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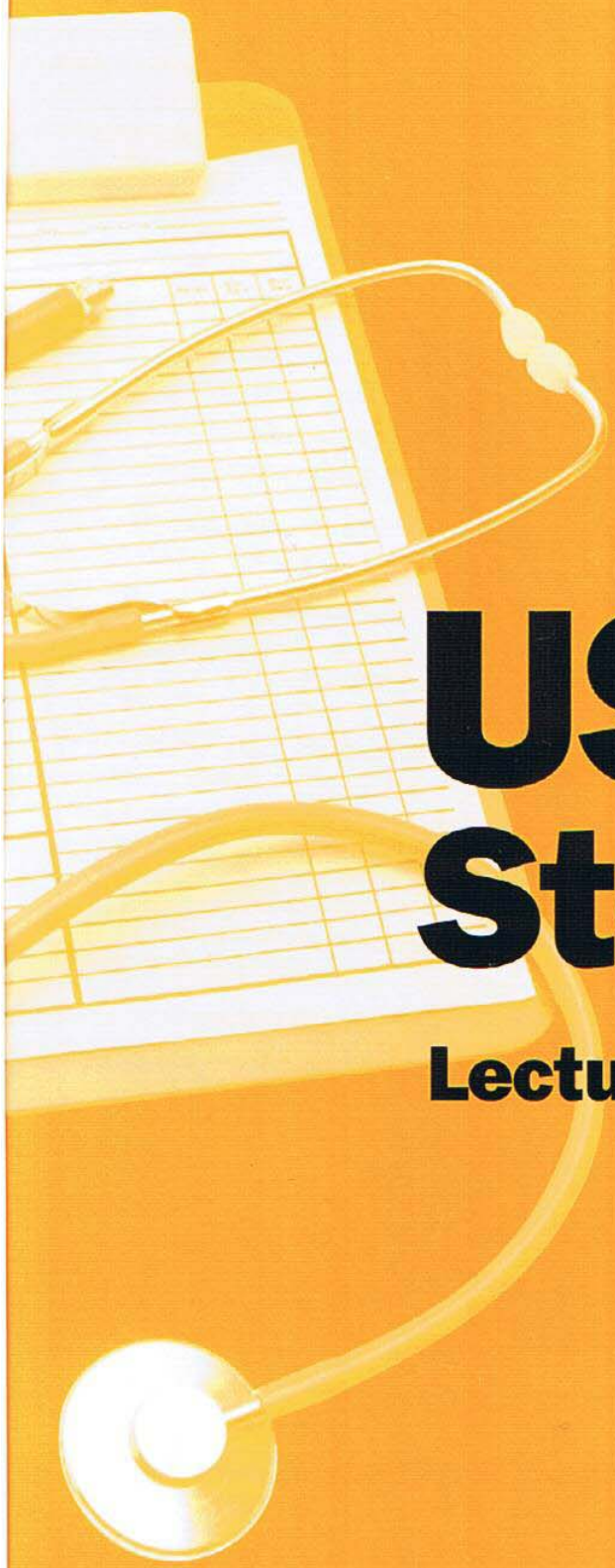

USMLE™* Step 2 CK

Lecture Notes

Pediatrics

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Newborn

APGAR SCORE

A newborn infant at birth is noted to have acrocyanosis, a heart rate of 140, grimaces to stimulation, and is active and with a lusty cry. What is her Apgar score?

Definition. The Apgar score is a useful tool for immediate assessment of the newborn. It helps identify those infants who require resuscitation. The score is also helpful in evaluating your resuscitation efforts. Scores are given at 1 and 5 min after birth and may be given every 5 min afterwards. Poor scores (0–3) at 1 min require resuscitation. Poor scores at 5 min do not predict subsequent cerebral palsy, although poor scores at 20 min are predictive of higher morbidity and mortality. A score of 8–10 is considered good. The table below demonstrates the scoring system.

Table 1-1. The Apgar Score

	0	1	2
Appearance (color)	Blue, pale	Body pink, extremities blue	All pink
Pulse (HR)	0	<100	>100
Grimace (reflex)	No response	Grimace	Cough
Activity (tone)	Limp	Some flexion	Active
Respiration (effort)	Absent	Slow, irregular	Good

SKIN

A newborn infant has a blue-gray pigmented lesion on the sacral area. It is clearly demarcated and does not fade into the surrounding skin. What is the most likely diagnosis?

Definition. Mongolian spots are more common in dark-skinned races, although they can be seen in white infants. These are flat blue or gray lesions with well-defined margins that generally disappear in the first few years of life. They can occur anywhere but are most common over the presacral area. They are secondary to melanin-containing melanocytes found in the dermal layer. They must be differentiated from the bruises of **child abuse**, which fade into the surrounding skin and have different colors.

Other skin findings in the newborn include:

Erythema toxicum—These are small papules or pustules on an erythematous base. They typically appear **after** the first day of life and may last several weeks. The pustules are full of **eosinophils** if scraped. The infant otherwise looks well. The lesions are benign but must be differentiated from **staphylococcal scalded skin syndrome.** These lesions are full of neutrophils, skin culture reveals *Staphylococcus aureus*, and the infant looks very ill. Differential diagnosis includes pyoderma and candidal infection.

Milia—These represent small inclusion cysts and are pearly white. In the mouth these are known as **Epstein's pearls.**

Cutis marmorata—This is a vasomotor response to cold stress. The skin assumes a lacy pattern similar to cobblestones. A persistent form is seen in trisomy 21, trisomy 18, and cutis marmorata telangiectasia congenita.

Neonatal acne—Neonates can develop open and closed comedones, possibly as a result of an increased response to circulating androgenic hormones. They rarely require therapy.

BIRTHMARKS

A newborn has a flat, salmon-colored lesion on the glabella, which becomes darker red when he cries. What is the best course of management?

The **salmon patch** is commonly seen over the eyelids, on the glabella, and in the nuchal area. It is a flat vascular lesion that disappears with time, except for those in the nuchal area, which may persist. Salmon patches must be distinguished from **port wine stains**, which are permanent and unilateral.

Other birthmarks are:

Capillary (strawberry) hemangiomas—These start out as macular lesions in the first few months and quickly grow in the first year of life. They can occur anywhere and are bright red, reminiscent of a strawberry. Treatment is usually not necessary because they regress spontaneously.

Nevus sebaceus (of Jadassohn)—Seen in infancy, these are yellow-orange hairless plaques resembling flat warts located on the scalp. Because they have a potential to become malignant, they are usually removed by adolescence.

Café-au-lait spots—These are tan or light brown flat lesions. They can occur anywhere, vary in size, and are sharply demarcated.

BIRTH INJURIES

On physical exam, a 12-h-old newborn is noted to have nontender swelling of the head that does not cross the suture line. What is the most likely diagnosis?

Definition. Birth injuries are avoidable and unavoidable injuries occurring during labor and delivery.

Birth injuries include:

Cephalhematoma—This is a subperiosteal bleed. Because it is limited to bone, it **does not cross** suture lines. It can be associated with an overlying nondepressed skull fracture. Slow bleeders, cephalhematomas are usually not present at birth and can increase in size over the first few days. A rim can be felt around the edge. Cephalhematomas resolve spontaneously over several months. Occasionally one can be fooled by bilateral cephalhematomas. Cephalohematoma is a common cause of jaundice.

Caput succedaneum—This is a swelling of the scalp, which involves the presenting part. It is caused by the pressure exerted on that part during labor and delivery. Involving the scalp only, the swelling **crosses suture lines** and resolves quickly over several days.

Subcutaneous fat necrosis—Look for a history of a difficult labor and delivery, particularly forceps or vacuum extraction. Rubbery, firm nodules are palpated on the cheeks or buttocks but also the back or extremities. The majority of these lesions resolve spontaneously, although occasionally calcium deposits occur in the lesions.

Brachial palsy—this type of injury occurs in large infants and is secondary to traction on the head during delivery. The two common presentations are **Erb-Duchenne paralysis and Klumpke paralysis.** Erb-Duchenne involves **C5–C6.** The arm is adducted and pronated and internally rotated. Occasionally, **C4** is affected, producing an **ipsilateral** diaphragmatic paralysis. Klumpke paralysis involves **C7–T1.** This produces paralysis of the hand. An ipsilateral **Horner syndrome** is seen if the sympathetic fibers of the first thoracic root are involved. Prognosis for both depends on the extent of damage to the nerves.

Facial palsy—This is usually a peripheral palsy, again secondary to difficult delivery. Because it is a flaccid paralysis, the **affected side does not move** when the baby cries.

Clavicular fracture—This is the most commonly fractured bone during delivery and is associated with babies who are large for gestational age and shoulder dystocia. Physical exam reveals a fussy baby with an asymmetric Moro reflex. Crepitus can be felt over the fracture. A healing callus is frequently palpated within the week. Treatment is usually not indicated.

Subconjunctival hemorrhage—These are also temporary and result from increased pressure during passage through the birth canal.

CONGENITAL ANOMALIES

These are numerous, and a brief list will be presented here by organ systems. Others will be covered in later chapters.

Eyes

Coloboma—a defect in the lid, ranging from a small notch to a large cleft. It can also involve the retina. There may be a coloboma of the iris.

Aniridia—absence of the iris. If it is associated with **hemihypertrophy**, always think of **Wilm** tumor.

Ears

Pre-auricular skin tags, pre-auricular pits, and malformed ears may be associated with hearing loss and/or genitourinary anomaly.

Neck

Branchial cleft cysts—These can form from incomplete closure of the branchial clefts. They are usually unilateral and can become infected, requiring antibiotic therapy.

Congenital torticollis—Also known as wry neck, this results from injury to the sternocleidomastoid during delivery, or less commonly from a congenital cervical anomaly. Muscular torticollis is usually treated with stretching exercises.

Chest

Breast hypertrophy—In the neonate, this is a temporary condition secondary to increased circulating hormones.

Supernumerary nipples (polythelia)—These usually occur along the mammary line. There is an association with renal and cardiovascular anomalies.

Poland syndrome—amastia, pectoralis muscle aplasia, rib deformities, webbed fingers, radial nerve aplasia.

Pectus excavatum (funnel), pectus carinatum (pigeon)—These are usually benign, isolated deformities of the chest. Surgical correction is usually for cosmetic reasons.

Abdomen

Masses—The cause of most abdominal masses in the newborn is renal, such as hydronephrosis and multicystic/polycystic kidney disease.

Umbilical hernias arise from incomplete closure of the fascia of the umbilical ring. They are associated with diastasis recti and usually close spontaneously by age 5 years.

Omphalocele is a herniation of peritoneum and abdominal contents into the base of the umbilical cord. Treatment is immediate surgical repair.

Gastroschisis is herniation without a sac, through an abdominal wall defect to the side of the umbilicus. Treatment is also immediate surgical repair.

Genitourinary

Epispadias occurs when the urethral opening is located on the dorsum of the shaft of the penis. It is usually repaired by 6–12 months of age.

Hypospadias is a urethral opening located on the ventral side of the shaft of the penis. A *ventral hood* is seen, and *chordee* is sometimes associated. Circumcision should be avoided because the foreskin is needed in the repair.

Undescended testes are usually in the inguinal canal and must be differentiated from **retractile testes.** Testes that have not descended by 1 year of age should have surgical intervention to avoid sterility or malignant degeneration. Retractile testes result from an active cremasteric reflex and do not require treatment.

Hydrocele is a collection of fluid in the scrotum, specifically the tunica vaginalis. It resolves in most cases by 1 year of age. Hydroceles that do not resorb by 1 year should undergo surgical correction. Diagnosis is made on transillumination. Reduction of a hydrocele by compression should raise the suspicion of a hernia.

Hernias in children are usually **inguinal,** usually indirect. They usually manifest as a bulge in the inguinal area or reducible scrotal swelling. Treatment is surgical.

SCREENING TESTS

A 1-month-old fair-haired, fair-skinned baby presents with projectile vomiting of 4 days' duration. Physical exam reveals a baby with eczema and a musty odor. Which screening test would most likely be abnormal?

Phenylketonuria

Definition. Phenylketonuria (PKU) results from a defect in hydroxylation of phenylalanine to tyrosine.

Risk Factors/Etiology. PKU is transmitted as an **autosomal recessive** trait and occurs with a frequency of 1:10,000.

Presentation. Affected infants are normal at birth until there is sufficient buildup of toxic metabolites. **Mental retardation** is the most common manifestation and is very severe. **Vomiting** can be projectile in nature and can be confused with pyloric stenosis. Infants tend to be **fair-haired, fair-skinned, and have blue eyes.** An **eczematous rash** and a **musty odor** have been described.

Diagnostic Tests. Routine newborn screening now picks up the diagnosis before most children exhibit symptoms. Blood screening is best performed after 48–72 h of life and after protein intake. After a positive test, blood levels of phenylalanine (high) and tyrosine (normal) should be drawn.

Treatment. PKU is treated with a diet low in phenylalanine. Some form of dietary control is needed for life.

Complications/Follow-up. Infants born to mothers with uncontrolled PKU have a higher rate of mental retardation, microcephaly, and congenital heart disease. Pregnant women with high levels of phenylalanine have a higher rate of spontaneous abortions.

Galactosemia

Etiology. Galactosemia results from a deficiency of **galactose-1-phosphate uridyl transferase.** Galactose-1-phosphate then accumulates, injuring kidney, liver, and brain. It is inherited in an autosomal recessive fashion, with several variants. The incidence is 1:60,000.

Presentation. Infants can present with a variety of symptoms, including jaundice, vomiting, hypoglycemia, seizures, cataracts, hepatosplenomegaly, and poor weight gain. Oftentimes the initial presentation is that of *Escherichia coli* sepsis.

Diagnostic Tests. Newborn blood screening provides the initial diagnosis. Reducing substances in the urine can be specific for galactosemia. Carrier testing and prenatal diagnosis are also available.

Treatment. Treatment is accomplished by eliminating galactose from the diet.

Complications/Follow-up. Even though early diagnosis and eliminating galactose from the diet have reversed many of the symptoms of galactosemia, patients still have developmental delay, speech disorders, and learning disabilities.

Hypothyroidism (see Endocrine Chapter)

INFANTS OF DIABETIC MOTHERS

> You are called to see a 9.5-pound newborn infant who is jittery. Physical exam reveals a large plethoric infant who is tremulous. A murmur is heard. Blood sugar is low.

Definition. Infants of diabetic mothers (**IDM**) are those infants whose mothers have or develop diabetes during their pregnancy.

Risk Factors/Etiology. Maternal hyperglycemia leads to fetal hyperglycemia, which in turn leads to fetal hyperinsulinemia. Insulin is a growth hormone, which, in combination with the hyperglycemia, contributes to the pathophysiology of the disease.

Presentation. Infants of diabetic mothers look a lot alike. Most have a **ruddy, plethoric complexion** and tend to be **large for gestational age**, which can lead to birth trauma. Jitters, tremors, and excitability result from **hypoglycemia**. Associated **hypocalcemia** and **hypomagnesemia** also occur. Because insulin can block surfactant production, IDM are more prone to **respiratory distress syndrome. Hypertrophic cardiomyopathy** is also common, as are **hyperbilirubinemia and polycythemia.** IDM are also at higher risk for **congenital anomalies**, including cardiac defects (ventricular septal defects, atrial septal defects, transposition, and most commonly, asymmetric septal hypertrophy), lumbosacral agenesis (caudal regression), and small (lazy) left colon.

Treatment. Therapy begins in utero, by controlling the mother's blood glucose and close follow-up. After birth, infant blood sugars are monitored closely, and hypoglycemia is treated aggressively.

Complications/Follow-up. IDM have a higher risk of developing subsequent diabetes, and larger babies may be predisposed to obesity as children.

SMALL FOR GESTATIONAL AGE (SGA)

A term infant weighs 4 pounds at birth. Physical exam reveals a small infant with a disproportionately larger head. Mother has a history of smoking during the pregnancy.

Definition. Small for gestational age (SGA) babies, also known as intrauterine growth retardation (**IUGR**), are those infants whose birth weights fall below the third percentile for their calculated gestational age. They are divided into **symmetric**, in which all the growth variables (weight, length, head circumference) are equally affected, and **asymmetric**, in which there is relative sparing of the head. Asymmetric IUGR is usually of later onset.

Risk Factors/Etiology. Factors that affect the growth of the fetus can be divided into:

- **Fetal** (chromosomal disorders, infections–TORCH (**T***oxoplasmosis*, **O**ther [syphilis, varicella], **R**ubella, **C**ytomegalovirus, and **H**SV), congenital anomalies, radiation, insulin deficiency)
- **Placental** (decreased weight, infarction, separation, twin–twin transfusion), and
- **Maternal** (toxemia, hypertension, malnutrition, tobacco, alcohol, narcotics).

Presentation. IUGR must be differentiated from preterm babies, which are proportionately small and whose weights fall in the normal range for their gestational age. The **Ballard** scoring system (see Figure 1-1) is helpful in determining gestational age, using physical and neuromuscular criteria. Both tend to have decreased subcutaneous fat.

Complications. Problems with SGA babies include fetal death, asphyxia, cold stress, hypoglycemia, and polycythemia/hyperviscosity from hypoxia.

ESTIMATION OF GESTATIONAL AGE BY MATURITY RATING

Symbols: X - 1st Exam O - 2nd Exam

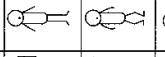
Side 1

Gestation by Dates _____ wks

Birth Date _____ Hour _____ am pm

APGAR _____ 1 min _____ 5 min

NEUROMUSCULAR MATURITY

	-1	0	1	2	3	4	5
Posture							
Square Window (wrist)	>90°	90°	60°	45°	30°	0°	
Arm Recoil		180°	140°-180°	110°-140°	90°-110°	<90°	
Popliteal Angle	180°	160°	140°	120°	100°	90°	<90°
Scarf Sign							
Heel to Ear							

MATURITY RATING

score	weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

PHYSICAL MATURITY

Skin	Sticky, friable, transparent	Gelatinous red, translucent	Smooth pink, visible veins	Superficial peeling and/or rash, few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar Creases	Heel-toe 40-50 mm = -1, <40 Mm = -2	Heel-toe >50 mm, No creases	Faint red marks	Anterior transverse crease only	Creases over anterior 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud	
Eye & Ear	Lids fused, Loosely = -1 Tightly = -2	Lids open, pinna flat, Stays folded	Slightly curved pinna, soft with slow recoil	Well-curved pinna, soft but ready recoil	Formed and firm, with instant recoil	Thick cartilage, ear stiff	
Genitals, male	Scrotum flat, smooth	Scrotum empty, Faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals, female	Clitoris prominent, Labia flat	Prominent clitoris, Small labia minora	Prominent clitoris, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	

Scoring system: Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. *J Pediatr.* 1991;119:417-423

Figure 1-1. The Ballard Scoring System

NEONATAL DRUG WITHDRAWAL

A 2-day-old infant is noticed to have coarse jitters and is very irritable with a high-pitched cry. A low-grade fever is reported, as well as diarrhea. Maternal history is positive for heroin use.

Definition. Infants born to actively addicted mothers will undergo withdrawal from whatever drug they were exposed to in utero.

Risk Factors/Etiology. Various drugs cross the placenta, with **heroin and methadone** being the most frequently associated with withdrawal.

Presentation. Timing of presentation depends on the drug, its half-life, and the last maternal dose. Signs include hyperactivity, irritability, fever, diarrhea, tremors/jitters, high-pitched crying, sneezing, restlessness, vomiting, nasal stuffiness, poor feeding, seizures, and tachypnea. **Heroin** withdrawal usually presents within **48 hours** after birth. Onset of symptoms for **methadone** withdrawal usually is **several weeks** (2–6), and there is higher risk for seizures. Phenobarbital withdrawal occurs at 1–2 weeks.

Diagnostic Tests. A good history and the clinical presentation usually are sufficient to make the diagnosis. Urine drug screening of the infant may be helpful.

Treatment. Treatment consists of use of narcotics, sedatives, and hypnotics, as well as swaddling and reducing noxious stimulation.

Complications. Infants of addicted mothers are at higher risk for low birth weight, IUGR, congenital anomalies (alcohol, cocaine), and sudden infant death syndrome, as well as of mother's complications such as sexually transmitted diseases, toxemia, breech, abruption, and intraventricular hemorrhage (cocaine).

RESPIRATORY DISTRESS SYNDROME

Shortly after birth, a 33-week gestation infant develops tachypnea, nasal flaring, and grunting and requires intubation. Chest radiograph show a hazy, ground-glass appearance of the lungs.

Risk Factors/Etiology. Respiratory distress syndrome (RDS) results from a developmental immaturity of **surfactant.** It occurs almost exclusively in **preterm** babies, and the incidence is inversely proportional to the gestational age. Surfactant is responsible for decreasing surface tension in the alveoli and preventing alveolar collapse at the end of expiration. Lack of or deficient surfactant results in **atelectasis** and **ventilation/perfusion mismatch.**

Presentation. Clinical manifestations occur fairly soon after birth. These include signs of **respiratory distress**—tachypnea, nasal flaring, retractions, cyanosis, and grunting. Apnea may occur as the infant tires. The patient's condition peaks at about the third day, and improvement is signaled by a spontaneous diuresis.

Diagnostic Tests. The diagnosis is made on clinical presentation. Chest radiograph usually demonstrates a reticular-granular pattern ("ground glass") with **air bronchograms.**

Treatment. Preventing the disease by reaching term is of utmost importance. **Steroids** given to the mother 48 h before delivery help decrease the incidence of RDS. Exogenous **surfactant** has greatly decreased mortality from RDS. Mechanical ventilation and good supportive care are extremely important.

Complications. Complications of RDS include pneumothorax, mucous plugging, intraventricular hemorrhage, sepsis, pulmonary interstitial emphysema, chronic lung disease, and patent ductus arteriosus.

Differential Diagnosis

- **Sepsis,** particularly from Group B Streptococcus.
- **Transient tachypnea of the newborn (TTN)**—This is usually self-limited and mostly seen in term infants or after cesarean section delivery. Tachypnea, mild retractions, and grunting may be present. Oxygen requirement is minimal. The chest x-ray shows fluid in the fissure and prominent vascular markings.
- **Meconium aspiration syndrome (MAS)**—This occurs when meconium is aspirated prior to, during, or immediately after delivery. Patients present with tachypnea and hypoxia. Chest radiograph shows patchy infiltrates. Pneumothorax is a common finding. Complications include primary pulmonary hypertension of the newborn, pneumothorax, and pneumomediastinum. Treatment includes mechanical ventilation, nitric oxide, and extracorporeal membrane oxygenation (ECMO).
- **Persistent fetal circulation (PFC;** also known as primary pulmonary hypertension of the newborn **[PPHN])**—This occurs when severe hypoxemia causes pulmonary vasoconstriction leading to right-to-left shunting through a patent ductus arteriosus or a patent foramen ovale. Echocardiogram shows increased pulmonary artery pressures and shunting. Treatment includes hyperventilation to avoid acidosis, maintaining optimal oxygenation to decrease pulmonary vasoconstriction, pulmonary vasodilators like nitric oxide, and extracorporeal membrane oxygenation.
- **Diaphragmatic hernia**—Failure of the diaphragm to develop allows abdominal contents to enter the chest, causing pulmonary hypoplasia on the affected side. Patients are born with respiratory distress and a scaphoid abdomen. Bowel sounds are easily heard in the chest, and a radiograph reveals bowel in the chest. The incidence is 1:200 births, and the treatment is surgical correction.

JAUNDICE

A 2-day-old infant is noticed to be jaundiced. He is nursing and stooling well. Indirect bilirubin is 11.2 mg/dL; direct is 0.4 mg/dL. Physical exam is unremarkable except for visible jaundice.

Definition. Neonatal jaundice occurs when indirect bilirubin is deposited in the skin. Hyperbilirubinemia in the newborn is classified as **physiologic** or **pathologic.** Bilirubin is also described as **unconjugated** or **conjugated.** Unconjugated bilirubin is potentially neurotoxic.

Risk Factors/Etiology. Hemoglobin is the major source of bilirubin. Bilirubin is metabolized via several steps, any of which, when affected, results in hyperbilirubinemia. Therefore, an increased load of bilirubin from hemolysis, increased red blood cell mass, and decreased red blood cell survival can cause hyperbilirubinemia. Likewise, deficiencies in enzymes involved in the metabolism of bilirubin contribute to jaundice.

Presentation. Jaundice presenting in the first day of life is pathologic and of concern. Jaundice begins on the face and progresses down the body as the level rises. **Physiologic jaundice** is not seen until after the first day of life, rarely exceeds 12.9–15 mg/dL, is unconjugated, and resolves by 1 week of age. Anything outside of that definition is considered pathologic jaundice. **Breast milk** jaundice usually presents at 1 week of age.

Diagnostic Tests. (*See* Table 1-2.) Serum bilirubin levels should be drawn, both conjugated and unconjugated. Hemoglobin levels are helpful in diagnosing polycythemia or hemolysis. White blood cell count is useful if sepsis is suspected. Mother and infant blood type and Rh group and Coombs test should be ordered.

Treatment. Phototherapy causes isomerization of unconjugated bilirubin to a form that is more easily excreted. If levels of conjugated bilirubin are elevated, phototherapy causes a **bronzed baby syndrome.** The level at which phototherapy should be initiated is not clear. **Exchange transfusion** is effective in removing bilirubin as well as removing circulating antibodies and restoring hemoglobin.

Complications. High levels of unconjugated bilirubin are associated with neurotoxicity and kernicterus. Conjugated hyperbilirubinemia, although not neurotoxic, is usually indicative of serious disease states.

Table 1-2. Differential Diagnosis of Pathologic Hyperbilirubinemia

<table>
<tr><th colspan="4">Direct Hyperbilirubinemia</th></tr>
<tr><td colspan="4">• Sepsis
• TORCH
• Prolonged total parenteral nutrition
• Hypothyroidism
• Galactosemia
• Tyrosinemia
• Cystic fibrosis
• Alpha-1 antitrypsin deficiency
• Choledochal cyst
• Giant hepatitis-biliary atresia spectrum</td></tr>
<tr><th colspan="4">Indirect Hyperbilirubinemia</th></tr>
<tr><th rowspan="2">Coombs Positive</th><th colspan="3">Coombs Negative</th></tr>
<tr><th>High Hgb</th><th colspan="2">Normal to Low Hgb</th></tr>
<tr><th></th><th></th><th>High Reticulocyte Count</th><th>Normal Reticulocyte Count</th></tr>
<tr><td rowspan="2">Isoimmunization
• Rh disease
• ABO incompatibility
• Minor blood groups</td><td rowspan="2">• Polycythemia
• Twin-twin transfusion
• Maternal-fetal transfusion
• Delayed cord clamping
• IUGR
• IODM</td><td>Characteristic RBC morphology:
• Spherocytosis
• Elliptocytosis</td><td rowspan="2">• Enclosed hemorrhage
• Increased enterohepatic circulation
• Decreased calories</td></tr>
<tr><td>Noncharacteristic RBC morphology:
• G6PD deficiency
• Pyruvate kinase deficiency</td></tr>
</table>

NEONATAL SEPSIS

A 3-week-old infant presents with irritability, poor feeding, temperature of 102°F, and grunting. Physical exam reveals a bulging fontanel, delayed capillary refill, and grunting.

Definition. Sepsis is a systemic response to infection. In newborns it can be classified as **early**, occurring in the first week of life, or **late onset**, manifesting between 8 and 28 days.

Risk Factors/Etiology. Risk factors for neonatal sepsis include maternal infection during pregnancy (urinary tract infection, chorioamnionitis), prematurity, and prolonged rupture of membranes. Common organisms causing sepsis in the newborn are group B *Streptococcus* (GBS), ***E. coli***, and ***Listeria***. Viral causes that should be considered are herpes simplex virus and enteroviruses.

Presentation. Signs and symptoms of neonatal sepsis are nonspecific. Babies may show grunting, tachypnea, cyanosis, poor feeding, irritability, apnea, bradycardia, jitters, tremors, and seizures. Newborns don't always develop fever, and hypothermia may be a presenting sign. A full fontanel may be palpated on physical exam. Infants rarely have nuchal rigidity.

Diagnostic Tools. Laboratory studies include complete blood count, lumbar puncture, and blood and urine cultures, as well as cultures of any lesions or drainage. Chest radiograph is also done to rule out pneumonia.

Treatment. Treatment consists of appropriate **antibiotics** (ampicillin + third-generation cephalosporin or ampicillin + aminoglycoside empirically pending cultures). Supportive care is just as important and requires meticulous attention to fluids, electrolyte, and hemodynamic status. Intrapartum penicillin or ampicillin given at least 4 h before delivery helps reduce the incidence of early-onset Group B *Streptococcus* infection.

Management of Perinatal Group B *Streptococcus* Infections. Intrapartum antimicrobial prophylaxis if vaginal/anorectal screening cultures are positive for GBS at 3 to 37 weeks or *at least one of* the following:

- Previous infant with invasive disease
- GBS bacteruria during pregnancy
- Delivery at <37 weeks
- Rupture of membranes >18 h
- Intrapartum temperature >38 C
- Unknown GBS status

Table 1-3. The Management of Neonatal Sepsis

Symptoms	Treatment
Signs of sepsis in baby	Sepsis workup and antibiotics
Gestational age <35 wk	Limited evaluation and observation >48 h
<2 doses of antibiotic Rx to mother before delivery	Limited evaluation and observation >48 h
≥ 2 doses of antibiotic Rx to mother before delivery	No evaluation or Rx; observe 48 h

Complications/Follow-up. Complications of neonatal meningitis include seizures, hearing loss, developmental delay, cerebral palsy, and hydrocephalus.

Differential Diagnosis. Differential diagnosis of neonatal sepsis includes diseases affecting other organ systems as well as other congenital infections. Respiratory diseases such as RDS and pneumonia have similar presenting symptoms as sepsis. Other considerations include congenital heart disease, metabolic diseases, and neurologic diseases such as intracranial hemorrhage. Congenital infections are classified as **(S)TORCH.**

TORCH Infections:

- Toxoplasmosis is transmitted by ingesting **undercooked or raw infected meat** or from handling of **infected cat feces.** Acquired infection is usually mild or asymptomatic in healthy individuals. Congenital infection is less common and more serious after maternal infection in the first trimester and more common but less serious if it occurs in the third trimester. Manifestations include **intracranial calcifications, IUGR, microcephaly,** seizures, blindness, and hepatosplenomegaly. Diagnosis is made from cultures, serologic testing (**IgM immunosorbent agglutination assay [ISAGA]** is best for congenital infection). Treatment of the pregnant woman is with spiramycin for the first trimester and pyrimethamine and sulfonamide afterward. Treatment of the newborn is with pyrimethamine, sulfonamide, and leucovorin (for hematologic side effects). Steroids are given for chorioretinitis.
- **CMV** is the most common congenital infection, usually transmitted in the first and second trimesters. Signs and symptoms include **IUGR,** prematurity, petechiae, hepatosplenomegaly, jaundice (direct), hearing loss, chorioretinitis, microcephaly, and **periventricular calcifications.** Diagnosis is made by **culture** or **polymerase chain reaction.** Prognosis is poor.
- **Congenital rubella** occurs in 80% of babies if the mother is infected in the first trimester. Manifestations include **IUGR** (most common), cataracts, mental retardation, microcephaly, **heart defects** (patent ductus arteriosus, pulmonary stenosis), hepatosplenomegaly, deafness, and **blueberry muffin lesions.** Diagnosis is made by culture or IgM titers. Prevention of disease is possible with **immunizations.**
- **HSV** usually is acquired from passage through an infected birth canal. Primary (first infection) disease in the mother has a high rate of transmission because there are no maternal antibodies, whereas recurrent disease has a low rate of transmission. Some babies acquire the disease postpartum from other infected family members (fever blisters). Infection follows three general patterns: **local** (skin, eyes, mouth) appearing at 5–14 days, **disseminated** (pneumonia, shock, hepatitis) at 5–7 days, and **CNS** (lethargy, seizures) at 3–4 weeks. **Mortality is highest with disseminated disease. Diagnosis** is by clinical pattern, culture, polymerase chain reaction in cerebrospinal fluid, and demonstration of antibodies. Therapy is with **acyclovir.** Delivery by cesarean section if there are active lesions helps prevent infection but is not a complete guarantee.
- **Syphilis** can be transmitted to the fetus at any stage of pregnancy, with fetal or perinatal death occurring in 40%. Manifestations are divided into early or late stages. **Early stage** manifestations appear before 2 years of age and include fever, anemia, failure to thrive, a maculopapular rash, snuffles, hepatosplenomegaly, periostitis of the long bones, and thrombocytopenia. **Late-stage** manifestations are skeletal and include saber shin, Hutchinson teeth, rhagades, saddle nose, and Clutton joints (usually knee synovitis).

