypothyroidism
      1. Know the etiology and clinical manifestations of congenital hypothyroidism
      2. Know the laboratory features and approach to therapy of congenital hypothyroidism
   d. Transient disorders of thyroid function
      1. Know how to evaluate and manage the causes of transient hypothyroidism in newborn infants
   e. Thyrotoxicosis
      1. Identify the etiology, clinical manifestations, laboratory features, and management of neonatal thyrotoxicosis

4. Glucose metabolism
   a. Normal fetal and neonatal carbohydrate metabolism
      1. General
         a. Know the amino acid substrates for gluconeogenesis
         b. Know the fuels used for brain metabolism
         c. Know the relationship of maternal blood glucose to fetal glucose uptake and metabolism
         d. Know the normal range of endogenous glucose production in term and preterm infants
      2. Hypoglycemia
a. Know the causes (including hyperinsulinemic hypoglycemia) of neonatal hypoglycemia syndromes
b. Recognize the clinical and laboratory features of neonatal hypoglycemia
c. Recognize the approach to therapy and prevention of neonatal hypoglycemia
d. Know the potential sequelae of neonatal hypoglycemia

3. Hyperglycemia
   a. Know the causes, including genetic disorders and other clinical conditions, of neonatal hyperglycemia, including transient diabetes mellitus
   b. Know the clinical and laboratory features and approach to therapy of neonatal hyperglycemia, including transient diabetes mellitus

b. Intermediary metabolism
5. Calcium, phosphorus, and magnesium metabolism
   a. Normal
      1. Know normal calcium, phosphorus, and magnesium metabolism during the prenatal and postnatal periods, including fetal accretion rates
      2. Know the interrelated effects of various hormones, including parathormone, calcitonin, and vitamin D on calcium, phosphorus, and magnesium metabolism in the fetus and neonate
   b. Abnormal
      1. Hypocalcemia/hypercalcemia
         a. Know the etiology and clinical manifestations of early and late neonatal hypocalcemia
         b. Know the laboratory features and approach to therapy of early and late neonatal hypocalcemia
         c. Know the etiology and clinical manifestations of neonatal hypercalcemia
         d. Know the laboratory features and approach to therapy of neonatal hypercalcemia
      2. Osteopenia of prematurity
         a. Know the etiology, clinical manifestations, radiographic features, and approach to treatment of osteopenia of prematurity
      3. Hypomagnesemia/hypermagnesemia
         a. Know the etiology, clinical manifestations, and approach to therapy of hypomagnesemia
         b. Know the etiology, clinical manifestations, and approach to therapy of hypermagnesemia

B. Inborn errors of metabolism
   1. Know the etiology, clinical manifestations, laboratory features, and management of infants with lysosomal and peroxisomal, and mitochondrial disorders
   2. Know the causes and differential diagnosis of metabolic encephalopathy
   3. Know the clinical manifestations, laboratory features, and treatment of disorders in the metabolism of amino acids
   4. Know the clinical manifestations, laboratory features, and treatment of disorders in the metabolism of fatty acids
   5. Know the clinical manifestations, laboratory features, and treatment of disorders in the metabolism of the urea cycle
6. Know the clinical manifestations, laboratory features, and treatment of disorders in the metabolism of carbohydrates (excluding glucose)
7. Know the clinical manifestations, laboratory features, and treatment of disorders of cholesterol synthesis
8. Know the clinical manifestations, laboratory features, and treatment of organic acid disorders

C. Thermal regulation
   1. Physiology of temperature regulation in the neonate
      a. General principles
         1. Know the mechanisms of heat gain and loss
      b. Neutral thermal environment and management of the thermal environment
         1. Know the definition and physiological implications of a neutral thermal environment
         2. Know the various types and mechanisms of action of devices to maintain a neutral thermal environment
      c. Hypothermia/hyperthermia
         1. Know the causes, metabolic consequences, and treatment of infants with hypothermia
         2. Know the causes, metabolic consequences, and treatment of infants with hyperthermia

9. Immunology
   A. Developmental biology of the immune system
      1. Know the timing and developmental stages of lymphoid tissues in the neonate and infant
      2. Know the two types of host defense mechanisms (innate and acquired immunity) and understand their role and interrelationship in normal development of the immune system
      3. Know the development, function, and potential clinical utility of pluripotent hematopoietic stem cells
      4. Know the types and functions of human hematopoietic growth factors (eg, GM-CSF, interleukins)
   B. Specific components of the immune system
      1. B-lymphocytes and immunoglobulins
         a. Development and function
            1. Know the normal immunoglobulin patterns in preterm and full-term newborn infants
            2. Know the activation and function of B-lymphocytes
            3. Know the function of immunoglobulins
            4. Know the mechanisms and gestational timing of the placental transfer of immunoglobulins
         b. Diagnosis and management of abnormalities
            1. Know the laboratory methods (eg, quantitation of immunoglobulins) for diagnosing immune deficiencies
      2. T-lymphocytes
         a. Development and function
1. Know the function and activation of T-lymphocytes, including the role of cytokines

b. Diagnosis and management of abnormalities
   1. Recognize the clinical features and know the evaluation and management of disorders associated with T-cell dysfunction, including DiGeorge sequence and HIV infection

3. Polymorphonuclear leukocytes (neutrophils)
   a. Development and function
      1. Know the role of neutrophils in host defense
      2. Know how to evaluate neutrophil function
      3. Know the changes that occur in circulating concentrations of polymorphonuclear neutrophils immediately after birth, under normal conditions

   b. Diagnosis and management of abnormalities
      1. Recognize the causes and consequences of alterations in number and distribution of neutrophils
      2. Know the consequences of leukocyte defects of chemotaxis, phagocytosis, or quantitative killing
      3. Know the etiology, pathophysiology, and differential diagnosis of neonatal leukopenia
      4. Know the evaluation and management of neonatal leukopenia
      5. Recognize the etiology, pathophysiology, and differential diagnosis of neonatal leukocytosis
      6. Know the evaluation and management of neonatal leukocytosis

4. Mononuclear phagocytes
   a. Know the normal development and function of monocytes and macrophages

5. The complement system
   a. Know the consequences of defects in the complement system
   b. Know the role of the complement system in host defense
   c. Know the activation pathways and components of the complement system

6. Circulating factors
   a. Know the role of C-reactive protein in host defense, and know the significance of elevated serum concentrations in the neonatal period

7. Inflammatory components
   a. Know the vascular components of acute inflammation
   b. Know the cellular components of acute inflammation
   c. Know the role of cytokines and chemokines in inflammation
   d. Know the role of extracellular matrix proteins in inflammation
   e. Know the role of reactive oxygen intermediates (oxygen free radicals, H2O2) in inflammation
   f. Know the role of eicosanoids (prostaglandins, leukotrienes) in inflammation

8. The Spleen
   a. Know the role of the spleen in normal host defenses
   b. Know the consequences, clinical manifestations, and management of altered spleen function, including asplenia

C. Abnormal function of the immune system
1. Know the clinical features and differential diagnosis of neonates with immune deficiencies
2. Know the initial screening tests and subsequent specific diagnostic tests used to evaluate neonates with possible defects in host defense mechanisms

