I. Introduction
   A. In order to fully comprehend and manage critically ill newborns, one must explore the biological aspects of pregnancy and maternal physiology that impact neonatal development and outcome.

II. Maternal antenatal fetal screening
   A. Overview
      1. Currently, the American College of Obstetricians and Gynecologists (ACOG) recommends that all pregnant women be offered the option of early screening for the presence of fetal aneuploidy and neural tube defects.
      2. Screening for such defects does not imply that parents are obligated to intervene in the pregnancy, but may present opportunities for intrauterine treatment, as well as for psychological preparation of the parents and family for the birth of a newborn with problems.
   B. First trimester screening
      1. Early ultrasound and evaluation of serum markers is performed between 10-4/7 weeks and 13-4/7 weeks of pregnancy.
      2. Ultrasound is performed to date the pregnancy using crown-rump measurements and to evaluate the fetus for the presence of nuchal translucency.
      3. The presence of nuchal translucency is a fetal marker that indicates a higher risk for the presence of aneuploidy and Down syndrome.
      4. If the translucency is >3.5 mm, the fetus should undergo a targeted ultrasound and a fetal echocardiograph, which detect up to 70% of cases of Down syndrome.
      5. If the presence of nuchal translucency is combined with the use of two maternal serum markers — pregnancy-associated plasma protein-A (PAPP-A) and human chorionic gonadotropin (hCG) — the antenatal detection rate for Down syndrome improves to 79%–90% of cases.
C. Second trimester screening

1. Screening in the second trimester of pregnancy is performed between 15 and 20-6/7 weeks to detect trisomies and the presence of neural tube defects.

2. An increase in maternal serum alpha-fetoprotein (AFP) may indicate the presence of an open neural-tube defect in the fetus.

3. AFP is a specific molecule produced by the fetal yolk sac, gastrointestinal tract, and liver.

4. Levels of AFP are lower in maternal serum than in fetal serum of liver tissue.

5. Maternal serum AFP levels are drawn between 15 and 20 weeks of gestation; the results are reported as multiples of mean (MoM) and are based on gestational age of the fetus.

6. AFP values greater than MoM are considered abnormal and should be repeated along with a targeted ultrasound assessment of the fetus.

7. Accurate timing of fetal gestational age is key to appropriate interpretation of AFP levels.

8. When maternal serum AFP levels are combined with hCG and unconjugated estriol levels, the testing array is called a “triple screen.”

9. The triple screen has an aneuploidy detection rate of 65%.

10. The addition of the maternal serum marker ("quad screen") increases the aneuploidy detection rate to 80% of trisomies and neural-tube defects.

11. The combination of nuchal translucency and the quad screen increases detection of trisomies and neural-tube defects to 90%.

12. AFP and amniotic acetylcholinesterase are also used to detect open neural-tube defects, with a 96% accuracy rate and a low false positive rate of 0.14%, which occurs when the sample has become contaminated with blood.

13. If a trisomy is suspected, the definitive diagnosis is a fetal karyotype obtained from fetal cells shed into the amniotic fluid.

14. An elevated maternal serum AFP in the second trimester that cannot be explained by a structural anomaly or underlying maternal conditions is associated with increased risk of fetal demise, abruption, and preeclampsia.
III. Diabetes

A. Overview
1. Diabetes is one of the most frequent complications of pregnancy.
2. 90% of all cases are caused by gestational diabetes.
3. Each year, 135,000–200,000 women are diagnosed with gestational diabetes.
4. Type 2 diabetes among women of childbearing age has increased 33%.
5. Neonates born to women with gestational diabetes have a 3- to 5-fold increase in the incidence of metabolic syndrome, obesity, and diabetes during their lives.
6. Diabetes, risk of obesity, and potential for adolescent obesity in offspring of diabetic women are major public health issues.

B. Maternal pathophysiology and clinical correlates
1. Severe hypoglycemia (serum glucose <60 mg/dL) and diabetic ketoacidosis are more common with type 1 diabetes.
2. Insulin resistance is more common in type 2 diabetes.

C. Type 1 insulin-dependent diabetes
1. Autoimmune disease characterized by islet B-cell destruction.
2. Islet cell autoantibodies, insulin autoantibodies, and other B-cell autoantibodies are present.
3. Type 1 diabetes may result in systemic effects on the cardiovascular system and blood flow to the kidneys and pelvic vessels.
4. Type 1 diabetics with pelvic vascular involvement may result in reduced uterine blood flow and, subsequently, fetal intrauterine growth restriction (IUGR).
5. Viruses, dietary factors, and environmental exposure to chemicals have been investigated as causes of the disorder.

D. Type 2 diabetes
1. Characterized by hyperglycemia caused by an increased hepatic glucose production, abnormal insulin secretion, and increased insulin resistance.
2. Decreased insulin action and increased glucagon secretion cause an increase in hepatic glucose production.
3. Pathophysiology of type 2 diabetes and gestational diabetes is similar; some researchers have identified them as the same disease with different names.
E. Gestational diabetes
1. Normal pregnancy is characterized by a state of hyperinsulinemia and insulin resistance caused by the diabetogenic effects on normal carbohydrate metabolism.
2. Women who develop gestational diabetes have a higher insulin resistance before conception, often associated with obesity.
3. Insulin resistance results in decreased glucose uptake by skeletal muscles, white adipose tissue, and liver, and in suppression of hepatic glucose production.
4. Women who develop gestational diabetes are more likely to develop metabolic syndrome and/or overt diabetes later in life.

F. Fetal exposure to increased glucose
1. Maternal glucose readily crosses the placenta; fetal glucose levels follow maternal levels.
2. Maternal insulin does not cross the placenta in clinically significant amounts.
3. High levels of fetal glucose stimulate increased secretion of fetal insulin.
4. Fetal hyperinsulinemia causes:
   a. Increased cellular glucose use
   b. Increased hepatic glycogen deposits
   c. Decreased mobilization of lipids
   d. Increased protein production
   e. Increased amino acid uptake and protein synthesis
   f. Decreased protein catabolism
5. In the last 12 weeks of gestation, infants of diabetic mothers (IDMs) deposit 50%–60% more fat than infants of non-diabetics.
6. All organs of IDMs are larger, except the kidneys and brain.
7. Growth abnormalities are a common risk in these infants.
   a. Macrosomia: In the United States, nearly 450,000 infants who are large for gestational age (LGA) are born each year.
      (1) Shoulder dystocia complicates ~50%–86% of LGA infants.
      (2) Infants whose birth weight is >4,000 g, and particularly those infants whose birth weight is >4,500 g, have higher mortality and morbidity than infants who are average for gestational age.
(3) Since fetuses gain 95% of their weight in the last half of pregnancy, maternal glycemic control during that time may reduce the risks of these macrosomic infants.

b. Small for gestational age (SGA)
   (1) 20% of IDMs will be SGA.
   (2) Impaired fetal growth in these infants is secondary to maternal renovascular disease.