Varicella can be **neonatal** (delivery <1 week before or after the onset of maternal disease) or **congenital.** Neonatal (perinatal) disease is treated with varicella-zoster immune globulin (VZIG) if mothers develop varicella **5 days before to 2 days after delivery.** All perinatal disease receives acyclovir. Congenital varicella is also associated with infection in the first and second trimesters and manifests with limb hypoplasia, cutaneous scars, microcephaly, chorioretinitis, cataracts, and cortical atrophy.

Table 1-4. The Most Prevalent Findings for the (S)TORCH Infections

Rubella	Toxoplasmosis
Intrauterine growth retardation (IUGR)	Chorioretinitis
Congenital heart defects	Intracerebral calcifications
Cataracts	Hydrocephalus
Congenital deafness	Hemolytic anemia
Hepatosplenomegaly (HSM)	HSM
Dermal erythropoiesis	Jaundice
Thrombocytopenia	Hepatitis
CMV	**Syphilis**
IUGR	IUGR
Chorioretinitis	Skin rash
Microcephaly	Bone abnormalities
Periventricular calcifications	Jaundice
Hearing loss	HSM
Jaundice	Hepatitis
HSM	Hemolytic anemia
Hepatitis	Thrombocytopenia
Hemolytic anemia	
Dermal erythropoiesis	
Thrombocytopenia	
Herpes simplex	
Skin rash	
Chorioretinitis	
Hydrocephalus	
Jaundice	
HSM	
Hepatitis	
Thrombocytopenia	
Meningoencephalitis	

Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) are nonspecific screening tests. The fluorescent treponemal antibody absorption test (FTA-ABS) is a confirmatory test. Treatment is with penicillin.

GASTROINTESTINAL

Tracheoesophageal Fistula

A newborn is noted to have choking and gagging with its first feed and then develops respiratory distress. Chest radiograph shows aspiration pneumonia. A feeding tube is coiled in the esophagus.

Definition. In approximately 85% of tracheoesophageal (TE) fistula, the esophagus is atretic and there is a fistula between the trachea and the distal esophagus. This allows air into the stomach and small intestine. There are other combinations of TE fistula.

Risk Factors/Etiology. Disorders in movement and formation of the foregut are responsible for TE fistulae and their variants.

Presentation. Esophageal disorders commonly present with coughing or choking with swallowing. In addition, TE fistula is associated with polyhydramnios, cyanosis, and coughing and choking with feeds.

Diagnostic Tests. Clinical presentation plus **inability to pass a catheter** into the stomach usually confirms the diagnosis. Chest radiographs may show evidence of aspiration.

Treatment. Treatment is surgical repair.

Complications/Follow-up. Patients with TE fistula have a higher risk of **congenital heart disease**, such as patent ductus arteriosus, vascular rings, and coarctation of the aorta. Look for other associated anomalies, such as found in the VACTERL association—abnormalities of vertebrae, anus, cardiovascular tree, trachea, esophagus, renal system, and limb buds.

Other gastrointestinal diseases of the newborn include:

- **Duodenal atresia**—This presents with bilious vomiting with every feed. The characteristic **"double bubble"** is seen on abdominal films. Patients with trisomy 21 are at higher risk. Treatment is surgical.
- **Hirschsprung**—This should be suspected in any newborn who fails to pass meconium in the first 24–48 h of life. Also known as congenital aganglionic megacolon, it results from absence of the ganglion cells. Barium enema reveals a dilated megacolon. The gold standard for diagnosis is biopsy showing absence of the ganglion cell. Treatment is surgical.
- **Necrotizing enterocolitis**—This is the most common medical and surgical GI emergency in the newborn. Ninety percent of cases occur in preterm infants, presenting in the first 2 weeks of life. Symptoms are usually related to **introduction of feeds**. These include bloody stools, apnea, lethargy, and abdominal distension once perforation has occurred. **Pneumatosis intestinalis** on plain abdominal film is pathognomonic. Treatment is **medical** with cessation of feeds, gut decompression, systemic antibiotics, and supportive care. **Surgical** management may also be necessary to resect necrotic bowel.

NEONATAL SEIZURES

In the newborn intensive care unit, an infant is noted to have sucking movements, tongue thrusting, and brief apneic spells. Blood counts and chemistries are normal.

Definition. Neonatal seizures are different from those in adults and children because of immaturity of the nervous system, which is why the classic tonic-clonic seizure is uncommon.

Risk Factors/Etiology. Neonatal seizures have multiple causes. **Hypoxic-ischemic encephalopathy** is the most common cause. Seizures usually present within 12–24 h after birth. **Intraventricular hemorrhage** is more common in preterm infants. It is rarely present at birth but occurs at 1–3 days of age. A bulging fontanel or bloody cerebrospinal fluid on lumbar puncture is seen. **Metabolic** causes of seizures include hypoglycemia and hypocalcemia. **Infections** are also responsible for seizures.

Presentation

- **Focal seizures**—rhythmic twitching, especially of the face and extremities. These are associated with structural lesions, infections, and subarachnoid hemorrhage.
- **Multifocal clonic**—Many muscle groups are involved.
- **Tonic**—rigid posturing of the extremities, fixed deviation of the eyes.
- **Myoclonic**—brief jerks of the extremities involving distal muscle groups.
- **Subtle**—chewing, tongue thrusting, apnea, staring, blinking, color changes.

Diagnostic Tests. Neonatal seizures are difficult to recognize; **electroencephalogram** may be normal. Complete blood counts, serum electrolytes, calcium, magnesium, phosphorous, and glucose should all be drawn. **Lumbar puncture** helps exclude meningitis/encephalitis or a bleed. Blood and urine cultures may be indicated. **Computed tomographic scan** and newborn screening for inborn errors of metabolism should be considered.

Maternal Diseases Affecting the Fetus/Neonate

Table 1-2

Disease	Effect
Cyanotic heart disease	Intrauterine growth retardation
Graves	Transient thyrotoxicosis
Hyperparathyroidism	Hypocalcemia
Idiopathic thrombocytopenia	Thrombocytopenia
Myasthenia gravis	Transient neonatal myasthenia
Systemic lupus erythematosus	Congenital heart block

Maternal Drugs Affecting Neonate

Table 1-3

Drug	Effect
Anesthetics	Respiratory, CNS depression
Barbiturates	Respiratory, CNS depression
Magnesium sulfate	Respiratory depression
Phenobarbital	Vitamin K deficiency
Sulfonamides	Displaces bilirubin from albumin

Teratogenic Drugs

Table 1-4

Drug	Effect
Alcohol	Fetal alcohol syndrome
Isotretinoin	Facial, ear anomalies, congenital heart disease
Phenytoin	Hypoplastic nails, typical facies, IUGR
Stilbestrol	Vaginal adenocarcinoma
Tetracycline	Enamel hypoplasia

Resuscitation

2

You are called to attend the delivery of a 22-year-old G1P0. She has been followed in the prenatal clinic, and all cultures are negative. The patient is term, with a single gestation; however, meconium is visualized.

Definition. Resuscitation is defined as revival after apparent death.

Risk Factors /Etiology. Risk factors for possible need of resuscitation in the **neonate** include **twin gestation, prematurity,** and presence of **meconium.** Risk factors for possible need of resuscitation in the **child** are usually **accidents** or **illnesses,** especially those that compromise **respiration.**

Presentation. The presentation will vary depending on the situation that leads to resuscitation. However, patients may have compromise of the respiratory system, cardiac system, or both.

Physical Examination. The physical examination will vary with presentation. However, there may be an absence or decrease of respiratory effort or of cardiac output. The patient may be cyanotic, pale, or mottled in appearance. If a foreign body was aspirated, drooling may be present. The patient may have **apnea**, i.e., the absence of breathing for >20 seconds. The patient may have tachycardia, bradycardia, or asystole. Remember that decrease in blood pressure is a late finding in children.

Table 2-1. Heart Rate

	Normal Heart Rate	
Age	**Average (bpm)**	**Mean (bpm)**
Newborn–3 months	94–190	140
3 months–1 year	124–180	140
1–3 years	98–160	126
3–5 years	65–132	98
5–8 years	70–115	96
8–12 years	55–107	79

Diagnostic Tests. The diagnostic tests that a physician orders will vary with the presentation of the patient as well as the extent of resuscitation needed. The **Apgar score** may be used to determine the stability of the newborn.

Treatment. Always remember your ABCs when performing resuscitation, i.e., Airway, Breathing, and Circulation. In the **neonate** a stepwise approach is important to having a good outcome. The **sequence** should be (*1*) position, suction, and tactile stimulation, (*2*) oxygen, (*3*) bag valve ventilation, (*4*) chest compressions, (*5*) intubation, and then (*6*) medication. Properly positioning, suctioning, and giving tactile stimulation may avoid the need for further steps in resuscitation. Keeping the infant **warm** will improve the response to resuscitation.

The need for intubation may arise (*1*) when bag ventilation is ineffective, (*2*) if tracheal suctioning is required, or (*3*) when prolonged positive-pressure ventilation is necessary. The tube size for the newborn is 2.5 to 3.5, **no cuff.** The vocal cords of the neonate must always be visualized, and intubation should never be done blindly.

Children usually respond to airway, ventilation, and fluids. It is important to assess the **ABCs.** The next steps should be to (*1*) secure an airway, (*2*) administer 100% oxygen, (*3*) start an intravenous, or intraosseous, route of administration, (*4*) check vital signs, and (*5*) for severe cardiorespiratory compromise, follow the algorithms.

If the need for intubation arises, remember that a **cuffed** endotracheal tube should be used in a child **>8 years old.** The proper endotracheal tube size can be estimated using the following formula:

$$\text{Tube size} = \frac{\text{Age (in years)} + 16}{4}$$

Children **older than 1 year of age** may receive the **Heimlich maneuver** for foreign body aspiration that is obstructing flow of air to the lungs. This maneuver consists of (*1*) wrapping your arms around the victim's waist from behind, (*2*) placing a fist on the abdomen between the rib cage and navel, and (*3*) administering **upward** abdominal thrusts. This maneuver should be performed until the foreign body dislodges.

Children **younger than 1 year of age** should not receive the Heimlich maneuver for foreign body aspiration that is obstructing flow of air to the lungs, but rather **back blows** and **chest thrusts** should be administered until the foreign body is visualized and can be removed from the mouth. Do not perform any blind finger sweeps.

Complications. Morbidity and mortality may be complications of resuscitation attempts.

Table 2-2. Summary of Basic Life Support Maneuvers in Infants and Children

Procedure	Child <1 Year	Child 1–8 Years
Airway	Use head tilt and chin lift. If trauma is present, use jaw thrust.	Head tilt and chin lift. If trauma is present, use jaw thrust.
Breathing		
Initial	Give two breaths at 1–1.5 s/breath.	Give two breaths at 1–1.5 s/breath.
Subsequent	Give 20 breaths/min (approximate).	Give 20 breaths/min (approximate).
Circulation		
Pulse Check	Brachial/femoral pulse	Carotid pulse
Compression area	Lower half of sternum	Lower half of sternum
Compression width	2 or 3 fingers	Heel of one hand
Depth	Approximately to 1/2 the depth of chest	Approximately to 1/2 the depth of chest
Heart Rate	At least 100 beats/min	100 beats/min
Compression–ventilation ratio	5:1 (pause for ventilation)	5:1 (pause for ventilation)
Foreign-body airway obstruction	Back blows/chest thrusts	Heimlich maneuver

Nutrition

BREAST FEEDING

A nursing mother asks if her 3-month-old baby requires any vitamin supplementation.

Human breast milk is the preferred food for full-term babies. It offers several advantages to both mother and infant. Breast milk is **premixed** at the right temperature and concentration. Breast milk has **immunologic factors** such as IgA, lactoglobulin, and maternal macrophages, which protect the infant from infections. Breast-fed babies have a lower incidence of upper respiratory tract infections and otitis media than their formula-fed counterparts. Breast milk also decreases the incidence of **allergic diseases. Maternal advantages** to breast feeding include a more rapid return to prepregnancy weight and faster uterine regression. Breast feeding also promotes maternal–infant bonding.

Supplementation of other nutrients is rarely needed in breast-fed infants. **Vitamin K** is present in low amounts in breast milk, and all newborn infants should receive vitamin K at birth to prevent hemorrhagic disease of the newborn. **Fluoride** is recommended after 6 months of age. **Vitamin D** should be given if the mother's intake is inadequate or if there is limited sun exposure. **Iron**-fortified foods are introduced at 4–6 months of age.

Contraindications to breast feeding are few but include active or untreated **tuberculosis, syphilis, HIV, galactosemia, and varicella. Herpes** is a contraindication if there are active lesions present on the breast. Relatively few **drugs** are contraindicated in breast feeding, but they include antineoplastics, radiopharmaceuticals, ergot alkaloids, iodides/mercurials, atropine, lithium, chloramphenicol, and cyclosporine, as well as nicotine and alcohol. **Relative contraindications** include neuroleptics, sedatives, tranquilizers, metronidazole, tetracycline, sulfonamides, and steroids. **Mastitis** is not a contraindication to nursing, and frequent nursing on the affected side is recommended to prevent engorgement.

FORMULA FEEDING

Formula feeding is used as a **substitute for** or to **supplement** breast milk. Most commercial formulas are cow milk–based with modifications to approximate breast milk. They contain **20 calories/ounce.** Specialty formulas (soy, lactose-free, premature, elemental) are modified to meet specific needs.

Whole Cow Milk

Whole cow milk is good for baby cows and any human over 1 year of age. It has a higher **renal solute load,** which can be damaging to the kidney. Cow milk can also create a potential for **intolerance** of whole milk protein, as well as increasing the incidence of **iron deficiency anemia.**

Comparison of Human Milk and Cow Milk

Table 3-1

Component	Human Milk	Cow Milk
Water/solids	Same	Same
Calories	20 cal/oz	20 cal/oz
Protein	1–1.5% (whey/casein 78:25)	3.3% (whey/casein 22:78)
Carbohydrate	6.5–7% lactose	4.5% lactose
Fat	3.5% (diet dependent)	3–4% (pooled)
Minerals	Iron better absorbed	Low iron and copper
Vitamins	Diet dependent, low in K	Low in C, D
Bacterial content	Uncontaminated	Harmless bacteria
Digestibility	Faster emptying	Same after 45 days

OTHER FOODS

Vitamins

Vitamin D is recommended only if the formula does not contain vitamin D, if the baby is low birthweight, or if there is poor milk intake. Breast-fed babies do not require vitamin D supplementation unless there is inadequate intake in the mother's diet, inadequate sun exposure, or in dark-skinned infants. Infants or children who drink **goat milk** should supplement with **folate.**

Iron

Most formulas are iron fortified. Breast milk iron is easily absorbed.

Solids

Solids should be introduced at 4–6 months of age. Before this time the risk for atopy is increased, and many infants are not yet developmentally ready to take solids. New foods should be introduced one at a time in small amounts. **Honey** is to be avoided in the first year of life because there is increased risk of **infantile botulism.**

Table 3-2. Development of Feeding Behavior in Infants

Age	Food Introduction
Birth to 2 mo	Infant is given breast milk or formula
4–6 mo	Introduce iron fortified cereals
6–7 mo	Strained vegetables and fruits Unsweetened fruit juices Avoid orange juice (citrus)
6–8 mo	Plain yogurt, cottage cheese, egg yolk (avoid egg whites). Start strained meats. Poultry and beans/lentils puree may also be given.
7–9 mo	Soft meats, poultry, mashed fruits and vegetables, cheese, and cereals
8–10 mo	Soft finger foods; meats, poultry, cooked vegetables in strips or slices
9–12 mo	Regular table foods: meats, poultry, cooked vegetables in strips or slices
12 mo	Can now include whole eggs, orange juice, cow's milk

"COLIC" (UNEXPLAINED CRYING)

A mother states that her infant has been having episodes of inconsolable crying every night for the past five nights. He draws his legs up, and his abdomen becomes rigid. The episodes resolve as quickly as they come on, and the rest of the day he acts normally.

Definition. Colic, the old term, is now known as unexplained crying and is not felt to have anything to do with abdominal pain.

Risk Factors/Etiology. The etiology of "colic"/unexplained crying is poorly understood but is generally self-limited and benign. It is thought that some infants are more sensitive to their environments and crying is a way of expressing discomfort.

Presentation. Episodes are characterized by excessive, loud, high-pitched crying and usually last for several hours. The infant may draw up his legs and pass flatus. These infants are difficult to console.

Diagnostic Tests. There are no diagnostic tests, and the diagnosis is purely made on the basis of history and physical exam.

Treatment. Gentle rocking motions, vibration, riding in a car, or white noise appear to help. In general, the episodes subside after 4 months of age. No treatment works consistently.

Differential Diagnosis. The baby should be examined for intussusception, hernia, strangulated hair, otitis media, hair in the eye, intestinal obstruction, hydrocephalus, glaucoma, gastroesophageal reflex, and anal fissures.

PROTEIN CALORIE MALNUTRITION (KWASHIORKOR)

A 3-year-old boy is seen for chronic illness. He appears edematous and apathetic, with thin hair. Generalized dermatitis is noted. Sparse hair and decreased muscle tone are noted.

Definition. Kwashiorkor (now called edematous malnutrition) is a result of a severe protein deficiency and inadequate caloric intake.

Risk Factors/Etiology. Decreased protein intake or abnormal protein losses account for kwashiorkor. Associated vitamin deficiencies contribute to the signs and symptoms.

Presentation. Kwashiorkor usually presents after weaning from the breast. Lethargy, apathy, or irritability are early signs. Muscle tone is lost and there is a decrease in subcutaneous tissue. Edema develops from the loss of oncotic pressure caused by hypoproteinemia. Dermatitis and sparse hair are common, as well as secondary infections.

Diagnostic Tools. Decreased **serum albumin** is the most common abnormality. Blood glucose is usually low, as are levels of essential amino acids. Anemia and vitamin and mineral deficiencies are evident.

Treatment. Treatment consists of **slow feeding** of dilute milk with **supplementation** of vitamins and minerals. Protein supplementation is also slowly increased to prevent liver problems. Dehydration and intercurrent infections are treated.

Complications. Mortality can reach 30–40% even when appropriately treated. Mental and physical retardation can be permanent.

Differential Diagnosis. Chronic infections and malabsorption states can mimic kwashiorkor. Nonedematous malnutrition is also known as marasmus.

VITAMINS

Table 3-3. Vitamins

Vitamin	Functions	Sources	Manifestations of Deficiency
A	Retinal pigments Bone and teeth development Epithelial maturation	Green and yellow vegetables Fruits	Ocular lesions Dry, scaly skin Anemia Increased intracranial pressure Mental retardation Growth retardation
B_1 Thiamine	Coenzyme in carbohydrate metabolism Generates NADP	Milk Vegetables Cereals Fruits Eggs	Beriberi—CNS Nausea Peripheral neuritis Congestive heart failure Ptosis Ataxia Increased intracranial pressure Paralysis of laryngeal nerve
Riboflavin	FAD—electron transport Normal tissue maintenance General growth Energy production	Liver Kidney Milk Cheese Eggs Leafy vegetables Cow milk 5× more than human breast milk	Glossitis Keratitis Conjunctivitis Photophobia Seborrhea
Niacin	NAD, NADP cofactors Glycolysis Electron transport	Liver Lean pork Salmon Poultry Red meat	Pellagra—classic triad: • Dermatitis • Diarrhea • Dementia Depression
B_6 Pyridoxine	Coenzyme for decarboxylation and transamination of amino acids Needed for adequate nervous system function and normal brain metabolism	Milk Cereals	Convulsions in infants Peripheral neuritis Dermatitis Anemia
C Ascorbate	Reducing agent in enzyme systems Formation of collagen and chondroitin sulfate	Fresh fruits and vegetables	Scurvy—bleeding, loose teeth, easy fractures, swelling of gums, anemia, sternal depression Costochondral rosary

(*Continued*)

Table 3-3. Vitamins (*cont'd*)

Vitamin	Functions	Sources	Manifestations of Deficiency
D	D_3 natural in skin—photoactivation	Low in breast and cow milk	Rickets—osteomalacia Tetany
E Alpha tocopherol	Nucleic acid metabolism	Green, leafy vegetables Nuts, legumes	Creatinuria Focal necrosis of striated muscle Weakness Premature—hemolytic anemia, increased platelet count
K	Oxidative phosphorylation Clotting factors	Naturally occurring—K_1 Bacteria—K_2 Liver Soybean Alfalfa Spinach Tomatoes Kale	Hemorrhage

Growth

DISORDERS OF HEIGHT

Short Stature

A father is worried that his 13-year-old son is short. The child has been very healthy. He is below the fifth percentile for height and has been all his life. Physical exam is normal. Father is 6 foot 3, mother is 5 foot 10. Father was a "late bloomer."

Definition. Growth is a continuum that involves changes in body size and form, changes in physiologic function, and biologic maturation. There is a corresponding increase in cell size and number. There is no true normal, rather an "average" (50th percentile) plus or minus two standard deviations (3rd–97th percentile). Measurements that fall below the 3rd percentile for height are termed **short stature.**

Risk Factors/Etiology. There are four basic patterns of proportional short stature: pathologic (postnatal onset), constitutional growth delay, familial short stature, and prenatal onset short stature (intrauterine growth retardation).

Presentation. Pathologic short stature and constitutional short stature both start out with the patient in the normal range for height. Over time, the patient with pathologic short stature starts falling off the height curve, crossing percentiles. In **constitutional short stature,** normal final adult height is reached, but the growth spurt and puberty are delayed. Patients with **familial short stature** stay parallel to the growth curve. There is a strong family history of short stature. **Prenatal short stature** also is parallel to the growth curve but is much more marked.

Diagnostic Tests. The **growth chart** is the single most important tool in evaluating disorders of growth. As many points as possible should be plotted to see trends. **Physical exam** is helpful in diagnosing syndromes and diseases associated with short stature. Any female being evaluated for short stature should have a **karyotype** (Turner syndrome). The single, most important diagnostic study is to obtain an x-ray of the left hand and wrist for bone age.

Treatment. Correction of the underlying disease state may help improve height. Some patients respond to human growth hormone.

Differential Diagnosis. Work-up for short stature.

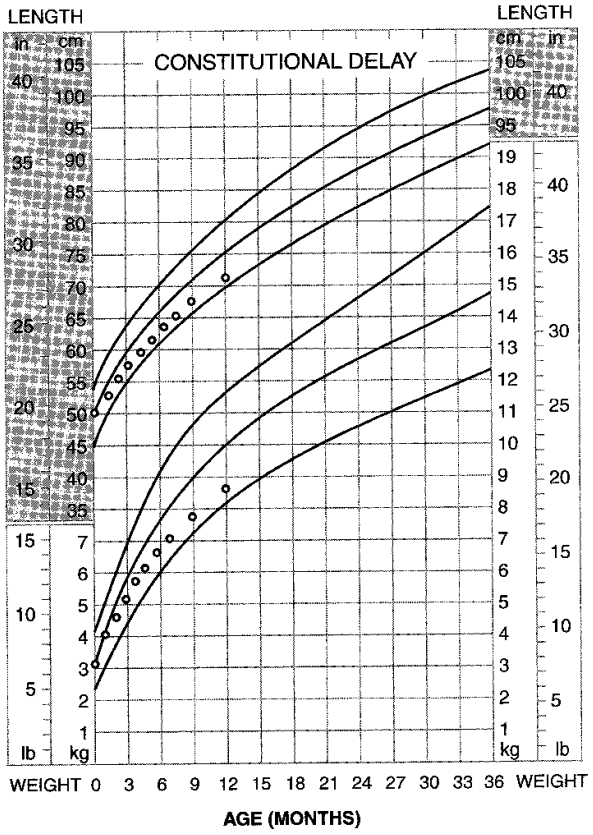


Figure 4-1. Growth Curve: Slow Growth but at a Normal Rate Consistent with Constitutional Delay

Tall Stature

Tall stature is usually a normal variant, **familial tall stature. Exogenous obesity** can also cause tall stature. **Endocrine** causes of tall stature include **growth hormone excess** (gigantism, acromegaly), **androgen excess** (tall as children but short as adults), and **hyperthyroidism.** Genetic syndromes and metabolic disorders responsible for tall stature include homocystinuria, cerebral gigantism, Beckwith-Wiedemann, Weaver-Smith, and Klinefelter syndromes. **Homocystinuria** is autosomal recessive, with an incidence of 1:200,000. Patients have a Marfanoid appearance with associated mental retardation or psychiatric illness. **Cerebral gigantism (Sotos syndrome)** are large for gestational age, have mental retardation, and a mild hydrocephalus.

Evaluation of Growth

Definitions

Growth velocity:	Yearly increments of growth; should follow a growth curve
Chronologic age (CA):	Actual age
Bone age (BA):	X-ray of left hand and wrist

Situations

I. **Ideal.** CA = BA with normal growth velocity

II. CA > BA

- with normal growth velocity: *constitutional delay*
- with abnormal growth velocity: *chronic systemic disease, endocrine disorders*

III. CA = BA

- with normal growth velocity: *genetic short stature*
- with abnormal growth velocity: *genetic, chromosomal, syndrome*

IV. CA < BA

- with normal growth velocity: *obesity*
- with abnormal growth velocity: *precocious puberty, congenital adrenal hyperplasia (CAH), hyperthyroidism*

DISORDERS OF WEIGHT

Failure to Thrive

A baby weighs 16 pounds at 1 year of age. Birth weight was 8 pounds. Parents state that the baby feeds well. Physical exam reveals a baby with little subcutaneous fat, long dirty fingernails, impetigo, and a flat occiput.

Definition. Failure to thrive is failure to gain weight or deceleration of weight growth.

Risk Factors/Etiology. Failure to thrive can result from **malnutrition** (starvation, deprivation, abuse), **malabsorption** (from infection, celiac disease, cystic fibrosis, disaccharidase deficiency, protein-losing enteropathy), **allergies, immune deficiency states,** and **chronic disease.**

Presentation. Again **growth charts** are invaluable. In infants, birth weight is doubled by 4–5 months of age and tripled by 1 year. Patients may show little subcutaneous fat, muscle wasting, rashes, poor tone, and weak cry.

Diagnostic Tests. Hospitalization for documentation of caloric intake and weight gain is sometimes necessary. Complete blood counts, urinalysis, liver function tests, and serum protein should be drawn. A **sweat chloride** test should be considered.

Obesity

Definition. Obesity is a generalized, excessive over-accumulation of fat. It may result from an increase in number or size of adipocytes.

Risk Factors/Etiology. Parental obesity and family inactivity can predispose to obesity. Feeding babies as a generic response to any crying can lead to obesity. Too much fruit juice in the first year of life has been linked with subsequent obesity. Some **syndromes** are related to obesity.

Presentation. Tall stature may sometimes be seen. Boys may present with increased adipose tissue in the mammary area mistaken for breast development. Abdominal **striae** are present. A large pubic fat pad gives the appearance of micropenis. Puberty may come early. Associated obesity of the proximal extremities is common.

Diagnostic Tests. Body mass index **(BMI)** >95% for age/sex or >30 in adolescents is used to define obesity.

Treatment. Exercise and a balanced diet are the keystones to effectively managing obesity.

Complications. Obese infants and children are at increased risk for becoming obese adults. This is related to more advanced age of onset and severity of obesity. Complications include **cardiovascular** (hypertension, increased cholesterol), **hyperinsulinism**, **slipped capital femoral epiphysis**, and **sleep apnea**.

Differential Diagnosis. This includes **endocrine** causes (Cushing, hypothyroidism, Prader-Willi) and **genetic causes** (Turner, Laurence-Moon-Biedl).

Fluids and Electrolytes

5

A 7-year-old is admitted to the hospital for an elective tonsillectomy. The surgeon has requested the pediatrician to keep the child NPO after midnight. The child weighs 22 kg.

MAINTENANCE

Can be calculated from caloric expenditures.

Maintenance water requirements are determined by water lost from feces and urine and insensible losses (i.e., losses through the lung and skin). However, fecal water losses are minimal, therefore, 100 ml for each 100 kcal expended may be used when calculating insensible and renal water losses.

Electrolytes, Na and K, are lost daily in the urine. These losses include 2–3 mEq/kg/d of Na, and 1–2 mEq/kg/d of K.

Maintenance should be administered using the following formulas:

0–10 kg:	100 ml/kg
11–20 kg:	1000 ml + 50 ml/kg for each kilogram >10 kg
>20 kg:	1500 ml + 20 ml/kg for each kilogram >20 kg

Example: Our patient weighs 22 kg. To calculate maintenance one would use the following formulas:

For the first 10 kg:	10 kg × 100 ml	= 1000 ml
For the second 10 kilograms:	10 kg × 50 ml	= 500 ml
For every kilogram > 20:	2 kg × 20 ml	= 40 ml

The patient needs a total of 1540 ml/24 h, which is equal to 64 ml/h maintenance IV fluids.

DEFICIT

There are different **types** of deficits that can develop:

- Isonatremic (isotonic): Na is 130–150 mEq/L with proportional losses of fluid and electrolytes from the extracellular space.
- Hyponatremia (hypotonic): Na <130 mEq/L; lose more Na than water.
- Hypernatremic (hypertonic): Na >150 mEq/L; lose more water.
- Deficit from extracellular and intracellular fluid compartments.

A **clinical assessment** should be made to assess the deficit. This can be done using the history, physical examination, and laboratory test results. Using clinical signs and symptoms, infants and small children may be estimated to have mild (5%), moderate (10%), or severe (15%) dehydration. Older children may be estimated to have mild (3%), moderate (6%), and severe (9%) dehydration.

Table 5-1. Assessment of Degree of Dehydration

	Mild	Moderate	Severe
Infant	5%	10%	15%
Adolescent	3%	6%	9%
Signs and symptoms (general appearance and condition)			
Infants/young children	Thirsty, alert, restless	Thirsty, restless, irritable	Lethargic, limp, cold, sweaty, cyanotic extremities; may be comatose
Tachycardia	Absent	Present	Present
Palpable pulses	Present	Present (weak)	Decreased
Cutaneous perfusion	Normal	Normal	Reduced/mottled
Skin turgor	Normal	Slight reduction	Reduced
Fontanel	Normal	Slightly depressed	Sunken
Mucous membrane	Moist	Dry	Very dry
Tears	Present	Present/absent	Absent
Respirations	Normal	Deep, may be rapid	Deep and rapid
Urine output	Normal	Oliguria	Anuria/severe oliguria
Blood pressure	Normal	Orthostatic hypotension	Hypotensive

FLUIDS

Isotonic fluids such as **normal saline** or **lactated Ringer's** should be used for volume resuscitation. **Oral rehydrating solutions**, such as Rehydralyte and Pedialyte, are available and contain Na 75 mM and 45 mM, respectively. The World Health Organization rehydrating solution contains 90 mM Na. Oral rehydrating therapy may be successful in mild and moderate dehydration.

THERAPY

Always re-evaluate.