10. Infectious Diseases
   A. Infections of organ systems
      1. Sepsis
         a. Know how infectious agents are transmitted to the neonate
         b. Know the clinical manifestations, laboratory features, and differential diagnosis of neonatal sepsis
         c. Understand the treatment and complications of sepsis
         d. Know the infectious agents that cause neonatal sepsis
         e. Know the maternal, perinatal, and neonatal risk factors for neonatal sepsis
      2. Respiratory infection (See IV.C.1.)
      3. Gastrointestinal infections (See XI.B.5.)
      4. Omphalitis
         a. Know the causative agents, pathogenesis, and differential diagnosis of neonatal omphalitis
         b. Know the clinical and laboratory features, treatment, and complications of neonatal omphalitis
      5. Ocular infections (See XVII.A.3.b)
      6. Otitis media
         a. Know the causative infectious agents and pathogenesis of neonatal otitis media
      7. Osteomyelitis and septic arthritis
         a. Know the causative infectious agents and pathogenesis of osteomyelitis and septic arthritis
         b. Know the clinical and laboratory features and differential diagnosis of osteomyelitis and septic arthritis
         c. Know the management and complications of osteomyelitis and septic arthritis
      8. Cutaneous infections (See XIII.C and D)
      9. Central nervous system (CNS) infections (see also XV.A.)
         a. Know the normal CSF counts and chemistries in preterm and term neonates and changes with infection
      10. Genitourinary infections
          a. Know the causative infectious agents, pathogenesis, and differential diagnosis of urinary tract infections
          b. Know the clinical and laboratory features, evaluation, treatment, and complications of urinary tract infections
   B. Etiologic agents
      1. Bacteria
         a. Non-clostridial anaerobes (eg, Bacteroides)
            1. Understand the epidemiology, pathogenesis, prevention, clinical manifestations, diagnostic features, and management of perinatal anaerobic bacterial infections
         b. Listeria monocytogenes (see also XIII.C.2.)
            1. Know the epidemiology, pathogenesis, prevention, clinical manifestations, and diagnostic features of perinatal Listeria monocytogenes infection
2. Know the treatment and complications of perinatal Listeria monocytogenes infection
c. Group B streptococcus
1. Know the epidemiology, prevention, and pathogenesis of perinatal/ neonatal group B streptococcal infections
2. Know the clinical manifestations and diagnostic criteria of group B streptococcal infections
3. Know the treatment and complications of group B streptococcal infections
d. Gonococcal infections (See also XVII.A.3.b)
1. Know the epidemiology, prevention, and pathogenesis of neonatal Neisseria gonorrhoea infections
2. Know the clinical manifestations, diagnosis, management, and complications of neonatal Neisseria gonorrhoea infections
e. Staphylococcal infections
1. Know the epidemiology, prevention, and pathogenesis of neonatal infection with Staphylococcus aureus and Staphylococcus epidermidis
2. Know the clinical manifestations and diagnostic features of neonatal infections with Staphylococcus aureus and Staphylococcus epidermidis
3. Know the management, including understanding of antibiotic resistance, and complications of neonatal infection with Staphylococcus aureus and Staphylococcus epidermidis
f. Mycoplasma and ureaplasma
1. Know the epidemiology, pathogenesis, and prevention of perinatal infection with mycoplasma and ureaplasma
2. Know the clinical manifestations, diagnostic features, management, and complications of perinatal infection with mycoplasma and ureaplasma
g. Syphilis (see also XII.C.2.)
1. Know the epidemiology, prevention, and pathogenesis of perinatal infections with Treponema pallidum
2. Know the clinical manifestations and diagnostic features of perinatal infections with Treponema pallidum
3. Know the management and complications of perinatal infections with Treponema pallidum
h. Escherichia coli and other gram-negative bacilli
1. Know the epidemiology, prevention, and pathogenesis of neonatal infections with Escherichia coli, Klebsiella, Enterobacter, Proteus, Citrobacter, Salmonella, and Pseudomonas
2. Know the clinical manifestations, diagnostic features, management, and complications of neonatal infections with Escherichia coli, Klebsiella, Enterobacter, Proteus, Citrobacter, Salmonella, and Pseudomonas
i. Haemophilus influenzae
1. Know the epidemiology, pathogenesis, and prevention of neonatal infection with Haemophilus influenzae
2. Know the clinical manifestations, diagnostic features, management, and complications of neonatal infection with Haemophilus influenzae
j. Chlamydial infections
1. Understand the epidemiology, pathogenesis, and prevention of neonatal infection with Chlamydia
2. Know the clinical manifestations, diagnostic features, management, and complications of neonatal infection with Chlamydia

k. Clostridial infections
1. Know the epidemiology and pathogenesis of Clostridial infections including Clostridium botulinum, difficile, and tetani
2. Know the prevention of Clostridial infections including Clostridium botulinum, difficile, and tetani
3. Know the clinical manifestations, diagnostic features, management, and complications of Clostridial infections including Clostridium botulinum, difficile, and tetani

l. Tuberculosis
1. Know the epidemiology, pathogenesis, and prevention of perinatal infections with Mycobacterium tuberculosis
2. Know the clinical manifestations, diagnostic features, management, and complications of perinatal infections with Mycobacterium tuberculosis

2. Viruses (Maternal screening covered in I.B.1)
   a. Herpes viruses
      1. Know the management of an infant born to a mother with active genital herpes lesions or with a history of genital herpes infection
      2. Know the epidemiology, prevention, and pathogenesis of perinatal infections with herpes 1, herpes 2, cytomegalovirus, Epstein-Barr virus, and varicella-zoster
      3. Know the clinical manifestations, diagnostic features, management, and complications of perinatal infections with herpes 1, herpes 2, cytomegalovirus, Epstein-Barr virus, and varicella-zoster

   b. Hepatitis viruses
      1. Know the management of an infant whose mother's serum contains hepatitis B surface antigen
      2. Know the epidemiology, prevention, and pathogenesis of perinatal infections with hepatitis A, hepatitis B, hepatitis C, and hepatitis D
      3. Know the clinical manifestations, diagnostic features, management, and complications of perinatal infections with hepatitis A, hepatitis B, hepatitis C, and hepatitis D

   c. Measles, mumps, and rubella (see also XIII.D.2.)
      1. Know the epidemiology, pathogenesis, and prevention of congenital infections with measles, mumps, and rubella
      2. Know the clinical manifestations, diagnostic criteria, treatment, and complications of congenital infections with measles, mumps, or rubella

   d. Enteroviruses
      1. Know the epidemiology, pathogenesis, and prevention of perinatal infections with coxsackievirus, echovirus, enterovirus, and poliovirus
      2. Understand the clinical manifestations, diagnostic criteria, treatment, and complications of perinatal infections with coxsackievirus, echovirus, enterovirus, and poliovirus
e. Influenza
   1. Know the epidemiology, clinical manifestations, diagnostic criteria, prevention, and management of perinatal infections with influenza
f. Respiratory syncytial virus
   1. Know the epidemiology, pathogenesis, and prevention of neonatal infections with respiratory syncytial virus
   2. Know the clinical manifestations, diagnostic features, management, and complications of neonatal infections with respiratory syncytial virus
g. Rotavirus
   1. Know the epidemiology, pathogenesis, and prevention of neonatal rotavirus infection
   2. Know the clinical manifestations, diagnostic features, management, and complications of neonatal rotavirus infection
h. HIV (see also I.A.2)
   1. Know the epidemiology, prevention, and pathogenesis of perinatal HIV infection
   2. Know the clinical manifestations and diagnostic features of perinatal HIV infection
   3. Know the treatment and complications of perinatal HIV infection
i. Parvovirus
   1. Know the epidemiology, pathogenesis, and prevention of perinatal parvovirus infections
   2. Know the clinical manifestations, diagnostic features, treatment, and complications of perinatal parvovirus infections
j. Metapneumovirus
   1. Know the epidemiology, pathogenesis, and prevention of congenital and neonatal metapneumovirus infections
   2. Know the clinical manifestations, diagnostic features, treatment, and complications of congenital and neonatal metapneumovirus infections
3. Fungi
   a. Know the epidemiology, prevention, and pathogenesis of neonatal fungal infections
   b. Know the clinical manifestations and diagnostic features of neonatal fungal infections
   c. Know the treatment and complications of neonatal fungal infections
4. Protozoa
   a. Know the clinical manifestations, diagnostic features, management, and complications of neonatal malaria
   b. Know the epidemiology, pathogenesis, and prevention of perinatal infections with toxoplasmosis
   c. Know the clinical manifestations, diagnostic features, management, and complications of perinatal infections with toxoplasmosis
C. Prevention of infections
   1. Know the effective techniques for control of healthcare associated infection in the nursery, neonatal intensive care unit, and obstetrical unit
   2. Recognize infectious agents that are transmitted in human milk
3. Plan the management of an exposure to varicella in the newborn nursery or newborn intensive care unit
4. Know the pathogenesis and prevention of transmission of infections with multi-drug-resistant bacteria
5. Know strategies to prevent and manage central line-associated bloodstream infections and understand their complications
6. Know strategies to prevent ventilator-associated pneumonia