G. Maternal hyperglycemia and resulting fetal hyperinsulinemia
1. Neonatal complications of maternal diabetes include:
   a. Fetal anomalies
   b. Metabolic, hematologic, and respiratory issues
   c. Increased NICU admissions and birth trauma
   d. Increased fetal growth and stillbirth

2. Congenital malformations account for 30%–50% of neonatal deaths, vs. 20%–30% for infants of non-diabetic mothers.

3. Rate of congenital anomalies:
   a. Similar for women with type 1 or type 2 diabetes
   b. 3- to 5-fold higher than in infants of non-diabetic mothers
   c. 4%–11% higher in fetuses of mothers with gestational diabetes
   d. Most common anomalies include central nervous system (CNS) and cardiovascular malformations (see Table 2-1)
   e. Most specific associated anomaly in IDMs is sacral agenesis
   f. Sacral agenesis 300–400 times more common in diabetic pregnancies (most common associated risk factor for sacral agenesis is diabetes mellitus)
   g. Other anomalies that develop as a result of embryologic disruption <8 weeks gestation (before completing organomegaly):
      (1) Cardiac: Transposition of great vessels most common
      (2) CNS: Neural tube defects and other anomalies
      (3) Genitourinary defects
      (4) Skeletal defects
      (5) Early glycemic control a key factor in reducing perinatal morbidity and mortality
### TABLE 2-1
Congenital Malformations and Lesions Found in Infants of Diabetic Mothers (IDMs)

<table>
<thead>
<tr>
<th>Systems</th>
<th>Defects</th>
<th>Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Nervous</strong></td>
<td>Neural tube defects</td>
<td>Meningocele, encephalocele, anencephaly</td>
</tr>
<tr>
<td></td>
<td>Caudal regression syndrome (sacral agenesis)</td>
<td>300–400 times more common in diabetic pregnancies</td>
</tr>
<tr>
<td></td>
<td>Holoprosencephaly</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>RDS</td>
<td>Transient tachypnea of the newborn</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Transposition of the great vessels; truncus arteriosus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ventricular and atrial septal defects</td>
<td>Tricuspid atresia</td>
</tr>
<tr>
<td></td>
<td>Left-sided obstructive lesions</td>
<td>Hypoplastic left heart, aortic stenosis, coarctation of the aorta, ventricular septal hypertrophy</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td>Renal agenesis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydronephrosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ureteral duplication</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cystic kidneys</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td>Intestinal atresias</td>
<td>Duodenal, anorectal</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td>Arthrogryposis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypoplastic femur</td>
<td></td>
</tr>
<tr>
<td><strong>FUNCTIONAL</strong></td>
<td><strong>Cardiac</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intraventricular septal hypertrophy, cardiomyopathy (with ventricular hypertrophy), cardiac failure</td>
<td></td>
</tr>
<tr>
<td><strong>Intestinal</strong></td>
<td>Small left colon syndrome, meconium plug syndrome</td>
<td></td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td><strong>Hematologic</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal vein thrombosis, adrenal hemorrhage, polycythemia, thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td><strong>Growth Anomalies</strong></td>
<td>Macrosomia (LGA) when hyperglycemic states are predominant; SGA when pelvic vascular disease has developed.</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic and Electrolyte</strong></td>
<td>Hypoglycemia, hypocalcemia, hypomagnesemia, iron abnormalities</td>
<td></td>
</tr>
<tr>
<td><strong>Increased Risks</strong></td>
<td>Asphyxia, hyperbilirubinemia, birth trauma, palsies (brachial plexus, Erbs, Klumpke)</td>
<td></td>
</tr>
</tbody>
</table>
H. Diagnosis
1. Type 1 or type 2 diabetes should be identified and treated by the first prenatal visit.
2. Gestational diabetes is identified when a woman with normal glucose control develops abnormal glucose while pregnant.
3. Approximately 2%–10% of diabetes classified as gestational are actually type 2 diabetes first identified during pregnancy.
4. Since diabetes carries long-term chronic disease implications, pregnancy remains an important screening period.
5. Because of the frequency of type 1 diabetes, type 2 diabetes, and obesity in childbearing women, all pregnant women should be screened with a 100-g glucose load and a 3-hour glucose tolerance test.
6. A single abnormal value probably indicates gestational diabetes and resultant risk for excessive fetal growth.
7. The National Diabetes Data Group, which is endorsed by ACOG and the American Diabetes Association, defines normal glucose levels (fasting) as shown in Table 2-2.
8. Women at risk for developing gestational diabetes mellitus present with:
   a. Abnormal fasting glucose
   b. Previous diagnosis of gestational diabetes before 20 weeks
   c. Previous infant of diabetic mother
   d. Obesity

I. Management during pregnancy
1. Goals
   a. Establish glycemic control prior to conception.
   b. Diminish rate of hyperglycemia and ketosis.

<table>
<thead>
<tr>
<th>Time</th>
<th>Range (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>95–105</td>
</tr>
<tr>
<td>1 hour</td>
<td>180–190</td>
</tr>
<tr>
<td>2 hours</td>
<td>155–165</td>
</tr>
<tr>
<td>3 hours</td>
<td>140–145</td>
</tr>
</tbody>
</table>
c. Achieving glycemic control (not the type of pharmacologic therapy) is key to improving perinatal outcomes in gestational diabetes.

2. Interventions
   a. Diet
   b. Exercise
   c. Medications
      (1) Oral anti-hyperglycemic agents
      (2) Insulin

J. Management during pregnancy that impacts fetal/neonatal well-being
   1. Establish best timing to begin fetal testing to prevent stillbirth and reduce fetal compromise.
   2. Establish timing of lung maturity to prevent respiratory distress syndrome (RDS).
      a. Use biochemical indices to determine lung maturation; do not rely on gestational age or fetal size.
      b. Test at 24–26 weeks, when fetus is viable to assist in timing of delivery.
      c. To prevent RDS in infants of diabetic women, determine lung maturation prior to delivery.
      d. Poor maternal glycemic control results in delayed lung maturation of phospholipid synthesis in the fetal lung by 1–2 weeks vs. non-diabetic pregnancies.
      e. Clinician must evaluate risks and benefits of delivering a fetus with immature lungs vs. continuing pregnancy of noncompliant or poorly controlled diabetes.
   3. Determine time and method of delivery, particularly if the fetus is macrosomic.
   4. Delivery should be term or earlier if macrosomia is present, if there is a history of previous stillbirth, or if there is poor compliance with testing or poor glycemic control.

K. Issues for fetus
   1. Poor glycemic control during pregnancy is associated with a higher incidence of early spontaneous abortion and fetal demise and late-gestation stillbirth.
   2. Maternal glucose crosses placenta; maternal insulin does not.
   3. Fetal glucose levels mirror those found in the mother.
   4. Fetal glucose levels stimulate beta cells of the fetal pancreas to secrete insulin.
5. Since insulin is one of the main fetal growth hormones, the infant undergoes increased protein synthesis and fat deposition and develops macrosomia.

6. Due to fetal beta cell hyperplasia and hyperinsulinemic state, loss of continual glucose infusion across the placenta may cause fetal hypoglycemia within a few hours of delivery.
   a. Hypoglycemia may be asymptomatic or may include jitteriness, cyanosis, irritability, seizures, and apnea.
   b. Monitor serum glucose levels frequently; early feedings and/or parenteral dextrose infusions may be necessary to maintain normal infant glucose levels.