Replacement includes Deficit + Maintenance + Ongoing losses = Total volume

When a child presents in **hypovolemic shock** (decreased blood pressure, increased time for capillary refill to 2–3 s), then rapid volume expansion is needed. An intravenous bolus of 20 ml/kg of isotonic fluid should be given. After the bolus, the patient should be reassessed, and if necessary, a second bolus of isotonic solution may be given. Subsequent therapy should be aimed at correcting the factors contributing to the hypovolemic shock.

- In **isonatremic dehydration,** the deficit should be replaced over 8–24 h.
- In **hyponatremic dehydration,** the deficit should be replaced over 8–24 h. In **severe hyponatremic dehydration,** Na may be given as a 3% NaCl solution. The following formula may be used to calculate the milliequivalents of Na to be administered.

(Desired Na – current Na) × (0.6 × kg) = amount of mEq Na that can be given as 3% NaCl solution.

- In **hypertonic dehydration,** the deficit should be replaced over 48 h. This prevents fluid shifts into the cells. A rapid decrease in serum Na decreases serum osmolality faster than intracellular osmolality, and therefore fluid goes into the cells, resulting in edema. Na should be lowered no faster than 10 mEq/L/d.

CASES

Isonatremic Dehydration

A 10-week-old infant is brought to the physician by his mother who states that the child has loose, watery, nonbloody stools that occur >15 times per day. The mother states that the child had been in his usual state of good health until 4 days ago when the symptoms started. The mother states that the child has had tactile fever, nonbilious emesis, and decreased urine output. Weight on admission is 5.3 kg. The vital signs are temperature of 38.4°C, heart rate 142 beats/min, and blood pressure 68/42 mm Hg. On physical examination the patient appears irritable. His anterior fontanelle is sunken, and his eyes are slightly sunken. The patient's oropharynx is dry, and the skin turgor is decreased. A urine specific gravity is 1.030. Laboratory tests show moderate dehydration. The Na is 136 mEq/L, K 4.9 mEq/L, Cl 111 mEq/L, blood urea nitrogen (BUN) 31 mg/dl, creatinine 0.8 mg/dl, venous pH 7.1, Pco_2 22 mm Hg, bicarbonate 10 mEq/L.

Treatment

Moderate dehydration in an infant is 10%.

1. **Give 20 mL/kg IV as a rapid bolus:** 20 mL/kg × 5.3 kg = 106 mL NS
2. **Calculate the pre-illness weight:** 0.90 (x) = 5.3
   x = 5.3/0.90 = 5.9 kg

3. **Calculate the 24-h maintenance fluids and electrolytes:**

   Fluid: 100 mL/kg × 5.9 kg = 590 mL

   Na^+: 3 mEq/kg = 3 × 5.9 = 17.7 mEq Na^+; round to 18 mEq Na^+

   K^+: 2 mEq/kg = 2 × 5.9 = 11.8 mEq K^+; round to 12 mEq K^+

4. **Calculate the deficit fluid:** 5.9 kg – 5.3 kg = 0.6 kg = 600 mL

5. **Calculate the electrolyte loss in the deficit fluid:**

   - For most cases of dehydration, the illness occurs over at least 3 days, in which case, the percent deficit from the extracellular fluid (ECF) is 60% and from the intracellular fluid (ICF) is 40%.
   - Na^+ and K^+ composition of the ECF and ICF:

	ICF (mEq/L)	ECF (mEq/L)
Na^+	20	140
K^+	150	4

   - Na^+ deficit = amount of Na^+ lost from the ECF during the dehydration period (ICF is negligible).
   - Na^+ deficit = fluid deficit (L) X% lost from the ECF X $[\text{normal } Na^+]_{ECF}$
   - K^+ deficit = amount of K^+ lost from the ICF during the dehydration period (ECF K^+ is negligible).
   - K^+ deficit = fluid deficit (L) X% lost from the ICF X $[\text{normal } K^+]_{ICF}$
   - Therefore:

     Na^+ deficit = (0.6 L) × 60% X [140] = 50 mEq Na^+

     K^+ deficit = (0.6 L) × 40% X [150] = 36 mEq K^+

6. **Maintenance and deficit fluid and electrolytes:**

	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	590	18	12
Deficit	600	50	36
Total	1,190	69	48

7. **Calculate the fluid schedule:**

   - We give the maintenance equally over 24 hours, and ½ the deficit over the first 8 hours, and the remaining deficit over the next 16 hours.

First 8 hours:	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	197	6	4
1/2 deficit	300	25	18

   - How do we get these numbers? The water is the maintenance (590 mL) divided equally over 24 hours and represents the amount in the first 8 hours: 590 mL/24 hours × 8 = 197 mL. Or alternatively, because 8 hours is 1/3 of a 24-hour period, the water maintenance is 590 mL/3 = 197 mL. The same calculations are used for the Na^+ and K^+.

8. **Calculate the IV rate:** Totals = maintenance + deficit, so...

   Water: 197 mL + 300 mL = 497 mL

   Na^+: 6 mEq + 25 mEq = 31 mEq Na^+

   K^+: 4 mEq + 18 mEq = 22 mEq K^+

   The 8 hour rate is then 497 mL/ 8 h = 62 mL/h

   The Na^+ concentration is 31 mEq/0.497 L = 62 mEq/L

   The K^+ concentration is 22 mEq/0.497 = 44 mEq K^+

9. **The next 16 hours is simply the remaining maintenance and the remaining ½ deficit of the fluid and electrolytes:**

Next 16 hours:	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Remaining maintenance	393	12	8
Remaining deficit	300	25	18

10. **Calculate IV rate and concentration:** Totals = maintenance + deficit, so...

    Water: 393 mL + 300 mL = 693 mL

    Na^+: 12 mEq + 25 mEq = 37 mEq Na^+

    K^+: 8 mEq + 18 mEq = 26 mEq K^+

    The 16-hour rate is then 693 mL/16 = 37 mL/h

    The Na^+ concentration is 37 mEq/(0.693 L) = 54 mEq Na^+

    The K^+ concentration is 26 mEq (0.693 L) = 38 mEq K^+

Hypernatremic Dehydration

A 5-month-old infant presents with a history of greenish, watery, loose stools for the past 4–5 days. The mother states that diarrhea occurs approximately 10 times per day and leaks out of the diaper onto the infant's socks. The patient has had tactile fever at home and decreased urine output. A home remedy for diarrhea is being administered. The grandmother feeds the child a homemade electrolyte solution of unknown composition to stop the diarrhea. On physical examination the patient has a temperature of 39°C, and a blood pressure of 80/50 mm Hg. The weight is 5.4 kg. The patient is cranky and has a decreased skin turgor that feels **doughy** in texture. Laboratory results include a Na 161 mEq/L, K 5.2 mEq/L, Cl 125 mEq/L, and bicarbonate 13 mEq/L. Arterial blood gas had a pH 7.28, creatinine 1.1 mg/dl, and urine specific gravity is 1.028.

Treatment

Moderate dehydration in an infant is 10%.

1. **Give 20 mL/kg IV as a rapid bolus:** 20 mL/kg × 5.4 kg = 108 mL
2. **Calculate the pre-illness weight:** 0.90 (x) = 5.4 kg

   x = 6 kg

3. **Calculate the 24-hour maintenance fluids and electrolytes:**

   Fluid: 100 mL/kg × 6 kg = 600 mL
   Na^+: 3 mEq/kg × 6 kg = 18 mEq
   K^+: 2 mEq/kg × 6 kg = 12 mEq

4. **Calculate the deficit fluid:**

   Deficit fluid = 6 kg – 5.4 kg = 600 mL

5. **Calculate the free water deficit:** The free water deficit is based upon the amount of free water required to decrease the Na^+ by 1 mEq/L and is based on the actual Na^+.

   For Na^+ <170 mEq/L = 4 mL/kg
   For Na^+ ≥170 mEq/L = 3 mL/kg

   Free water deficit = 4 mL/kg (or 3) × weight (kg) × (Na^+ present – Na^+ desired)
   Free water deficit = 4 mL/kg × 6 kg × (162 – 145) = 384 mL

6. **Calculate the solute deficit:** This is simply the remaining deficit fluid from which the electrolyte deficit occurs.

   600 mL – 384 mL = 216 mL

7. **Calculate the Na^+ and K^+ deficit from the solute deficit:**

   Na^+: 0.6 × 0.216 × 140 = 18 mEq
   K^+: 0.4 × 0.216 × 150 = 13 mEq

8. **Calculate the 24-hour totals:** Total = maintenance + deficit.

   Water: 600 mL + 600 mL = 1,200 mL
   Na^+: 18 mEq + 18 mEq = 36 mEq Na^+
   K^+: 12 mEq + 13 mEq = 25 mEq K^+

9. **Calculate the first 24-hour fluid schedule:** In hypernatremic dehydration, we give all of the maintenance equally, plus half the free water deficit and the entire solute deficit over the first 24 hours, and the maintenance and the other half of the free water deficit over the next 24 hours.

	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	600	18	12
½ Free water deficit	192	—	—
Solute deficit	216	18	13
Totals	1,008	36	25

10. **Calculate the first 24-hour IV rate and electrolyte concentrations:**

    IV rate = 1,008 mL/24 hour = 42 mL/h
    Na^+ concentration = 36 mEq/1.008 L = 36 mEq
    K^+ concentration = 25 mEq/1.008 = 25 mEq K^+

11. The next 24 hours is the maintenance again, plus the other half of the free-water deficit:

	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	600	18	12
½ Free water	192	—	—
Totals	792	18	12

IV rate = 792 mL/24 hour = 33 mL/h

Na^+ concentration = 18 mEq/0.792 L = 23 mEq/L Na^+

K^+ concentration = 12 mEq/0.792 L = 15 mEq K^+

Severe Hyponatremic Dehydration

A 9-month-old is admitted with a 4-day history of increased temperature at home and a copious amount of watery diarrhea. The mother was giving the baby "flat" carbonated soda pop to replace the fluids that the patient lost. The patient had a little formula, but no solid food. The mother states that the child has not had a wet diaper in 12–15 h. Weight 7.7 kg, heart rate is 164 beats/min, and blood pressure is 48/30 mm Hg. Physical examination reveals the patient to be lethargic, limp, and with dry mucous membranes. The patient's respirations are deep. The infant's eyes are extremely sunken. During the physical examination the patient had a generalized seizure. Multiple doses of diazepam were given but the **child continued to seize.** Laboratory results were Na 113 mEq/L, K 4.6 mEq/L, Cl 80 mEq/L, and bicarbonate 7 mEq/L. The arterial blood gas result was pH 7.17, Pco_2 20 mm Hg, BUN 58 mg/dl, and creatinine 2 mg/dL, urine specific gravity is 1.031, Na 5 mEq/L, and creatinine 50 mg/dL.

Treatment

Severe dehydration in an infant is 15%.

1. **Give 20 mL/kg IV as a rapid bolus:** 20 mL/kg × 7.7 kg = 154 mL NS
2. **Calculate the pre-illness weight:** 0.85 x = 7.7 x = 7.7/0.85 = 9.0 kg
3. **Correct the serum Na^+ up to 125 mEq/L:**

   Amount of 3% NaCl needed = (125 mEq/L – 113 mEq/L) × 9 kg × 0.6 L/kg
   = 12 mEq/L × 9 kg × 0.6 L/kg = 65 mL,

   where 0.6 L/kg is the volume of distribution for Na^+.
4. **Calculate the 24-hour maintenance fluids and electrolytes:**

   Fluid: 100 mL/kg × 9 kg = 900 mL
   Na^+: 3 mEq/kg × 9 kg = 27 mEq
   K^+: 2 mEq/kg × 9 kg = 18 mEq
5. **Calculate the deficit fluid:** 9.0 kg – 7.7 kg = 1.3 kg = 1,300 mL

6. **Calculate the electrolyte loss in the deficit fluid:**

   Na^+ deficit = 1.3 L × 60% × 140 mEq/L = 109 mEq Na^+

   K^+ deficit = 1.3 L × 40% × 150 mEq/L = 78 mEq K^+

7. **For hyponatremia, calculate the extra Na^+ deficit after raising the Na^+ to 125 mEq/L:**

   Extra Na^+ deficit = (140 mEq/L – 125 mEq/L) × 0.6 L/kg × 9 kg = 81 mEq

8. **Tabulate the totals for the 24-hour period:**

	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	900	27	18
Deficit	1,300	109	78
Extra Na^+ deficit	—	81	—

9. **Calculate the fluid schedule:**

First 8 hours	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	300	9	6
½ Deficit	650	95	39
		(= ½[109 + 81])	
Totals	950	104	45

   IV rate = 950 mL/8 hour = 119 mL/h

   Na^+ concentration = 104 mEq/0.950 L = 109 mEq/L

   K^+ concentration = 45 mEq/0.950 L = 47 mEq/L

10. **The fluid schedule for the next 16 hours is:**

Next 16 hours	Water (mL)	Na^+ (mEq)	K^+ (mEq)
Maintenance	600	18	12
½ Deficit	650	95	39
Totals	1,250	113	51

    IV rate = 1,250 mL/16 h = 78 mL/h

    Na^+ concentration = 113 mEq/1.250 L = 90 mEq

    K^+ concentration = 51 mEq/1.250 L = 41 mEq/L

Development/Behavior

DEVELOPMENT

An infant can sit up with its back straight, has started crawling, has a pincer grasp, and plays peek-a-boo. What age is most appropriate for this baby?

Definition. Development reflects changes in and acquisition of new functions. It can be classified as:

- *Neurodevelopmental*—changes in behavior over time, e.g., reflexes, gross/fine motor skills
- *Cognitive*—includes thought, learning, problem solving
- *Psychosocial*—environmental interactions, interpersonal relationships

Development in infants and children can be monitored by standardized developmental tables such as the Denver Developmental Screening Test (DDST).

Primitive newborn reflexes appear and disappear in a certain order. Absence or persistence indicates CNS dysfunction. The majority of newborn reflexes are present at birth and disappear by 4–6 months. Table 6-2 (following page) is a list of common reflexes of infancy.

Table 6-1. Newborn Reflexes

Reflex	Description	Appears	Disappears	CNS Origin
Moro	Extend head → extension, flexion of arms, legs	Birth	4–6 mo	Brain stem vestibular nuclei
Grasp	Finger in palm → hand, elbow, shoulder flexion	Birth	4–6 mo	Brain stem vestibular nuclei
Rooting	Cheek stimulus → turns mouth to that side	Birth	4–6 mo	Brain stem trigeminal system
Trunk incurvation	Withdrawal from stroking along ventral surface	Birth	6–9 mo	Spinal cord
Placing	Steps up when dorsum of foot stimulated	Birth	4–6 mo	Cerebral cortex
Tonic neck	Fencing posture when supine	Birth	4–6 mo	Brain stem vestibular nuclei
Parachute	Simulate fall → extends arms	6–8 mo	Never	Brain stem vestibular

Behavioral and developmental milestones are monitored at each health supervision visit to recognize any delays. Not all children reach the same milestone at the same age; rather, there is a range of normal. The following are some common milestones.

Table 6-2. 0–3 Months

Age	Prone	Ventral	Supine	Visual
Newborn	Turns head, nose touches	Flexed around supporting hand	Flexed	Prefers face, doll's eyes, moves in cadence with sound
1 mo	Turns head, clears surface, chin up	Lifts head to plane of body	Relaxed in tonic neck, head lag	Watches person, follows moving object, may smile
2 mo	Lifts head and chest	Sustains head in plane of body	Tonic neck, head lag, follows 180°	Smiles on social contact, attends to voice, and coos
3 mo	Lifts head and chest, with arms extended	Lifts head above plane of body, with legs extended	Tonic neck, reaches at objects, may fail to grasp, less head lag, head bobs on sitting	Sustained social smile, listens to music, some vowel sounds, "aah"

Table 6-3. 4–6 Months

Age	Prone	Supine	Sit/Stand	Manipulate	Social
4 mo	Head to vertical, legs extended	Symmetrical posture, hands to midline, grasps objects, brings to mouth	No head lag, head steady, sits with truncal support; held erect, pushes with feet	Regards pellet	Laughs out loud, displeased if social contact broken
6 mo	Rolls over, pivots, may creep, crawl	Lifts head, rolls over, squirms	Sits with pelvic support, back rounded, leans forward on hands	Rakes at pellet, turns body to extend reach and grasp	Prefers mother, repetitive vowels

Table 6-4. 6–12 Months

Age	Sit/Stand	Locomotor	Manipulative	Cognitive	Social
9 mo	Sits alone, back straight	Creeps/crawls, "walks" with hands held	Pincer grasp assisted	Alert to sound of own name, object permanence	Peek-a-boo, bye-bye, repetitive consonant
12 mo	Cruises, may stand	Walk with one hand held	Unassisted pincer, releases on request, pellet into bottle	One or more words	Plays ball, adjusts posture to dressing

Table 6-5. Second Year

Age	Locomotor	Large Object	Small Object	Crayon	Social
15 mo	Walks alone, crawls up stairs	3 cube tower	Dumps pellet if shown	Makes line, scribbles	Indicates by pointing, hugs parents
18 mo	Runs stiffly, sits on small chair, walks down stairs, one hand held	4 cube tower	Dumps pellet on request	Imitates stroke	Feeds self, 10 words, seeks help, "NO," body parts
24 mo	Runs well, up/down stairs (one step), opens doors, climbs on furniture, jumps in place (both feet off)	7 cube tower, 4 cube train	Threads shoelace	Imitates vertical stroke, circular, folds paper imitatively	Handles spoon well, helps undress, listens to stories, 30–50 words, 2–3 word sentences, "I," "you," parallel play

Table 6-6. Preschool (2–5 Years)

Age	Motor	Manipulative	Crayon	Social
30 mo	Upstairs alternating feet, stand on one foot	9 cube tower, adds chimney to train	Imitates vertical/ horizontal strokes, not cross, imitates circular stroke with closure	Refers to self as "I," knows name, helps put things away, pretends in play
36 mo	Down stairs, (alternating), broad jump(both feet), rides tricycle	10 cube tower, imitates 3 cube bridge	Imitates cross, copies circle, tries to draw person	Knows age and sex, counts 3 objects, understands taking turns
48 mo	Hops on one foot, throws ball overhand, climbs well	Copies 3 cube bridge	Copies cross, square, draws figure with head, 2–4 parts	Counts 4 objects, tells a story, group play, goes to toilet alone
60 mo	Skips		Copies triangle, draws figure, 8–10 parts	

Language Development

Table 6-7. Language Development

	Expressive Language	Receptive Language
First year	Social smile at 6 wk Coo at 3 mo Babble at 6 mo "Dada" inappropriate at 9 mo "Dada" appropriate at 10 mo First word at 11 mo	Oriented to voice at 4 mo Gesture games at 10 mo Understands "no" at 10 mo One-step command with gesture at 12 mo
Second year	3–5 words at 15 mo 8–10 words at 18 mo 20 words at 21 mo 50 words at 20 mo Two words together at 21 mo	One-step commands without gesture at 15 mo Body parts at 18 mo Identifies pictures at 18 mo Points to show at 18 mo Two-step commands at 24 mo

BEHAVIOR DISORDERS

Attention Deficit Hyperactivity Disorder

A 6-year-old boy is doing poorly in school. Teachers report that he is distractible, impulsive, and fidgety. Parents state that he is always "on the go" at home and has been a discipline problem.

Definition. Attention deficit hyperactivity disorder (ADHD) encompasses those disorders characterized by inability to attend to the task at hand, increased motor activity, and impulsivity.

Risk Factors/Etiology. The actual cause is unknown. Patients with ADHD have problems with **filtering** environmental stimuli and **controlling** their own behavior to socially acceptable norms. Imaging studies show a difference in brain structure and function between patients with ADHD and normal control subjects. ADHD occurs more frequently in **boys (4:1)** and is associated with other childhood behavior disorders.

Presentation. ADHD presents with problems in **attention, hyperactivity, and impulsivity.** Using DSM IV criteria these can be defined by the following:

- **Inattentiveness**—makes mistakes due to not paying attention, has difficulty paying attention, doesn't seem to listen, doesn't follow through on tasks, has difficulty getting organized, dislikes/avoids sustained mental effort, loses things easily, is easily distracted, is forgetful
- **Hyperactivity**—fidgets, is out of seat often, does excessive running/climbing, has difficulty playing quietly, is always on the go, talks excessively
- **Impulsivity**—blurts out answers, has difficulty awaiting turn, interrupts/intrudes

Diagnostic Tests. ADHD is a **clinical diagnosis.** Diagnosis requires at least **six criteria** from inattentiveness, six from hyperactivity/impulsiveness, or both. Symptoms must be seen by **7 years** of age, last at least 6 months, be observed in **more than one setting**, be more than age appropriate, and **impair function.** Psychologic testing helps in the differential diagnosis, but there is no specific test for ADHD.

Treatment. Treatment consists of a combination of **pharmacologic** and **psychosocial** management as well as management of any **associated learning disabilities.** Pharmacologic management includes methylphenidate, dextroamphetamine, pemoline, tricyclic antidepressants, clonidine, and bupropion. **Diets** (e.g., low-sugar, dye-free) have absolutely **no value** in the management of ADHD.

Complications. About half of patients with ADHD have normal adult lives. Those who continue to be affected may demonstrate antisocial personalities and alcohol and drug abuse. Aggressive, defiant children tend to do worse as adults.

Differential Diagnosis. Other psychiatric disorders can mimic many of the characteristics of ADHD.

Enuresis

A 7-year-old boy has problems with bedwetting. The mother says that during the day he has no problems but is usually wet 6 of 7 mornings. He does not report dysuria or frequency, and has not had increased thirst. The mother also says that he is a deep sleeper.

Definition. Enuresis is the involuntary passage of urine in a child who is reasonably expected to be toilet trained. Day and night bladder control is usually attained by age **5 years.**

Risk Factors/Etiology. Incidence of enuresis declines with age. There is a strong genetic predisposition for primary nocturnal enuresis.

Presentation. Enuresis can be divided into two major types: **primary enuresis** (90%), in which the patient has never achieved dryness for any significant period of time, and **secondary enuresis**, in which a previously continent child becomes incontinent. Secondary enuresis is usually secondary to **emotional difficulties** (e.g., birth of a sibling, significant loss, family discord). It is usually transient and has a better prognosis. Primary enuresis can be further divided into nocturnal only, diurnal only, and nocturnal/diurnal. **Nocturnal enuresis** is associated with maturational developmental delay of the bladder and may be a disorder of sleep and arousal. Diurnal enuresis is associated with waiting too long to void, urinary tract infections, constipation, diabetes, and stress incontinence.

Diagnostic Tests. Usually there is no pathologic condition associated. Anatomic abnormalities are uncommon. History and physical exam, as well as a screening urine analysis, are all that are indicated.

Treatment. Treatment of any associated anomaly or pathology is indicated. Reward systems, alarm systems, and pharmacotherapy are all used with varying degrees of success. All have relapse rates of up to 30%. **Imipramine and desmopressin** are commonly used.

Encopresis

Definition. Encopresis is fecal incontinence after the age of 4 years.

Risk Factors/Etiology. Encopresis occurs more commonly in boys (4–6:1). The cause is usually psychological, secondary to toilet phobia, overly aggressive management of constipation, starting toilet training too early, or painful defecation after diarrhea, fissures, or severe perianal rashes.

Presentation. Encopresis is usually secondary to stool retention, resulting in leakage of loose stool around the obstruction.

Treatment. Treatment consists of counseling for the child and parents, as well as gentle cleaning of impacted stool out of the colon.

PERVASIVE DEVELOPMENTAL DISORDERS

Autism

A 4-year-old child speaks in unintelligible mumbles, prefers to play by himself, and rocks back and forth constantly. Parents state that as an infant he had a delayed social smile and was never very playful or interactive.

Definition. Autism is a developmental disorder characterized by **impaired social relatedness, deficits in verbal and nonverbal communication,** and unusual responses to the environment.

Risk Factors/Etiology. Autism develops **before 30 months** of age. The cause is unknown. It is more common in **boys (4:1).**

Presentation. Clinical features include **failure to attach as an infant, delayed/absent social smile,** and failure to anticipate interaction with the caretaker. Patients demonstrate a **delay in verbal** and **nonverbal communication** skills. **Stereotypical movements** and a need for **sameness** and routines are characteristic. **Outbursts** of anger are common, as well as **self-injurious behavior.** Autistic children are content to play alone. Seventy-five percent of patients with autism are mentally retarded, although testing is difficult.

Treatment. Treatment consists of behavioral and educational programs geared to the individual patient's needs. Pharmacotherapy can be used for treating some target behaviors.

Prognosis. Prognosis is poor. A very small minority will grow up to be marginally self-sufficient. The majority will end up institutionalized. A better prognosis is associated with patients who demonstrate functional speech and higher intelligence.

Asperger Syndrome

These patients are **more communicative, appear more socially aware,** and do not have language impairments found in autism. They do have social impairments, repetitive behaviors, and sometimes obsessional interests.

Rett Syndrome

Rett syndrome is **X-linked dominant,** affecting exclusively girls. Development is normal until 1 year of age, when language and motor milestones regress and an **acquired microcephaly** is seen. **Hand wringing and sighing** are characteristic, and they develop autistic behavior.

Poisonings

7

INTRODUCTION

Poisoning is the fourth most common cause of accidents in children. There are two groups of children that are prone to poisoning: (*1*) **children** <5 years of age, and (*2*) the **adolescent** population. Accidental ingestions are most common in children <5 years. Adolescent ingestions are usually a result of suicidal attempt or experimentation with illicit drugs. Any self-poisoning in a child >5 years old should be considered intentional. Ninety-one percent of all poisonings occur in the home, the most common sites being the kitchen and the bathroom.

PREVENTION

Accidental poisonings occur most frequently when routines are disrupted, e.g., moving and vacations. Child safety caps have helped decrease the number of childhood poisonings; however, they are **not** 100% effective and should not give a false sense of security. All potential poisons should be properly labeled, stored out of reach of children, and locked. Medications should not be taken in front of small children. Parents should receive anticipatory guidance regarding poisoning and should have the number for Poison Control.

FIRST AID

If the poisoning occurs at home, Poison Control should be called first. If the poison is an inhalant, remove the patient from the area. If the poisoning is affecting the skin, remove the clothing and wash the skin thoroughly unless a dry powder is the cause of the poisoning. If the patient has swallowed the poison, induce vomiting if appropriate and take the patient to the hospital. If the poison is in the eye, flush the eye thoroughly.

EMERGENCY CENTER

When caring for poisoning in the emergency center always remember the ABC's (airway, breathing, and circulation). Review the patient's history and perform a pertinent, focused physical examination. Treat the patient for shock, burns, and pain. If a narcotic is suspected, give naloxone. The goal is to prevent absorption. This may be done using (*1*) emesis, particularly in the first 4 h, (*2*) gastric lavage, (*3*) activated charcoal, (*4*) cathartics, and (*5*) diuresis. Ipecac is no longer recommended. Indications for **gastric lavage** include coma or impending coma, seizures, or a depressed gag reflex. Gastric lavage is most effective within 1 h of ingestion, and the largest possible orogastric tube should be used. Gastric lavage should be performed only in older children. **Activated charcoal** has no real contraindications and is the treatment of choice to prevent absorption of poisoning when the patient is present in the emergency center. However, charcoal is ineffective against cyanides, metals, Na, K, Cl, acids, and bases. **Cathartics** decrease absorption by increasing the rate of excretion. Magnesium should not be used if the

patient has renal failure. **Diuresis** may be performed using hemodialysis, hemoperfusion, and peritoneal dialysis. Exchange transfusion should only be performed if the patient is unresponsive to appropriate care.

SPECIFIC POISONINGS

Acetaminophen

> A 3-year-old was playing doctor with his 4-year-old sister. The sister told him that he was very ill and "prescribed" 25 acetaminophen tablets, which the younger child ingested.

Definition. Acetaminophen is an analgesic and antipyretic that is metabolized in the liver. Acetaminophen poisoning causes an *N*-acetyl-*p*-benzoquinoneimine (NAPQI) metabolite that produces hepatotoxicity in the absence or depletion of glutathione.

Risk Factors/Etiology. In children <12 years of age the toxic dose of acetaminophen is 150 mg/kg. A single ingestion of 7.5 g is considered to be a minimum toxic dose in adolescents and adults.

Presentation/Physical Examination. There are four stages of acetaminophen poisoning if the patient is left untreated.

- Stage 1—In the first 24 h after ingestion, the patient may develop nausea, vomiting, and diaphoresis.
- Stage 2—During the next 24–48 h, there is clinical improvement. During this time serum glutamic-oxaloacetic transaminase, serum glutamate pyruvate transaminase, bilirubin, and prothrombin increase. The patient develops right upper quadrant pain.
- Stage 3—From 72 to 96 h after ingestion, the patient has peak liver function abnormalities. GI symptoms may again develop.
- Stage 4—From 4 days to 2 weeks after ingestion, the patient's hepatic problems resolve. There are no sequelae 3 months to 1 year later. However, <1% will develop fulminant hepatic necrosis.

Diagnostic Tests. Absorption may be delayed 4 h in overdose; therefore a plasma level for acetaminophen should be measured ≥4 h after ingestion. The Rumack-Matthew nomogram should be used to plot the level of acetaminophen. See Figure 7.1.

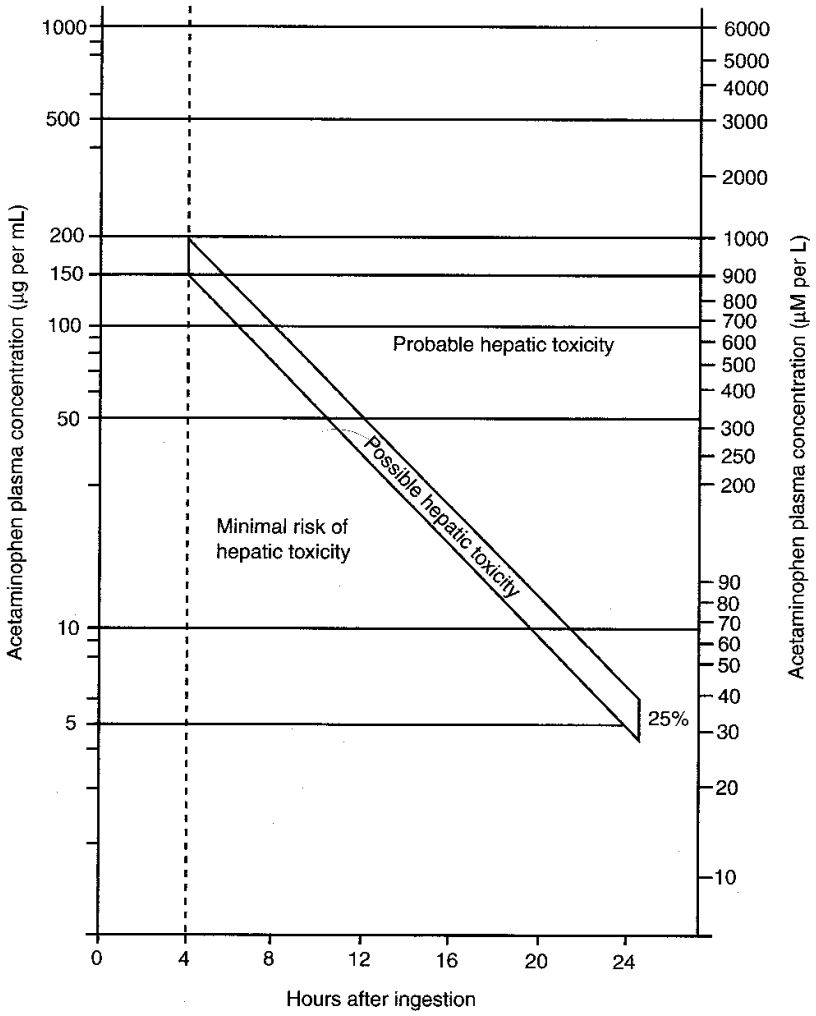


Figure 7-1. Semilogarithmic Plot of Plasma Acetaminophen Levels Versus Time

Treatment. The use of **activated charcoal** should be considered, as many poisonings are multidrug poisonings and not solely poisonings with acetaminophen. ***N*-Acetylcysteine** is the antidote for acetaminophen poisoning. If the acetaminophen level is ≥150 μg/ml treat with *N*-acetylcysteine. *N*-Acetylcysteine works best if started within 8 h of ingestion but can be given up to 16 h after ingestion. In severe cases Poison Control may advise *N*-acetylcysteine to be given as late as 24–36 h after ingestion. In this country *N*-acetylcysteine is given orally. Liver enzymes, bilirubin levels, and prothrombin time should be monitored in patients within the toxic range of the acetaminophen nomogram.