D. Immunization
1. Know the immunizations recommended by the American Academy of Pediatrics and the appropriate schedules for immunizing preterm and full-term infants

11. Gastroenterology
A. Development of gastrointestinal (GI) anomalies
1. The gastrointestinal tract
   a. Morphogenesis
      1. Know the modes of inheritance of various inherited and genetic disorders of the GI tract
      2. Know the morphogenesis of the GI tract and factors that lead to congenital malformations
   b. Cellular proliferation, differentiation and maturation
      1. Know the dietary and hormonal agents that have trophic effects on the infant's GI tract
   c. Development of digestive and absorptive capabilities
      1. Protein digestion and absorption (See also VI.A.2.c.)
         a. Know the changes that occur in gastric acidity in term and preterm infants during the immediate neonatal period
         b. Know the factors involved in protein digestion and absorption
      2. Carbohydrate digestion and absorption (See also VI.A.2.e.)
         a. Know the developmental pattern of enzymes required for carbohydrate digestion
         b. Know other factors involved in carbohydrate digestion and absorption
      3. Lipid digestion and absorption (See also VI.A.2.d.)
         a. Know the factors involved in the process of lipid digestion and absorption and how it differs in infants fed breast milk vs. commercial infant formula
         b. Know the difference between the digestion and absorption of medium versus long-chain fatty acids
   d. Development of motility
      1. Identify the developmental pattern for motility of various segments of the alimentary canal
      2. Know the factors that may inhibit or improve intestinal motility
   e. Development of immune function of the intestinal tract
      1. Recognize the immaturity of the immune function of the GI tract during development
2. Developmental anomalies
   a. General
      1. Know the differential diagnosis of bilious and non-bilious vomiting and abdominal distention in the neonate
2. Understand the differential diagnosis of delayed passage of meconium

b. Mouth and pharynx
c. Esophagus
   1. Know the clinical manifestations of duplications of the esophagus
   2. Know the various types and diagnostic features of tracheoesophageal fistulae and esophageal atresias
   3. Know the management and the complications of surgical repair of tracheoesophageal fistulae and esophageal atresias
   4. Know the clinical manifestations and diagnostic features of gastroesophageal reflux in neonates
   5. Know the management of gastroesophageal reflux in neonates
d. Stomach
   1. Recognize the clinical manifestations of the developmental defects of the stomach, including absence, volvulus, pyloric stenosis, and pyloric atresia
   2. Know the approach to diagnosis and management of the developmental defects of the stomach, including absence, volvulus, pyloric stenosis, and pyloric atresia
e. Small intestine
   1. Know the pathogenesis of atresias, stenosis, diverticulae, and duplications of the small intestine including those associated with annular pancreas
   2. Know the clinical manifestations of atresias, stenosis, diverticulae, and duplications of the small intestine including those associated with annular pancreas
   3. Know the approach to diagnosis and management of atresias, stenosis, diverticulae, and duplication of the small intestine including those associated with annular pancreas
   4. Know the pathogenesis and clinical manifestations of infants with malrotation and/or volvulus of the small intestines
   5. Know the approach to diagnosis and management of infants with malrotation and/or volvulus of the small intestine
f. Large intestine
   1. Understand the consequences of resection of the distal ileum and cecum
   2. Know the pathogenesis and clinical manifestations of atresias, stenosis, and diverticulae of the large intestine
   3. Know the approach to diagnosis and management of atresias, stenosis, and diverticulae of the large intestine
   4. Know the etiology, clinical manifestations, diagnostic features, and management of the small left colon syndrome
   5. Know the pathophysiology, clinical manifestations, diagnostic features, and management of the meconium plug syndrome
g. Rectum and anus
   1. Know the pathogenesis of rectal and anal malformations and associated anomalies
   2. Know the diagnosis and management of rectal and anal malformations and associated anomalies
3. Know the pathological, clinical, and diagnostic features of Hirschsprung disease, including other associated clinical conditions
4. Know the management and complications of treatment of Hirschsprung disease

h. Pancreas
1. Recognize the clinical manifestations, diagnosis, and treatment of pancreatic aplasia and hypoplasia, including Shwachman syndrome
2. Know the clinical manifestations and pathophysiology of cystic fibrosis in the newborn infant
3. Know the diagnosis and management of cystic fibrosis in newborn infants
4. Know the clinical manifestations, diagnosis, and management of meconium ileus in the preterm and term neonate
5. Know the clinical manifestations, diagnosis, and management of meconium peritonitis in the neonate

i. Abdominal wall defects
1. Gastrochisis
   a. Know the pathogenesis, clinical manifestations, and associated abnormalities of gastrochisis
   b. Know the approach to management, the complications, and the difficulties in providing enteral nutrition to neonates with gastrochisis
2. Omphalocele
   a. Know the pathogenesis and anomalies associated with omphalocele
   b. Know the approach to management, clinical manifestations, the differential diagnosis of, and the complications of treatment of omphalocele in neonates

j. Syndromes associated with gastrointestinal malformation
1. Recognize the association of major congenital anomalies involving the GI tract and abdominal wall with those involving other organs

B. Acquired disorders of the GI tract
1. GI bleeding
   a. Know the clinical manifestations and differential diagnosis of GI bleeding in newborn infants, including the various coagulation disorders that cause GI hemorrhage
   b. Know the laboratory and radiographic findings, evaluation, and management of GI bleeding in newborn infants
2. Necrotizing enterocolitis (NEC)/GI Perforations
   a. Recognize the clinical manifestations, diagnosis, and management of infants with perforations of the gastrointestinal tract (including gastric and intestinal)
   b. Know the pathophysiology of NEC
   c. Know the clinical and diagnostic features, evaluation, management, and complications of NEC
   d. Know the clinical features, complications, and management of short bowel syndrome
3. Neonatal intussusception
   a. Recognize the clinical signs, imaging features, and treatment of neonatal intussusception
4. Strictures of the intestines
a. Know the etiology, clinical manifestations, diagnosis, and management of GI strictures

5. Infectious enteritis and colitis (see also X.B.1.h)
   a. Identify the etiological agents, modes of transmission, and clinical manifestations of infectious enteritis and colitis in the neonate
   b. Know the differential diagnosis, diagnostic and laboratory features, and approach to management of infectious enteritis and colitis in the neonate

6. Allergic enteritis and colitis
   a. Know the clinical manifestations, diagnosis, and management of allergic enteritis and colitis such as milk protein allergy

C. Malabsorption syndromes
   1. Know the causes, clinical manifestations, diagnosis, and management of congenital or acquired malabsorption syndromes

D. Liver disease of the newborn infant
   1. Congenital malformations of the liver and bile ducts
      a. Choledochal cysts
         1. Know the clinical manifestations, diagnostic features, and treatment of infants with choledochal cysts
      b. Intrahepatic biliary hypoplasia
         1. Know the pathogenesis and clinical features, differential diagnosis, and treatment of intrahepatic biliary hypoplasia
      c. Extrahepatic biliary atresia
         1. Know the pathogenesis and clinical manifestations of extrahepatic biliary atresia
         2. Know the clinical, laboratory, and diagnostic features of extra-hepatic biliary atresia that differentiate it from neonatal hepatitis and other causes of cholestasis in the neonate and know the approach to management of extrahepatic biliary atresia

2. Cholestasis of the neonate
   a. Metabolic and familial causes of cholestasis
      1. Know the etiology, clinical manifestations, and differential diagnosis of metabolic and familial causes of cholestasis in the neonate
      2. Know the laboratory and imaging features and management of metabolic and familial causes of cholestasis in the neonate
   b. Cholestasis associated with TPN (See V.I.D.3.)