7. Infants born to mothers with type 1 diabetes are at risk for developing:
   a. Hypoglycemia
   b. Asphyxia
   c. RDS
   d. Hyperbilirubinemia
   e. Electrolyte disturbances (hypocalcaemia, hypomagnesemia)
   f. IUGR

8. In addition, infants born to mothers with type 2 or gestational diabetes have an increased incidence of:
   a. Adolescent obesity
   b. Metabolic syndrome
   c. Type 2 diabetes later in life

9. Although breast-feeding is best for all infants, it has even greater importance in infants of diabetic mothers; reducing long-term risks of obesity, type 2 diabetes, hypertension, and cardiovascular disease; even if breast-fed for only 2 months.

10. Due to their hyperinsulinemic condition, all infants born to diabetic mothers must be carefully screened and evaluated for hypoglycemia in the first few days of life, particularly if breast feeding.

L. Issues for very low birth weight (VLBW) infants
1. Fetal growth abnormalities
   a. Macrosomia
      (1) Characteristic appearance includes generous adipose tissue deposits, organomegaly, a full round face, and plethora.
(2) Kidneys and brain size are not enlarged in IDMs.
(3) Frequently, infants have abundant vernix; placenta and umbilical cord are also large.
(4) Even in low birth weight infants, can experience greater than expected growth in response to maternal hyperglycemia and fetal hyperinsulinemia.
(5) VLBW infants may appear larger than expected for gestational age; since gestation was shortened, they have not been exposed to maternal hyperglycemia for as long and they do not exhibit typical facial or body morphological appearance of IDMs.
(6) Larger size does not indicate greater maturity; evaluate based on gestational age.

b. Fetal growth restriction
(1) Up to 3-fold more common in infants born to insulin-dependent diabetic mothers vs. non-diabetic population.
(2) May be related to abnormalities in fetal cell replication and reduction in number of cells, resulting in an impaired pattern of fetal growth that is early in onset and symmetrical in distribution.
(3) Early-onset growth restriction may be related to fetal malformations.
(4) Low maternal glucose levels and vasculopathy of pelvic vessels result in fetal growth restriction.
(5) IUGR infants have higher risk of asphyxia, immune deficiency, polycythemia/hyperviscosity, pulmonary hemorrhage, meconium staining, and intrauterine fetal death.
(6) Developmental outcome and postnatal growth are dependent upon the degree and cause of IUGR.
(7) Temperature instability is common.

2. Congenital anomalies: Cause 50% of perinatal mortality for IDMs
a. Increased 2- to 3-fold in insulin-dependent diabetics; also increased anomalies in gestational diabetics, but not in diabetic fathers.

b. Frequency is increased if there has been poor diabetic control and elevated hemoglobin A1C in early gestation.
c. The most common anomalies involve the cardiac, musculoskeletal, and central nervous systems (see Table 2-1).

d. Congenital anomalies are thought to result from maternal hyperglycemia during the first seven weeks of pregnancy.

e. The incidence of congenital heart disease (most commonly transposition of the great arteries, septal defects, and coarctation of the aorta) is 3–5 times higher than in the general population.

f. Skeletal anomalies include delayed ossification and osseous defects; caudal regression syndrome (sacral agenesis) and hypoplasia of the femur are much more common in IDMs.

g. CNS anomalies include hydrocephalus, neural tube defects, and anencephaly. Small left colon is a rare functional, rather than structural, disorder that results in partial intestinal obstruction and delayed passage of meconium. Usually resolves over the first few days of life without need for surgical intervention.

3. Hypoglycemia

a. The American Academy of Pediatrics (AAP) target glucose screen is >45 mg/dL for SGA infants, IDMs, and late preterm infants.

b. Nadir of hypoglycemia occurs at 30–90 min of age. Most infants are asymptomatic but should be corrected with parenteral glucose solution.

c. Mini bolus of 2mL/kg of D10W can be given to hypoglycemic infants, followed by a constant glucose infusion rate of 5–8 mg/kg/min of dextrose to maintain glucose between 40 and 50 mg/dL.

d. Since most VLBW infants are started on parenteral glucose infusions after delivery and have their serum glucose levels monitored closely, this complication is not seen as frequently as in infants born at later gestational ages.

e. Shortened gestation period in preterm infants results in decreased level of pancreatic beta cell hyperplasia from fetal hyperglycemia.

f. Carefully monitor glucose infusion rate and serum glucose, particularly as feedings are being initiated and advanced.
4. RDS
   a. Maternal hyperglycemia and resulting fetal hyperinsulinemia inhibit production of phospholipids and decrease the synthesis of pulmonary surfactant, resulting in RDS.
   b. There is usually a 2-week delay in pulmonary maturation for IDMs.
   c. Fortunately, due to improved antenatal testing, administration of antenatal steroids, and the wide availability of surfactants, this complication of maternal diabetes is not as problematic today.

5. Hypocalcemia and hypomagnesemia
   a. Frequently seen in infants of insulin-dependent diabetic mothers.
   b. Symptoms resemble hypoglycemia; these parameters must be followed closely.
   c. Hypocalcemia (<7 mg/dL) develops in the first 72 hours after birth in infants born to insulin-dependent diabetics; may be due to diminished parathyroid response, persistently elevated levels of calcitonin, and, possibly, alterations in vitamin D metabolism.
   d. Neonatal hypomagnesemia (<1.5 mg/dL) is usually transient, with uncertain physiologic significance.
   e. Since VLBW infants are started on total parenteral nutrition within an hour after birth, these electrolytes may need to be adjusted or added to standard mixtures.

6. Polycythemia and renal vein thrombosis
   a. Seen frequently in IDMs; thought to be due to relative chronic hypoxic state in the fetus, which stimulates red blood cell production.
   b. Symptoms include jitteriness, tachypnea, cyanosis, and priapism; oliguria in larger infants.
   c. In VLBW infants, stimulation of red blood cell synthesis is interrupted by shortened gestation time; polycythemia is much less common.
   d. Treatment of a partial reduction exchange transfusion may be needed; rarely needed in VLBW infants.
   e. When present, however, polycythemia may lead to hyperviscosity and intravascular thrombosis, including renal vein thrombosis.
   (1) Symptoms of renal vein thrombosis include hematuria and a palpable renal mass.
(2) Medical treatment may be necessary to dissolve the thrombus; nephrectomy may be required, but is rare.

7. Myocardial dysfunction in IDMs
   a. Myocardial dysfunction and neonatal heart failure is related to fetal ventricular septal hypertrophy and left ventricular outflow obstruction.
   b. Even in asymptomatic infants, diastolic function is altered, along with decreased passive compliance of the ventricle.
   c. The infant presents with delayed peripheral capillary refill time, diminished perfusion, and decreased pulses.
   d. Placing the infant on inotropes increases the outflow obstruction; cardiac function deteriorates as the inotropes cause the ventricular wall to press into the hypertrophied septum below the aortic valve, further obstructing outflow.
   e. Stopping the inotropes and beginning an infusion of isoproterenol mediates this condition.
   f. This condition, now rare, usually occurs in infants whose mothers had very poor glycemic control.
   g. The condition is transient and disappears spontaneously within 6 months after birth.