Complications/Follow-up. Fulminate hepatic necrosis and death may occur. A liver transplantation may be necessary in patients with severe hepatic problems.

Alcohol

A high school senior arrives in the emergency center immobilized on a backboard with cervical spine collar in place after a motor vehicle accident. The patient was a restrained passenger in the backseat passenger side. He states that he and the five other teens in the motor vehicle had just left a party when their car was struck. The smell of alcohol is present on physical examination.

Definition. Alcohol (ethyl alcohol or ethanol) is a solvent that is used as a beverage, topical antiseptic, in colognes, and in some instances a rubbing alcohol.

Risk Factors/Etiology. Alcohol use may be seen in adolescents and may affect their normal function as well as threaten society, especially if the adolescent is driving under the influence of alcohol.

Presentation/Physical Examination. The effects of alcohol depend on the **level.** The alcohol level depends on the quantity of alcohol ingested, the size of the patient, and whether food was ingested. A person in most states is **medico-legally intoxicated** at **100 mg/dl.** At **50–150 mg/dl** the patient is uncoordinated and has blurred vision and a slow reaction time. At **150–300 mg/dl** the patient has visual impairment, staggering, and slurred speech. Levels of **300–500 mg/dl** produce stupor, hypoglycemia, and coma. A level of **>500 mg/dl** is **fatal** if the patient has no tolerance.

Diagnostic Tests. An alcohol and blood glucose level should be obtained.

Treatment. The treatment is supportive. Hypoglycemia and acidosis should be treated. Artificial ventilation may be needed for respiratory failure. Alcohol is rapidly absorbed from the gut and is not adsorbed by activated charcoal, therefore GI decontamination of patients presenting >2 h after ingestion is rarely performed. Gastric lavage should be used in earlier presentations. However, activated charcoal should be administered to adolescents because of the potential drug coingestion. Dialysis should be considered for blood alcohol levels >400 mg/dl.

Complications/Follow-up. Hypoglycemia and seizures may occur. Death may result from respiratory failure.

Amphetamines

The guidance counselor refers a 10th-grade student to the school nurse for weight loss, insomnia, and depression.

Definition. Amphetamines are stimulants. Methamphetamine "ice" is very popular with adolescents.

Risk Factors/Etiology. Amphetamines are one of the most frequently reported illicit drugs in high school seniors.

Presentation/Physical Examination. Patients with acute toxicity from amphetamines may have symptoms that include diarrhea, palpitations, arrhythmia, syncope, hyperpyrexia, and hyperreflexia progressing to convulsions and coma.

Patients with chronic toxicity from amphetamines develop tolerance to the drug. Symptoms may include restlessness, nervousness, depression, insomnia, and suicidal behavior.

Diagnostic Tests. A urine drug screen can be performed to determine the presence of amphetamines.

Treatment. Patients may need to be hospitalized. Supportive therapy is important. Cooling blankets may be used for hyperthermia. Sedation may be obtained with lorazepam, or diazepam. Haloperidol may be given for agitation and delusions. Hypertension and arrhythmias should be treated.

Aspirin (Salicylates)

> A teenage girl is brought by ambulance to the emergency center because her mother found her ingesting a bottle of aspirin. The patient states that "she wants to die," as her boyfriend has decided to date someone else.

Definition. Aspirin (salicylate) is an analgesic and antipyretic. Methyl salicylate is found in oil of wintergreen.

Risk Factors/Etiology. Salicylates are the most common cause of drug poisoning in the United States. Salicylates uncouple oxidative phosphorylation and increase the metabolic rate, resulting in tachypnea, tachycardia, fever, and hypoglycemia. The Krebs cycle is also inhibited, causing a metabolic acidosis. In addition, damage to hepatocytes occurs, causing liver toxicity, prolonged prothrombin time, platelet inhibition, and prolonged bleeding time.

Presentation/Physical Examination. The presentation and physical examination will vary according to the amount of salicylate ingested. Vomiting, hyperpnea, fever, lethargy, and mental confusion are seen in **mild** salicylate ingestion. Convulsions, coma, and respiratory and cardiovascular collapse are seen in **severe** salicylate ingestion. Hyperventilation, dehydration, bleeding disorders, seizures, and coma are seen in **chronic** salicylate ingestion.

There are three phases of salicylate ingestion:

- Phase 1—The patient has respiratory alkalosis from direct stimulation of the respiratory center, and potassium and sodium bicarbonate are excreted in the urine. This phase lasts approximately 12 h in an adolescent but may not be evident in a small child. **Remember** that clinical signs and symptoms of acute calculate poisoning may simulate diabetic ketoacidosis.
- Phase 2—As alkalosis continues, a "paradoxical aciduria" occurs approximately 12–24 h after salicylate ingestion in the adolescent. This phase may begin shortly after salicylate ingestion in the young child. The aciduria may lead to hypokalemia.
- Phase 3—**Metabolic acidosis, dehydration, and hypokalemia appear 4–6 h after ingestion of salicylates in an infant, and ≥24 h after ingestion in an adolescent.** Metabolic acidosis results from lactic acidosis. The hyperpnea in this phase is secondary to acidosis rather than to stimulation of respiratory centers.

Diagnostic Tests. The white blood cell count, hematocrit, and platelets will be increased. The blood urea nitrogen and creatinine are also increased. Patients may have hypernatremia, or hyper- or hypokalemia. The patient may have hyper- or hypoglycemia. The arterial blood gas will show a metabolic acidosis with respiratory compensation in children and a respiratory alkalosis alone in adolescents.

In acute overdose, the salicylate serum level is predictive of the clinical course at 6 h after ingestion. This serum level should be plotted on the Done's nomogram. See Figure 7.2.

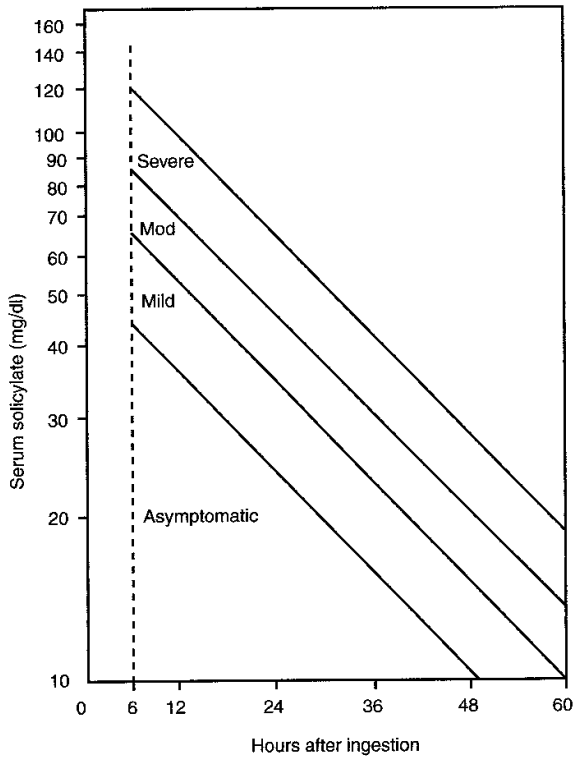


Figure 7-2. Done's Nomogram

If the patient's serum salicylate level is **<35 mg/dl,** the patient will be **asymptomatic.** If at 6 h after ingestion, the salicylate level is **35–70 mg/dl,** the patient will have **mild to moderate** toxicity. A patient with a salicylate level between **70 and 100 mg/dl** will have **severe** toxicity. A salicylate level **>100 mg/dl** is **potentially fatal.**

Treatment. Gastric decontamination should be performed, and the patient should be hydrated. To enhance the excretion of salicylate the intravenous route should be used to administer bicarbonate. Urine pH should be raised to a pH of 7.0–7.5. Hemodialysis may be required in severe cases of salicylate toxicity (salicylate level >100 mg/dl).

Complications/Follow-up. Some causes of death from salicylate ingestion include respiratory failure, cerebral edema, hemorrhage, and cardiovascular collapse.

Carbon Monoxide

A 5-year-old is brought to the emergency center for first-time seizure. The child was previously well, and has never had a seizure. The father states that the child was traveling cross-country in an older model vehicle when the seizure occurred. The child was sleeping on the floor of the vehicle, and there were five adults who were smoking tobacco at the time of the event. On physical examination the child appears drowsy, but otherwise, the physical examination is unremarkable. The pulse oximetry reads 97%.

Definition. Carbon monoxide is a colorless, odorless gas produced from the combustion of carbon-containing fuel.

Risk Factors/Etiology. The affinity of carbon monoxide to hemoglobin is 250 times that of oxygen. This results in the formation of carboxyhemoglobin, decreasing the oxygen carrying capacity of blood. Unintentional carbon monoxide poisoning claims approximately 500 lives each year.

Presentation/Physical Examination. Symptoms depend on the carboxyhemoglobin levels

0–10%:	None
11–20%:	Mild headache
21–30%:	Throbbing headache, irritability
31–40%:	Severe headache, lethargy, nausea, vomiting
41–50%:	Confusion, syncope, tachycardia, tachypnea
51–60%:	Syncope, coma, seizures
61–70%:	Coma, hypertension, respiratory failure, death
>70%:	Death

Diagnostic Tests. Presence or absence of the classic cherry-red skin color is of no diagnostic value. A carboxyhemoglobin level as well as an arterial blood gas analysis should be obtained. Patients with severe carbon monoxide poisoning may have muscle breakdown; therefore, a urinalysis for myoglobin should be obtained. A complete blood count and electrolytes are also useful.

Treatment. The patient should be removed from the environment, and 100% supplemental oxygen, or hyperbaric oxygen in severe cases, should be administered until the carboxyhemoglobin level is ≤5%. Urine output should be >1 ml/kg/h.

Complications/Follow-up. Behavior changes, memory loss, and blindness are reported in as many as 10–30% of cases, even after a single exposure.

Caustics (Acids and Alkalis)

A 2-year-old presents to the emergency center with his parents who say that they found the patient drinking some Red Devil lye. The patient is crying profusely, and has blisters and burns in his mouth. The patient is drooling.

Definition. Caustics include both acids and alkali (bases). Examples of acids include metals, toilet bowel cleaners, and batteries. Examples of bases are Purex, Drano, dishwashing detergent, Red Devil lye, and Liquid Plummer.

Risk Factors/Etiology. Acids coagulate proteins, resulting in tissue necrosis, and alkalis produce liquefaction necrosis with the risk of perforation if the burn is located in the intestinal tract. Serious injuries tend to occur with a pH <2 or >12.

Presentation/Physical Examination. Burns of the mucous membranes may be visualized. The patient may drool and refuse to swallow secondary to pain. Esophageal strictures may be found. Acids may be responsible for delayed gastric emptying from pylorus scarring.

Diagnostic Tests. A complete blood count should be ordered, as well as an abdominal radiograph.

Treatment. The caustic should be removed by flushing copiously with water. Emesis and gastric lavage are contraindicated in caustic patients, nor should activated charcoal be used. Endoscopy should be completed in the first 24 h if the patient is symptomatic or the history is suggestive of burns from caustic ingestion. The use of steroids is controversial, and prophylactic antibiotics do not seem to improve outcome.

Cocaine

A 15-year-old is brought to the emergency center with pupilary dilatation, tachycardia, and chest pain. A classmate reports that she thinks she saw the patient "snorting" in the locker-room.

Definition. Cocaine is an alkaloid extracted from *Erythroxylon coca* and is supplied as a hydrochloride salt in crystalline form. It is absorbed from the nasal mucosa, detoxified in the liver, and excreted in the urine. The half-life for cocaine is approximately 1 h.

Risk Factors/Etiology. All cocaine is not "pure" as drugs such as PCP, heroin, or amphetamines may be added or substituted for cocaine. It may be snorted (nasal application), injected, or smoked (freebasing).

Presentation. Cocaine gives a feeling of euphoria. Patients may have CNS stimulation, i.e., restlessness, excitement, agitation, increased motor activity, increased respiratory rate, and hypertension. Later, the patient may experience hypotension with seizure, coma, and respiratory depression. Often patients complain of chest pain secondary to myocardial injury that ranges from angina pectoris to myocardial infarction. There may be nausea, insomnia, and emaciation in the chronic user.

Physical Examination. There may be a perforated nasal septum from snorting.

Diagnostic Tests. A urine drug screen may be done. If smuggling is suspected, a flat-plate abdominal roentgenogram will show opaque densities within the bowel highlighted by a gas halo.

Treatment. GI decontamination with activated charcoal is only indicated when "body packing" with cocaine is suspected. Intensive supportive therapy applied to the clinical manifestations is the treatment of choice. The half-life for cocaine is approximately 1 h, and prognosis is good if there is adequate support.

Complications/Follow-up. Hypertension may lead to a cerebrovascular accident. Chronic cocaine users may develop a cardiomyopathy that leads to depressed cardiac function and death.

Hydrocarbons

A 2-year-old is brought to the pediatric emergency center because the patient ingested gasoline. The gasoline had been placed in a soda pop bottle to be used for the lawn mower. The patient does not appear to be in any respiratory distress, but wheezing is present in the right base.

Definition. Hydrocarbons are carbon compounds that become liquid at room temperature.

Risk Factors/Etiology. Hydrocarbons can be found in fuels, solvents, household cleaners, and polishes. Aspiration of hydrocarbons may cause a chemical pneumonitis.

Presentation. The patient may have cough, emesis, and fever. However, symptoms may be delayed for 6 h.

Physical Examination. Shortness of breath, wheezing, rales, dullness to percussion, and respiratory difficulty may be found on physical examination.

Diagnostic Tests. A chest roentgenogram should be ordered and may show an infiltrate.

Treatment. Gastric lavage is contraindicated, unless there is a risk of severe poisoning, e.g., CNS involvement from the ingestion. If gastric lavage is necessary, a cuffed endotracheal tube should be inserted into the patient's airway before lavage.

Patients who are symptomatic on arrival, become symptomatic during the first 6 h after ingestion, or have ingested toxic hydrocarbons should be admitted to the hospital for treatment and observation. Patients who remain asymptomatic after 6 h and have a negative chest roentgenogram may be discharged home.

Antibiotics are not indicated unless a secondary bacterial infection declares itself. Corticosteroids are not beneficial.

Complications/Follow-up. Recovery occurs in most cases, but the course may include lethargy, seizures, and coma. Complications include pneumothorax, pleural effusions, and secondary bacterial infections. Some patients develop respiratory failure and death.

Organophosphates

A young boy who is visiting his grandfather's farm is brought to the emergency center by ambulance. The grandfather says that the child had been playing in a newly fertilized field when he developed drooling, tearing, and emesis. At present the patient is areflexive and has defecated and urinated in his trousers. The patient appears lethargic.

Definition. Organophosphates are acetylcholinesterase inhibitors that may be ingested, inhaled, or absorbed through the skin. They are commonly found in insecticides.

Risk Factors/Etiology. Organophosphates are used as nerve gases in chemical warfare agents. Because organophosphates may be dissolved in hydrocarbon bases, the health-care provider must be prepared to treat hydrocarbon pneumonitis.

Presentation/Physical Examination. The presentation and physical examination may include muscarinic, nicotinic, and CNS signs and symptoms. The **muscarinic** symptoms include salivation, lacrimation, urination, defecation, GI cramping, and emesis. The **nicotinic** symptoms include cramps, fasciculations, twitching, weakness, and areflexia, and paralysis of voluntary muscles, including respiration, occurs after the muscarinic effects. The nicotinic symptoms are not seen in mild poisoning. **CNS** symptoms include anxiety, ataxia, dizziness, headache, convulsions, and coma.

Diagnostic Tests. A history of exposure to organophosphates and clinical presentation are the most helpful clues to making the diagnosis. The diagnosis may be suspected with the odor of insecticide. A decreased red blood cell cholinesterase is the best laboratory test; however, it is not available on a stat basis. Treatment should not be delayed waiting for the results.

Treatment. Attention should be given to airway, breathing, and circulation (ABC's). Gastric decontamination with gastric lavage and activate charcoal should be performed on patients who ingested organophosphates. If exposure was via skin, the patient should be washed with soap and water, and contaminated clothing placed in a plastic bag. Health-care workers should take precautions not to get organophosphate on their skin. **Atropine** should be administered for the **muscarinic** symptoms, and **pralidoxime** should be administered for the **nicotinic** symptoms. The goal of therapy is relief of neurologic and cholinergic signs.

Iron

Risk Factors/Etiology. The most common cause of death from poisoning in childhood is **iron poisoning**. The severity of the poisoning depends on the amount of elemental iron ingested. Adult preparations are responsible for serious poisonings.

Presentation/Physical Examination. Iron poisoning occurs in four stages:

- **Stage 1** occurs 30 min–6 h after ingestion, with symptoms of nausea, vomiting, and diarrhea and abdominal pain. Hemorrhagic gastroenteritis may be present in more serious iron ingestion.
- **Stage 2** occurs 6–12 h after ingestion, and relative clinical improvement may be mistaken for recovery **(honeymoon phase).**
- **Stage 3** occurs 24–48 h after ingestion and is associated with severe poisoning, progressive circulatory collapse **(shock)**, hepatorenal failure, bleeding, metabolic acidosis, and coma.
- **Stage 4 occurs 1–2 months after ingestion and causes GI scarring and obstruction, as well as pyloric stenosis.**

Diagnostic Tests. The diagnosis is based on history and development of symptoms. **Serum iron levels** should be obtained. Serum iron levels of >500 μg/dl is considered severe poisoning. Iron is radiopaque, and iron tablets may be seen on **plain abdominal films.** Children's multivitamins may not be visualized on roentgenogram because of their low iron concentration.

Treatment. Syrup of ipecac may be used to remove iron tablets from the stomach if there is no evidence of gastroenteritis. **Whole bowel irrigation** should be used to flush tablets from the intestine. If tablets continue to adhere to the gastric mucosa, then they must be removed by **endoscopy** or **surgery.** Treatment is **supportive** and includes airway and fluids if the patient is in shock. The **antidote** for iron poisoning is **deferoxamine,** administered as an intravenous infusion. Deferoxamine should be administered (*1*) to symptomatic patients, and those with hypotension and lethargy regardless of the serum iron level and total iron binding capacity (TIBC), (*2*) if the serum iron is greater than the total iron binding capacity (TIBC), or (*3*) if the serum iron level is >350 μg/dl. The urine turns **"vin rose"** when free iron binds with deferoxamine. Treatment should continue until the patient is symptom free.

Complications/Follow-up. Iron is corrosive to the GI mucosa, and may cause hypotension and metabolic acidosis, and coagulopathies. Drowsiness and coma may develop. Toxic ingestions may result in death.

Lead

A 24-month-old child has a lead level of 19 μg/dl on a routine screening for a well-child check. The patient is asymptomatic, but lives in a historic home that is being renovated by his parents.

Definition. Lead poisoning is a chronic disorder often seen in children who are near environmental exposure risk, such as ingestion of paint chips or putty or plaster from old buildings.

Risk Factors/Etiology. Sources of lead include household dust, paint removal, and contaminated soil and water. Living in close proximity to lead production facilities increases the risk of lead poisoning. Exposure to lead may also occur from contaminated work clothes of a parent. Pipes may cause mild to moderate lead poisoning. Rarely, folk remedies, lead objects (shot, fishing weights), and lead-glazed pottery also contribute to lead poisoning.

Presentation/Physical Examination. Presentation and physical examination depends on the blood lead level and age of the child. Most have no symptoms and are picked up on routine screen. Anorexia, apathy, lethargy, anemia, decreased play activity, aggressiveness, and poor coordination may all be symptoms of lead intoxication. Symptoms of **chronic exposure** are apathy, clumsiness, nausea, and vomiting. **Acute** symptoms include apathy, nausea, and vomiting, followed by coma and seizures.

Diagnostic Tests. Elevated blood lead levels and signs of interference with hemoglobin synthesis, such as an increase in free erythrocyte protoporphyrin and increased lead excretion in the urine after administration of a chelating agent such as calcium EDTA, make the diagnosis. Minimal lead screening should be done for patients who are 6 months–6 years of age. Children at risk for lead poisoning should be screened by **finger stick blood lead.** Blood lead levels of >10 μg/dl are abnormal. The patient may have evidence of sideroblastic anemia. Roentgenogram findings may show lead lines at the metaphyses of the long bones and radiopaque foreign material within the small bowel.

Treatment. The goal of management is to eliminate or remove the child from the source of lead.

Table 7-1. Management of Lead Poisoning

Level (in μg/dL)	Management
10–14	Repeat within 3 mo Evaluate sources Education
15–19	Repeat in 2 mo Evaluate sources Education Department of Health referral
20–44	Repeat 1 mo all stated above
44–70	Treat with single drug, preferably DMSA
>70	*Immediate hospitalization and two drugs:* • *EDTA + DMSA/BAL without encephalopathy* • *EDTA + BAL with encephalopathy*

Complications/Follow-up. Encephalopathy can occur after 3–6 weeks of actively ingesting lead (<3 years).

Antihistamines

A 2-year-old took his brother's allergy medication. He is brought to the hospital by ambulance because of tremors and hyperactivity. The medics report that the child had a seizure before arriving at the hospital. On physical examination the patient has fever, flushed skin, tachycardia, and fixed dilated pupils.

Definition. Antihistamines are used as sedatives, for allergies, for antinausea, and for motion sickness. They are available over the counter and as prescription. They may be found in some cold medications such as liquid cough medication.

Risk Factors/Etiology. Antihistamines may depress or stimulate the CNS. Some liquid cough and cold preparations that contain antihistamines may also contain ethanol.

Presentation/Physical Examination. The presentation will vary. Some patients will be drowsy, but others will have insomnia, nervousness, and restlessness. Children may be hyperactive and experience hallucinations. In addition they may have tonic-clonic seizures. Anticholinergic effects such as flushed skin, fever, tachycardia, and fixed dilated pupils may also be present.

Diagnostic Tests. There are no special diagnostic tests that need to be ordered.

Treatment. The treatment of antihistamine poisoning requires an accurate history of the time of ingestion and the type of drug ingested because of the many sustained-release antihistamines. **Activated charcoal** should be administered unless a sustained-release antihistamine was ingested. In cases of ingestion of **sustained-release antihistamine, whole bowel irrigation** should be considered. Seizures should be controlled. Supportive therapy should be given.

Complications/Follow-up. Death may result from uncontrolled seizures leading to coma and cardiopulmonary arrest.

Barbiturates

A 3-year-old arrives with his parents after ingesting his brother's seizure medication (phenobarbital). The patient has constricted pupils and appears to be in coma.

Definition. Barbiturates are sedatives used for seizure disorders, induction of anesthesia, and management of increased intracranial pressure.

Risk Factors/Etiology. Barbiturates enhance the inhibitory neurotransmitter γ-aminobutyric acid (GABA) and are general depressants to nerve and muscle tissue.

Presentation. Mild to moderate barbiturate toxicity mimics alcohol intoxication. Severe acute barbiturate toxicity results in CNS problems, including lethargy and coma.

Physical Examination. Constricted pupils, confusion, hypotension, poor coordination, respiratory depression, and coma may be found on physical examination.

Diagnostic Tests. Although a barbiturate serum level may be obtained, the clinical presentation predicts the seriousness of the overdose.

Treatment. Attention must be given to the ABC's (airway, breathing, and circulation.) Gastric lavage and multiple doses of activated charcoal may be used to decontaminate the GI system. Intravenous fluids and forced diuresis and alkalinization should be used for long-acting barbiturate intoxication. In severe cases, hemodialysis may be necessary.

Complications/Follow-up. Early deaths are usually a result of shock or cardiopulmonary arrest. Later deaths are usually the result of pulmonary complications such as aspiration pneumonia or pulmonary edema.

Tricyclic Antidepressants

A 3-year-old presents to the emergency center after taking her brother's bed-wetting medicine. She is noted to be drowsy, and on electrocardiogram the patient has a QRS widening, and QT and QTc prolongation.

Definition. The cyclic antidepressants produce sedation, α-blocking, anticholinergic, and quinidinelike effects. In the central and peripheral nervous systems, norepinephrine, 5-hydroxytryptamine, and dopamine are blocked.

Risk Factors/Etiology. Ingestion of tricyclic antidepressants is a serious problem in the pediatric population because of the availability of these in the home when prescribed for depression and bed-wetting. Poisoning with tricyclic antidepressants is a leading cause of death.

Presentation/Physical Examination. The **CNS** and the **heart** are the two main systems that are affected. Symptoms include drowsiness, delirium, hallucination, disorientation, seizures, coma, hypertension, later hypotension, and arrhythmias.

Diagnostic Tests. An electrocardiogram should be obtained to check for QRS widening and QT and QTc prolongation.

Treatment. Supportive therapy should be given, including intubation if necessary. **Activated charcoal** should be given to prevent further absorption. **Sodium bicarbonate** should be administered to treat and prevent dysrhythmias. Treat the arrhythmias not responding to sodium bicarbonate with lidocaine. Hypotension may be treated with fluids and norepinephrine (in some cases). Seizures usually resolve without treatment. Symptomatic patients should be monitored in an intensive care unit. Patients who are completely asymptomatic after 6 h of observation may be discharged home.

Complications/Follow-up. Seizures and arrhythmias are the most important life-threatening complications.

TOXIDROMES

Definition: Grouping of physical findings that suggest a specific toxin or class

Table 7-2. Toxidromes

Organ System	Anticholinergic	Sympathomimetic	Cholinergic	Opiate
Pupil	Large, nonreactive	Large, reactive	Small	Pinpoint
CNS	Confusion	Hyperactive	Lethargy	Depressed
Cardiovascular	Tachycardia	Tachycardia	Brady./Nl.	Brady/Nl.
Skin	Dry	Wet	Wet	Nl.
Bowel sounds	Decreased	Increased	Increased	Increased

Definitions: Brady., bradycardia; Nl., normal.

Table 7-3. Antidotes

Poison/Toxic Sign	Antidote
Acetaminophen	*N*-acetylcysteine
Anticholinergics	Physostigmine sulfate
Anticholinesterases	Atropine sulfate Pralidoxime (2-PAM) chloride
Carbon monoxide	Oxygen
Cyanide	Amyl nitrite Followed by sodium nitrite
	Followed by sodium thiosulfate
Digoxin	Antidigoxin Fab fragments
Ethylene glycol	Ethanol
Extrapyramidal signs	Diphenhydramine hydrochloride Benztropine mesylate
Heavy metals (e.g., arsenic, copper, gold, lead, mercury)	Chelators Calcium disodium edetate (EDTA) Dimercaprol (BAL) Penicillamine 2,3-dimercaptosuccinic acid (DMSA, Succimer)
Iron	Deferoxamine mesylate
Isoniazid (INH)	Pyridoxine
Methanol	Ethanol
Methemoglobinemia	Methylene blue
Opioids	Naloxone hydrochloride
Warfarin and related drugs	Vitamin K1 (phytonadione) Fresh-frozen plasma

Accidents/Emergencies

HEAD TRAUMA

A 5-year-old fell approximately 6 ft from a tree and is brought to the emergency center because he had loss of consciousness at the scene for 1 minute. The patient is awake and alert on arrival, and his Glasgow Coma Score is 15. The patient has an obvious deformity of his right forearm and some bruises. Otherwise, the physical examination is unremarkable.

Risk Factors/Etiology. Head trauma is a common cause of childhood hospitalization. Serious head trauma is usually secondary to motor vehicle accidents, sports, recreation, and violence.

Presentation. Presentation varies according to the injury. A patient may present with neurologic deficit or without neurologic deficit. Some patients with head trauma will stabilize and other patients may deteriorate. Children with neurologic deficits may have a history of a lucid interval and relapse into coma, or they may have remained abnormal after the injury.

Physical Examination. The physical examination will vary according to the injury. Some patients may have linear or depressed skull fractures. Basilar skull fractures are associated with Battle sign (a subcutaneous bleed over the mastoid), hemotympanum, and cerebrospinal fluid (CSF) rhinorrhea and otorrhea.

Some Types of Head Injuries

- **Cerebral concussion** is the most common head injury seen in children. Patients with concussion may have a history of brief (seconds to minutes) unconsciousness, then normal arousal. Disturbance of vision and equilibrium may also occur. Concussion can be divided into **three grades**:
  - In grade I, the patient has confusion, but no amnesia, and no loss of consciousness.
  - In grade II, the patient has confusion and amnesia, but no loss of consciousness.
  - In grade III, the patient has confusion, amnesia, and loss of consciousness.
- **Recommendations** for returning to play in **contact sports** (including practice) after a concussion are as follows:
  - A patient with a grade I concussion, if asymptomatic, may return to contact sports in 20 minutes.
  - A patient with a grade II concussion, if asymptomatic for 1 week, may return to contact sports in 1 week.
  - A patient with a grade III concussion, if asymptomatic for 1 week, may return to contact sports in 1 month.

  - A second-time grade I concussion may return to play contact sports in 2 weeks after being asymptomatic for a week, and a second-time grade II may return to play contact sports 1 month after being asymptomatic for a week.
  - However, if the patient has **repeated concussions** after contact sports, grade I (×3), grade II (×2), grade III (×2), then it should be recommended that the **season is over.**
- **Mild concussion** is usually not associated with any sequelae. However, a **slightly greater injury** can be associated with both antegrade and retrograde amnesia (not able to remember events before or after the injury). The amount of time that the amnesia is present correlates with the severity of the injury. In some cases patients may develop the **postconcussion syndrome,** which includes memory difficulties, dizziness, and depression.
- **Epidural hematoma** is a rapidly accumulating hematoma between the dura and the cranium. These patients have a history of head trauma with loss of consciousness, then a lucid period, followed by loss of consciousness. Clinical onset occurs over minutes to hours. Many of these injuries are associated with laceration of the **middle meningeal artery.** A **lenticular extracerebral hemorrhage** will be noted on computed tomography (CT) of the head. The need for an operation should be determined by a neurosurgeon. Although death is a potential complication, the prognosis is good when this injury is recognized and treated.
- **Subdural hematoma** occurs when there is tearing of a bridging vein between the cerebral cortex and a draining venous sinus. At times they may be caused by arterial lacerations on the brain's surface. Patients may have a history of loss of consciousness but recover. Clinical onset occurs over hours. A **crescent-shaped hemorrhage** compressing the brain will be noted on CT of the head. **Surgical evacuation** is the treatment. Complications include uncal herniation, focal neurologic deficits, and death. The prognosis is guarded.
- **Cerebral contusion** is bruising of the brain parenchyma. The majority of contusions occur in the frontal and temporal lobes. **Multiple low-density areas** and **punctate hemorrhages** will be noted on the CT of the head. **Complications** may include cerebral edema and transtentorial herniation. The goal of treatment should be to treat the increased intracranial pressure. The prognosis is guarded.

Diagnostic Tests. A **CT of the head** should be performed on (*1*) children who have a history of loss of consciousness for >1 min, (*2*) children for whom the time of loss of consciousness is unknown, (*3*) children with abnormal neurologic findings, and (*4*) those who have a neurologic status that is deteriorating. **Cervical spine** films should be obtained on children with head trauma suspected of having an associated neck injury.