3. Infectious diseases of the liver (See also X.B.2.b, etc)
   a. Know the various etiologies, including bacterial, viral, and protozoal agents, and clinical manifestations of hepatitis in the newborn
   b. Know the approach to the diagnosis and management of various types of hepatitis in the newborn including those caused by bacterial, viral, and protozoal agents

E. Abdominal masses/Neonatal ascites
   1. Know the etiology, clinical and laboratory features, and management of abdominal masses in the neonate
   2. Know the etiology, clinical manifestations, diagnostic features, and management of neonatal ascites

12. Bilirubin
A. Biochemistry, metabolism, and measurement

1. Biochemistry and metabolism
   a. Know the factors that affect the biological properties of bilirubin, including its solubility and tissue distribution
   b. Know bilirubin physiology, including pathways of synthesis, transport, and metabolism, in the fetus and neonate
   c. Know the factors, including red cell life span, enzyme defects, and red cell structural abnormalities, associated with an increase in bilirubin production
   d. Know the factors associated with a decrease in neonatal serum bilirubin excretion, including those that affect the enterohepatic circulation of bilirubin

2. Measurement
   a. Know the differences between physiologic and nonphysiologic jaundice
   b. Know how to use a pre-discharge bilirubin measurement to predict the risk of severe hyperbilirubinemia

B. Bilirubin toxicity and pathologic hyperbilirubinemia

1. Bilirubin toxicity
   a. Pathophysiology
      1. Know the pathologic findings of kernicterus
      2. Know the factors affecting the binding of bilirubin to albumin and know the pharmacologic agents which affect binding
      3. Know the factors that increase the risk of the development of kernicterus
   b. Acute manifestations
      1. Know the clinical features of acute bilirubin encephalopathy in newborn infants
   c. Sequelae
      1. Know the clinical features of kernicterus

2. Pathologic indirect hyperbilirubinemia
   a. Etiology and differential diagnosis
      1. Know the differential diagnosis and evaluation of infants with indirect hyperbilirubinemia
   b. Management
      1. Know the indications for and risks and complications of exchange transfusions
      2. Know the indications for use, the mechanism of action, the efficacy, and the dose-response relationship of phototherapy in the treatment of neonatal hyperbilirubinemia
      3. Know the side effects and complications of phototherapy
      4. Know the effects of drugs and other therapeutic agents in the treatment of hyperbilirubinemia

C. Physiologic and human milk jaundice

1. Physiologic jaundice
   a. Influencing factors
      1. Know the mechanisms for physiologic jaundice
      2. Know the course of physiologic jaundice in the newborn infant
      3. Know the range of normal serum bilirubin concentration and the effects of an infant's age, race, and feeding circumstances on serum bilirubin

2. Breast-feeding jaundice
   a. Influencing factors
1. Know the pathogenesis, clinical course, diagnosis, and management of breast-feeding jaundice

13. **Skin Disorders**
   A. Skin development and function (see also VII.A.1.c)
      1. Know the development of the human skin and understand the differences between preterm and full-term skin
      2. Know the rationale for various treatment strategies designed to decrease rates of transepidermal water loss in preterm infants
      3. Know the complications and management of various neonatal skin injuries including IV infiltrates and chemical and thermal burns
      4. Know the potential toxicity of various drugs applied topically to newborn skin, including antiseptics, lidocaine, and mydriatic agents
   B. Hair and nail disorders
      1. Know the diagnoses associated with abnormalities of hair and nails
   C. Vesicobullous lesions
      1. General
         a. Know the etiology and differential diagnosis of bullous skin lesions
         b. Know the management of bullous skin lesions in the newborn infant
      2. Infectious (see also X.B.)
         a. Know the cutaneous manifestations of congenital syphilis
         b. Know the cutaneous manifestations of severe candidiasis
         c. Know the cutaneous and laboratory manifestations and management of bullous impetigo
         d. Know the cutaneous manifestations of herpes simplex and varicella zoster
         e. Know the cutaneous manifestations of *Listeria monocytogenes*
         f. Know the cutaneous and laboratory manifestations of scalded skin syndrome
         g. Know the treatment of scalded skin syndrome
      3. Non-infectious
         a. Know the cutaneous and laboratory manifestations and management of acrodermatitis enteropathica
         b. Know the inheritance patterns, cutaneous and laboratory manifestations, management, and outcome of epidermolysis bullosa
   D. Maculopapular eruptions
      1. Petechial or purpuric
         a. Infectious (see also X.B.2.a. and c.)
            1. Know the pathogenesis and cutaneous manifestations of CMV
            2. Know the cutaneous manifestations of rubella
         b. Noninfectious (see also XIV.C)
            1. Know the cutaneous manifestations of neonatal hematologic disorders such as thrombocytopenia and coagulation disorders
      2. Common neonatal dermatoses
         a. Know the etiology and cutaneous manifestations of common neonatal skin lesions, including erythema toxicum, neonatal pustular melanosis, and neonatal acne
         b. Know the management of common neonatal dermatoses, including diaper dermatitis
   E. Scaly disorders
1. Know how to recognize, diagnose and manage scaly disorders of the skin, including neonatal ichthyoses

F. Vascular lesions
1. Know how to diagnose and manage capillary and cavernous hemangiomas
2. Know how to diagnose and manage Kasabach-Merritt syndrome
3. Know how to diagnose and manage port wine stain and know the association with Sturge-Weber syndrome

G. Other
1. Pigmentary anomalies
   a. Know the differential diagnosis and syndromes associated with hyperpigmented lesions, including café au lait spots, Peutz-Jeghers syndrome, giant hairy nevus, incontinentia pigmenti, and pigmented nevi
   b. Know the differential diagnosis and syndromes associated with hypopigmented lesions (e.g., ash leaf macules, white forelock) and hypopigmentation, including albinism, partial albinism, phenylketonuria, Chediak-Higashi syndrome, tuberous sclerosis, and Waardenburg syndrome

2. Other
   a. Know the differential diagnosis and management of ectodermal dysplasias
   b. Know the cutaneous manifestations of neonatal lupus erythematosus
   c. Know the diagnostic approach and genetic basis of heritable disorders of the skin, including ichthyoses, incontinentia pigmenti, cutis laxa, and cutis aplasia
   d. Know how to evaluate and manage disorders of the umbilical cord, including granulomas, persistent omphalomesenteric duct remnant, and patent urachus

14. Hematology/Oncology
A. Erythrocytes
1. Biology of hemoglobin
   a. Know the biochemical characteristics of fetal hemoglobin
   b. Know the developmental biology of hemoglobin types
   c. Know the clinical and laboratory features of neonatal hemoglobinopathies, including the thalassemias
   d. Know the indications for and approaches to screening for hemoglobinopathies in the newborn population
2. Erythropoiesis
   a. Know normal erythropoiesis in the fetus and neonate
   b. Know the factors regulating erythropoiesis in the fetus and neonate including erythropoietin
3. Anemia
   a. General
      1. Know the causes of and diagnostic approach to an infant who is anemic at birth
   b. Hypoproduction
      1. Know the mechanisms resulting in anemia of prematurity
      2. Know the causes of and approaches to management of an infant with anemia of prematurity
      3. Understand the mechanism and gestational timing of placental transfer of iron to the fetus and its effect on iron stores in newborn infants
4. Recognize the causes of iron deficiency anemia and various prevention measures
5. Recognize the clinical and diagnostic features, laboratory findings, management, and long-term consequences of iron deficiency anemia

c. Hemolysis
   1. Know the etiology and pathophysiology of hemolytic anemias in the neonate
   2. Know the clinical and laboratory features of hemolytic anemia in the neonate
   3. Know the management of hemolytic anemia in the neonate

d. Blood loss (see I.C.2.)