8. Hyperbilirubinemia
   a. Unconjugated bilirubin may be increased because of increased red blood cell mass, diminished activity of the hepatic glucuronidase enzymes, withholding of early enteral feedings, and delayed passage of meconium from small left colon syndrome.
   b. Peak bilirubin is increased and hyperbilirubinemia is prolonged for IDMs.

IV. Maternal thyroid disease
   A. Overview
      1. Maternal and fetal thyroid disorders are closely tied.
      2. Drugs used to treat maternal thyroid disease also affect the fetal thyroid gland.
      3. Maternal thyroid autoimmune disorders have been associated with increased early spontaneous abortions and uncontrolled thyrotoxicosis.
      4. Undertreated hypothyroidism can result in adverse pregnancy outcomes.
5. Fetal thyrotropin-releasing hormone (TRH) is detectable in mid-pregnancy and the level remains stable throughout gestation.

6. Maternal thyroid-stimulating hormone (TSH) does not cross the placenta; thyroxine (T4) does.

7. Throughout pregnancy, maternal T4 is used for normal fetal brain development, especially prior to the development of the fetal thyroid gland.

8. Despite fetal thyroid function beginning as early as 12 weeks, transfer of maternal T4 accounts for 30% of T4 in fetal serum at term.

9. The major maternal thyroid disorders include hyperthyroidism and hypothyroidism.

10. Most maternal thyroid disorders are linked to the presence of autoimmune antibodies, which may stimulate thyroid function, block thyroid function, or result in thyroid inflammation, leading to thyroid follicular cell destruction.

11. Thyroid-stimulating autoimmune antibodies bind to TSH receptors and activate the cells, resulting in thyroid hyperactivity and growth.

12. Thyroid-stimulating autoimmune antibodies are found in most patients with Graves’ disease (hyperthyroid); thyroid-blocking autoimmune antibodies are found in women with Hashimoto’s thyroiditis (hypothyroid).

13. The presence of thyroid-peroxidase autoimmune antibodies is associated with early pregnancy loss and postpartum thyroid dysfunction.

B. Hyperthyroidism (Graves’ disease)

1. Overview
   a. Pregnancy outcomes depend upon whether metabolic control and a euthyroid state can be achieved.
   b. Women with excessive T4 levels have greater early pregnancy loss and a higher incidence of preeclampsia, heart failure, and adverse perinatal outcomes.
   c. Systemic hyperthyroidism or thyrotoxicosis develops in 1 in 1,000 to 1 in 2,000 pregnancies; causes are Graves’ disease or Hashimoto’s thyroiditis.
   d. Mild thyrotoxicosis may be difficult to assess due to the natural changes in levels of TSH and T4 during pregnancy; they mimic the clinical findings of hyperthyroidism.

2. Thyroid storm: An acute, life-threatening hypermetabolic state, rare in pregnancy
a. Excessive levels of T4 cause pregnant women to develop pulmonary hypertension and heart failure from cardiomyopathy.

b. A pregnant woman with thyrotoxicosis has minimal cardiac reserve and decompensates if preeclampsia, anemia, and/or sepsis develop.

c. Gestational thyrotoxicosis, a transient condition, develops when the normal pregnancy levels of hCG stimulate maternal TSH receptors to secrete massive amounts of T4, which causes suppression of endogenous TSH secretion and hyperemesis gravidarum.

3. Issues for the fetus

a. Abnormalities of maternal thyroid function and treatment may affect the neonate.

b. TSH receptor antibodies cross the placenta, stimulate the fetal thyroid gland, and cause a fetal goiter; maternal administration of thionamides may be therapeutic for the fetus.

c. Although thionamides have the potential to cause fetal complications, these are uncommon.

d. After pre-pregnancy maternal radioiodine thyroid ablation, fetal thyrotoxicosis may still develop as a result of transplacental passage of long-lived thyroid-stimulating antibodies.

e. In most cases, the neonate is euthyroid; however, hyper- or hypothyroidism can develop, with or without a goiter.

f. Approximately 1% of neonates born to mothers with Graves’ disease develop fetal hyperthyroidism from the transplacental passage of thyroid-stimulating antibodies.

g. Placental transfer of autoimmune antibodies may result in fetal goiter and thyrotoxicosis, which may progress to nonimmune hydrops and fetal demise. Fetal sonogram evaluation of thyroid volume can be performed antenatally.

h. The lowest level of fetal risk for thyroid dysfunction is associated when no maternal antithyroid medications are required, the mother is euthyroid, and there is an absence of anti-thyroid autoimmune antibodies in the third trimester.
i. Women who require anti-thyroid medications and have thyroid receptor antibodies present have a higher incidence of a fetus with goiters and either hyper- or hypothyroidism.

4. Issues for the VLBW infant
   a. Infants who are hyperthyroid at delivery may have tachycardia, cardiac failure, and an increased metabolic rate.
   b. Increased metabolic rate places the VLBW infant at greater risk for intolerance to labor, perinatal asphyxia, intrauterine and postnatal growth failure, and hypoglycemia.
   c. After delivery, neonatal thyrotoxicosis may require short-term anti-thyroid therapy.
      (1) Symptoms of neonatal thyrotoxicosis include poor weight gain or excessive weight loss, goiter, irritability, tachycardia, flushing, and exophthalmos.
      (2) Many infants are SGA.
      (3) May have elevated or high-normal T4 and suppressed TSH levels.
      (4) Large goiters may cause tracheal obstruction; cardiac failure may need to be treated with propranolol.
      (5) Onset of thyrotoxicosis develops within the first week of life but may be delayed until the second week of life.
      (6) Dysrrhythmias, such as paroxysmal atrial tachycardia and cardiac failure, and death may occur if thyrotoxicity is severe.
      (7) Prognosis is good as thyrotoxic state is transient; most resolve by 9 months of age.
      (8) May have rapid advance in skeletal maturation and advanced bone age, premature closure of cranial sutures.

C. Hypothyroidism (Hashimoto’s thyroiditis)
   1. Overview
      a. The most common cause of hypothyroidism in pregnancy is Hashimoto’s thyroiditis, caused by glandular destruction of the thyroid by autoimmune antibodies, particularly anti-thyroid peroxidase antibodies.
b. This disorder complicates from 2 in 1,000 to 3 in 1,000 pregnancies.
c. Overt maternal hypothyroidism or inadequate treatment results in a greater frequency of adverse perinatal outcomes; adequate T4 replacement therapy during pregnancy minimizes the risk of adverse outcomes.
d. Transplacental passage of maternal TSH receptor-blocking antibodies may cause fetal hypothyroidism without the development of goiter.
e. Fetal thyroid begins to produce T4 at 14 weeks of gestation; prior to that time, normal maternal thyroid hormone production is important for fetal neurologic development.

2. Congenital hypothyroidism
a. May be caused by thyroid agenesis, errors of T4 synthesis, genetic factors, and drug-induced environmental factors.
b. Universal newborn screening mandates testing of all newborns for hypothyroidism.
c. In the United States, 1 in 2,500 newborns annually are diagnosed with this condition, 80%–90% resulting from thyroid agenesis or hypoplasia.
d. Early and aggressive T4-replacement therapy is critical for these infants.
e. Severity of the hypothyroidism, not timing of replacement therapy, is an important factor in long-term cognitive outcomes.