Treatment. Attention should be paid to airway, breathing, and circulation (ABCs). Bleeding should be controlled if present. Head injury may be associated with a neck injury; therefore, one should have a high suspicion for a cervical spine injury, especially if there are bruises on the back or neck, or if the patient has back pain or pain radiating to the arms. If a cervical spine injury is suspected, the patient should be immobilized and a cervical collar applied.

Complication/Follow-up. It is common for head trauma patients to have **drowsiness (but easily aroused), headaches,** and **vomiting** after the injury. This is of no concern if the neurologic examination is normal and consciousness is preserved. But if these symptoms persist >1 or 2 days, a CT of the head should be performed.

In some cases **transient neurologic disturbance** may occur, lasting minutes to hours and causing occipital blindness and a state of confusion. Malignant **posttraumatic cerebral swelling** can develop unexpectedly in stable patients after an injury, as can **posttraumatic seizures.** The child

with **worsening neurologic signs** (change in level of consciousness, respirations, blood pressure, pulse, seizures, etc.) must be suspected of having subarachnoid or subdural bleeding. **Recovery** in children **with neurologic deficits** will vary. Children with neurologic deficits who improve daily or within days of the injury are more likely to recover completely. Children who are vegetative for months are less likely to improve. Most patients **without neurologic deficits** have **full recovery.**

Table 8-1. Pediatric Glasgow Coma Scale

Action	Total Points	Point Breakdown	
Eye opening	**4**		
		Spontaneous	4
		To voice	3
		To pain	2
		None	1
Verbal response	**5**		
Older child			
		Oriented	5
		Confused	4
		Inappropriate	3
		Incomprehensible	2
		None	1
Infant			
		Smiles, fixes, follows	5
		Consolable cry	4
		Persistently irritable	3
		Restless/agitated	2
		None	1
Motor response	**6**		
		Obeys	6
		Localizes pain	5
		Withdraws	4
		Flexion	3
		Extension	2
		None	1
Highest possible total	**15***		

*If score is 8, intubate/resuscitate.

DROWNING

A 15-month-old was found with his head stuck in a bucket filled with cleaning agent. The mother says that she received a telephone call while mopping the floor. She was only speaking on the telephone for 5 min.

Definition. Drowning is defined as death within 24 h of submersion. **Near drowning** is defined as survival >24 h after submersion whether a person later survives or not. Submersion causes hypoxia, aspiration, and hypothermia. It is important to note that asphyxia may occur with or without pulmonary aspiration. Fluid may be aspirated into the lungs, or laryngospasm may prevent aspiration. Remember that pulmonary aspiration hastens hypoxemia and respiratory failure.

Risk Factors/Etiology. Drowning is the leading cause of accidental deaths in children >1 year old. It is estimated that there are approximately 8,000 deaths per year from drowning in the United States, and 40% of these deaths are in children **≤4 years of age.** Most infants and toddlers drown at home in pools, bathtubs, hot tubs, and buckets. **Adolescent boys**, because of their risk-taking behaviors and alcohol and drug use, are also at high risk for drowning. Therefore, boys have a greater risk than girls of drowning, and nonwhites have a greater chance than whites. Ninety-eight percent of drowning occurs in freshwater.

Presentation. The clinical presentation varies according to the circumstances surrounding the drowning or near drowning. Children with brief submersions may be awake and alert on arrival, yet others may have respiratory distress or cardiopulmonary arrest.

Physical Examination. Findings on physical examination will vary according to the presentation. Vital signs should be monitored. The Glasgow Coma Scale should be assessed. Patients who drown or have near drowning in **freshwater** may have more lung damage secondary to the hypotonic fluid washing out surfactant. Patients who drown or have near drowning in **saltwater** may be prone to more pulmonary edema.

Diagnostic Tests. Diagnostic studies should include a chest roentgenogram and an arterial blood gas or pulse oximetry.

Treatment. Patients who receive **cardiopulmonary resuscitation (CPR)** at the scene have a better outcome. There should not be an attempt to drain the lungs. The Heimlich maneuver or abdominal thrusts and back blows should only be administered if one is suspecting a foreign body. The **cervical spine** should be protected with a cervical collar if the patient has altered mental status or suspected traumatic injury. **Cricoid pressure** and **nasogastric** or **orogastric decompression** should be performed to decrease the risk of emesis and aspiration. **Electrocardiographic monitoring** should be done to diagnose and treat any arrhythmias (asystole, ventricular fibrillation or tachycardia, or bradycardia). **Hypothermia** should be treated as patients with severe hypothermia may look clinically dead but in rare cases have full recovery. Although patients who are exposed to saltwater may have hypernatremia, and patients exposed to freshwater may have hyponatremia, these electrolyte imbalances are rarely seen on arrival to the emergency center. Therefore, **isotonic fluid** is usually given to these patients to establish perfusion. Dextrose-containing solutions should be given to children who are hypoglycemic. **β_2-agonist therapy** may help children with bronchospasm. Prophylactic antibiotics are not recommended unless the child has been exposed to contaminated water. It is imperative to establish an airway and deliver oxygen to prevent further hypoxia.

Complications/Follow-up. Neurologic injury is the main cause of mortality and morbidity for drowning and near drowning victims. Adult respiratory distress syndrome (ARDS), pneumothorax, pneumomediastinum, and pulmonary edema are other complications that may occur in these victims. Rhabdomyolysis may be seen after cold saltwater drowning. The prognosis is better for patients who enter the intensive care unit awake and aroused rather than comatose.

BURNS

A 2-year-old comes to the emergency center after being splashed with hot coffee that fell off the table when he pulled the tablecloth. He has first- and second-degree burns.

Definition. Burns result from an act, process, instance, or result of burning that causes injury from fire, heat, electricity, caustics, or some types of radiation.

Risk Factors/Etiology. Burns are the second leading cause of death in children. Scald burns account for 85% of the burns in children <4 years of age. Child abuse should be suspected if the history does not match the burn pattern that would be expected on physical examination.

Presentation/Physical Examination. Burns can be divided into three types. **First-degree** burns involve only the epidermis. The skin is painful and erythematous. **Second-degree** burns involve both the epidermis and dermis. Painful blisters are usually associated with superficial second-degree burns. Deep second-degree burns may be white and painless and may require grafting. These burns may progress to a full-thickness burn with wound sepsis. **Third-degree** burns are full-thickness burns that involve the epidermis and all of the dermis, are painless, and require grafting.

Diagnostic Tests. Estimation of **body surface area (BSA)** of the burn should be performed. This can be done using **burn charts** for children of different ages (<14 years), or by using the **"rule of nines"** used in adults for those children >14 years. The **"rule of palm"** may be used for burns <10% of BSA, in which the child's palm equals 1% of the child's BSA.

Treatment. The Parkland formula should be used for fluid resuscitation for children (4 ml of Ringer's lactate/kg body weight/%BSA burned). One half the fluid should be given in the first 8 h calculated from the hour that the injury first occurred. The second half of the fluid should be given during the next 16 h. Do not apply cold water to a person with extensive burns. Pain medication should be administered in small, frequent doses by the intravenous route only. Prophylactic antibiotics are not indicated until a secondary infection declares itself.

Complications/Follow-up. The extent and severity of burn injury may change over the first several days of the injury.

Orthopedics

LIMPING

Legg-Calvé-Perthes

A 5-year-old boy has developed progressive limping. At first painless, it now hurts to run and walk. The pain is in the anterior thigh. The pain is relieved by rest. Parents recall no trauma.

Definition. Legg-Calvé-Perthes disease is an **avascular necrosis** of the femoral head. It should be considered in any limping child 4–12 years of age.

Risk Factors/Etiology. The cause of Legg-Calvé-Perthes is unknown. The femoral head has a tenuous vascular supply, which, when interrupted, can lead to necrosis. **Trauma, transient synovitis, venous congestion, hyperviscosity, and coagulation abnormalities** have all been implicated. **Boys** predominate 4–5:1. Twenty percent of cases are bilateral. Other associations include poverty, low birth weight, hernias, and undescended testes.

Presentation. Limping is the hallmark of Legg-Calvé-Perthes. At first it is painless, but it can proceed to pain that is worsened by activity and relieved by rest. Pain is reported in the groin, hip, thigh, or knee.

Diagnostic Tests. Radiographs show a wide articular space, then necrosis. Follow-up films during reconstitution reveal a flattened femoral head; later it becomes spherical.

Treatment. Legg-Calvé-Perthes is a self-healing process. The goal of therapy is to **maintain joint mobility**. This is done through the concept of **containment**—maintaining the hip in the acetabulum. This is accomplished by close observation, bracing with orthoses, or surgically with osteotomies.

Complications. Osteoarthritis is a complication of Legg-Calvé-Perthes.

Differential Diagnosis. Acute trauma is the most common cause of limping in children. Other causes of limping can be divided according to age. **Developmental dysplasia of the hip (DDH)** occurs in the newborn period but should be considered up to 3 years of age. Twenty percent of patients have a positive family history. Ligamentous laxity, maternal estrogens, breech position, and torticollis are associated with DDH. **Barlow, Ortolani, and Galeazzi** signs are all useful in diagnosing DDH. **Ultrasound** is the best test in newborns; later, frog lateral radiographs of the pelvis are useful in older infants and children. **Treatment** varies with extent of disease. Containment is the key and can be achieved by harnesses, casting, and osteotomies. DDH can lead to avascular necrosis of the femoral head. **Slipped capital femoral epiphysis (SCFE)** is seen in adolescents. This is a displacement of the femoral head from the femoral neck because of a stress

fracture through the femoral capital epiphyseal plate. Although its cause is unknown, an **endocrine basis** is suggested. Typically, patients are **obese** with delayed skeletal maturation or tall and thin with a recent growth spurt. **Chronic** SCFE is associated with **obesity, deficient gonadal development**, and **hypothyroidism**. Manifestations depend on the degree of slippage and its classification (preslip, acute, acute on chronic, chronic). Chronic SCFE is the most common type and presents with groin pain referred to anteromedial knee and thigh, limp, and accentuated external rotation. **Radiographs** show medial displacement of the epiphysis, a bare upper portion of the femoral neck, and a wide growth plate. **Treatment** consists of pinning, external fixation, bone grafts, and casting.

SCOLIOSIS

A 12-year-old girl is seen for routine physical exam. She voices no complaints. Exam is remarkable for asymmetry of the posterior chest wall on bending forward. One shoulder appears higher than the other when she stands up.

Definition. Scoliosis is an abnormal curvature of the spine caused by misalignment in the frontal plane.

Risk Factors/Etiology. The majority of cases of scoliosis are **idiopathic**. Congenital, neuromuscular, and compensatory scoliosis are less frequent. Although the male-to-female ratio is fairly equal, girls tend to have a higher risk of progression that requires treatment.

Presentation. Idiopathic scoliosis is usually painless and is diagnosed on routine physical exam. Asymmetry on standing, a prominent shoulder blade, and spinal curvature are seen. The curve progresses during periods of rapid growth.

Diagnostic Tests. Forward bending (**Adams test**) is the best way to screen for scoliosis. **Radiographs** of the spine are the gold standard for evaluating suspected scoliosis.

Treatment. Mild curves need no therapy. **Bracing** is recommended to slow down progression of curves. **Surgery** (fusion, fixation rods) is considered on curves greater than 45 degrees.

Exercise and electrical stimulation have no effect.

Complications. Complications of idiopathic scoliosis include degenerative joint disease, cardiorespiratory disease, and poor self-esteem.

Differential Diagnosis. Idiopathic scoliosis can be divided into three types—**infantile** (0–3 years), **juvenile** (4–10 years), and **adolescent** (>11 years). **Congenital scoliosis** is caused by vertebral anomalies such as a **hemivertebra**. It is associated with genitourinary anomalies (renal agenesis horseshoe kidneys, obstructive uropathy), congenital heart disease, and spinal dysraphism. **Early surgical treatment** is indicated because of the underlying pathophysiology (hemivertebra). Many **neuromuscular** disorders (e.g., cerebral palsy) course with scoliosis. **Syndromes** such as neurofibromatosis, Marfan, VACTERL, and Goldenhar (malar/maxillary hypoplasia, microtia, hemivertebrae) are also associated with scoliosis.

INTOEING

Talipes Equinovarus

A newborn is noted to have a foot that is stiff and slightly smaller than the other one. The affected foot is medially rotated and very stiff, with medial rotation of the heel.

Definition. Talipes equinovarus (clubfoot) is a deformity of the foot and lower leg.

Risk Factors/Etiology. Although the cause is **unknown**, clubfoot can be related to in utero displacement and malalignment. Inheritance plays a part, and there is probably a neuromuscular basis. Half of all cases are bilateral. **Associated disorders** include developmental hip dysplasia, amniotic bands, spina bifida, and arthrogryposis. Clubfoot is more common in boys.

Presentation. Isolated congenital clubfoot is the most common presentation. The foot is in medial rotation (in hindfoot equinus, adduction), is stiff, and is usually smaller than a normal foot.

Treatment. Treatment includes serial casting and surgery.

Differential Diagnosis. Other causes of intoeing include the following:

- Metatarsus adductus (metatarsus varus)—The forefoot is adducted, but the hindfoot is normal. The forefoot can be brought to the neutral position. Observation, passive range of motion, and casting may treat this condition.
- Tibial torsion—Tibial torsion is usually secondary to in utero positioning. Treatment is not necessary because this condition resolves on its own.
- Femoral anteversion—This is more common in children older than 2 years and is more frequent in girls. It is affected by sitting position. Treatment is usually an attempt to correct sitting position.

TUMORS

Tumors of bone are usually seen during periods of **rapid bone growth**; therefore, they are more common during **adolescence**. The two primary neoplasms of bone are **osteosarcoma**, the most common, and **Ewing** sarcoma. Ewing is more common in the second decade of life. **Retinoblastoma** has a higher association with osteosarcoma. Osteosarcoma can also be induced by exposure to **radiation**. Osteosarcoma is most common in the **long bones** at the metaphysis (e.g., distal femur, proximal humerus, proximal tibia). It usually presents with **pain at the tumor site**. Limitation of motion and a palpable, visible tumor are other findings. Deep bone pain awakening an adolescent at night should make one suspicious. Radiographs show a typical **"sunburst"** appearance. Ultimately, diagnosis is made by **biopsy**. **Lung** and bone are common sites of metastasis. Treatment is with **surgery and chemotherapy.** Up to 75% of patients with nonmetastatic osteosarcomas are cured. Pelvic tumors present a worse prognosis. **Ewing** sarcoma presents similarly to osteosarcoma. The radiographic presentation is that of **"onion skin"** periosteal elevation. **Metastasis** is also to the lung and bone. Definitive diagnosis is by **biopsy. Treatment** includes surgery, radiation, and chemotherapy. Prognosis is worse if the primary tumor is in the pelvis or with metastatic disease at the time of diagnosis.

OTHER

Pes planus (flat feet)—This occurs when there is no longitudinal arch of the foot. It is a variation of normal feet. It is usually seen in children older than 6 years of age, is usually asymptomatic, and requires no treatment. Occasionally pes planus is associated with heel cord contractures and cerebral palsy.

Popliteal cyst (Baker cyst)—This arises from the capsule or tendon sheaths. It appears as a painless **nonpulsatile swelling** on the posterior aspect of the knee. It becomes more prominent on knee extension. Treatment is usually not necessary because it resolves spontaneously. Excision is recommended for large, painful lesions. Differential diagnosis includes lipoma, aneurysm, neuroma, and rarely tumors.

Osgood Schlatter disease is a traction apophysitis of the **tibial tubercle** caused by overuse. It is more common in physically active **boys** around puberty. Patients present with **localized tenderness** and swelling over the tibial tubercle. The pain is exacerbated by running and jumping and is relieved by rest. Radiographs show soft tissue swelling over the tubercle. Nonsteroidal anti-inflammatory drugs usually do not help. Resolution occurs over 12–24 months.

Radial head subluxation (nursemaid's elbow) occurs after **sudden traction** on the arm, usually in children younger than 4 years. The child cries immediately and won't move the arm. The arm is held partially flexed at the elbow and supinated. Radiographs are not needed but are normal. Treatment consists of reduction by gentle supination with pressure over the radial head. A click may be heard.

Immunizations

10

A 6-month-old patient is being seen for routine care. The baby is doing well, and physical examination, growth, and development are normal. The mother states that after the last set of immunizations the baby had a temperature of 103°F and cried for 2 h but was consolable. What is your advice to this mother before administering the next set of immunizations?

Definitions

- A **vaccine** is a suspension of attenuated live or killed microorganisms administered to induce immunity.
- A **toxoid** is a modified bacterial toxin, now nontoxic, which stimulates formation of antitoxins.
- **Active immunity** results when an antibody is produced in response to a vaccine or toxoid.
- **Passive immunity** occurs when preformed antibodies are given, resulting in temporary immunity.
- **Herd immunity** results when enough persons are immunized to prevent transmission of disease to unimmunized persons.

Table 10-1. Classification of Vaccines

Live Attenuated		
	Viral	*MMR, varicella,* yellow fever
	Bacterial	BCG, oral typhoid
Inactivated		
Whole	Virus	*Polio,* rabies, hepatitis A
Fractional		
	Protein based	Subunit: *hepatitis B, influenza, acellular pertussis*
		Toxoid: *diphtheria, tetanus*
	Polysaccharide based	Pure: *pneumococcal, Hib, meningococcal*
		Conjugate: *Hib, pneumococcal*

COMPOSITION OF VACCINES

Table 10-2

Vaccine	Composition
DTaP (diphtheria, tetanus, acellular pertussis)	Inactivated DT toxins (toxoid), inactivated *Bordetella pertussis* cells
OPV*	Live attenuated poliovirus
IPV	Killed poliovirus
HiB (*Haemophilus influenza*)	Capsular polysaccharide polyribosylribitol + protein carrier
MMR (measles, mumps, rubella)	Live attenuated virus
HBV (hepatitis B vaccine)	Inactivated (recombinant)
Varicella	Live attenuated virus
Influenza	Both live attenuated and inactive vaccines are available
Pneumococcal	Capsular polysaccharide

*No longer licensed in the United States.

IMMUNIZATION RULES

Simultaneous Administration of Vaccines

- Inactivated vaccines may be given simultaneously at separate sites, except cholera, typhoid, and plague.
- Live virus vaccines given on different days should be administered 1 month apart.
- Pneumococcal polysaccharide and whole virus influenza can be given simultaneously, at different sites.

Hypersensitivity

Avoid it.

- **Egg** hypersensitivity can occur with influenza and yellow fever vaccines.
- **Neomycin** is contained in IPV, measles, mumps, rubella, and MMR.
- **Streptomycin** is contained in IPV and MMR.
- Vaccines are now **thimerosal free**.

Contraindications and Precautions

Contradictions to Vaccines

Permanent:

- Severe allergy to a prior dose of vaccine or to a component
- Encephalopathy following pertussis vaccine

Temporary:

- Pregnancy and immunosuppression—vaccine deferral as indicated

Misconceptions

The following are *not* contraindications to immunizations:

- A reaction to a previous DPT of temperature <105°F, redness, soreness, and swelling.
- A mild, acute illness in an otherwise well child.
- Concurrent antimicrobial therapy.
- Prematurity—immunize at the chronological age.
- A family history of seizures.
- A family history of sudden infant death syndrome.

Table 10-3. Immunizations in Special Circumstances

Immunocompromised	*No live virus vaccine* But poor response to inactivated
Preterm infants	Immunize at chronologic age Do *not* reduce dosage
Hepatitis B in <2 kg	Start series if hospitalized at 2 months HBsAg– mother: at DC if 2 kg or at 1–2 mo HBsAg+ mother: birth dose and HBIG, but get 4 doses

DELAYED IMMUNIZATIONS

Give as many immunizations as possible. You do not have to start all over again for any missed immunizations.

General Rules for Catch-Up Vaccines

- For lapsed vaccines, resume schedule as if usual interval has elapsed; do not repeat doses.
- HiB and PCV7 are not needed again if immunocompetent child is ≥5 years old.
- Second-dose HiB indicated only if first dose is given >15 months of age.
- Second-dose PCV7 only if child <2 years.
- If unsure and no proof of immunizations, assume none and vaccine from beginning.

Recommended Scheduling of Immunizations

Please refer to Table 10-4.

It is required that for school the student must have four doses of DPT (the fourth dose must be after 4 years old), three doses of poliovirus, and two doses of MMR (35 states).

Table 10-4. Immunization Recommendations for HIV Infection

Vaccine	Mild/Moderate Immunosuppression, Known Asymptomatic	Severe Immunosuppression, Known Symptomatic
DtaP	Yes	Yes
OPV	No	No
IPV	Yes	Yes
MMR	Yes	No
HiB	Yes	Yes
Pneumococcal	Yes	Yes
Influenza	Yes	Yes
HBV	Yes	Yes
Varicella	Consider	Consider

INDIVIDUAL IMMUNIZATIONS

DtaP

Common reactions to the DTaP vaccine include fever up to 105°F in the first 24 h, redness, or swelling and soreness at the injection site. **Less common reactions** include inconsolable crying for >3 h, temperature >105°F, and a high-pitched cry. Rarely, seizures occur, probably from the fever. There is no evidence to date that the pertussis vaccine causes brain damage. DTaP is **contraindicated** if there was a serious CNS problem within 7 days of receiving the vaccine, if there was an anaphylactic reaction, or if there is an unstable encephalopathy. In those cases, **DT should be substituted. Acetaminophen** helps reduce the discomfort of the side effects. In patients with prior history of pertussis, the pertussis component may be left out of subsequent vaccines.

Polio

It is now recommended that only the killed polio vaccine (IPV, Salk) be administered. Contraindications to the IPV include anaphylaxis to neomycin or streptomycin.

MMR and Separate Vaccines

Common side effects of the MMR include a sore arm for 1–2 days. **Most effects, however, occur 1–2 weeks after immunization.** These include signs or symptoms of the components of the vaccine. Measles can cause a rash, fever, or upper respiratory infection symptoms. Mumps can cause slight salivary gland swelling. Rubella may present with cervical lymph adenopathies

and arthralgia. The MMR vaccine can present with all of the above. **All the vaccines can cause febrile seizures and a reversible encephalopathy. The MMR should be delayed** for pregnancy or possibility of pregnancy in the patient, for anything more than a minor illness, and if the patient has received gammaglobulin in the past 3 months. **Contraindications** include anaphylaxis to any of its components or immunodeficiency such as cancer, leukemia, severe HIV immunosuppression, radiation therapy, chemotherapy, and steroids. **There is no proof that MMR vaccination causes autism.**

HiB

Side effects of HiB include local swelling and low-grade fever. **Invasive HiB disease** under 2 years of age does not confer immunity, and therefore the patient still requires immunization. One dose of HiB given after 15 months of age confers immunity, and there is no need to give the entire series.

Pneumoccoccus

Pneumococcal vaccine is now recommended for all children beginning at 2 months of age. The current vaccine in use is a heptavalent conjugated vaccine. In addition, all children >2 years of age with sickle cell anemia, functional or anatomic asplenia, and immunosuppression should receive pneumococcal vaccine (23 valent).

Hepatitis B Vaccine

This is now universally recommended. Patients born to hepatitis B surface antigen-negative mothers receive vaccine in the usual time schedule. Patients born to hepatitis B surface antigen-positive mothers also require hepatitis B immune globulin along with the first dose of vaccine.

Hepatitis B

Perinatal Transmission

If mother is HBsAg+ and HbeAg:

- 70–90% infants infected
- 90% infected become carriers

If mother only HBsAg+:

- 20% infants infected
- 90% infants become carriers

Prevention of Perinatal HBV Infection

- Begin prevention within 12 h of birth
- HBV and HBIG at different sites
- 85–95% successful

Adolescent HBV Alternative

- Two-dose adolescent schedule (11–15 years) separated by 4–6 months

Meningococcal Vaccine

- Does not cover all serogroups; active immunization against serotypes A, C, Y, and W-135; *not* protective for those <2 years of age.
- Indications for vaccination include:
  - Travelers
  - College freshmen (although not routine)
  - Military
  - Asplenia (anatomic or functional)

Varicella Vaccine

Live attenuated vaccine scheduled for all children 12–18 months of age and all children without a history of varicella. Patients aged 12 months to 12 years have a 95% seroconversion rate. Children younger than 12 years of age receiving the vaccine require two doses at least 4 to 8 weeks apart for effective seroconversion.

The vaccine is 100% protective against severe disease; however, breakthrough infections can occur that may result in mild disease. Mild varicella <50 lesions may still be contagious.

Postexposure prophylaxis with VZIG

- Newborn and mother—5 days prior to delivery to 2 days after
- Susceptible pregnant women
- Immune deficiency
- Hospitalized preterm infant born at <28 weeks or weighs <1,000 grams

Contraindications

- Moderate to severe acute illness
- Malignancy or T-cell defect, including HIV infected with CD4 counts <25%
- High-dose steroid treatment
- Pregnancy
- Component allergy

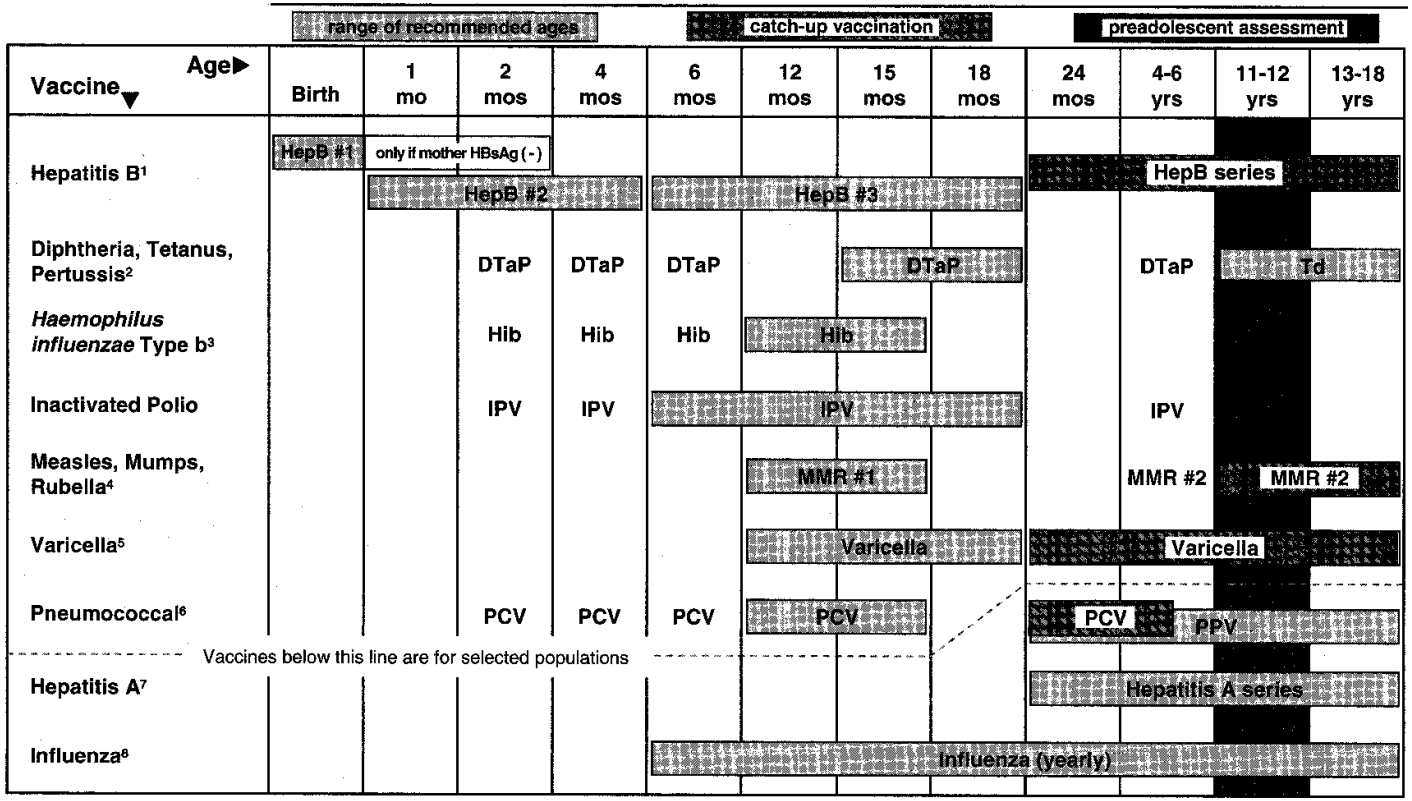
Influenza Vaccine

Inactivated vaccine produced in embryonated eggs. Duration of immunity is <1 year; thus, schedule 1 dose annually. Avoid the flu shot in patients with egg anaphylaxis; consider live attenuated intranasal influenza vaccine.

Recommendations

- All persons >50 years
- Infants 6–23 months
- Persons >6 months with chronic illness
- Pregnant women—at least 14 weeks
- Those 6 months to 18 years receiving salicylates
- Split dose <9 years old

Recommended Childhood and Adolescent Immunization Schedule -- United States, 2004



For Children and Adolescents Who Start Late or Who Are >1 Month Behind

The tables below give catch-up schedules and minimum intervals between doses for children who have delayed immunizations. There is no need to restart a vaccine series regardless of the time that has elapsed between doses. Use the chart appropriate for the childís age.

Catch-up schedule for children age 4 months through 6 years

Dose 1 (Minimum Age)	Minimum Interval Between Doses			
	Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
DTaP (6 wk)	**4 wk**	**4 wk**	**6 mo**	**6 mo**[1]
IPV (6 wk)	**4 wk**	**4 wk**	**4 wk**[2]	
HepB[3] (birth)	**4 wk**	**8 wk** (and 16 wk after first dose)		
MMR (12 mo)	**4 wk**[4]			
Varicella (12 mo)				
Hib[5] (6 wk)	**4 wk:** if first dose given at age <12 mo **8 wk (as final dose):** if first dose given at age 12-14 mo **No further doses needed:** if first dose given at age ≥15 mo	**4 wk**[6]**:** if current age <12 mo **8 wk (as final dose)**[6]**:** if current age ≥12 mo and second dose given at age <15 mo **No further doses needed:** if previous dose given at age ≥15 mo	**8 wk (as final dose):** this dose only necessary for children age 12 mon5 y who received 3 doses before age 12 mo	
PCV[7]**:** (6 wk)	**4 wk:** if first dose given at age <12 mo and current age <24 mo **8 wk (as final dose):** if first dose given at age ≥12 mo or current age 24-59 mo **No further doses needed:** for healthy children if first dose given at age ≥24 mo	**4 wk:** if current age <12 mo **8 wk (as final dose):** if current age ≥12 mo **No further doses needed:** for healthy children if previous dose given at age ≥24 mo	**8 wk (as final dose):** this dose only necessary for children age 12 mon5 y who received 3 doses before age 12 mo	

Catch-up schedule for children age 7 through 18 years

Minimum Interval Between Doses		
Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Booster Dose
Td: 4 wk	**Td:** 6 mo	**Td**[8]**:** **6 mo:** if first dose given at age <12 mo and current age <11 y **5 y:** if first dose given at age ≥12 mo and third dose given at age <7 y and current age ≥11 y **10 y:** if third dose given at age ≥7 y
IPV[9]**:** 4 wk	**IPV**[9] 4 wk	**IPV**[2,9]
HepB: 4 wk	**HepB: 8 wk** (and 16 wk after first dose)	
MMR: 4 wk		
Varicella[10]**:** 4 wk		

1. **DTaP:** The fifth dose is not necessary if the fourth dose was given after the fourth birthday.
2. **IPV:** For children who received an all-IPV or all-oral poliovirus (OPV) series, a fourth dose is not necessary if third dose was given at age ≥4 years. If both OPV and IPV were given as part of a series, a total of 4 doses should be given, regardless of the childís current age.
3. **HepB:** All children and adolescents who have not been immunized against hepatitis B should begin the HepB immunization series during any visit. Providers should make special efforts to immunize children who were born in, or whose parents were born in, areas of the world where hepatitis B virus infection is moderately or highly endemic.
4. **MMR:** The second dose of MMR is recommended routinely at age 4 to 6 years but may be given earlier if desired.
5. **Hib:** Vaccine is not generally recommended for children age ≥5 years.
6. **Hib:** If current age <12 months and the first 2 doses were PRP-OMP (PedvaxHIB or ComVax [Merck]), the third (and final) dose should be given at age 12 to 15 months and at least 8 weeks after the second dose.
7. **PCV:** Vaccine is not generally recommended for children age ≥5 years.
8. **Td:** For children age 7 to 10 years, the interval between the third and booster dose is determined by the age when the first dose was given. For adolescents age 11 to 18 years, the interval is determined by the age when the third dose was given.
9. **IPV:** Vaccine is not generally recommended for persons age ≥18 years.
10. **Varicella:** Give 2-dose series to all susceptible adolescents age ≥13 years.