4. Polycythemia
   a. Know the causes of neonatal polycythemia
   b. Know the clinical manifestations, evaluation management, and outcomes of neonatal polycythemia

5. Blood groups; physiology and pathophysiology
   a. Know the inheritance patterns of the major blood groups

B. Granulocytes, monocytes, and macrophages (see IX.B.3.a.(5))

C. Platelets and coagulation
   1. Platelets
      a. Developmental biology
         1. Know the normal pattern of platelet production and maturation
      b. Thrombocytopenia/thrombocytosis (see also XIII.D.1.b.)
         1. Know the causes and pathophysiology of neonatal thrombocytopenia and thrombocytosis
         2. Know the clinical and laboratory manifestations and management of neonatal thrombocytopenia and thrombocytosis
   2. Coagulation
      a. General (see also VII.B.3.a. and XIII.D.1.b.)
         1. Know the inheritance patterns of the common coagulation factor deficiencies
         2. Know the causes and pathophysiology of congenital and acquired thrombotic disorders
         3. Know the clinical and laboratory features, management, and potential adverse effects of treatment of congenital and acquired thrombotic disorders
         4. Know the causes and pathophysiology of acquired defects in hemostasis
         5. Know the clinical and laboratory features and management of acquired defects in hemostasis including intravascular coagulation and hemorrhagic disease of the newborn
         6. Know the causes and pathophysiology of congenital defects in hemostasis
         7. Know the clinical manifestations, laboratory findings, and management of congenital defects in hemostasis
         8. Know the pathogenesis and complications of catheter related thrombi including umbilical arterial and central venous catheters
   
D. Oncology
   1. Leukemias
      a. Know the clinical and laboratory features of congenital leukemia
   2. Solid tumors and others (eg, histiocytosis)
a. Know the cutaneous and laboratory manifestations, including imaging studies, and management of Langerhans cell histiocytosis
b. Know the clinical, laboratory, and imaging features and management of neonatal teratoma
c. Know the clinical, laboratory, and imaging features and management of hemangiomas in the newborn
d. Know the clinical, laboratory, and imaging features and management of neuroblastoma in the newborn
e. Know the clinical and laboratory features and management of rhabdomyomas in the newborn and its association with tuberous sclerosis
f. Know the clinical, laboratory, and imaging features of Wilms tumor

E. Transfusions and component therapy
1. Know the clinical indications for use of blood products in neonates, as well as the manifestations and prevention of potential complications of transfusion

15. Neurology
A. Neurologic evaluation
1. Physical examination (see XVI.A.1.)
   a. Recognize the ocular signs associated with increased intracranial pressure
   b. Know the differential diagnosis of fixed dilated pupils
   c. Realize the importance and neurodevelopmental consequences of optic atrophy
   d. Know the neuroanatomic basis, function, and methods of testing cranial nerve function in the newborn infant
   e. Know the normal integrated (primitive) reflexes that are present in the newborn infant (such as Moro, tonic neck, rooting, and grasping) and their maturation
   f. Know how a newborn infant's posture, spontaneous activity, and elicited movements are influenced by postmenstrual age and neurologic status
   g. Identify the various maneuvers used to evaluate active and passive tone in newborn infants, and know how they change with maturation
   h. Know the significance of persistent neuromotor abnormalities in infancy (including asymmetries)
   i. Recognize normal deep tendon reflexes (DTRs) in newborn infants, including unsustained clonus
   j. Know physical findings indicative of neonatal encephalopathy
   k. Know the significance and differential diagnosis of jitteriness and irritability in neonates

2. Neurodiagnostic tests (See also XVII.B.2.)
   a. Know the indications for and limitations of various neurodiagnostic tests
   b. Understand the indications for, contraindications, and interpretation of spinal fluid analysis

3. Neuroimaging studies
   a. Know the indications for and limitations of various neuroimaging studies and be able to recognize normal and abnormal structures and changes during development and growth
   b. Know the major patterns of injury resulting from term neonatal hypoxic-ischemic injury evident from neuroimaging studies
c. Know the major patterns of injury resulting from preterm brain injury evident from different neuroimaging studies

B. Development of the nervous system
1. CNS morphogenesis
   a. Know the normal developmental course of neuronal proliferation, migration, and myelination and the factors affecting these processes
   b. Know the clinical and imaging findings, treatment, and outcomes of abnormalities of neuronal proliferation, migration, and myelination (e.g., holoprosencephaly, agenesis of the corpus callosum, lissencephaly, and schizencephaly)
   c. Know the embryology, prevention, incidence, and differential diagnosis of myelomeningocele and encephalocele
   d. Know the clinical and imaging findings, treatment, and outcome of myelomeningocele and encephalocele
2. Cerebral blood flow
   a. Know the effects of variations in arterial and venous blood pressure, blood gas tensions, and hemoglobin concentration on cerebral blood flow, cerebral vascular resistance, and cerebral perfusion
   b. Know the effects of various therapeutic measures, including use of drugs (e.g., indomethacin, caffeine, dopamine) on cerebral perfusion
3. Neurotransmitters
   a. Know the important neurotransmitters and their physiological role
   b. Know the major drugs that interact directly with and their effect on neurotransmitter receptors in the developing brain
4. Macrocephaly/Hydrocephalus
   a. Know the familial/genetic features of neurologic disorders associated with increased head circumference
   b. Know the etiology, familial/genetic features, and abnormalities associated with hydrocephalus
   c. Know the management and outcome of an infant with hydrocephalus
   d. Know the significance and management of mild ventriculomegaly detected on a prenatal ultrasound examination
5. Microcephaly
   a. Know the causes, diagnosis, management and outcome of an infant with microcephaly

C. Encephalopathy
1. Hypoxic-ischemic (see also II.A.1.)
   a. Know the causes, clinical features, evaluation, and management of hypoxic-ischemic encephalopathy
   b. (3320) Know the outcome of infants with hypoxic-ischemic encephalopathy
   c. Know the neuroimaging features of hypoxic-ischemic injury in term infants
2. Metabolic
   a. Know the causes, clinical features, laboratory evaluation, and acute management of metabolic encephalopathies in newborn infants

D. Intracranial hemorrhage and vascular injury
1. Prenatal vascular injury (see also XV.D.4)
a. Know the risk factors (including genetic abnormalities) for and evaluation and management of a fetus or infant with prenatal vascular brain injury

2. Periventricular-intraventricular hemorrhage (PIVH)
   a. Know the risk factors for development, proposed mechanisms, clinical and laboratory features, and diagnosis of PIVH
   b. Know the proposed prevention strategies, evolution, early complications, management, and long-term consequences of PIVH
   c. Know the appropriate monitoring of acute and subacute PIVH during the neonatal period