3. Issues for the fetus
a. Maternal and fetal thyroid abnormalities are inescapably related.
b. Both require adequate iodide intake; deficiency early in pregnancy results in both maternal and fetal hypothyroidism.
c. Transplacental passage of maternal TSH receptor-blocking antibodies results in destruction of the fetal thyroid gland and hypothyroidism.
d. Anti-thyroid peroxidase and anti-thyroglobulin antibodies seem to have little to no effect on fetal thyroid function, despite their transplacental passage.
e. Women with Hashimoto’s thyroiditis typically have fetuses with normal thyroid function.
f. Any fetus inadvertently exposed to radioactive iodine should be carefully evaluated for hypothyroidism after birth; potential for fetal hypothyroidism depends on the size and timing of the dose and the gestational age of the fetus.

4. Issues for the VLBW infant
   a. Infants with decreased thyroid function are at greatest risk for cognitive delays, which are related to the severity of hypothyroidism, rather than simply the timing of replacement therapy.
   b. Hypothyroidism during the critical first weeks of embryologic neurologic development results in neurodevelopmental delay, even with early replacement therapy.
   c. Results of universal newborn screening tests for congenital hypothyroidism should be readily available with treatment prior to one month of age.
   d. After diagnosis of hypothyroidism, thyroid hormone (L-thyroxine) should be provided in sufficient doses to achieve a high euthyroid state within 2 weeks of starting therapy.
   e. After starting thyroxine therapy, T4 levels are monitored early in therapy (first 4–6 weeks).
   f. After 4–6 weeks of therapy, the TSH level is the best indicator of adequate treatment.
   g. If the TSH level remains elevated, then the dose of thyroxine needs to be increased.

V. Preeclampsia and HELLP syndrome
   A. Overview
      1. This can be fatal to both the mother and the fetus.
      2. The term “pregnancy-induced hypertension” is misleading; does not address the underlying cause of hypertension.
      3. The NIH work group defined four categories of hypertension seen during pregnancy:
         a. Preeclampsia/eclampsia
         b. Gestational hypertension
         c. Chronic hypertension
         d. Preeclampsia/eclampsia superimposed on chronic hypertension
   B. Pathophysiology
      1. The fundamental abnormality that underlies preeclampsia/eclampsia is uteroplacental ischemia.
2. Reduced uteroplacental perfusion is demonstrated by ischemic lesions and atherosis of the vascular bed of the placenta, restricted fetal growth secondary to decreased uteroplacental blood flow, and radionucleotide studies.

C. Diagnosis of preeclampsia
1. Symptoms include new-onset hypertension with proteinuria and with or without edema.
2. Proteinuria >30 mg in a random specimen or >300 mg in a 24-hour collection is abnormal.
3. Pathologic edema consists of rapid weight gain (>2.25 kg/week), edema in nondependent sites, or persistent facial edema after patient is upright for a few hours.
4. The classic definition of hypertension is blood pressure (BP) >140/90 or mean of 105.
5. BP in the first half of pregnancy is generally lower than the patient’s baseline; an increase in systolic BP of 30 and/or an increase in diastolic pressure of 15 do not reliably identify preeclampsia.
6. Women who later develop preeclampsia have greater decreases in BP in the first half of pregnancy.
7. Eclampsia presents with seizures, coma, or both, in the setting of preeclampsia.
8. Severe preeclampsia occurs when a woman with a BP ≥160/110 who meets the basic criteria for a diagnosis of preeclampsia develops other complications, such as a platelet count <100,000, impaired liver function, renal insufficiency, pulmonary edema, visual disturbances (particularly black spots or flashes), epigastric pain, cerebral symptoms (persistent frontal headache), or cyanosis.

D. Assessment and screening during pregnancy
1. Screening for hypertension and proteinuria is an essential component of standard prenatal care.
2. Monitoring the progression of hypertension and proteinuria help to distinguish preeclampsia from gestational hypertension (with onset after the 20th week of pregnancy) and chronic hypertension (diagnosed before pregnancy or before the 20th week of gestation).
3. Preeclampsia is a progressive disease with increasing severity; chronic hypertensive disorders are stable. Both diseases may coexist.
4. The management goal for preeclampsia is to maximize perinatal outcome within the bounds of maternal and fetal safety.
5. Preeclampsia is more common in first pregnancies and occurs more commonly at the extreme ages of childbearing.

6. Higher levels of proteinuria are more common among African Americans.

7. Preeclampsia may occur more frequently in daughters and sisters of preeclamptic women.

8. The incidence of preeclampsia is higher in lower socioeconomic strata, in twin pregnancies, and diabetic pregnancies.

E. Management during pregnancy

1. Severe hypertension results in serious cerebrovascular events, including parenchymal ischemia and hemorrhage.

2. Antihypertensive therapy includes sublingual nifedipine and intravenous boluses of hydralazine or labetalol.

3. Caution should be taken when using nifedipine; it may cause inadvertent precipitation of angina and myocardial infarction.

4. Corticosteroids are used safely in patients with preeclampsia to accelerate fetal lung maturity and improve neonatal outcomes.

5. Magnesium sulfate infusion is the agent of choice to prevent maternal seizures and can be used in conjunction with nifedipine.

6. Infuse magnesium as a bolus of 2–4 g over 5–30 min, followed by a continuous infusion starting at 1 g/hour and increasing the dose to maintain therapeutic levels of 4–6 meq/L.

7. Monitor maternal deep-tendon reflexes and urine output in preeclamptic women.

F. Issues for the fetus

1. Greatest risks are due to chronic uteroplacental insufficiency, restricted fetal growth, and fetal hypoxia.

2. These infants have little to no placental reserve and are often intolerant of labor.

3. Interventional preterm delivery, a complication in maternal preeclampsia, is a major cause of perinatal morbidity.

4. The highest fetal death rates occur in women with the greatest increases in hypertension, proteinuria, and uric acid levels.

5. Fetal growth restriction increases the risk of postnatal hypoglycemia and maladaptation to extrauterine life.
6. Chronic fetal hypoxia may result in perinatal asphyxia, abruption, placental insufficiency from placental infarcts, polycythemia, hyperviscosity, neurologic impairment, and fetal death.

G. Issues for VLBW infants
1. Interventional prematurity is the major complication for VLBW infants, due to deteriorating maternal condition, and may result in hypoglycemia, growth abnormalities, increased risks of intraventricular hemorrhage, RDS, patent ductus arteriosus, necrotizing enterocolitis, and an increased risk of infection.
2. Women may present with rapidly progressive, severe preeclampsia and a fetus with a poor biophysical profile, necessitating delivery prior to corticosteroid therapy for fetal lung maturation.
3. If the mother was treated with magnesium sulfate, the fetal serum level is very similar to the maternal level and may result in hypotonia, respiratory depression, hypocalcemia, and poor feeding.
4. Although Apgar scores do not closely correlate to maternal magnesium levels, fetuses exposed to magnesium in utero have a higher frequency of hypotonia for their age, as well as decreased intestinal motility and decreased diaphragmatic strength until the magnesium is cleared from their system by renal excretion.
5. Intrauterine growth is frequently impaired in a fetus born to a preeclamptic mother and these infants must be screened for hypoglycemia.
6. Infants born to preeclamptic mothers frequently have a reduced total white blood cell count, neutropenia, and thrombocytopenia.
7. Alterations in white blood cell counts may result in increased susceptibility to infections and bleeding.
8. Impaired placental perfusion seen in this condition may negatively affect transplacental passage of maternal antibodies and reduce passive immunity.