Reporting Adverse Reactions
Report adverse reactions to vaccines through the federal Vaccine Adverse Event Reporting System. For information on reporting reactions following immunization, please visit www.vaers.org or call the 24-hour national toll-free information line (800) 822-7967.

Disease Reporting
Report suspected cases of vaccine-preventable diseases to your state or local health department.

For additional information about vaccines, including precautions and contraindications for immunization and vaccine shortages, please visit the National Immunization Program Web site at www.cdc.gov/nip or call the National Immunization Information Hotline at 800-232-2522 (English) or 800-232-0233 (Spanish).

Infectious Diseases

11

FEVER/OCCULT BACTEREMIA IN CHILDREN <3 YEARS

A 5-month-old infant presents with fever. The temperature is 39°C, and the mother states that the patient is less active and has a decreased appetite. On physical examination no focus of infection can be found.

Definition. Fever is defined as temperature >38°C (100.4°F) rectally. There are different categories of fever: (*1*) fever of short duration with localizing signs, (*2*) **fever without a focus,** lasting <1 week duration, in children <36 months old, and (*3*) fever of unknown origin defined as lasting >14 days in a child, and lasting >21 days in an adolescent or adult. In this section we will discuss **fever without a focus,** which occurs in about 5% of children <36 months old.

Bacteremia is defined as having bacteria in the blood. Occult bacteremia (bacteremia without an obvious focus of infection) is usually secondary to *S. pneumoniae, N. meningitidis, H. influenzae* B, and *Salmonella.*

Risk Factors/Etiology. Children at **high risk** for serious bacterial infection (e.g., meningitis, sepsis, urinary tract infections, septic arthritis) are those children **<24 months of age.** Some organisms responsible for fever without a focus include group B streptococci, *Listeria monocytogenes,* and *Escherichia coli.* These patients may also be exposed to *Salmonella, Neisseria meningitides, Streptococcus pneumoniae, Haemophilus influenzae* B, and *Staphylococcus aureus.* Viral pathogens may also be identified.

A temperature greater than or equal to **38°C (100.4°F)** in patients **<3 months** of age is significant, and the physician should consider the possibility of meningitis, urinary tract infection, or pneumonia and work up accordingly. Children **older than 3 to 36 months** of age with temperature **>38.9°C (102°F)** are also at risk for serious bacterial infections when there is no focus for the fever. Patients with history of chronic disorder such as sickle cell disease, congenital heart disease, or immunodeficient disorders, e.g., AIDS, agammaglobulinemia, or malignancy, are at increased risk for serious bacterial disease.

Table 11-1. Children at High Risk for Occult Bacteremia

Age of child	Increased risk if younger then 24 months
Fever	Temperature >38.9°C (102°F). Increased risk if >40°C (104°C)
History of chronic disorder	Sickle cell disease, immunodefient disorders ie. AIDS, or malnourishment.
Contact history	Children in day care centers may carry highly infectious organisms ie., *N. Meningitis* and *H. Influenza*
Signs and symptoms	Child may be ill appearing, irritable, or lethargic, with loss of appetite. May have petichae.

Presentation. There are usually no abnormal signs indicating fever, and presentation varies from patient to patient. Some nonspecific findings in infants and young children might be decreased activity, poor feeds, and increased fussiness. Children with occult bacteremia look relatively well.

Physical Examination. Although fever is present, there is no focus of fever that can be found on physical examination. In occult bacteremia, there are no localizing signs of infection.

Diagnostic Tests. After careful history and physical examination of children without an identified source of fever, a high index of suspicion for bacteremia, meningitis, and other serious illness should be formed. Children with white blood cell (WBC) counts >15,000 are at higher risk. Blood cultures are positive more frequently if the temperature is >40°C (104°F).

Treatment. All infants **<1 month** of age should be **admitted** to the hospital to receive **prophylactic antibiotics** for group B streptococci, *L. monocytogenes,* and *E. coli.* Infants >1 month who appear well and have been in good health are unlikely to have serious bacterial illness if they have a total WBC count between 5,000 and 15,000 cells/μL (absolute band count <1,500 cells/μL) and normal urinalysis.

Ceftriaxone may be given to the patient who **appears well,** but has no source for fever and has a **WBC count >15,000.**

If the patient is **ill-appearing,** then they should be **admitted to the hospital,** and **empiric antibiotics** should be started after appropriate cultures are obtained. Ceftriaxone (children >2 months) or cefotaxime and ampicillin (for *L. monocytogenes* and enterococci) in children <2 months are effective for initial therapy for patients without a source of fever. If meningitis with *S. pneumoniae* is a possibility, then vancomycin should be added to the regimen.

Complications/Follow-up. A physician should follow up with patients who are discharged home (while awaiting cultures) in 24 h.

Differential Diagnosis. Before diagnosing fever without a source, diagnoses that should be **considered** are meningitis, septicemia, urinary tract infection, otitis media, and pneumonia.

Management of previously healthy <3-mo-old with fever without a source

Nontoxic, 28- to 90-day old, and low risk with rectal temperature >38.0°C (100.4°F)

Table 11-2. Low-Risk Criteria

Clinical	Previously healthy Nontoxic No focal bacterial infection on exam (other than OM)
Lab results	WBC 5–15,000/mm^3 <1,500 bands If respiratory symptoms, normal chest x-rays If diarrhea, <5 WBCs/hpf Normal urine analysis (<5 WBCs/hpf)

Outpatient Management

Option 1: BC, UC, LP, ceftriaxone, return in 24 hours

Option 2: BC, UC, careful observation

Follow-up

- All cultures negative, afebrile, well: *careful observation*
- BC negative, well, febrile: *careful observation, second dose of ceftriaxone (?)*
- BC positive: *admit*
- UC positive, persistent fever: *admit*

Management of previously healthy 91-day-old to 36-month-old child with fever without a source

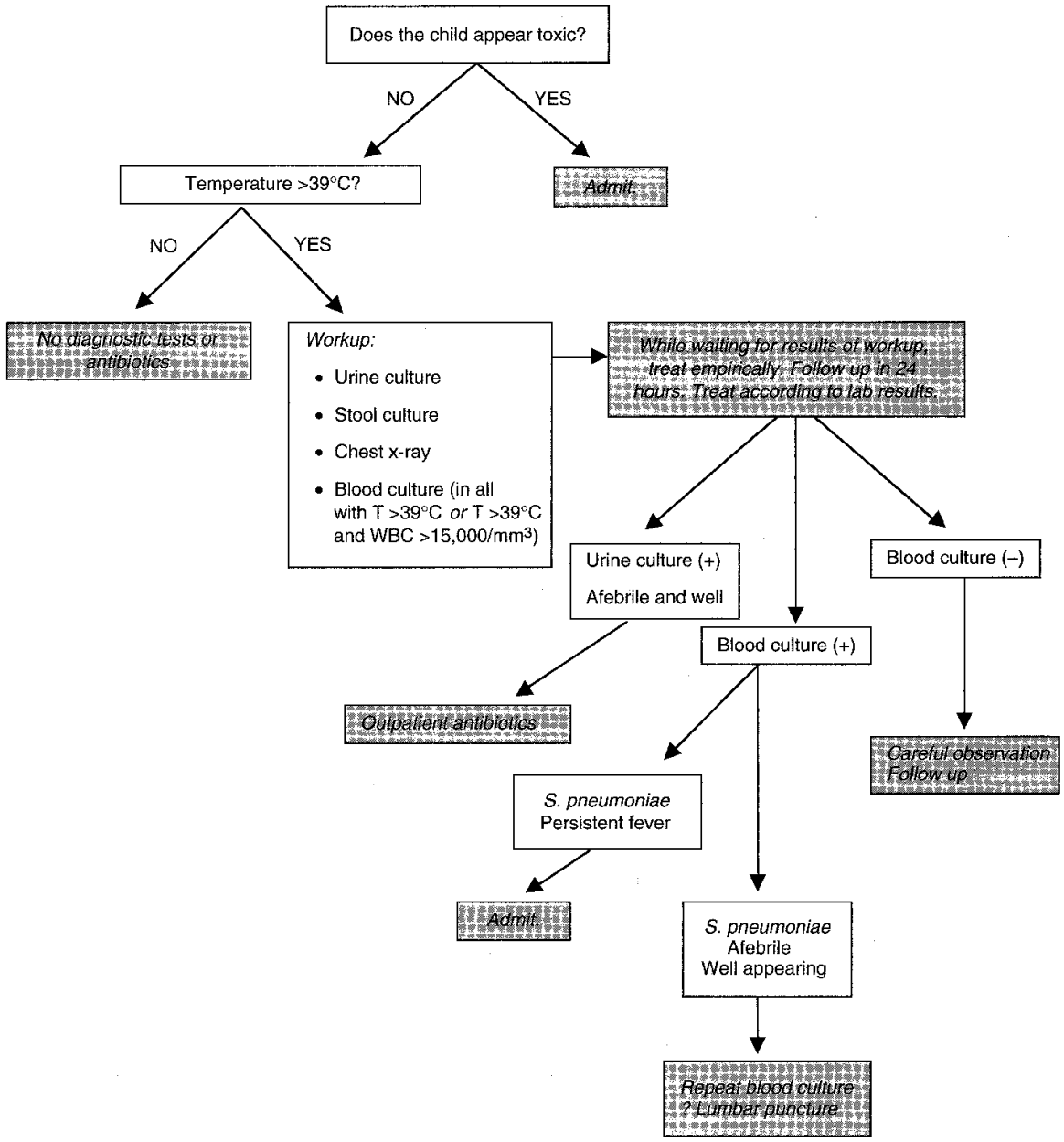


Figure 11-1

MENINGITIS

A 6-year-old presents to the physician with the chief complaint of headache, vomiting, neck stiffness, and photophobia. Physical examination reveals an ill-appearing child unable to flex his neck without eliciting pain. Kernig and Brudzincki signs are positive.

Definition. Meningitis is caused by inflammation of the leptomeninges.

Risk Factors/Etiology. Bacterial meningitis usually occurs from hematogenous dissemination of microorganisms from another site of infection. Some risk factors include lack of immunity, occult bacteremia, splenic dysfunction, meningomyelocele, attending day care, male sex, black race, and poverty.

The agents are usually group B streptococci, *L. monocytogenes,* and *E. coli* in patients <3 months old; and *N. meningitides, S. pneumoniae,* and *H. influenzae* B in the child >3 months old. Patients with sickle cell disease and CSF leaks are prone to pneumococcal infections. Patients with CSF shunt infections may have *Staphylococcus epidermidis* infections.

Presentation. The presentation depends on the age. Infants may have history of irritability, restlessness, and poor feeding. Older children may present with fever, headache, neck pain, photophobia, and vomiting. Rarely a patient may present with shock, purpura, and disseminated intravascular coagulation (DIC).

Physical Examination. A bulging fontanelle may be seen in infants. Older children may have neck pain with flexion. Both **Brudzinski** sign (involuntary flexion of the knees and supine hips after flexion of the neck while supine) and **Kernig** sign (flexion of the hip 90° with subsequent pain on extension of the leg) may be elicited in older children.

Diagnostic Tests. The diagnosis depends on examination of CSF obtained by lumbar puncture. Latex particle agglutination tests are helpful for diagnosis if the patient has received antibiotics previously.

Table 11-3. CSF Findings in Various Types of Meningitis

	Pyogenic	Partially Treated	Granulomatous	Aseptic	Neighborhood Reaction*
Cells/mL	200–5,000	200–5,000	100–500	100–700	100–500
Cytology	PMN	Mostly PMN	L	PMN → L	Variable
Glucose†	Low	Low	Low	Normal	Normal
Protein	High	High	High	Slightly high	Variable
Gram stain	Positive	?Positive	Negative	Negative	Negative
Culture	Positive	?Negative	Positive	Negative	Negative
CIE or LA	Positive	Positive	Negative	Negative	Variable
Lactic acid	High	High	High	Normal	Normal
Pressure	High	High	High	Normal	Variable

Definition of Abbreviations: CIE = counterimmunoelectrophoresis; L = lymphocyte; LA = latex agglutination; PMN = polymorphonuclear neutrophil.

*Neighborhood reaction refers to a localized focus of infection near the subarachnoid space that may spill some products of inflammation into the CSF. Such a site could be a brain abscess, an epidural abscess, sinusitis, or mastoiditis.

†CSF glucose concentration should be considered in relation to blood glucose concentration; normally CSF glucose is 50–70% of blood glucose.

Treatment. Antibiotic therapy is the same as for the suspected microorganisms of sepsis. Data suggest that the administration of **corticosteroids** (intravenous dexamethasone) given to children >6 weeks of age with acute bacterial meningitis may reduce the incidence of hearing problems, decrease fever, and lower CSF protein and lactate levels. However, experience with dexamethasone has been positive with *H. influenzae*, but not with other bacterial pathogens. If there is a **delay** in obtaining the lumbar puncture, then the administration of **antibiotics** should be given before obtaining CSF. **Supportive care** should also be given.

Aseptic meningitis usually occurs in the summer and fall. The origin is usually **viral.** If the cause of aseptic meningitis is **not viral,** then **partially treated meningitis** should be considered. The clinical presentation is similar to bacterial meningitis. A lumbar puncture is performed, and analysis of the CSF is made. **Treatment** for aseptic meningitis is **supportive, except** for **herpes virus** in which case **acyclovir** should be prescribed.

Complications. Neurologic complications are common and may include seizures, hearing loss, mental retardation, language impairment, and behavioral problems. Other problems include ataxia, palsies, stroke, cerebral or cerebellar herniation, and subdural effusions. Syndrome of inappropriate antidiuretic hormone, thrombocytosis, and anemia may also be present.

Differential Diagnosis. Toxins, malignancy, and collagen vascular disease can cause generalized inflammation of the CNS.

Prevention. Rifampin should be given for family contacts of patients with *H. influenzae* and *N. meningitides*. Vaccines may be given to prevent *H. influenzae*, *S. pneumoniae*, and *N. meningitides*.

ARBOVIRAL ENCEPHALITIS

A 10-year-old presents with fever and altered mental status. The parents state that over the past 24 h the patient has been extremely combative. There is no evidence of trauma or drug ingestion.

Definition. Arboviral encephalitis is an acute inflammation of parenchyma of the brain caused by different arthropod-borne viruses.

Risk Factors/Etiology. The main causes of arboviral encephalitis are **St. Louis encephalitis (SLE),** which is spread by birds; **California encephalitis (CE),** carried by rodents and spread by mosquitoes; **Western equine encephalitis (WEE),** carried by mosquitoes and birds; **Eastern equine encephalitis,** spread by mosquitoes and birds; and **Colorado tick fever,** transmitted by the wood tick *Dermacentor andersoni.*

Presentation/Physical Examination. The clinical presentation is similar to aseptic meningitis, but the patient has more abnormalities of mental function noted, e.g., confusion, delirium, hallucinations, and combative ataxia.

Diagnostic Tests. The history is extremely important, i.e., exposure to persons or animals that may be a source of infection. Testing of acute phase serum using an indirect immunofluorescence test or an enzyme-linked immunosorbent assay (ELISA) IgM-capture makes the diagnosis. Brain tissue obtained by biopsy or at autopsy also establishes the diagnosis. The CSF is normal or similar to aseptic meningitis. Electroencephalography, computed tomography, and magnetic resonance imaging (MRI) may aid in the diagnosis of encephalitis.

Treatment. Patients need supportive care, including seizure control.

Complications. Eastern equine encephalitis produces death in one third of the patients acquiring this disease.

Differential Diagnosis. Differential diagnoses include encephalopathy from toxins, hypoglycemia, Reye syndrome, and inborn errors of metabolism. Postinfectious encephalitis may occur from mumps, measles, and varicella. Rare causes of encephalitis are trypanosimiasis and malaria.

Prognosis. The prognosis is good for St. Louis, California, Western, and Colorado tick fever encephalitis. The Eastern equine encephalitis has an abrupt course, and patients can develop coma, seizures, and death.

OSTEOMYELITIS

A 12-month-old infant presents to the physician with the chief complaint of refusing to bear weight on his left lower extremity. The mother states that the child had an ear infection 1 week ago. The patient was prescribed antibiotics, but the mother states she did not fill the prescription.

Definition. Osteomyelitis is an infection of bone. Osteomyelitis may occur by (*1*) acute hematogenous spread (most common in children), (*2*) contiguous spread (from soft tissue infection), or (*3*) direct inoculation from penetrating wounds.

Risk Factors/Etiology. Osteomyelitis is usually seen in children 3–12 years of age. It is found more commonly in boys at a 2:1 ratio. *S. aureus* is the most common organism. Group B streptococci and gram-negative enteric bacilli are also important pathogens in the neonate. Patients with sickle cell disease are predisposed to both *S. aureus* and *Salmonella*. Osteomyelitis caused by *Pasteurella multicida* may be seen after dog or cat bites. *Pseudomonas aeruginosa* infections may be associated with puncture wounds of the foot through a sneaker.

Presentation. Infants usually do not appear ill and may only have pain on movement of the affected area. Older children usually have an acute onset of fever and localized signs. The patient may refuse to bear weight on the infected extremity, and may have decreased range of motion.

Physical Examination. The patient may have pain, tenderness, warmth, and swelling at the site. The patient may limp if the hip is involved.

Diagnostic Tests. The history and physical examination aids in the diagnosis. The WBC count and erythrocyte sedimentation rate (ESR) may be normal during the first days of infection. Blood cultures are positive 60% of the time. A **periosteal bone culture** should be performed to confirm the diagnosis. Radiographs turn positive after 10–14 days, showing soft tissue swelling and periosteal elevation. If radiographs are negative, but there is still a suspicion, then an MRI should be performed as the next step.

Treatment. Therapy is based on laboratory results. One should always cover for *Staphylococcus*. ESR and CRP are the best ways to determine response to therapy. The patient should be treated for 4–6 weeks. The patient is treated in the hospital with IV antibiotics for approximately 3 weeks and than switched to oral antibiotic for the rest of the course. Chronic osteomyelitis needs surgical intervention and a few months of antibiotics.

SEPTIC ARTHRITIS

A 5-year-old presents with a fever, knee pain, and a limp. On physical examination the knee is red, warm, and swollen. Full range of motion of the knee is not possible on physical examination.

Definition. Septic arthritis is an infection of a joint space.

Risk Factors/Etiology. In newborns *S. aureus*, group B streptococci, and gram-negative bacilli are important agents of septic arthritis. In children up to 5 years of age, the pathogens may be *S. aureus*, streptococci, *H. influenzae* (in children not immunized with *H. influenzae* vaccine). Patients >5 years usually are infected with gram-positive **cocci.** As with osteomyelitis, septic arthritis may be spread by acute hematogenous, contiguous, or direct inoculation, or from osteomyelitis.

Presentation. There is usually an acute onset of fever. The patient may refuse to bear weight on the infected extremity, and may have decreased range of motion.

Physical Examination. Pain, tenderness, warmth, and swelling may be elicited at the site. The patient may limp if the hip is involved. Remember that **hip pathology refers pain to the knee.**

Diagnostic Tests. The WBC and ESR are elevated. The **arthrocentesis** is the test of choice for quick diagnosis. Soft tissue swelling and widening of the joint space may be found on roentgenogram. Sonography is very useful for septic arthritis of the hip.

Treatment. The treatment is similar to osteomyelitis. Treatment is for 10–21 days depending on the organism, and whether the ESR rate has returned to normal and symptoms resolve. Immunocompromised patients require prolonged courses of therapy.

Differential Diagnosis. Cellulitis, rheumatic fever, juvenile rheumatoid arthritis, toxic synovitis, and leukemia should be considered in the differential diagnosis for these patients.

TUBERCULOSIS (TB)

A 10-year-old child is referred from the school nurse because of a positive tuberculin skin test. The patient has been well, without any associated complaints.

Definition. TB is caused by *Mycobacterium tuberculosis.*

Risk Factors/Etiology. The elderly, immigrants, and patients with AIDS are reservoirs for TB. It is more common in crowded societies, and in those with lower socioeconomic status. TB infection occurs after the inhalation of infective droplet nuclei containing *M. tuberculosis.* Congenital TB (transmission via a lesion in the placenta, or aspiration of infected amniotic fluid) is rare, and most neonates are infected by airborne transmission from an adult with infectious pulmonary TB.

Presentation/Physical Examination. A healthy host usually walls off the organism. Primary pulmonary TB is usually asymptomatic in children. Patients who are symptomatic usually complain of malaise and low-grade fever. Children with progressive pulmonary TB have bronchopneumonia. Patients with progressive pulmonary TB have fever, weight loss, night sweats, and hemoptysis. Patients with upper respiratory tract TB have involvement of the larynx and

middle ear. These patients may have a croupy cough and sore throat. They may also have hearing loss. Infection of the CNS with TB may cause meningitis that may be fatal. Bone and joint TB may lead to Pott disease (destruction of vertebral bodies leading to kyphosis).

Diagnostic Tests

- The Mantoux tuberculin skin test should be used to make the diagnosis. A reaction of **≥5 mm** of induration is a **positive** result for patients who have been **exposed to TB**, have **illnesses consistent with TB,** or are **immunocompromised.** For other **high-risk** groups (e.g., homeless, health-care workers, children exposed to high-risk adults), a reaction of **≥10 mm** of induration is positive. For **low-risk** persons **≥15 mm** may be considered a positive reaction. Previous vaccination with **Bacilli Calmette-Guerin (BCG)** may cause a **false-positive** reaction. However, prior vaccination with BCG is never a contraindication to tuberculin skin test. Patients who are **immunocompromised, malnourished,** or received **live-virus vaccines** may have a **false-negative** reaction.
- A **roentgenogram** should be done to look for pulmonary involvement. Older children and adolescents may have an upper lobe infiltrate.
- Early morning **gastric aspirates** should be obtained in an attempt to isolate *M. tuberculosis* from the pooled secretions that the child swallowed overnight.
- If TB meningitis is suspected, then a **lumbar puncture** should be performed.

Treatment. The basic management of TB in children is the same as for adults. Several drugs must be used because of the high incidence of resistant strains, except in cases of asymptomatic skin test conversion. The most **commonly used antituberculosis drugs** include isoniazid (INH), rifampin, pyrazinamide, streptomycin, ethambutol, and ethionamide.

Table 11-4. Side Effects of TB Drugs

Drug	Side Effect
INH	Hepatotoxicity Neuritis
Rifampin	Hepatotoxicity Thrombocytopenia
Pyrazinamide	Hepatotoxicity
Streptomycin	Ototoxicity Nephrotoxicity
Ethambutol	Ocular toxicity
Ethionamide	Hepatitis

Children and adolescents with **asymptomatic skin test conversion** or those who have received **BCG and test positive on PPD** should be treated with 9 months of **INH** prophylaxis.

If the **mother has suspected TB at delivery,** then the infant should be separated from the mother until a chest radiograph is taken. If the chest radiograph is positive, then the infant should remain separated from the mother until the mother's sputum is acid-fast tested. If the mother shows evidence of active disease, then the mother should begin anti-TB therapy and the infant placed on INH. Separation from the mother in this instance is no longer required. Separation from the mother is only necessary if she is hospitalized for the illness, or she has suspected drug-resistant TB.

Complications. The incidence of drug-resistant TB has increased.

Progression of the disease is more common in the first year after infection and in children <5 years old. Reactivation is more common in adolescents, especially in the apical segments of the upper lobes and superior segments and lower lobes. Patients with reactivation have fever, night sweats, etc. Miliary TB has a hematogenous spread. TB meningitis may be seen within 6 months of primary infection. Pott disease TB of the bone (spine) causes kyphosis.

Prevention. To prevent TB, one must identify carriers of the disease and treat them. BCG vaccination may help to control TB for selected populations (e.g., children with prolonged exposure to untreated adults, and children with continuous exposure to people with drug-resistant TB).

PERTUSSIS

A 10-month-old child who is delayed in immunizations presents with a paroxysmal cough. The patient appears ill and continuously coughs throughout the examination. The patient has facial petechiae, and conjunctival hemorrhages. In addition the patient has posttussive emesis.

Definition. Pertussis is an acute respiratory infection caused by the agent *Bordetella pertussis*. This is sometimes referred to as whooping cough because patients with this illness may have a forceful inspiratory gasp **(whoop)** after a paroxysmal cough. The whoop does not usually occur in a patient <3 months of age or in those who are tired from coughing or lack muscle strength to form sudden negative intrathoracic pressure.

Risk Factors/Etiology. The incubation period is 3–12 days. Children at highest risk for the disease are <5 years of age. Neither natural disease nor vaccination prevents recurrence of the disease.

Presentation. Infants may present with apnea, cyanosis, and cough. Older children experience three stages of the disease: **stage 1,** the **catarrhal stage,** lasting 1–2 weeks and consisting of rhinorhea, conjunctival injection, and cough; **stage 2,** the **paroxysmal stage,** lasting 2–4 weeks and consisting of coughing spasms, inspiratory whoop, and facial petechiae; and **stage 3,** the **convalescent stage,** lasting 1–2 weeks and consisting of decreased frequency of symptoms.

Physical Examination. Patients may have conjunctival hemorrhages or petechiae on the upper part of their body. Evidence of lower respiratory tract illness should not be found.

Diagnostic Tests. The diagnosis is made by **history,** particularly of **incomplete immunizations.** Fever, hoarseness, sore throat, wheezing, and rales are usually absent. Infants may present with apnea or cyanosis before the cough appears. There may be **leukocytosis** caused by absolute **lymphocytosis. Culture** of *B. pertussis* is the **gold standard. Direct fluorescent antibody (DFA)** testing of nasopharyngeal secretions is a rapid test that may be helpful if a patient has received antibiotics, but is not always reliable. Depending on the severity of the disease or complications, **chest radiograph** may show a perihilar infiltrate, edema, atelectasis, pneumothorax, pneumomediastinum, or air in the soft tissues.

Treatment. Treatment consists of **supportive care**. Patients at risk for **severe disease** should be **hospitalized**. These high-risk patients include infants <6 months of age, premature infants or children with underlying heart, lung, muscular, and neurologic disorders, and children of any age with complications from the illness. **Erythromycin** (the standard treatment) shortens the period of communicability. Treatment does not affect duration of the paroxysmal stage.

Standard pertussis immune globulin is **not recommended. Household members** and **close contacts** should receive **erythromycin** for 14 days. **Health-care providers** exposed to pertussis do not routinely receive antimicrobial prophylaxis. **Close contacts <7 years of age** who have **delayed immunizations** should receive the pertussis-containing vaccine. Children <7 years of age, who received a third dose of pertussis-containing vaccine ≥6 months before exposure, or a fourth dose ≥3 years before exposure, should receive a **booster vaccination.** Children who have proven *B. pertussis* infection are usually exempt from further pertussis immunizations.

Complications. Some complications that may be associated with pertussis include apnea, pneumonia, atelectasis from mucus plugging, pneumothorax from forceful cough, seizures, encephalopathy, and death. Most fatalities occur in children <6 months of age.

CAT SCRATCH

A 6-year-old presents with a swollen 3×5-cm tender, erythematous, anterior cervical neck node. He denies fever, weight loss, chills, night sweats, or sore throat. The patient's pets include a kitten, a turtle, and goldfish.

Definition. Cat scratch disease is a regional lymphadenitis caused by *Bartonella hensalae.*

Risk Factors/Etiology. Cat scratch disease may occur in a patient after he or she is scratched or bitten by a kitten or cat. The mechanism of cat to human transmission is not clear. Kittens appear to cause a higher incidence of transmission. The range for incubation is 3–30 days, so the patient may not remember cat exposure.

Presentation. Small red papules occur at the site of inoculation, appearing in linear fashion similar to a cat scratch. **Chronic regional lymphadenitis** is **characteristic,** and tender nodes are usually evident in 1–4 weeks. The affected lymph nodes usually remain enlarged for approximately 2 months. The patient may be febrile and have associated symptoms such as headache, anorexia, and malaise. **Parinaud occuloglandular syndrome** (unilateral conjunctivitis, preauricular lymphadenopathy, and ± cervical lymphadenopathy) after rubbing the eye with the hands after cat contact is an atypical presentation.

Physical Examination. As noted in the presentation, the patient usually has an enlarged lymph node that is tender with overlying erythema. The patient may have fever, temperature of 38–39°C.

Diagnostic Tests. This disease should be suspected with clinical evidence and history of cat exposure. Routine laboratory tests are not helpful. If tissue specimens are obtained, then gram-negative bacilli may be seen with the **Warthin-Starry** stain. An indirect immunofluorescent assay (IFA) has shown good correlation with disease.

Treatment. Cat scratch disease resolves spontaneously in 2–4 months, and usually no treatment is necessary. If the lesion is large and painful, then needle aspiration may be performed. The prognosis for cat scratch disease is good.

Complications. Some complications of cat scratch disease include encephalopathy, seizures, altered mental status, macular retinopathy, thrombocytopenic purpura, and leukocytoclastic vasculitis.

Differential Diagnosis. Some differential diagnoses for cat scratch disease include lymphoma, adenitis, tuberculosis, and mononucleosis.

RASH DISEASES

Lyme Disease

A 6-year-old child presents with a rash after camping on Long Island with his family. On physical examination the rash has a red raised border with central clearing.

Definition. Lyme disease is a vector-borne disease caused by the agent *Borrelia burgdorferi.* The vector is *Ixodes scapularis,* i.e., the deer tick.

Risk Factors/Etiology. The risk factor is a tick bite of *I. scapularis.*

Presentation/Physical Examination

- **Early localized disease** has a rash, **erythema migrans,** which begins 3–32 days (mean, 7 days) after the tick bite. The rash begins as a papule that expands to form a red raised border with central clearing. The patient may complain of malaise, lethargy, fever, and arthralgias. The signs will resolve without treatment in a month.

or

- **Early disseminated disease** may include neurologic and cardiac manifestations. Neurologic manifestations include "aseptic" meningitis, Bell palsy, and a neuropathy. Cardiac manifestations include myocarditis and varying degrees of heart block.

then

- **Late disease** includes arthritis that may occur months after the tick bite.

Diagnostic Tests. The diagnosis is made by a history of a tick bite and a rash. Confirmation of diagnosis is based on demonstration of antibodies to *B. burgdorferi* in the patient's serum.

Treatment. Treatment for **early disease** is doxycycline or amoxicillin. Children <8 years of age should not receive doxycycline. Erythromycin or cefuroxime may be prescribed for those not able to take either doxycycline or amoxicillin. Treatment for **disseminated disease** is ceftriaxone or penicillin G for 14–21 days. Bell palsy should be treated the same as for erythema migrans for 21–30 days. Steroids should not be used. Treatment for **late disease** is the same as for erythema migrans, except treatment lasts 30 days. If symptoms fail to resolve after 2 months or there is a recurrence, then give either a second course of orally administered antimicrobials for 30 days or treat as for late neurologic disease.

Prognosis. The prognosis for children with Lyme disease is excellent.

Prevention. The most effective way to avoid Lyme disease is to wear protective clothing in tick-infested areas and check for and remove ticks after spending time in such areas.