3. Intraparenchymal cysts, echodensities, & periventricular leukomalacia
   a. Know the risk factors for development, proposed mechanisms, clinical and laboratory features, and diagnosis of intraparenchymal cysts/ periventricular leukomalacia, and intraparenchymal echodensities
   b. Know the proposed prevention strategies, evolution, early complications, management, and long-term consequences of intraparenchymal cysts/periventricular leukomalacia, and intraparenchymal echodensities
   c. Know the appropriate monitoring of intraparenchymal cysts/periventricular leukomalacia, and intraparenchymal echodensities during the neonatal period

4. Perinatal cerebral/cerebellar infarction (see also XV.D.1.)
   a. Know the pathogenesis, clinical and imaging features, diagnosis, management, and outcome associated with perinatal cerebral and cerebellar infarction

5. Subarachnoid hemorrhage
   a. Know the pathogenesis, clinical and imaging features, diagnosis, management, and outcome associated with subarachnoid hemorrhage

6. Subdural hematoma
   a. Understand the pathogenesis, clinical and imaging features, diagnosis, management, and outcome associated with subdural hematoma

E. Cranial and neurologic trauma (see also XV.D.5. and D.6.)
   1. Extracranial hemorrhage
      a. Know the diagnostic, clinical, and imaging features of extracranial hemorrhage, including cephalohematoma and subgaleal hemorrhage
      b. Know the management, complications, and outcomes of extracranial hemorrhage, including cephalohematoma and subgaleal hemorrhage
   2. Nerve injury
      a. Recognize the clinical features of cranial nerve, cervical root, and brachial plexus palsies, including risk factors
      b. Know the diagnosis, management, and outcome of cervical root and brachial plexus injury
   3. Spinal cord injury
      a. Know the diagnosis, clinical and imaging features, management and outcome of spinal cord injury
   4. Skull fracture
      a. Know the diagnosis, clinical and imaging features, management, and outcome of skull fracture

F. Seizures
   1. Classification
a. Understand the spectrum of seizures in the newborn infant

2. Diagnosis and management
   a. Understand the differential diagnosis and evaluation of neonatal seizures
   b. Understand the management of neonatal seizures, including the role of neurophysiologic monitoring
   c. Understand the clinical manifestations of neonatal seizures, and their prognosis
   d. Understand the prognostic significance of electroencephalographic patterns, such as burst suppression

G. Infections
   1. Know the causative infectious agents and pathogenesis of early and late-onset meningitis as well as meningitis associated with ventricular drainage devices
   2. Know the clinical manifestations and laboratory features of meningitis and meningoencephalitis
   3. Know the management, complications, and outcomes of meningitis and meningoencephalitis

H. Neonatal abstinence and withdrawal syndromes (see also I.A.4.)
   1. Know the drugs associated with neonatal abstinence syndromes including maternal substance abuse and those administered in the NICU
   2. Know the clinical and laboratory features of neonatal abstinence syndromes
   3. Know the management of neonatal abstinence syndromes

I. Other
   1. Hypotonia/neuromuscular weakness
      a. Know the basis for (including genetic), clinical and laboratory features (including associated abnormalities), differential diagnosis, evaluation, management, and outcomes of neonatal hypotonia/neuro-muscular weakness
   2. Arthrogryposis
      a. Know the pathogenesis, evaluation, clinical and laboratory features, management, and outcomes of neonatal arthrogryposis
   3. Vascular malformations
      a. Know the clinical features and evaluation, management, complications of management, and outcome of intracranial arteriovenous malformations
   4. Congenital cerebral neoplasms
      a. Know the clinical features, diagnosis, management, and outcome of cerebral neoplasms
   5. Neurocutaneous disorders (see also XIII.F.)
      a. Know the clinical features, diagnosis, management and outcome of neurocutaneous disorders including neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, etc.

16. Neurodevelopmental outcomes
   A. Incidence
      1. Know the risks of neurodevelopmental impairments in term infants, late preterm infants, moderately preterm infants, and extremely preterm infants, with and without neurologic risk factors
      2. Know the risks of neurodevelopmental impairments after fetal high risk conditions such as the in utero death of a monozygotic twin and intrauterine growth restriction
3. Know the risks of neurodevelopmental impairments in full-term infants with medical risk factors such as pulmonary hypertension, congenital heart disease and chronic lung disease

B. Etiologies (see also XVII.A.3.d.)
1. Know the importance of prenatal and postnatal nutrition on neurodevelopmental outcomes, including the importance of breast milk for brain development
2. Know the neonatal conditions that are associated with vision loss in preterm and full-term infants

C. Clinical features
1. Know the evolution of neurodevelopmental impairments during development and the difference between transient and permanent impairments in NICU graduates (eg, developmental delay vs. intellectual disability; tone abnormalities vs. cerebral palsy)
2. Know the value and limitations of the Bayley Scales of Infant Development and other tests of psychomotor development in assessing current function and predicting long-term outcomes

D. Effects of the environment
1. Know the maternal and infant conditions that may interfere with maternal-infant bonding and the potential effects on subsequent development
2. Know the effects of neonatal positioning on skull shape, muscle tone and early patterns of motor development
3. Know the effects of family risk factors (low socioeconomic status, mental health problems) on cognitive outcomes
4. Know the effects of socioeconomic factors on the results and generalizability of outcome studies of neonatal intensive care unit graduates
5. Know the rationale for early intervention programs for infants at risk for cognitive and behavioral problems

17. Eyes, Ears, Nose, Mouth, Throat, and Neck

A. Eyes
1. Normal development and anatomy
   a. Know the normal anatomy and ophthalmologic findings of the developing eye
2. Abnormalities of the eye
   a. Congenital abnormalities
      1. Recognize the importance of corneal opacifications
      2. Know the syndromes associated with abnormalities of the eye including cranio-facial abnormalities, coloboma, abnormalities of the orbit, the eyebrows, the eyelids, the eyelashes, the cornea, the iris, and the retina
      3. Identify the conditions associated with a white pupil (ie leukokoria)
      4. Recognize the signs of and know the conditions associated with congenital glaucoma
      5. Recognize the signs of, and know the conditions associated with, neonatal cataracts
   b. Acquired abnormalities, other than retinopathy of prematurity
      1. Know the ocular findings associated with congenital infections
      2. Know the benefits and complications of eye prophylaxis (e.g. obstructed nasolacrimal duct)
3. Know the causes and clinical and laboratory features of acute neonatal infections of the eyes, including ophthalmia neonatorum
4. Know the management and complications of acute neonatal infections of the eyes, including ophthalmia neonatorum
5. Know the findings and management of the ophthalmic complications of eye trauma that may occur in difficult deliveries or in the "shaken baby" syndrome
6. Know the causes and management of excess tearing
c. Tumors of the eye
   1. Know the inheritance pattern, clinical manifestations, treatment and outcomes (including associated conditions) of retinoblastoma
d. Retinopathy of prematurity
   1. Know the normal vascularization of the retina
   2. Know the risk factors for and pathophysiology of retinopathy of prematurity, and approaches to prevention
   3. Know the clinical features and course of retinopathy of prematurity and the staging of severity according to the international classification
   4. Know the treatment and outcome of retinopathy of prematurity in relation to severity and therapy

B. Ears
   1. Normal development and anatomy
      a. Know the normal anatomy and positioning of the ear
   2. Abnormality of the ear
      a. Congenital (see also XV.A.2. and XVI.E.2.)
         1. Recognize the association of abnormalities of the ear and congenital syndromes
         2. Know the incidence, causes, risk factors, and management of congenital hearing loss in the neonate
      b. Acquired (otitis media covered in X.A.6)
         1. Know the incidence, causes, risk factors, and approaches to evaluation and management of acquired hearing loss in the neonate
      c. Evaluation
         1. Know the methods used to screen and evaluate hearing in newborns, including auditory brainstem responses and otoacoustic emissions