VI. Human immunodeficiency virus (HIV)
A. Overview
1. In the last several years, women represent the greatest number of new HIV cases; more than 50% are among African-American women.
2. Current estimates indicate 110,000–150,000 asymptomatic HIV carriers in the United States.
3. With appropriate recognition and treatment of HIV in pregnancy, the risk of transmission to the newborn, which was once certain, is now <2%.
4. Universal HIV screening in pregnancy is recommended by ACOG and is mandatory in many states.

B. Pathophysiology
1. HIV infection leads to a progressive incompetence of the immune system, leading to opportunistic infections and unusual neoplasms.
2. Diseases may present as AIDS, the condition of an HIV infection, along with opportunistic infections, neoplasia, dementia encephalopathy (wasting syndrome), CD4 counts <200, cervical cancer, pulmonary tuberculosis, and/or recurrent pneumonia.
3. Pregnancy does not alter the progression of HIV disease.
4. Diagnosis is made by rapid testing using enzyme-linked immunoabsorbant assay and is confirmed by a Western blot.

C. Treatment of HIV-positive mothers during pregnancy
1. Treatment during pregnancy involves multiple, potent antiviral medications (nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors), which provide the best long-term control over viral replication.
2. The goal of treatment in pregnancy is to control maternal disease and prevent vertical transmission.
3. All pregnant women who are HIV positive should be treated with antiviral agents (even if they do not meet criteria for non-pregnant women), based on the reduction of vertical transmission to the newborn.
4. Antiviral therapy should drive the viral load below limits of detection.

D. Risks to the fetus
1. Transplacental transmission of HIV has been documented; the virus has been isolated from early trophoblastic tissue, amniotic fluid, membranes, placenta, and breast milk.
2. HIV-positive women in the United States, where formula is readily available, should not breast feed.
3. Intrapartum infections account for 70%–80% of vertical transmission; without treatment, 25%–30% of these infants develop HIV infections.
4. Considerations to reduce vertical transmission include:
   a. Decrease instrumentation.
   b. Reduce length of time membranes are ruptured prior to delivery.
   c. Reduce episiotomies.
   d. Perform operative deliveries before the onset of labor, rupture of membranes, or if viral load is >1,000 copies/mL.
   e. The risk of vertical transmission is correlated to viral load; there is a 1% risk of transmission with viral loads <50 copies/mL.

E. Treatment of HIV-positive mothers during labor
   1. To reduce fetal transmission, intrapartum intravenous zidovudine is recommended for all HIV-infected pregnant women, regardless of their antepartum regimen.
   2. For HIV-positive women in labor who have not received any antepartum antiretroviral therapy, intravenous zidovudine is recommended.
   3. Infants born to HIV-infected women who have not received antepartum antiretroviral drugs should receive prophylactic treatment of a combination antiretroviral drug regimen; begin as soon as possible after birth and continue for 6 weeks.
      b. For up-to-date parental and teaching information, refer to http://aidsinfo.nih.gov/contentfiles/Perinatal_FS_en.pdf.
   4. A randomized, controlled trial has shown that a 2-drug regimen of zidovudine given for 6 weeks, combined with 3 doses of nevirapine in the first week of life (at birth, 48 hours after the first dose, and 96 hours after the second dose), is as effective as, but less toxic than, a 3-drug regimen.
   5. The 3-dose regimen for nevirapine antiretroviral therapy in the first week of life is:
      a. Infants with birth weights of 1.5–2 kg:
         8 mg/dose x 3 doses
      b. Infants with birth weights of >2 kg:
         12 mg/dose x 3 doses
6. Neonatal antiretroviral prophylaxis includes 6 weeks of zidovudine for all HIV-exposed neonates to reduce perinatal transmission of HIV.

7. Zidovudine should be initiated as close to the time of birth as possible, preferably within 6–12 hours of delivery.

8. The 6-week course of zidovudine prophylaxis is recommended at age-appropriate doses.

9. The dosing schedule for zidovudine should be given either intravenously or orally (not both). See Table 2-3.

F. Testing

1. If an infant is born to a mother with unknown HIV status, rapid HIV testing of the mother and/or infant should occur as soon as possible after birth; immediately start antiretroviral treatment for the newborn if the rapid test is positive.

2. If the rapid test is positive, confirm with Western blot. Do not wait for the results of the Western blot before initiating antiviral prophylaxis.

3. If the Western blot is positive, perform an HIV DNA polymerase chain reaction (PCR) test on the infant.

4. If the HIV DNA PCR is positive, discontinue the antiretroviral therapy; immediately refer the infant to a pediatric infectious disease specialist for diagnostic confirmation and management.

### TABLE 2-3

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>IV Dose/Interval</th>
<th>PO Dose/Interval</th>
<th>Length of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥35 weeks</td>
<td>3.0 mg/kg/dose Q 12 hours</td>
<td>4 mg/kg/dose Q 12 hours</td>
<td>6 weeks</td>
</tr>
<tr>
<td>≥30–&lt;35 weeks</td>
<td>1.5 mg/kg/dose Q 12 hours for the first 2 weeks of life, then increase to 2.3 mg Q 12 hours for the next 4 weeks</td>
<td>2 mg/kg/dose Q 12 hours for first 2 weeks of life, then increase to 3 mg Q 12 hours for next 4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>&lt;30 weeks</td>
<td>1.5 mg/kg/dose Q 12 hours for the first 4 weeks of life, then increase to 2.3 mg Q 8 hours for the next 2 weeks</td>
<td>2 mg/kg/dose Q 12 hours for the first 4 weeks of life, then increase to 3 mg Q 8 hours for the next 2 weeks</td>
<td>6 weeks</td>
</tr>
</tbody>
</table>

Note: Verify all dosages with your institution’s guidelines and current practice.
VII. Herpes simplex virus (HSV)

A. Overview
1. HSV is a double-stranded-DNA virus that only infects humans.
2. There are two serotypes: HSV-1 and HSV-2.
3. HSV is one of the most common sexually transmitted infections worldwide and responsible for 70%–80% of genital ulcers.
4. There are more than 600,000 new cases annually in the United States; 50 million people in the United States have been exposed to HSV.
5. There are three types of HSV genital infections:
   a. A primary infection can result from exposure to HSV-1 or HSV-2, without prior exposure to either serotype.
   b. A non-primary first episode can occur when the first clinical episode with HSV-1 or HSV-2 is in an individual with prior exposure to the other serotype.
   c. A recurrent infection is reactivation of a latent virus.
6. Primary infections are associated with multiple, painful genital lesions with pelvic lymphadenopathy; systemic symptoms include malaise and fever.
7. Manifestations of non-primary and recurrent infections are not as severe and tend to resolve more quickly.
8. Recurrences are common; 80%–85% of women with primary HSV-1 have at least one recurrence in their lifetimes.
9. Of the women who are seropositive for HSV, 20%–30% have never been symptomatic.
10. Asymptomatic viral shedding occurs in 3%–16% of pregnant women and may be as high as 33% in women who are infected during pregnancy.
11. Viral shedding is more common in the following cases:
   a. After infection with HSV-2 (rather than HSV-1)
   b. When a second infection occurs soon after the primary outbreak resolves
   c. In a patient who is subject to frequent recurrences

B. Diagnosis and treatment
1. Perform viral cultures of skin (eye, rectal, conjunctiva, nasopharyngeal) and obtain blood and cerebral spinal fluid for HSV DNA detection using PCR techniques with HSV type-specific serology.
2. There are three viral agents used to treat HSV:
   a. Acyclovir
   b. Valacyclovir
   c. Famciclovir
3. Acyclovir has been used in pregnancy extensively and reduces viral shedding by 90%.
4. An estimated 2% of pregnant women develop a primary HSV infection during pregnancy; the fetus is infected by vertical transmission.