Erythema Infectiosum (Fifth Disease)

A 4-year-old is brought to the physician's office because she developed red cheeks that appear as if someone has slapped her, and a lacy rash on her upper extremities and trunk.

Definition. Erythema infectiosum is a benign, self-limited exanthematous illness.

Risk Factors/Etiology. The etiology of erythema infectiosum is parvovirus B19, a DNA virus. Humans are the only known host, and they transmit the virus via respiratory secretions and blood. This disease is commonly seen in the spring. The incubation period ranges from 4 to 28 days.

Presentation. The patient usually presents with mild systemic symptoms, including low-grade fever, headache, and upper respiratory tract symptoms such as pharyngitis. Some patients may have arthritic symptoms.

Physical Examination. The patient usually has an intensely red "slapped cheek" appearance, followed by a lacy-appearing rash over the trunk and proximal extremities. The palms and soles are spared. The rash lasts 2–40 days (mean, 11 days). The patient is not contagious after the rash appears.

Diagnostic Tests. The diagnosis of erythema infectiosum is usually made clinically. Laboratory tests for the diagnosis of B19 are not available routinely. Detection of viral DNA in fetal blood aids in making the diagnosis of B19-induced fetal hydrops.

Treatment. The treatment is supportive care only. IgG given intravenously may be considered in an immunocompromised patient. Intrauterine transfusions may be given to fetuses with hydrops and anemia.

Complications. Patients with hemolytic anemias such as **sickle cell anemia** are at risk for **aplastic crisis** if infected with parvovirus B19. **Fetuses** exposed to erythema infectiosum may develop **fetal hydrops** and **death.**

Measles (Rubeola)

A mother presents to the physician with her adopted daughter, who has just arrived in the United States from a foreign country. The immunization record is not up-to-date. The child has coryza, cough, conjunctivitis, and fever. The mother states that the child also has a rash that began cephalad and spread caudad. On physical examination a morbilliform rash is seen over the body including the palms. Tiny grayish white dots are seen on the buccal mucosa next to the third molar.

Definition. Measles is a viral infection characterized by high fever and a maculopapular rash.

Risk Factors/Etiology. The agent for measles is the measles virus, an RNA paramyxovirus. It usually occurs in unimmunized preschool children, or in high school and college students. Measles is extremely contagious. Incubation lasts 10–12 days before prodromal symptoms appear.

Presentation/Physical Examination. Patients have a prodrome that consists of the **"3 Cs"**, i.e., **cough, coryza,** and **conjunctivitis.** It is during this stage that Koplik spots, grayish white dots on the buccal mucosa, appear. The final stage consists of a high fever and appearance of a rash. The rash is macular and starts at the head, spreads downward, and fades in the same manner. Cervical lymphadenitis may also be noted.

Diagnostic Tests. The diagnosis is usually made clinically, and laboratory evaluation is rarely necessary. However, a rise in the convalescent sera will help confirm the diagnosis, as do the presence of multinucleated giant cells in nasal mucosal smears during the prodromal stage.

Treatment. Treatment is supportive. Vitamin A is recommended for some children, such as those with vitamin A deficiency, malnutrition, malabsorption, young hospitalized infants with measles, and immigrants from countries with high mortality from measles.

Prevention. The patient must be isolated from the seventh day after exposure until 5 days after the rash appears. Immunization helps prevent the disease. Passive immunization with immune globulin is effective for prevention of measles if given within 6 days of exposure.

Complications. Otitis media is the most common problem associated with measles infection. Pneumonia and encephalitis are other major complications.

Differential Diagnosis. There are many diseases associated with rash that should be differentiated from measles such as rubella, roseola, scarlet fever, Kawasaki disease, and drug rashes.

Roseola (Exanthem Subitum)

> A 15-month-old infant is brought to the physician because of a rash. The mother states that the patient had a fever of 104°F for the last 3 days without any source of infection. She explains that the fever has resolved, but now the child has pink, slightly raised lesions on the trunk, upper extremities, face, and neck.

Definition. Roseola is a febrile illness with exanthem that occurs in young children usually <5 years old (peak, 6–15 months of age).

Risk Factors/Etiology. Human herpesvirus 6 (HHV-6) is the agent responsible for roseola, and the incubation period is 5–15 days. Infection with HHV-6 usually occurs early in life, with peak incidence at 6–15 months.

Presentation. The classic presentation is a high fever, up to 41°C (106°F), that lasts 3–4 days with minimal physical findings. The fever resolves by the third or fourth day, and a maculopapular rash appears on the trunk, arms, neck, and face.

Physical Examination. Before the rash, physical findings are minimal but may include mild upper respiratory signs such as rhinorrhea, and conjunctival redness. **Occipital lymphadenopathy** may be found. The **rash** is **rose colored** and begins as papules on the trunk, then spreads to the neck, face, and proximal extremities.

Diagnostic Tests. No diagnostic studies are necessary. The diagnosis is based on age of the patient, history, and physical findings.

Treatment. Supportive therapy with antipyretics and fluids is the treatment for roseola.

Complications. Rarely HHV-6 invades the brain, liver, and other organs. In most cases the course is benign and the prognosis excellent.

Differential Diagnosis. Drug hypersensitivity, rubella, rubeola, erythema infectiosum, and scarlet fever may resemble roseola.

Rubella (German, Three-Day Measles)

A 5-year-old child who has delayed immunizations presents with low-grade fever, a pinpoint rash, postoccipital and retroauricular lymphadenopathy, and rose spots on the soft palate.

Definition. Rubella is a viral infection that is characterized by rash and enlargement and tenderness of the postoccipital, retroauricular, and cervical lymphadenopathy. It is infrequently seen.

Risk Factors/Etiology. The rubella virus, the cause of rubella, is an RNA virus. Most cases of rubella occur in adolescents and young adults. The incubation period is 14–21 days. Patients are contagious 2 days before the rash begins and 5–7 days after the rash.

Presentation. The patient presents with retroauricular and posterior occipital lymphadenopathy. The patient may present with pharyngitis, low-grade fever, and upper respiratory infection symptoms.

Physical Examination. The patient has a rash that is erythematous and maculopapular. It begins on the face, and spreads to the body, lasting 3 days. Retroauricular, posterior cervical, and postoccipital lymphadenopathy are characteristic of rubella. Forscheimer spots, rose spots on the soft palate, may appear before onset of the skin rash. There is no photophobia. Adolescent females may have polyarthritis.

Diagnostic Tests. The diagnosis may be made clinically from the history and physical examination. However, it should be confirmed by serology or virus culture.

Treatment. Supportive treatment is given.

Complications. The prognosis of rubella in childhood is excellent as complications are uncommon. Rubella infection in a pregnant woman can lead to congenital rubella syndrome.

Prevention. Immunization, usually as measles-mumps-rubella (MMR), helps to prevent the disease.

Differential Diagnosis. Some illnesses with skin rashes that need to be differentiated from rubella are roseola, rubeola, scarlet fever, infectious mononucleosis, and drug rashes.

Rocky Mountain Spotted Fever

A 17-year-old presents to the emergency center with his friends because of fever, headache, and a rose-colored rash that began on his ankles and is spreading. The patient and his friends have been camping in Virginia.

Definition. Rocky Mountain spotted fever is a rickettsial disease that is associated with fever, headache, and a rash.

Risk Factors/Etiology. *Rickettsia rickettsii* is the agent. The vector is a tick. The reservoir is rodents and mammals. The distribution of this illness is on the East Coast and in southeastern and western states. *R. rickettsii* causes vasculitis, tissue hypoperfusion, and end-organ damage.

Presentation. There is a nonspecific onset. The patient may complain of fever, myalgia, nausea, and vomiting. Headache, fever, and a pale, rose-colored, blanching maculopapular rash are the triad of the illness. The rash begins on the extremities and spreads to involve the entire body, including palms and soles.

Physical Examination. The patient has a **pale, rose-red maculopapular rash,** which begins peripherally and spreads to the entire body, including the palms and soles, and which turns into petechiae.

Diagnostic Tests. The diagnosis is made by history (tick exposure, fever, headache) and physical examination (rash especially on the palms and soles). There is no one single laboratory test that establishes early diagnosis. Confirmation is made by serology, which is performed in convalescence, usually by IFA assay. Thrombocytopenia, a low leukocyte count, and low serum sodium aid in making the diagnosis.

Treatment. Treatment should be initiated on clinical diagnosis alone. **Tetracycline** or **doxycycline** is the treatment of choice. In cases of Rocky Mountain spotted fever, tetracyclines, or doxycycline, can be used in children <8 years of age because tooth discoloration is dose dependent, and it is not likely that children <8 years of age should require multiple courses of the drug. Chloramphenicol should be used for patients not able to take tetracycline.

Complications. Delay in treatment can result in death. Rickettsial vasculitis may cause gangrene of the digits, ear lobes, nose, scrotum, or entire limbs. Patients may also have meningoencephalitis. Long-term neurologic sequelae may also occur secondary to infection.

Differential Diagnosis. Some other diseases that should be considered in the differential diagnosis are meningococcemia, Henoch-Schönlein purpura, hemolytic uremic syndrome, and drug rashes.

Prevention. There are no vaccines. Therefore, prevention depends on elimination of tick infestations.

Varicella

A 5-year-old child is brought to the emergency center because he has a temperature of 102°F and is developing a pruritic rash. The rash appears to be in various stages of papules, vesicles, and crusts. It began on his trunk and spread to his extremities.

Definition. Varicella zoster virus (chickenpox) is a neurotropic human herpes virus.

Risk Factors/Etiology. Varicella zoster virus is transmitted via respiratory secretions. The varicella zoster virus develops a latent infection in the sensory ganglia cells in individuals with primary infection. If the latent virus is reactivated, herpes zoster develops. Herpes zoster is rare in children because it is the reactivation of latent varicella zoster virus. However, children who are immunocompromised are susceptible to herpes zoster.

Children may become infected with varicella after exposure to adults with herpes zoster. However, varicella does not cause herpes zoster.

Presentation. The illness begins 14–16 days after exposure, but the incubation period ranges from 10 to 21 days. Fever and mild abdominal pain may occur 1–2 days before the rash appears. The patient has a **pruritic rash** consisting of papules, vesicles, pustules, and crusted lesions in crops in various stages. The patient is contagious from 1 to 2 days before the rash develops and until all the lesions are crusted (±7 days).

Physical Examination. The **varicella rash** consists of papules, vesicles, and crusted lesions in different stages. The rash begins as a papule that progresses to a vesicle then a pustule, and finally crusts. **Crops of lesions** in **various stages** are **characteristic.**

Diagnostic Test. The diagnosis is made clinically, and no laboratory evaluations are necessary.

Treatment. Treatment is symptomatic. Acyclovir and varicellar zoster immune globulin may be helpful in high-risk cases.

Complications. The most common complication from varicella in a normal host is scarring caused by secondary infections with group A streptococci and *S. aureus*. The disease is worse in neonates, adolescents, and the immunocompromised. Pneumonia is a complication in 15–20% of adults and the immunocompromised. Neurologic sequelae include Guillain–Barré, encephalitis, and cerebellar ataxia. Varicella may cause congenital infection and neonatal transmission. Other complications may occur, which are beyond the scope of this text.

Differential Diagnosis. The differential diagnosis would include vesicular rashes such as insect bites, herpes simplex virus, and *S. aureus*.

Scarlet Fever

A 7-year-old complains of a headache and a sore throat. On physical examination he has a temperature of 103°F, 3+ tonsils with exudate, and a strawberry tongue. In addition he has circumoral pallor, and a "sandpaper" rash on his face, trunk, and upper extremities. Pastia lines are also noted.

Definition. Scarlet fever is caused by a streptococci infection.

Risk Factors/Etiology. Group A β-hemolytic streptococci are the agent. It usually is associated with pharyngitis. However, it may follow wound infections, burns, and streptococcal skin infections.

Presentation. The patient typically presents with an abrupt onset of fever, chills, headache, and sore throat. The patient may have abdominal pain with vomiting before the onset of a maculopapular rash. The rash begins in the axilla, groin, and neck and becomes generalized in 24 h.

Physical Examination. Pertinent findings on physical examination are a **"strawberry" tongue, circumoral pallor, maculopapular or sandpaper rash, Pastia lines,** and **miliary sudamina** (small vesicular lesions over the hands, abdomen, and feet). The tonsil may be inflamed, enlarged, and covered with exudates. Desquamation can be found on the face by the end of the first week and later proceeds to the trunk, hands, and feet.

Diagnostic Tests. If the patient has pharyngitis, a rapid strep or throat culture should be obtained.

Treatment. Penicillin is the **drug of choice** for the treatment of scarlet fever. Alternatives for patients allergic to penicillin include erythromycin, clindamycin, or first-generation cephalosporins.

Complications. Some complications that may occur as a result of streptococcal infection include bacteremia, sinusitis, otitis media, cervical adenitis, and osteomyelitis. Late complications include rheumatic fever and glomerulonephritis.

Differential Diagnosis. Scarlet fever may resemble roseola. However, scarlet fever is very rare in infancy, and its rash has sandpaperlike lesions. Scarlet fever has also been confused with Kawasaki disease, but patients with scarlet fever have no conjunctival involvement, and there is recovery of group A streptococci. Viral exanthems such as measles and rubella, as well as sunburn, should also be included in the differential diagnosis of scarlet fever.

MUMPS

A 4-year-old unimmunized child presents with fever and unilateral parotid swelling.

Definition. Mumps is a viral infection that causes painful enlargement of the salivary glands, predominantly the parotid glands.

Risk Factors/Etiology. Mumps virus, which is a Paramyxovirus, causes mumps. Transmission of mumps virus occurs by airborne droplets, direct contact, and fomites contaminated by saliva. It is more commonly seen in the winter and spring. Outbreaks are related to lack of immunization. The patient is contagious 1 day before and 3 days after the swelling. The incubation period ranges from 14 to 24 days.

Presentation. Initially the patient with mumps presents with fever, headache, muscle pain, and malaise. This prodrome is usually followed by pain and swelling in the parotid.

Physical Examination. The patient with mumps has swelling of the parotid. Parotid swelling may be unilateral or bilateral. Erythema and swelling may also be present around Stenson's duct.

Diagnostic Tests. The diagnosis is usually made clinically by history and physical examination. Routine diagnostic studies are nonspecific. An elevation of the serum amylase is common. Virus can be isolated in the saliva, urine, CSF, blood, and any infected tissues. There is also a rise in serum antibodies, and enzyme immunoassay for mumps immunoglobulin IgG and IgM antibodies is most often used for diagnosis.

Treatment. Treatment is supportive. Orchitis is treated with local support and bed rest. Immunization against mumps will prevent the disease. Mumps arthritis should be treated with nonsteroidal antiinflammatories or corticosteroids.

Complications. The most frequent complication is meningoencephalomyelitis. Orchitis may also be a complication of mumps. It rarely occurs before puberty, and occurs bilaterally in approximately 30% of patients. Infertility is rare even with bilateral orchitis. Postpubertal females may develop oophoritis; however, fertility is not impaired. Mild pancreatitis is common. Other complications are thyroiditis, myocarditis, deafness, dacryoadenitis, and arthritis.

Differential Diagnosis. Examples of other viral causes of parotitis are HIV infection, cytomegalovirus, and coxsackievirus. A salivary calculus may cause intermittent swellings. Cervical lymphadenitis should also be considered in the differential.

Table 11-5. Common Childhood Infections with Exanthems

	Measles	Rubella	Mumps	Varicella	Fifth Disease	Roseola	Scarlet Fever
Virus	RNA/Paramyxovirus	RNA/Rubivirus	RNA/Paramyxovirus	Neurotropic herpes	DNA/erythro	Human herpes 6 & 7	Group A strep erythrogenic
Incubation (days)	8–12	14–23	16–18	14–16	4–14	9–10	2–5
Prodrome	Cough, coryza, conjunctivitis; high fever	Mild constitutional symptoms	HA, fever, malaise, muscle pain	Low-grade fever, malaise, URI sx	Mild URI sx	URI sx, abrupt onset high fever, then breaks	Sore throat
Enanthem	Koplik spots	Forchheimer spots	(Glandular swelling)	None	None	None	Exudative pharyngitis, strawberry tongue
Exanthem	Macules—hairline, face, neck, then to trunk and extrem.	Similar to measles; posterior cervical & auricular nodes	Swollen parotid & submandibular glands	Crops of papules vesicles, crusts at same time; central to peripheral	Slapped cheek, then to trunk, then central clearing—lacey	Fever falls rapidly, then fine macular rash on trunk and spreads to extrem.	Fine maculopapular rash; feels like sand paper; esp. in antecubitus and inguinal areas; Pastia lines
Complications	Pneumonia, enceph., SSPE	Congenital rubella—teratogenic	Encephalitis, orchitis, pregnancy—aqueductal stenosis; pancreatitis	Superinfection, zoster, pneumonia, hepatitis, enceph., congenital varicella	Aplastic anemia	Pneumonia	ARF, GN
Return to school	At least 2 weeks after appearance of rash	7 days after onset of rash	9 days after onset of parotid swelling	When all lesions have crusted	Once rash develops, no longer infectious	No control measures	24 hours after start of antibiotics

Definition of abbreviations: ARF, acute renal failure; enceph., encephalitis; extrem., extremities; GN, glomerular nephritis; HA, headache; SSPE, subacute sclerosing panencephalitis; sx, symptoms; URI, upper respiratory tract.

AIDS (ACQUIRED IMMUNODEFICIENCY SYNDROME)

An 18-month-old has failure to thrive and developmental delay. The patient also has a history of recurrent ear infections, oral thrush, and chronic diarrhea. The patient on physical examination today is noted to have lymphadenopathy.

Definition. The acquired immunodeficiency syndrome (AIDS) has HIV types 1 and 2 as its agent. Infection with HIV-2 is rarely found in children.

Risk Factors/Etiology. Most HIV-infected children are born in developing countries. The majority of HIV cases are acquired via vertical transmission from mother to child. Cesarean section combined with prenatal, intrapartum, and neonatal zidovudine (ZDV) therapy significantly reduces transmission of HIV. In developing countries breast-feeding is an important route of transmission. Other cases of HIV are obtained from parental exposure to blood products. Sexual contact is a major route of transmission of HIV in adolescents.

Presentation. Three patterns of disease have been described in children: (*1*) HIV-infected newborns with rapid onset of symptoms and AIDS during the first few months, (*2*) perinatally infected newborns with slower progression of the disease, and (*3*) long-term survivors with minimal or no progression of disease and normal CD4 counts. Clinical status and degree of immunologic impairment are used to classify HIV in children.

Physical Examination. In the majority of infants the physical examination at birth is normal. However, over a period of time the infant may develop failure to thrive. Problems such as lymphoid interstitial pneumonia, chronic otitis media, persistent diarrhea, hepatosplenomegaly, recurrent bacterial sepsis, and candidiasis may be seen. Older children have physical findings similar to adults.

Diagnostic Tests. The detection of antibody is by ELISA and Western blot analysis. Passively acquired maternal antibodies last up to 15 months. All infants born to HIV-positive mothers have positive antibody tests at birth because of passive transfer of maternal antibodies. HIV DNA polymerase chain reaction is the preferred virologic assay for infants in developing countries. HIV culture is not recommended for infants <1 month because of the potential for false-positive results. HIV disease can be excluded in children ≥18 months of age who have at least two HIV antibody tests that are negative, absence of hypogammaglobulinemia, and no clinical evidence of HIV disease.

Treatment. Treatment with antiretroviral therapy in children infected with HIV depends on the viral load, CD4 count and percentage, and clinical condition. Decisions regarding therapy should be made in consultation with an expert in pediatric HIV infection. Opportunistic infections should be treated. Nutritional support should be given.

Table 11-6. Pediatric HIV Classification System

	Clinical Categories	Diagnostic Criteria
N:	Not Symptomatic No signs or symptoms of HIV infection or only one of the conditions listed in Category A	If <18 mo of age has positive results on separate determinations from one or more of the following: (a) HIV culture (b) HIV PCR or (c) HIV p24 antigen If ≥18 mo is HIV antibody positive by repeatedly reactive ELISA and confirmatory test (e.g., Western blot or IFA)
A:	Mildly Symptomatic Two or more of the conditions listed, but none of the conditions listed in Category B or C	Lymphadenopathy (>0.5 cm at more than two sites bilateral = one site) Hepatomegaly Splenomegaly Dermatitis Parotitis Recurrent or persistent upper respiratory infection, sinusitis, or OM
B:	Moderately Symptomatic Symptoms of HIV infection other than those listed for Categories A or C. Examples include but are not limited to those listed.	Anemia (<8), neutropenia (<1,000), or thrombocytopenia (<100,000) persisting ≥30 days Bacterial meningitis, pneumonia, or sepsis (single episode) Candidiasis, oropharyngeal thrush, persisting >2 mo in children >6 mo old Cardiomyopathy CMV infection, onset before 1 mo of age Diarrhea, recurrent or chronic Hepatitis HSV stomatitis, recurrent (more than 2 episodes within 1 year) HSV bronchitis, pneumonitis, or esophagitis with onset before 1 mo of age Herpes zoster (shingles)—two episodes or more than one dermatome Leiomyosarcoma LIP or pulmonary lymphoid hyperplasia (AIDS defining, report to State) Nephropathy Nocardiosis Persistent fever (lasting >1 mo) *Toxoplasmosis*, onset before 1 mo of age Varicella, disseminated (complicated chickenpox)

(*Continued*)

Table 11-6. Pediatric HIV Classification System (*cont'd*)

	Clinical Categories	Diagnostic Criteria
C:	Severely Symptomatic Any condition listed in the 1987 surveillance case definition for AIDS with the exception of LIP	Serious bacterial infection; 2 in 2 yr; sepsis, pneumonia, meningitis, bone or joint infection; abscess of organ or body cavity (excludes OM, skin or mucosal abscesses, and indwelling catheter infections) Candidiasis (esophageal, tracheal, bronchial, pulmonary) Coccidioidomycosis, disseminated or extrapulmonary Cryptococcosis, extrapulmonary Cryptosporidiosis or isosporiasis >1 mo duration CMV disease (onset >1 mo), other than liver, spleen, or lymph nodes Encephalopathy: >1 finding for >2 mo and no illness that explains: (a) failure to attain or loss of milestones or intellectual ability shown by neuropsychologic tests; (b) impaired brain growth or acquired microcephaly shown by OFC measurements or brain atrophy or MRI (serial imaging needed if <2 years old); (c) acquired symmetric motor deficit with >2 of paresis, pathologic reflexes, ataxia, or gait disturbances Herpes simplex (ulcer >1 mo duration or pneumonia or esophagitis >1 mo old) Histoplasmosis, disseminated or extrapulmonary Kaposi sarcoma Lymphoma, primary, in brain Lymphoma, B cell, non-Hodgkin, lymphoma *Mycobacterium tuberculosis*, disseminated or extrapulmonary *Mycobacterium* infection, noncutaneous, extrapulmonary or disseminated (except leprosy) *Pneumocystis carinii* pneumonia Progressive multifocal leukoencephalopathy *Salmonella* (nontyphoid) sepsis, recurrent Toxoplasmosis of the brain, onset >1 mo old Wasting syndrome—in absence of other illness that explains: (a) weight loss >10% of baseline *or* (b) downward crossing of ≥ two percentile lines on the weight chart in a child >1 yr *or* (c) <5th% on weight for height on 2 consecutive measures >30 days apart *plus* (1) chronic diarrhea (>2 loose stools/day for >30 days) *or* (2) documented fever for >30 days, intermittent or constant

Definition of Abbreviations: AIDS = acquired immunodeficiency virus; CMV = cytomegalovirus; CT = computed tomography; HSV = herpes simplex virus; LIP = lymphoid interstitial pneumonia; MRI = magnetic resonance imaging; OFC = occipitofrontal circumference; OM = otitis media; PCR = polymerase chain reaction.

Modified from Centers for Disease Control and Prevention MMWR 43(RR-12);1-19, 1994.

MONONUCLEOSIS

A 17-year-old presents with fever, fatigue, and headache. He also complains of a sore throat and left upper quadrant pain. On physical examination he is noted to have generalized lymphadenopathy, enlarged tonsils, and hepatosplenomegaly.

Definition. The agent for mononucleosis is Epstein-Barr virus (EBV).

Risk Factors/Etiology. The disease is spread by intimate contact and saliva.

Presentation. Infants infected with EBV have mild clinical symptoms or are asymptomatic. Older children experience a prodrome, which lasts 1–2 weeks, and consists of fever, malaise, fatigue, headache, and nausea.

Physical Examination. Patients may have pharyngitis with exudates and petechiae. Generalized lymphadenopathy, splenomegaly, and hepatomegaly may also be present. An urticarial rash occurs in 5–15% of patients.

Diagnostic Tests. A preliminary diagnosis of EBV may be made by the presence of typical clinical symptoms plus atypical lymphocytosis in the peripheral blood. Serologic testing confirms the diagnosis.

Approximately 5% of EBV-infected patients have throat cultures positive for group A β-hemolytic streptococci. This represents pharyngeal streptococcal carriage.

Treatment. Supportive care is the treatment for the disease. Treatment with acyclovir with or without corticosteroids does not alter the outcome of the disease. Contact sports should be avoided for 2–3 weeks or until splenomegaly has resolved.

Complications. Eighty percent of patients develop an ampicillin rash.

Differential Diagnosis. As mentioned above, group A β-hemolytic throat infections can be confused with mononucleosis. Sometimes patients with mononucleosis develop very high or very low WBC counts with thrombocytopenia. In these cases a bone marrow biopsy should be performed to exclude the diagnosis of leukemia.

OTHER VIRUSES

Influenza

A 14-year-old is seen by his physician because of fever, headache, myalgia, chills, and a cough.

Definition. Influenzae viruses are RNA viruses divided into three types: A, B, and C.

Risk Factors/Etiology. Types A and B are responsible for epidemics. Type C is a sporadic cause of upper respiratory tract infections.

Presentation/Physical Examination. Older children have symptoms similar to adults. There is abrupt high fever, flushed face, headache, myalgia, cough, and chill symptoms that last 2–5 days;

and nasal congestion and cough may last 4–10 days. These viruses are less common in younger children, who have laryngotracheitis, bronchiolitis, bronchitis, and upper respiratory tract infections as a result of infection.

Diagnostic Tests. The diagnosis may be made (*1*) from nasopharyngeal secretions, (*2*) by ELISA, or (*3*) by serologic confirmation.

Treatment. Amantadine and rimantadine may be given for severe cases. These antivirals are not effective for influenzae B.

Complications. Secondary bacterial infections such as otitis media and sinusitis may occur.

Differential Diagnosis. It is difficult to distinguish influenzae from other viral infections (e.g., respiratory syncytial virus, parainfluenza virus).

Adenovirus

A 12-year-old patient presents with fever, sore throat, and follicular conjunctivitis.

Definition. Adenovirus is a DNA virus responsible for respiratory tract infections in infants. It may cause other types of infections, such as follicular conjunctivitis, pharyngoconjunctival fever, myocarditis, and intussusception.

Risk Factors/Etiology. These viruses usually occur in the spring and summer. The incubation period is usually 2–14 days.

Presentation. Patients have fever, pharyngitis, and occasionally diarrhea.

Physical Examination. Patients may have conjunctivitis, cervical adenopathy, and rhinitis.

Diagnostic Tests. Laboratory diagnosis of adenovirus may be made with serology or by viral culture or polymerase chain reaction.

Treatment. Supportive care is the therapy for adenovirus.

Enterovirus Including Coxsackie A, Coxsackie B, and Poliovirus

Hand, foot, and mouth disease (coxsackie A)

A 2-year-old presents with a vesicular rash in his mouth and on his palms and soles. The mother states that he also has a rash on his buttocks.

Definition. Hand, foot, and mouth disease is caused by infection with coxsackievirus A16.

Risk Factors/Etiology. The incubation period is 4–6 days, and it is seen more frequently in the summer and fall.

Presentation. The patients have an enanthem-exanthem.

Physical Examination. Ulcerative lesions are present in the oropharynx. Lesions may be also present on the hands and feet. Buttock lesions are very common.

Diagnostic Tests. The diagnosis is made clinically.

Treatment. Supportive treatment is given.

Complications. Dehydration may occur if the patient is unable to take liquids.

PARASITES

Enterobiasis (Pinworms)

A mother brings her 4-year-old child to the physician with history of anal itching. The patient attends day care, and you are told that the child's favorite activity is playing in the sandbox.

Definition. Enterobiasis is the most common parasite infection of children in temperate zones.

Risk Factors/Etiology. *Enterobius vermicularis* are small, white worms approximately 1 cm in length. The gravid female deposits eggs in the perianal region at night. Worms live in the cecum, appendix, ileum, and ascending colon. Children are infected via hand to mouth transmission.

Presentation. The history of nocturnal pruritus ani suggests infection of pinworms. The patient may have a history of restless sleep.

Physical Examination. Excoriations around the perianal area may be seen from scratching. Perianal granulomas are rare. Other sites that enterobiasis has been located are the female genital tract, the appendix, liver, and spleen.

Diagnostic Tests. Inspection of the worm under the microscope or collecting eggs with the cellophane tape test aids in the diagnosis. Eosinophilia is **not** seen in enterobiasis.

Treatment. Drug therapy should be given to infected and symptomatic individuals. Medications that may be prescribed for the treatment of pinworms are albendazole, mebendazole, and pyrantel pamoate. A repeat dose of these medications should be readministered in 2 weeks. Bed linens, undergarments, and nightclothes should be laundered in hot water.

Prevention. If exposure is constant then repeated treatments might be necessary every 3–4 months. Personal cleanliness is desirable but has not been proven to have an important role in control of this disease.

Ascariasis (*Ascaris lumbricoides*)

A patient is brought to the physician's office because the mother found a worm in the diaper.

Definition. Ascariasis is a helminthic disease.

Risk Factors/Etiology. Infection is usually seen in young children (preschool or early school age).

Ascariasis is caused by *Ascaris lumbricoides.* It is found in warm climates, and is a soil-transmitted infection. The use of human feces as fertilizer is the cause of this disease. The mode of

transmission is hand to mouth. Raw foods contaminated by human fertilizer or flies also cause *A. lumbricoides.* The life cycle of *A. lumbricoides* is as follows:

The human host ingests the eggs. → Larvae are released and penetrate the intestinal wall. → Larvae migrate to the lungs via the venous circulation. → Larvae break through the lung tissue into the alveolar spaces. → Larvae travel up the bronchial tree and are reswallowed. → Adult worms are formed.

Presentation/Physical Examination. Children may present with colicky abdominal pain and bile-stained emesis. Pulmonary ascariasis may occur with the clinical features being cough and bloodstained sputum.

Diagnostic Tests. A direct fecal smear examination helps to make the diagnosis. Pulmonary and gastrointestinal ascariasis complicated by obstruction is made clinically.

Treatment. Treatment includes albendazole, pyrantel pamoate, and mebendazole. No chemotherapeutic treatment is effective for ascariasis during the pulmonary phase. Piperazine is used if intestinal obstruction has occurred. In severe obstruction surgery may be required.

Scabies (*Sarcoptes scabiei*)

A mother brings her three children to you because they all have a pruritic rash that has been present for the past 3 weeks. The mother states that both she and the children's father have a similar rash that began in the webs of the fingers and has spread to the wrists, elbows, and axilla.

Definition. *Sarcoptes scabiei* is the agent that burrows in the skin and releases toxic and antigenic substances, resulting in a pruritic rash.

Risk Factors/Etiology. Children and sexual partners of affected individuals are at highest risk for developing scabies, because transmission depends on extent and duration of physical contact. Fomite transmission is rare.

Presentation. Patients typically present with an intense itch. Family members may have similar symptoms.

Physical Examination. The **burrow** is the classic lesion of scabies. A rash may be seen between the fingers, and on the wrists, elbows, and axilla. Infants may not have burrows but instead may have pustules, wheals, papules, and eczematous dermatitis located on the face, scalp, palms, and soles. The face is spared in adults and older children.