C. Nose, mouth, throat, and neck
   1. Normal development of the nose, mouth, throat, and neck
   2. Congenital abnormalities
      a. Know the clinical and diagnostic features of the DiGeorge sequence (velocardiofacial syndrome, 22q11 deletion)
      b. Know the clinical manifestations of branchial cleft cysts
      c. Know syndromes associated with abnormalities of nasal development including low nasal bridge, broad nasal ridge, short and anteverted nostrils
      d. Know the various causes of stridor in the newborn and how to assess severity
      e. Know the incidence, genetics, evaluation, and management of cleft lip and palate
      f. Know the incidence, clinical manifestations, and management of bilateral and unilateral choanal atresia
      g. Know the clinical manifestations and approaches to therapy of neck masses in the newborn infant
h. Know the associations and clinical features and management of macroglossia and hypoplastic mandible, including the Pierre-Robin syndrome

3. Acquired abnormalities
   a. Know the complications of tracheal intubation, including tracheal perforation and subglottic stenosis
   b. Know the etiology and clinical features of necrotizing tracheitis
   c. Know the indications for and the complications of tracheostomies

18. Basic Principles of Pharmacology
   A. Drug disposition and pharmacokinetics
      1. Absorption
         a. Know the physiological and pathophysiological factors that influence drug absorption and bioavailability and the clinical implications of how this changes in the newborn period
      2. Distribution
         a. Know the physiological and pathophysiological factors involved in the distribution of a drug (ie, factors influencing peak serum concentration of a drug) and the clinical implications of how this changes in the newborn period
         b. Know the physiological and pathophysiological factors that determine protein-binding of a drug in plasma and the clinical implications of how this changes in the newborn period
         c. Know the factors that affect transplacental passage of a drug
         d. Know the definition of the steady state of a drug during administration
      3. Metabolism and elimination
         a. Know the general mechanisms by which various drugs are metabolized and the clinical implications of how this changes in the newborn period
         b. Know the mechanisms by which various drugs are eliminated and the clinical implications of how this changes in the newborn period
         c. Know how to modify drug therapy in the presence of renal or hepatic disease
      4. Pharmacokinetics
         a. General
            1. Know basic pharmacokinetics and basic pharmacokinetic definitions including the basic definitions of linear (single compartment) and nonlinear (multiple-compartment) pharmacokinetics
            2. Know the definitions of drug dose, serum concentrations, and volume of distribution, and know how these values are mathematically related
            3. Know the definitions of drug half-life, elimination rate constant, and clearance, and know how these values are mathematically related
            4. Know the application of pharmacokinetic principles (both first-order and zero-order kinetics) in administration of drugs by continuous infusion
         b. Basic calculations of dosages
            1. Know how to calculate a drug dose in order to achieve a certain serum concentration
            2. Know how to use serum drug concentrations to adjust the dosing regimen of drug eliminated by first-order kinetics
   B. Clinical toxicology
1. Recognize drugs that, when taken by a nursing mother, are known to present health risks to her breast-feeding infant, and know the factors that modify these risks
2. Recognize drugs that cross the placenta and are known to present health risks to the developing fetus or to the newborn infant
C. Indications/mechanisms/adverse reactions of specific types of drugs
   1. For antibiotics used commonly in the neonate, know indications for their use, clinical effects, side effects, and toxicity
   2. For therapeutic drugs commonly used in the neonate (eg, opiates, methylxanthines, barbiturates, etc), know indications for their use, clinical effects, side effects, and toxicity
   3. Know the implications of FDA approval, drug labeling, and off-label use

19. Health Services Delivery, Ethical Issues, and Family Counseling
   A. The organization and issues of perinatal and neonatal care
      1. The organization of perinatal care
         a. Know the issues in the organization of perinatal care (e.g., regionalization, transport, practice guidelines, benchmarking data, quality improvement)
      2. Awareness of public health issues, services and delivery
         a. Definitions
            1. Know the definitions of perinatal, neonatal, postneonatal, and infant mortality
         b. Immunizations (See Section IX.)
         c. Control of infection (See Section X.)
   B. Ethical and legal issues and death and dying
      1. Ethical and legal issues
         a. Maternal versus fetal rights
            1. Know the evolving issues of maternal versus fetal rights
         b. Limit of viability
            1. Recognize the controversies associated with treating extremely premature infants
         c. Limits of technology
            1. Recognize the controversies associated with the introduction of new technologies to treat previously fatal disorders, such as an experimental therapy that may save a life, prolong a life, or prolong death
            d. Genetic testing and gene therapy
               1. Recognize the controversies associated with the introduction of new genetic tests for rare and common diseases that present in the neonatal period
               2. Recognize the controversies associated with the development of gene-based therapies to treat neonatal conditions
      2. Death and dying
         a. Know the components of bereavement counseling prior to, during, and after the death of a newborn infant, including palliative care
         b. Recognize the importance of obtaining an autopsy and understand the proper way to seek consent from and to share the results with the parents

20. Core Knowledge in Scholarly Activities
   A. Principles of Use of Biostatistics in Research
      1. Types of variables
         a. Distinguish types of variables (eg, continuous, categorical, ordinal, nominal)
b. Understand how the type of variable (e.g., continuous, categorical, nominal) affects the choice of statistical test

2. Distribution of data
   a. Understand how distribution of data affects the choice of statistical test
   b. Differentiate normal from skewed distribution of data
   c. Understand the appropriate use of the mean, median, and mode
   d. Understand the appropriate use of standard deviation
   e. Understand the appropriate use of standard error

3. Hypothesis testing
   a. Distinguish the null hypothesis from an alternative hypothesis
   b. Interpret the results of hypothesis testing

4. Statistical tests
   a. Understand the appropriate use of the chi-square test versus a t-test
   b. Understand the appropriate use of analysis of variance (ANOVA)
   c. Understand the appropriate use of parametric (e.g., t-test, ANOVA) versus non-parametric (e.g., Mann-Whitney U, Wilcoxon) statistical tests
   d. Interpret the results of chi-square tests
   e. Interpret the results of t-tests
   f. Understand the appropriate use of a paired and non-paired t-test
   g. Determine the appropriate use of a 1- versus 2-tailed test of significance
   h. Interpret a p-value
   i. Interpret a p-value when multiple comparisons have been made
   j. Interpret a confidence interval
   k. Identify a type I error
   l. Identify a type II error

5. Measurement of association
   a. Differentiate relative risk reduction from absolute risk reduction
   b. Calculate and interpret a relative risk
   c. Calculate and interpret an odds ratio
   d. Understand the uses and limitations of a correlation coefficient
   e. Interpret a hazard ratio

6. Regression
   a. Identify when to apply regression analysis (e.g., linear, logistic)
   b. Interpret a regression analysis (e.g., linear, logistic)
   c. Identify when to apply survival analysis (e.g., Kaplan-Meier)
   d. Interpret a survival analysis (e.g., Kaplan-Meier)

7. Diagnostic tests
   a. Recognize the importance of an independent "gold standard" in evaluating a diagnostic test
   b. Calculate and interpret sensitivity and specificity
   c. Calculate and interpret positive and negative predictive values
   d. Understand how disease prevalence affects the positive and negative predictive value of a test
   e. Calculate and interpret likelihood ratios
   f. Interpret a receiver operator characteristic curve
   g. Interpret and apply a clinical prediction rule
8. Systematic reviews and meta-analysis
   a. Understand the purpose of a systematic review
   b. Understand the advantages of adding a meta-analysis to a systematic review
   c. Interpret the results of a meta-analysis
   d. Identify the limitations of a systematic review
   e. Identify the limitations of a meta-analysis