C. Risk to the fetus
1. If the primary infection develops in the first trimester, there is an increased incidence of early spontaneous abortion, stillbirth, and prematurity.
2. Infants infected during the first trimester may be born with hallmark skin vesicles or scarring (10%–15%), chorioretinitis (40%–50%), microcephaly (60%), and microphthalmia (25%). Intracranial calcifications (15%), seizures (30%), or evidence of hydranencephaly may be present.
3. Infants may be born with symptoms or develop them in the first day of life; ~66% of infants are ill by the end of the first week of life, but can develop symptoms of skin, eyes, and mouth (SeM) disease at 10–11 days of life.
4. Congenital HSV infection occurs in 4% of infected infants; 40% have disease confined to skin, eyes, or mouth; 34% have disease confined to the CNS; 22% of infected infants have the disseminated infection.
5. Mortality rate is 40%–80%, depending upon organ system involvement, despite treatment with acyclovir; one-half of survivors are expected to have significant long-term residual problems, including psychomotor delay, seizure disorder, spasticity, blindness, and deafness.
6. The major risk of infection for the fetus is intrapartum exposure to an infected birth canal. The risks are increased when the maternal infection is primary, when multiple lesions are present on the cervix, when the infant is premature, when there is prolonged rupture of membranes, and if fetal scalp electrodes/invasive instrumentation are used.
7. Vaginal deliveries in women with asymptomatic primary infections infect 30%–50% of neonates.
8. About 60%–80% of infants with HSV infection are born to mothers who are asymptomatic at time of delivery or in whom there is no history of HSV infection.

9. If lesions are from recurrent disease, the risk of transmission is reduced to 3%–5% and further reduced to 0.004% in the presence of asymptomatic viral shedding.

10. Neonatal manifestations involve SEM disease, SEM disease plus CNS involvement, or disseminated disease.

11. Although most infected infants are born with SEM disease, 60%–70% progress to SEM plus CNS or disseminated disease.

12. Most infants with herpes infections are born to mothers who have no history of HSV and have never had symptoms, making the neonatal diagnosis more challenging.

13. Prevention of vertical transmission can be accomplished by performing a cesarean section before or shortly after rupture of membranes, when active lesions are present.

14. Prophylactic acyclovir from 36 weeks onward reduces the recurrence of genital lesions and positive cultures at the time of labor; fewer cesarean sections are required.

VIII. Hepatitis viruses

A. Overview

1. Hepatitis infections are common and highly contagious.

2. Hepatitis B and hepatitis C can be sexually transmitted; the fetus can be infected by vertical transmission.

B. Hepatitis B (HB)

1. Overview
   a. There are three major structural antigens:
      (1) HBsAG
      (2) HBcAG
      (3) HBeAG
   b. HB virus (HBV) is responsible for 40%–50% of acute hepatitis cases in the United States.
   c. 300,000 new cases occur annually.
   d. 12,000–20,000 of those infected develop a chronic-carrier state.
   e. The incubation period lasts from 2 to 4 months.
   f. It manifests with nausea, vomiting, malaise, weakness, abdominal pain, jaundice, hepatic tenderness, and weight loss.
g. The acute course lasts 3–4 weeks, but may persist for months.

h. After infection, 80%–85% have complete resolution with development of protective anti-HBs antibodies.

i. 10%–15% become chronic carriers.
   (1) HBsAG persists in the serum.
   (2) HBeAG may persist for years, followed by a gradual seroconversion to HBeAG antibodies.

j. Asymptomatic carriers have normal liver function tests and HBsAG and anti-HBcAG.

k. Fulminant hepatitis occurs in <1% with acute hepatic failure, encephalopathy, coma, and death.

2. Diagnosis
   a. After exposure to HBV, HBsAG develops and is present for 2–4 weeks before the onset of clinical symptoms and acute infection.
   b. HBeAG develops at this time and the antigen disappears before the symptoms resolve.
   c. Anti-HBeAG develops.
   d. During the convalescent period, anti-HBsAG develops and is evidence of immunity.

3. HB infection in pregnancy
   a. Complicates 1 in 1,000 to 2 in 1,000 pregnancies; chronic-carrier states complicate from 5 in 1,000 to 15 in 1,000 pregnancies.
   b. If maternal infection develops during the first or second trimester, the infection is rarely transmitted to the fetus.
   c. If maternal infection develops during the third trimester, there is an 80%–90% risk of neonatal infection.
   d. Most infants are infected by genital tract secretions or mixing of maternal blood.
   e. The best predictor of neonatal infection is the presence of HBeAG in maternal blood or secretions.
   f. If the mother is a chronic HB carrier and anti-HBeAG positive, the risk of fetal transmission is reduced to 10%–20%.
   g. Most infants who are infected at birth and untreated become chronic carriers and can develop cirrhosis, chronic active hepatitis, or hepatocellular carcinoma.
4. Recommendations in pregnancy and perinatal period
   a. All pregnant women should be screened for HBsAG during pregnancy; repeat for high-risk patients.
   b. Infants who are exposed to HBV or born to mothers with unknown HB status should receive prompt administration of HB immune globulin (HBIG) and HB vaccine.
   c. HBIG reduces the infection rate from 94% to 75% and reduces the carrier state from 91% to 22%.
   d. HBIG should be given within 12 hours of delivery.
   e. HB vaccine further reduces chronic carrier state from 14% to 9%.
   f. HB vaccine should be given within the first week of life.
   g. All newborns should receive HB vaccine after birth, even if the mother is HB negative.
   h. Breast-feeding is not contraindicated.

C. Hepatitis C (HC)
   1. Overview
      a. HC is sometimes called non-A, non-B hepatitis.
      b. The major source of infection occurs by parenteral route, with only a minor percentage as result of sexual transmission.
      c. It is the most common blood-borne infection, responsible for 20%–40% of acute hepatitis cases.
      d. The incubation period is 30–60 days; the disease is asymptomatic in 75% of cases.
      e. Symptoms, when they occur, are milder than HB.
      f. Seroconversion begins by 8–9 weeks; 97% of patients have seroconversion by 6 months.
      g. Fulminant hepatitis is rare; most patients develop chronic liver disease demonstrated by persistence of the HC virus (HCV), RNA, and abnormal liver function tests.
      h. The disease progression is slow and insidious, sometimes taking 20 years.
      i. There is no effective treatment and no vaccine presently available.
      j. HCV occurs in 1%–3% of pregnancies.
      k. Risk factors include IV-drug use, multiple sexual partners, the presence of other infections such as HIV or HBV, and absence of prenatal care.
l. 30%–60% have no identifiable risk factor.
m. The risk of vertical transmission is 5%; if the mother also has HIV disease, incidence of vertical transmission is increased to 23%.

n. Most infected neonates develop a chronic-carrier state and chronic hepatitis.
o. There is no treatment available and immunoprophylaxis is not effective.

p. The mode of delivery does not affect transmission rates.

q. Breast-feeding is not contraindicated, particularly if viral load is low.