B. Principles of Epidemiology and Clinical Research Design
1. Study types
   a. Distinguish between Phase I, II, III, and IV clinical trials
   b. Recognize a retrospective study
   c. Understand the strengths and limitations of retrospective studies
   d. Recognize a case series
   e. Understand the strengths and limitations of case series
   f. Recognize a cross-sectional study
   g. Understand the strengths and limitations of cross-sectional studies
   h. Recognize a case-control study
   i. Understand the strengths and limitations of case-control studies
   j. Recognize a longitudinal study
   k. Understand the strengths and limitations of longitudinal studies
   l. Recognize a cohort study
   m. Understand the strengths and limitations of cohort studies
   n. Recognize a randomized-controlled study
   o. Understand the strengths and limitations of randomized-controlled studies
   p. Recognize a before-after study
   q. Understand the strengths and limitations of before-after studies
   r. Recognize a crossover study
   s. Understand the strengths and limitations of crossover studies
   t. Recognize an open-label study
   u. Understand the strengths and limitations of open-label studies
   v. Recognize a post-hoc analysis
   w. Understand the strengths and limitations of post-hoc analyses
   x. Recognize a subgroup analysis
   y. Understand the strengths and limitations of subgroup analyses

2. Bias and confounding
   a. Understand how bias affects the validity of results
   b. Understand how confounding affects the validity of results
   c. Identify common strategies in study design to avoid or reduce bias
   d. Identify common strategies in study design to avoid or reduce confounding
   e. Understand how study results may differ between distinct sub-populations (effect modification)

3. Causation
   a. Understand the difference between association and causation
   b. Identify factors that strengthen causal inference in observational studies (eg, temporal sequence, dose response, repetition in a different population, consistency with other studies, biologic plausibility)

4. Incidence and prevalence
a. Distinguish disease incidence from disease prevalence

5. Screening
   a. Understand factors that affect the rationale for screening for a condition or disease (eg, prevalence, test accuracy, risk-benefit, disease burden, presence of a presymptomatic state)

6. Decision analysis
   a. Understand the strengths and limitations of decision analyses
   b. Interpret a decision analysis

7. Cost-benefit, cost-effectiveness, and outcomes
   a. Differentiate cost-benefit from cost-effectiveness analysis
   b. Understand how quality-adjusted life years are used in cost analyses
   c. Understand the multiple perspectives (eg, of an individual, payor, society) that influence interpretation of cost-benefit and cost-effectiveness analyses

8. Sensitivity analysis
   a. Understand the strengths and limitations of sensitivity analysis
   b. Interpret the results of sensitivity analysis

9. Measurement
   a. Understand the types of validity that relate to measurement (eg, face, construct, criterion, predictive, content)
   b. Distinguish validity from reliability
   c. Distinguish internal from external validity
   d. Distinguish accuracy from precision
   e. Understand and interpret measurements of interobserver reliability (eg, kappa)
   f. Understand and interpret Cronbach's alpha

C. Applying Research to Clinical Practice

1. Assessment of study design, performance & analysis (internal validity)
   a. Recognize when appropriate control groups have been selected for a case-control study
   b. Recognize when appropriate control groups have been selected for a cohort study
   c. Recognize the use and limitations of surrogate endpoints
   d. Understand the use of intent-to-treat analysis
   e. Understand how sample size affects the power of a study
   f. Understand how sample size may limit the ability to detect adverse events
   g. Understand how to calculate an adequate sample size for a controlled trial (eg, clinically meaningful difference, variability in measurement, choice of alpha and beta)

2. Assessment of generalizability (external validity)
   a. Identify factors that contribute to or jeopardize generalizability
   b. Understand how non-representative samples can bias results
   c. Assess how the data source (eg, diaries, billing data, discharge diagnostic code) may affect study results

3. Application of information for patient care
   a. Estimate the post-test probability of a disease, given the pretest probability of the disease and the likelihood ratio for the test
   b. Calculate absolute risk reduction
   c. Calculate and interpret the number-needed-to-treat
d. Distinguish statistical significance from clinical importance

4. Using the medical literature
   a. Given the need for specific clinical information, identify a clear, structured, searchable clinical question
   b. Identify the study design most likely to yield valid information about the accuracy of a diagnostic test
   c. Identify the study design most likely to yield valid information about the benefits and/or harms of an intervention
   d. Identify the study design most likely to yield valid information about the prognosis of a condition

D. Principles of Teaching and Learning
   1. Educational theory
      a. Understand the basic principles of adult learning theory (eg, adult learners are self-directed, goal-oriented, practical; need to feel respected, build on life experiences; learn best when learning is based on an existing framework)
      b. Understand the attributes of an effective learning environment
      c. Understand the importance of "reflective practice" in teaching and learning
      d. Identify strategies that motivate learners
      e. Recognize the impact of the "hidden curriculum" on learning

2. Feedback and evaluation
   a. Identify components of effective feedback
   b. Distinguish between formative and summative feedback
   c. Distinguish between evaluation and feedback
   d. Understand the strengths and weaknesses of various methods to evaluate learners

3. Teaching methods
   a. Understand the strengths and weaknesses of various teaching methods (eg, lecture, small group discussion, bedside teaching, simulation)
   b. Understand that individuals may learn more effectively with certain teaching methods (eg, reading, hearing, doing) than with others

4. Education planning
   a. Understand the role of needs assessment in educational planning
   b. Distinguish between goals and learning objectives
   c. Identify components of well-formulated learning objectives
   d. Recognize the strengths and weaknesses of various educational outcome measures (eg, participant satisfaction, acquisition of knowledge and skills, behavioral change, patient outcomes)

E. Ethics in Research
   1. Conflicts of interest and commitment
      a. Evaluate whether an investigator has a conflict of interest during the course of a study
      b. Understand ways to manage a conflict of interest
      c. Understand what constitutes a conflict of commitment

2. Professionalism and misconduct in research
   a. Identify forms of research misconduct (eg, plagiarism, fabrication, falsification)
   b. Differentiate honest error and differences of opinion from research misconduct
   c. Understand the criteria for authorship of clinical research publications
3. Principles of research with human subjects
   a. Understand and apply the three main principles of research ethics articulated in the Belmont Report (eg, respect for persons, beneficence, and justice)
   b. Understand the role of analysis of risks and benefits in the ethical conduct of research
   c. Understand the federal regulatory definitions regarding which activities are considered research
   d. Understand the federal regulatory definitions regarding when research includes the use of human subjects
   e. Understand the federal regulatory definition of minimal risk
   f. Understand the functions of an Institutional Review Board
   g. Understand when an exemption from review by the Institutional Review Board is permissible
   h. Understand the functions of a Data Safety Monitoring Board
   i. Understand the importance of clinical equipoise in research with human subjects
   j. Understand the impact of "therapeutic fallacy" on clinical research with human subjects
   k. Understand the ethical considerations of study design (eg, placebo, harm of intervention, deception, flawed design)
   l. Understand the privacy rules regarding recruitment and participation of subjects in a research study and reporting the results of that study

4. Principles of consent and assent
   a. Understand what constitutes informed consent in research
   b. Understand how undue influence can affect obtaining consent for research
   c. Understand how coercion can affect obtaining consent for research
   d. Understand the special ethical considerations related to research utilizing children because of their inability to give informed consent
   e. Distinguish among consent, assent, and permission in research involving children

5. Vulnerable populations
   a. Recognize that the definition of "children" is related to the underlying clinical intervention in the jurisdiction in which the child is located rather than a fixed nationwide notion of age
   b. Recognize the types of protections that might be accorded to vulnerable populations (eg, incarcerated individuals, pregnant women, fetuses, children, mentally disabled individuals, educationally or economically disadvantaged individuals)
   c. Understand the concept of minimal risk as it applies to research involving children
   d. Understand the circumstances under which research that involves children and that entails greater than minimal risk may be permissible