IX. Gonorrhea

A. Overview

1. Gonorrhea remains one of the most common sexually transmitted communicable diseases in the United States.

2. More than 300,000 new cases are reported each year; more than 80% occur in 15- to 29-year-olds.

3. The Gram-negative diplococcus is found in the genitourinary tract, pharynx, and conjunctiva, and may cause sepsis and arthritis in infected individuals.

4. Gonorrhea infections during pregnancy tend to be asymptomatic, with only some vaginal discharge and dysuria.

5. Screening is done on the first prenatal visit by culturing the cervix; repeat cultures may be indicated for high-risk women.

6. Untreated gonorrhea infection during pregnancy may result in endometritis, premature rupture of membranes, chorioamnionitis, IUGR, or neonatal sepsis.

7. Treatment of maternal gonorrhea during pregnancy incorporates the use of cephalosporins; strains of gonorrhea in the United States are becoming penicillinase-producing and thus, resistant to penicillin.

B. Treatment of the fetus

1. Newborns born to untreated gonorrhea-positive mothers should be given a single dose of ceftriaxone.

2. Newborn eyes should be treated with erythromycin ointment or tetracycline ointment, which reduces the incidence of neonatal gonorrhea ophthalmitis from 10% to <0.5%.
3. Gonorrhea ophthalmitis develops within 4 days with frank, purulent discharge from both eyes. If left untreated, corneal ulceration develops, which leads to corneal scarring and blindness.

X. Syphilis

A. Overview
1. Syphilis is a serious, highly contagious, sexually transmitted disease caused by the organism *Treponema pallidum*.
2. Rates of syphilis vary widely across the country, with higher rates seen in women who are prostitutes, have multiple random partners, and who have little to no prenatal care.
3. The incubation period is 10–90 days after exposure to the organism.
4. The hallmark lesion of primary syphilis infection — a painless chancre, which is indurated with raised borders — develops at the site of exposure, usually the penis or cervix.
5. Primary syphilis is a local infection.
6. If primary syphilis is not treated, secondary syphilis develops 4–10 weeks later and is a systemic infection, which is disseminated throughout the body by the bloodstream.
7. Symptoms of secondary syphilis include fever, lymphadenopathy, condyloma lata, and a generalized maculopapular rash on the trunk, limbs, palms and soles.
8. After the rash fades, a latent period begins which may last for years.
9. If untreated, one-third of those infected develop tertiary syphilis, with involvement of the CNS and cardiovascular system, and gumma formation within 10–30 years.

B. Diagnosis
1. Non-treponema antigen screening tests include rapid plasma reagin (RPR) and the Venereal Disease Research Laboratory (VDRL).
2. False positives occur in 1%–2% due to subclinical autoimmune disease, recent fever, and laboratory error.
3. Confirm all positive results from either the RPR or VDRL with a specific antibody test using microhemagglutination assay or fluorescent treponemal antibody absorption test to detect antibodies to *T pallidum*.
C. Management and treatment
1. Prenatal care identifies women who have been exposed and infected with syphilis.
2. Individuals with syphilis require treatment with penicillin.
3. The number of doses depends upon the stage of the disease at the time of treatment.
4. Penicillin is safe to use in pregnancy; test of cure should be done to assure adequate treatment.
5. Erythromycin does not cross the placenta and does not treat the fetus; tetracycline causes fetal dental darkening; both drugs should be avoided.
6. The mother should be monitored monthly with either RPR or VDRL screening to detect an increase in titers or a lack of a 4-fold increase in titers over 3 months, which indicates a need for re-treatment.
7. Women who test positive for syphilis should also be screened for HIV, a known comorbidity.

XI. Congenital syphilis
A. Overview
1. Infants can be infected during the transplacental passage of the organism to the fetus during pregnancy or from fetal contact with active genital lesions during labor and delivery.
2. Up to 40–50% of congenital syphilis cases are fatal.
3. Early fetal infection may result in spontaneous abortion due to overwhelming infection of the placenta and the development of non-immune hydrops.
4. While nearly all infants born to mothers with primary or secondary syphilis have treponemes transmitted to them, only 50% of the infants are symptomatic.
5. If the infant is born in the early latent stage, there is a 40% chance of organism transmission, whereas if the infant is born during the late latent stage, the risk of transmission is 6%–14%.
6. Even with treatment, 11% of fetuses have CNS involvement.

B. Symptoms of untreated congenital syphilis include:
1. Non-immune hydrops
2. IUGR
3. Hemolytic anemia
4. Hepatosplenomegaly
5. Jaundice rhinitis
6. Maculopapular rash
7. Condyloma lata
8. Bone abnormalities, such as periostitis and osteochondritis
9. CNS involvement

C. Infections that occur late in pregnancy or are undertreated result in neurologic involvement, hearing loss from damage to the eighth cranial nerve, hydrocephalus, dental abnormalities (Hutchinson’s teeth, mulberry molars), rhagades, saddle nose, saber shins, and clutton joints.

XII. *Chlamydia trachomatis*

A. Overview
1. More than 4 million infections occur annually.
2. *C. trachomatis* is an obligate intracellular bacterium that depends upon the invaded cell for its energy supply and destroys that cell with its replication.
4. High-risk groups include inner-city women, particularly African Americans.
5. 40%–60% of women with positive gonorrhea cultures are also positive for chlamydia.
6. The cervix is the primary site of infection.
7. The woman may be asymptomatic or the infection may cause hypertrophic cervical erosion and copious mucopurulent discharge.
8. Chlamydial infections are a common cause of tubal infertility.

B. Diagnosis and treatment
1. Diagnosed with nucleic acid amplification tests.
2. Treatment of choice in pregnancy is azithromycin; erythromycin and amoxicillin are alternatives.

C. Risks to the fetus
1. Untreated chlamydia may cause a higher incidence of premature rupture of membranes, birth weight <2,500 g, and lower incidence of neonatal survival.
2. Newborns delivered to mothers with active chlamydial cervical infections have a 25%–60% chance of becoming infected.
3. The clinical presentation of chlamydial infection include conjunctivitis, which develops in 18%–45% of infants; and neonatal pneumonia, which develops in 20%.
4. Conjunctivitis is treated with erythromycin ointment.
5. Neonatal chlamydial pneumonia develops 4–11 weeks after birth and manifests with signs of congestion and obstruction, little nasal discharge, minimal fever, tachypnea, and a prominent staccato cough.
6. Bilateral infiltrates and lung hyperexpansion are found on chest radiograph.
8. Approximately 50% of these infants had conjunctivitis after delivery.

References