Diagnostic Tests. The **diagnosis** may be made clinically. Confirmation is made by microscopic identification of mites from skin scrapings.

Treatment. Permethrin 5% cream or **1% lindane** is the treatment of choice for children **>2 months of age.** Lindane should not be used in small infants because of its potential for neurotoxicity. In children **<2 months of age, 6% sulfur in petrolatum** may be prescribed. All family members and caretakers of the child should be treated. All bed linens and clothes should be laundered in hot water.

Complications. Pruritus may persist for several days after treatment because of hypersensitivity to mite antigens. If the pruritus persists >2 weeks after treatment the patient should be reexamined for mites; if mites are present, the patient should be retreated.

Lice (*Pediculus humanus corporis, Pediculus humanus capitis, Phthirus pubis*)

The school nurse refers a first-grade student to you because of nits in the child's hair.

Definition. Lice are obligate parasites of the human host. There are three types: (*1*) body or clothing lice, (*2*) head lice, and (*3*) pubic lice.

Risk Factors/Etiology. A risk factor for *Pediculus corporis* and *Pediculus capitis* is **poor hygiene.** *Phthirus pubis* is usually transmitted via **sexual contact** with an infested individual. *P. corporis* and *P. pubis* are rarely seen in children, although sexually active adolescents are at risk for *P. pubis.*

Presentation. Pruritus accompanies **all** types of lice infestation.

Physical Examination. *P. corporis* may manifest as a macule or papule with a hemorrhagic punctate lesion on the shoulders, trunk, or buttocks. In *P. capitis* nits are attached to the hair shaft close to the scalp. Nits may also be seen in the pubic hair when infested with *P. pubis.*

Diagnostic Tests. There are no diagnostic studies. A diagnosis is usually made on clinical findings such as nits on the hair shaft. A microscopic examination may be used to identify lice.

When *P. pubis* is present patients should be tested for venereal disease.

Treatment. Treatment for ***P. corporis*** (body lice) is **permethrin cream.** If the eyelashes are infested with lice **petrolatum** should be applied to alleviate the problem. ***P. capitis*** (head lice) is treated with permethrin1% cream rinse. Nits can be removed from the hair with a fine-tooth comb. Treatment for ***P. pubis*** is application of a pyrethrin shampoo. In addition, clothes, bed linens, and towels must be **laundered** in hot water for all types of lice.

Hookworm (*Ancylostoma duodenale, Necator americanus*)

A 5-year-old presents with complaint of anorexia, abdominal pain, and diarrhea. The patient is noted to have a yellow-green pallor.

Definition. Hookworm is a helminthic disease that can cause blood loss, iron deficiency, anemia, and protein malnutrition.

Risk Factors/Etiology. *Ancylostoma duodenale,* and *Necator americanus* cause classic hookworm. Hookworms are found in warm, moist soil, especially in rural areas where human feces is used as fertilizer. There may be penetration through the skin (*A. duodenale* and *N. americanus*), or ingestion (*A. duodenale*). No matter what the mode of entry, these helminths eventually attach to the wall of the intestine.

Presentation. There is pruritus at the site of penetration. The patient may complain of abdominal pain, fullness, and diarrhea.

Physical Examination. Children with chronic hookworm disease may have a yellow-green pallor known as chlorosis. Infants may be failing to thrive.

Diagnostic Tests. Anemia is a major manifestation. Diagnosis is made by direct fecal examination for eggs.

Treatment. Mebendazole or albendazole is the treatment of choice to eliminate hookworms from the intestine. Pyrantel pamoate is an alternative therapy that may be given in liquid form. Patients with iron deficiency anemia should receive iron salt replacement.

Prevention. Avoidance of human feces as fertilizer, sanitation, and education will help prevent hookworm infection.

FUNGAL INFECTIONS

Cutaneous/Mucocutaneous

Oral candidiasis/thrush

A newborn is noted to have white plaques on his buccal mucosa that are difficult to remove.

Definition. Oral thrush is an infection of the oropharynx caused by *Candida albicans.*

Risk Factors/Etiology. *Candida* infection of the mouth occurs in infants, the immunosuppressed, patients with poor oral hygiene, and patients taking inhaled steroids. Oral thrush is commonly seen in neonates because of contact with the organism in the birth canal.

Presentation. Thrush causes painful inflammation of the tongue, palates, and buccal mucosa.

Physical Examination. The lesions of oral thrush look like "**milk curds.**" However, the white plaques of thrush, which may cover all or part of the oropharyngeal mucosa, are difficult to wipe off. When removed, inflammation and pinpoint hemorrhages may be seen.

Diagnostic Tests. The diagnosis is confirmed by microscopic examination of KOH smears and by culture scrapings from the lesions.

Treatment. Topical nystatin solution is used for treatment.

Complications. Discomfort from this infection may cause a problem with feeding.

Diaper rash caused by *Candida* may coexist with oral thrush. Treatment for this is topical nystatin cream or ointment.

Tinea corporis (ringworm)

The school nurse refers a student to your clinic because of an annular rash that has scaling and central clearing. Other members of the child's family have similar lesions.

Definition. Tinea corporis is a fungal infection of the skin that excludes the palm, the soles, and the groin.

Risk Factors/Etiology. Tinea corporis may be caused by most dermatophyte species, but ***Trichophyton rubrum*** and ***Trichophyton mentagrophytes*** are the most prevalent agents.

Presentation. The patient presents with a rash.

Physical Examination. An annular lesion that has a raised border, scaling, and central clearing, i.e., **ringworm** is found on inspection.

Diagnostic Tests. The diagnosis is confirmed by the presence of hyphae on KOH preparation of epidermal scrapings and cultures. Tinea corporis should not fluoresce with a Wood's lamp.

Treatment. Topical treatment with an antifungal agent is recommended for treatment of these lesions.

Differential Diagnosis. The differential diagnosis includes pityriasis rosea, seborrheic dermatitis, psoriasis, and granuloma annulare.

Tinea capitis

A child is brought to the clinic by his mother because he has patches of hair loss as well as "knots" in the back of his scalp.

Definition. Tinea capitis is a dermatophyte infection of the scalp usually caused by *Trichophyton tonsurans,* and at times *Microsporum canis.*

Risk Factors/Etiology. It more commonly found in Hispanic and black children.

Presentation. The presentation varies; however, most children are brought to a physician because of hair loss or scalp pruritus.

Physical Examination. Occipital adenopathy may be present. Small circular patches of alopecia with hairs broken off close to the scalp, the **"black dot"** sign, is seen with infection by *T. tonsurans.*

Diagnostic Tests. The **Wood's lamp** may be helpful in the diagnosis of tinea capitis. Hairs infected with the *Microsporum* species fluoresce blue-green; most *Trichophyton* species do not fluoresce. **Cultures** of the infected material and **KOH preparations** are also used.

Treatment. Griseofulvin is the treatment of choice for all forms of tinea capitis. Treatment should continue until the fungal culture is negative; and may be necessary for 2–3 months.

Complications. An inflammatory reaction may produce a boggy granulomatous mass called a **kerion.** This is an id reaction and is treated with griseofulvin plus a tapering dose of steroid.

Differential Diagnosis. Seborrheic dermatitis, alopecia areata, trichotillomania, and psoriasis may be mistaken for tinea capitis.

Systemic

Coccidioidomycosis (San Joaquin); *Coccidiodes immitis*

A 14-year-old living in the Southwest presents with fever, headache, malaise, chest pain, a rash, and tibial erythema nodosum.

Definition. Coccidioidomycosis is an infection caused by the fungus *Coccidiodes immitis* that is found in soil.

Risk Factors/Etiology. Coccidioidomycosis is found in areas of California's San Joaquin Valley, Arizona, and southwest Texas. Transmission of *C. immitis* occurs through inhalation or, rarely, through injured skin. The average incubation period is 10–16 days. Persons with blood group type B are at higher risk for dissemination. In the normal host, recovery from the infection gives permanent immunity.

Presentation. There are three forms of the illness: (*1*) a benign, self-limited, primary infection, (*2*) residual pulmonary lesions, and (*3*) disseminating fatal disease. The patient may present with influenzalike symptoms, chest pain, and a maculopapular rash. Tibial erythema nodosum may be seen with or without erythema multiforme.

Physical Examination. Examination of the chest rarely shows abnormalities even though roentgenography usually reveals consolidation. Pleural effusions may compromise respiratory status.

Diagnostic Tests. Sputum should be obtained by gastric aspirates or bronchoalveolar lavage. The diagnosis is confirmed by culture, DNA probe, or histologic examination. Skin tests and serology may also be used as adjuncts. Diagnosis of the disseminated disease is by biopsy or autopsy. Hilar adenopathy and pulmonary consolidations may be seen on roentgenogram.

Treatment. Primary disease is **self-limiting**, and no treatment is necessary. **Amphotericin B** should be prescribed for severe *Coccidioides*. However, amphotericin B does not cross the blood–brain barrier; therefore, if the patient has **coccidioidal meningitis, fluconazole** should be used. There is limited information about the azoles and their use in children; however, **fluconazole** taken orally is useful in the treatment of disseminated coccidioidomycosis. Persistent pulmonary cavities may need surgical intervention.

Complications. In residual disease pulmonary granulomas persist, which are sometimes confused with TB or neoplasm. Meningitis is the most serious problem associated with disseminated coccidioidomycosis.

Histoplasmosis (*Histoplasma capsulatum*)

A 10-year-old who had been exploring caves with his friends presents to the physician with flulike symptoms.

Definition. Histoplasmosis is a fungal infection found in three forms in humans: (1) acute pulmonary infection, (2) chronic pulmonary infection, and (3) progressive disseminated disease.

Risk Factors/Etiology. *Histoplasma capsulatum* thrives in soil rich in nitrates and heavily contaminated with bird droppings. It has also been found in bat guano along bridges frequented by bats and in caves. It is prevalent in the Mississippi, Missouri, and Ohio river valleys.

Presentation/Physical Examination

- **Acute pulmonary histoplasmosis** develops after inhalation of microconidia. The majority of patients are asymptomatic, but children usually are symptomatic with flulike symptoms. Symptomatic infections may be associated with respiratory distress necessitating intubation.
- **Chronic pulmonary histoplasmosis** is an opportunistic infection with centrilobular emphysema that is rarely seen in children.
- **Progressive disseminated histoplasmosis** is seen in infants and immunosuppressed hosts. Fever, hepatosplenomegaly, anemia, and thrombocytopenia are found in the majority of patients <1 **year** of age with this disease. In **immunosuppressed non-HIV-infected patients** with disseminated histoplasmosis, presentation usually includes unexplained fever, weight loss, interstitial pulmonary disease, oropharyngeal ulcers, and meningitis. Disseminated histoplasmosis in **HIV-infected individuals** is an **AIDS-defining illness**. Fever, weight loss, lymphadenopathy, skin rashes, and meningoencephalitis may manifest.

Diagnostic Tests. Sputum cultures are usually negative in patients with symptomatic or asymptomatic acute pulmonary histoplasmosis. However, **seroconversion** helps make the diagnosis. **Fungal antigen by radioimmunoassay** is the most efficacious laboratory evaluation for diagnosing **disseminated histoplasmosis.**

Treatment. The disease is self-limited in asymptomatic or mildly symptomatic persons. For disseminated histoplasmosis, treat with amphotericin. Prophylactic itraconazole should be used for children living in endemic areas who have severe immunodeficiency and HIV. A nonsteroidal antiinflammatory should be used for sarcoidlike disease. Surgery may be necessary for complications of pulmonary histoplasmosis.

Allergies/Immunology

12

ALLERGIC RHINITIS

An 8-year-old patient comes to the physician because of runny nose, sneezing, and mouth breathing. The mother states that the patient gets these symptoms every spring when the lilacs start to bloom. The physical examination is pertinent for allergic shiners, a nasal crease, clear rhinorrhea and boggy turbinates.

Definition. Allergic rhinitis that is **seasonal** consists of symptoms that present after exposure and sensitization of pollens. Allergic rhinitis that is **perennial** occurs year-round because of allergens that the patient is exposed to on a continual basis.

Risk Factors/Etiology. Approximately 5–9% of children will develop seasonal allergic rhinitis, and it is rare before the age of 5 years. The pathophysiology stems from the inhalation of spores, pollens, and animal and mite antigens that are deposited on the nasal mucosa. IgE is produced and stimulates the release of mast cells.

Presentation. The patient may complain of sneezing, profuse watery rhinorrhea, and nasal obstruction. The patient may also have itching of the nose, palate, pharynx, eyes, and ears.

There may be a history of snoring or mouth breathing.

Physical Examination. The nasal passages are boggy, edematous, blue, and pale. The patient may have a nasal salute or nasal crease. Allergic shiners may be present.

Diagnostic Tests. The diagnosis is made on clinical grounds. However, a **nasal smear** of patients with allergic rhinitis may be overabundant with **eosinophils**. In addition, a family history of asthma or eczema may be obtained.

Treatment. The patient should **avoid the allergen**. **Antihistamines** and **decongestants** are useful in treating allergic rhinitis, especially if seasonal. **Cromolyn** nasal solution is useful in both seasonal and in perennial allergic rhinitis. **Topical** use of **corticosteroids** is the most effective treatment. If **infection** is suspected, a broad-spectrum **antibiotic** should be administered.

Differential Diagnosis. Hypertrophy of the tonsils, malignancy, nasal polyposis, foreign body, rhinitis medicamentosa, and unilateral choanal atresia are other causes of nasal obstruction.

URTICARIA-ANGIOEDEMA

A 5-year-old boy presents to the emergency center because he was stung by a bee and has developed a wheal-like raised rash over his body. He denies respiratory distress, dizziness, or emesis. On physical examination vital signs are stable, and there is no tongue swelling and no wheezing. He has well circumscribed raised lesions of various sizes on his trunk and upper extremities that are pruritic.

Definition

- **Urticaria,** or hives, are erythematous raised skin lesions (wheals or welts) of various sizes that may be localized or generalized. These lesions are usually well circumscribed but may occasionally be coalescent.
- **Angioedema** (angioneurotic edema) is difficult to distinguish from urticaria; however, the lesions appear to differ in that the deeper layers of skin, subcutaneous, or other tissues are involved. The upper respiratory and gastrointestinal tracts are commonly affected.

Risk Factors/Etiology. Urticaria is seen more frequently in girls than in boys. It is an IgE-mediated response. Release of histamine is responsible for the wheal-flare reaction. A second mediated pathway for urticaria uses C3a and C5a to cause histamine release from mast cells and basophils. A third mediated pathway uses bradykinin to increase vascular permeability and causes hives.

There are many **causes** of urticaria. Some of these causes include food, drugs, viruses (e.g., infectious mononucleosis, hepatitis), bacteria (e.g., *Streptococcus,* mycoplasma), malignancy, hyperthyroidism, and cold.

Presentation. The patient may complain of a pruritic rash.

Physical Examination. On physical examination a localized or generalized well circumscribed erythematous rash (wheals or welts) is seen. The individual hive may last 48 hours; however, new ones may appear.

Diagnostic Tests. The diagnosis of urticaria and angioedema is clinical. Therefore, the physician must be aware of the various forms of urticaria. If urticarial vasculitis is suspected, a skin biopsy should be obtained.

Treatment. The treatment is usually self-limited and requires only antihistamines (hydroxyzine, diphenhydramine, loratadine, cetirizine). Severe urticaria may be treated with epinephrine 1:1,000.

Complications. If the hives last longer than 6 weeks, then the patient has chronic urticaria. Chronic urticaria may persist for years because it is difficult to treat.

Differential Diagnosis. Erythema multiforme with target lesions and sometimes mucosal involvement may be confused with urticaria. Urticaria pigmentosa seen in young children is associated with systemic mastocytosis infiltrating liver, spleen, stomach, and lymph nodes. Exercise-induced anaphylaxis presents with hypotension, urticaria, angioedema, and wheezing and laryngeal obstruction after exercise. Urticarial vasculitis is associated with pigmented lesions that persist in the same location for 24 hours and has poor response to antihistamines. Fever and a high erythrocyte sedimentation rate may also be present.

ATOPIC DERMATITIS

A mother brings her 5-year-old daughter to the physician's office because the child has developed a rash in the antecubital area. The rash is pruritic. On physical examination an erythematous rash with excoriations is noted in the antecubital area.

Definition. Atopic dermatitis is an inflammatory skin disorder characterized by erythema, edema, pruritus, exudation, crusting, and scaling.

Risk Factors/Etiology. Patients with atopic dermatitis may have a family history of asthma, hay fever, and atopic dermatitis.

Presentation. In **infancy** the patient may present with an erythematous, pruritic rash with weepy patches on the cheeks, neck, wrist, hands, and extensor aspects of the extremities. Atopic dermatitis in infancy frequently coincides with introduction of foods.

Older **children** characteristically have the rash in the antecubital and popliteal fossae. There is a drying and thickening of the skin with age.

Physical Examination. This is described in the presentation.

Diagnostic Tests. Diagnosis may be made on clinical grounds with the characteristic lesions plus pruritus. A family history of atopy, an increased IgE, and an increase in eosinophils support the diagnosis. Atopic pleats (Dennie lines and Morgan folds) may be seen on physical examination and aid in the diagnosis.

Treatment. Some treatments for atopic dermatitis are **bathing less** frequently and using **bath oils**. The **environmental** causes of itch should be **controlled.** The patient should avoid extremes in **temperature**. The patient should wear smooth-textured clothes and **avoid wool**. **Antihistamines** may be prescribed for itch. The patient may use **topical corticosteroids** to help heal the rash. **Antibiotics** should be given for **secondary infection.**

Complications. Secondary infections are a complication seen with atopic dermatitis. The pruritus leads to infection causing secondary infections.

Differential Diagnosis. Scabies, seborrheic dermatitis, allergic contact dermatitis, Wiskott-Aldrich, X-linked agammaglobulinemia, and phenylketonuria are some of the disease entities that should be included in the differential diagnosis of atopic dermatitis.

IMMUNE DEFICIENCIES

In immunodeficiency, infections are characterized by increased frequency, unusual severity, a prolonged course or persistence of infection, and at times unusual organisms. Some common clinical manifestations that may be seen in immunodeficiency are recurrent sinopulmonary infections, failure to thrive, persistent thrush, diarrhea, and malabsorption. Associated conditions may include skin lesions such as eczema and pyoderma. Patients may have autoimmune disease and hematologic abnormalities such as anemia, neutropenia, and thrombocytopenia. Patients may also have hepatosplenomegaly.

The child with **recurrent infections** should have a (*1*) complete blood count and manual differential and (*2*) an erythrocyte sedimentation rate. If an immunodeficiency is suspected, screening tests targeting the suspected deficiency may be performed. Suggested **screening tests**

for **B-cell deficiency** are (*1*) immunoglobulin levels, (*2*) antibody titers, and (*3*) IgG subclasses. **Screening tests** for **T-cell deficiency** should include (*1*) an absolute lymphocyte count and (*2*) skin test for delayed hypersensitivity. If phagocytic deficiency is suspected, screening tests should include (*1*) an absolute neutrophil count and (*2*) measurement of the neutrophil respiratory burst after phorbol ester stimulation. If **complement deficiency** is suspected, then CH50 should be obtained because it measures the intactness of the entire complement pathway.

Table 12-1. Evaluation of Immunodeficiency

Antibody deficiency	Ig levels Ab titers to protein Ags (diphtheria, tetanus) Ab titres to polysaccharide Ags (pneumococcal vaccine) IgG subclasses B-cell enumeration
Cell-mediated immunity	Total lymphocyte count HIV evaluation Delayed hypersensitivity (skin tests—*Candida*, mumps, tetanus toxoid) CD3, CD4, CD8 In vitro T-cell proliferation to mitogens Chest x-ray-thymic hypoplasia FISH 22 for DiGeorge
Antibody and cellular immunity	All of the above
Splenic dysfunction	Howell Jolly bodies Hb electrophoresis Tc-99 spleen scan
Phagocytic function (CGD, Chediak-Higashi)	WBC neutrophil count and morphology NBT test (CGD) Chemotactic assay Phagocytic assay
Complement	CH50 Individual complement assays

B Cell

X-Linked agammaglobulinemia (XLA or Bruton)

A 15-month-old child presents to the physician with fever of 39°C. On physical examination the patient is noted to have a right tympanic membrane that is erythematous and bulging and that has obscure landmarks and no mobility. On review of the medical record you note that since 9 months of age this patient has had multiple infections with otitis media, sinusitis, and pneumonia.

Definition. Patients with Bruton agammaglobulinemia have severe hypogammaglobulinemia caused by defects in B lymphocytes.

Risk Factors/Etiology. Bruton is an X-linked disease that involves all three major classes of immunoglobulins.

The abnormal gene in Bruton is q22 on the long arm of the X chromosome.

Presentation. Most boys with Bruton present after maternal antibodies fall at about age 6–12 months. These patients are susceptible to repeated infections such as pneumonias, persistent otitis media, and sinusitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae.*

Physical Examination. There may be hypoplasia of tonsils and adenoids. There is no lymphadenopathy or splenomegaly.

Diagnostic Tests. Carriers are detected by direct mutation analysis or by finding nonrandom X-chromosome inactivation in B cells. Prenatal detection of Bruton is done by mutation analysis.

The diagnosis should be considered in patients with extremely low levels of IgG, IgA, IgM, and IgE (compared with matched controls for age and race) and in the absence of circulating B cells.

Treatment. The patient may be given prophylactic antibiotics and immunoglobulin therapy.

Complications. Paralysis after live polio vaccine has occurred. Infections with *Mycoplasma*, hepatitis, and enteroviruses are difficult for these patients.

Differential Diagnosis. Transient hypogammaglobulinemia of infancy may mimic Bruton agammaglobulinemia.

IgA deficiency

A 3-year-old child is brought to your office because of recurrent upper respiratory infections and recurrent urinary tract infections, as well as chronic diarrhea.

Definition. IgA deficiency is the most common humoral antibody deficiency.

Risk Factors/Etiology. The basic defect for IgA deficiency is unknown. It is thought to be an autosomal dominant inheritance.

Presentation. Patients with IgA deficiency are susceptible to recurrent respiratory and urinary tract infections as well as chronic diarrhea.

Complications/Follow-up. There is a high association with systemic lupus erythematosus and rheumatoid arthritis as well as an increased incidence of cancer. One must be very careful when administering blood and blood products to patients with IgA deficiency. These patients may develop anti-IgA antibodies causing anaphylactic reactions after intravenous administration of blood products containing IgA.

IgG subclass deficiency

A 2-year-old child presents to your office with more than seven sinopulmonary infections in the past year. The patient does not have siblings and does not attend day-care, and no one is ill in his household. The patient does not have any pets or animal exposure. There has been no recent travel. The patient is not failing to thrive. He is at the 50th percentile for height and weight for his age.

Definition. There are four subclasses of IgG (IgG1, IgG2, IgG3, and IgG4). IgG subclass deficiency occurs when there is a low IgG subclass concentration and a deficient antibody response to that subclass. At times a person may have an insufficient IgG subclass, but the total IgG serum concentration is normal or elevated.

Risk Factors/Etiology. Most patients with IgG2 deficiency have IgA deficiency. It is speculated that IgG subclass deficiency is a marker for general immune dysfunction.

Presentation. Patients have a history of sinopulmonary infections but have a normal growth pattern.

Diagnostic Tests. Quantitation of IgG subclasses is used in evaluation of immunodeficiency. There is age-dependent variation, and it is important that all levels be interpreted using age-appropriate standards.

Treatment. Gamma-globulin replacement therapy is sometimes used to treat these patients.

T Cell

DiGeorge syndrome

A 3-week-old infant presents with a generalized seizure. The patient was born to a 22-year-old white woman, G1P1, full term, via spontaneous vaginal delivery. The mother had good prenatal care and denies tobacco, drugs, and alcohol. There were no complications at delivery. The patient weighed 7 lb 6 oz at birth and has gained weight. The infant has been feeding and sleeping well. On physical examination the patient has hypertelorism, low-set ears, micrognathia, and a fish mouth.

Definition. DiGeorge syndrome, or thymic hypoplasia, results from injury to the cephalic crest cells, which contribute to the **third** and **fourth** pharyngeal pouches, causing **hypoplasia** or **aplasia** of the **thymus** and **parathyroid glands**. Other structures forming at the same gestational age may also be affected. Therefore, some other **features** of children with DiGeorge Syndrome may include congenital heart disease, hypertelorism, esophageal atresia, a bifid uvula, and micrognathia.

Risk Factors/Etiology. DiGeorge syndrome occurs in both boys and girls. Microdeletions of specific DNA sequences from chromosome 22q11.2 is found in the majority of cases.

Presentation. The diagnosis is often made in the newborn period after the patient presents with a hypocalcemic seizure. Total aplasia of the thymus and parathyroids is rare, and they usually have some functionality. Children with partial DiGeorge syndrome have little trouble with infections and grow normally. Children with complete DiGeorge syndrome are susceptible to

low-grade or opportunistic infections as well as graft-versus-host disease (GVHD) from nonirradiated blood transfusions.

Physical Examination. Some features of patients with DiGeorge syndrome include epicanthal folds to the eyes, hypertelorism, low-set ears, a bifid uvula, a short philtrum, micrognathia, a fish mouth, and congenital heart disease (atrial septal defect, ventricular septal defect).

Diagnostic Tests. Although DiGeorge syndrome should be suspected from history and physical examination, polymerase chain reaction (PCR)-based genotyping may be performed.

Concentrations of serum immunoglobulins are usually normal, but IgA may be decreased and IgE increased.

Treatment. Thymic tissue transplants and unfractionated HLA-identical bone marrow transplantation may correct immune deficiency in the complete DiGeorge syndrome.

Differential Diagnosis. Patients with fetal alcohol syndrome have similar facial features and heart lesions as DiGeorge patients. Velocardiofacial syndrome (VCFS) and the conotruncal anomaly face syndrome (CTAFS) share similarities with DiGeorge syndrome (i.e., 22q deletions and conotruncal heart defects).

B and T Cell

Wiskott-Aldrich syndrome

> A 1-year-old infant presents to his physician with severe eczema. On physical examination the patient is noted to have draining ears as well as a petechial rash. Review of the medical record reveals that the patient has recurrent infections, including otitis media and pneumonia.

Definition. Wiskott-Aldrich is an X-linked recessive disease characterized by recurrent infection, thrombocytopenia, and eczema.

Risk Factors/Etiology. Wiskott-Aldrich has an abnormal gene on the X chromosome causing problems in the lymphocyte and megakaryocyte cell lineage.

Presentation. The patient may present with eczema, petechiae, and a history of recurrent infections.

Physical Examination. Otitis media or pneumonia may be found on physical examination. The patient may have petechiae. Hepatomegaly, splenomegaly, and cervical lymphadenopathy may be present. The skin may be eczematous.

Diagnostic Tests. The serum level of IgA and IgE is elevated. IgG is normal or low, and IgM is low. Carriers of Wiskott-Aldrich disease can be detected with genetic testing.

Treatment. Splenectomy may correct the thrombocytopenia but increases the patient's risk of infection. Therefore, after splenectomy the patient requires antibiotic prophylaxis. Bone marrow transplant is the treatment and cure for Wiskott-Aldrich syndrome.

Complications. Infections, malignancy, and bleeding may lead to early death.

Ataxia-telangiectasia

A 3-year-old child presents with ataxia, masklike facies, drooling, tics, and irregular eye movements. According to the mother, the ataxia began at approximately 1 year of age. On examination of the patient's eyes he is noted to have telangiectasias. In addition, he also has a history of recurrent respiratory infections.

Definition. Ataxia-telangiectasia is a syndrome that consists of ataxia, telangiectasia of the eyes and skin, chronic sinopulmonary disease, and endocrine abnormalities. There is humoral and cellular immunodeficiency.

Risk Factors/Etiology. Ataxia-telangiectasia is an autosomal recessive disease caused by a mutated gene on chromosome 11.

Presentation. Cerebellar ataxia is the **first neurologic sign** and usually becomes evident after the patient begins walking. The patient may have a history of **recurrent sinopulmonary disease.**

Physical Examination. On physical examination the patient has **masklike facies** with drooling, tics, and irregular eye movements.

Diagnostic Tests. The patient has IgA deficiency. IgE and IgM levels are low. $CD3^+$ and $CD4^+$ T cells are moderately reduced, with moderate or increased numbers of $CD8^+$. Both the helper T cells and intrinsic B cells have defects.

Complications. Children are usually confined to a wheelchair by age 12 years. Fatal varicella has occurred in patients with ataxia-telangiectasia.

Eye 13

DEVELOPMENT OF THE EYE

A normal newborn's eye is about 65–75% adult size. **Binocular fixation** is present by 3–4 months of age; before that, eyes commonly cross. **Normal acuity** is approximately 20/200–20/400. **Acuity** reaches 20/30–20/40 by 3 years of age, 20/40 by 4 years, and 20/20 by 5 years. Newborn infants see black and white best. Color blindness is usually red-green and sex-linked recessive.

LID ABNORMALITIES

Congenital Abnormalities

Coloboma is a defect of the lid that can range from a small indentation to a large cleft, which can lead to ulceration from excessive drying. Coloboma can also extend to the iris, lens, retina, and choroid. They are associated with chromosomal disorders and malformation syndromes. **Epicanthal folds** are folds of skin on the nasal side of the eye. Usually more prominent at birth and receding with time, they are responsible for pseudostrabismus by making the eyes appear closer together. **Ptosis**, or drooping of the upper eyelid, is the most common anomaly of the eyelid. It is usually an isolated finding but can be seen in systemic disorders such as botulism and myasthenia gravis.

Infections

Blepharitis is an inflammation of the lid margins. It is associated with pain, itching, burning, and eyelid redness. **Hordeolum**, or stye, is an infection (usually staphylococcal) of the ciliary follicle and glands along the lid margin. **Treatment** consists of warm compresses and topical antibiotics. **Chalazion** is a chronic lipogranuloma caused by retention of secretions of the Meibomian glands. They do not have acute inflammatory signs and tend to regress spontaneously but may require **excision**.

CONJUNCTIVAL ABNORMALITIES

Conjunctivitis

A 12-hour-old newborn is noted to have bilateral conjunctival injection, tearing, and some swelling of the left eyelid. Physical examination is otherwise normal.

Definition. Conjunctivitis is an inflammatory response of the conjunctival vessels to a variety of insults.

Risk Factors/Etiology. Ophthalmia neonatorum is caused by chemicals or infection. **Chemical conjunctivitis** caused by instillation of silver nitrate is the most common cause of conjunctivitis presenting in the first 24 hours of life. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are common infectious causes of neonatal conjunctivitis. ***Chlamydia*** is the most common infectious cause of ophthalmia neonatorum. Acute purulent conjunctivitis is usually **bacterial** in cause (*Haemophilus,* streptococci, staphylococci, pneumococcus). **Viruses** (adenovirus, enterovirus) can also be responsible for conjunctivitis. Some systemic viral diseases with exanthems also cause conjunctivitis. Conjunctivitis can be a manifestation of **allergies.**

Presentation. Tearing, conjunctival injection, lid edema, and **discharge** are the hallmarks of conjunctivitis. Pain, photophobia, and decreased vision are rare and should make one suspicious of corneal disease. Gonococcal conjunctivitis is purulent and can occur at birth but usually occurs at 5 days of age or later if the patient has received topical antibiotic prophylaxis. Chlamydial conjunctivitis occurs about 5–23 days after birth.

Diagnostic Tests. Gram stain and culture may be helpful in identifying an infectious cause.

Treatment. Gonococcal conjunctivitis is treated with **ceftriaxone.** Prevention is with topical **silver nitrate or topical erythromycin. Chlamydial** conjunctivitis is treated with **erythromycin** topically and systemically to prevent pneumonia. Acute purulent conjunctivitis is treated with topical antibiotic drops, whereas allergic conjunctivitis is treated with decongestant drops, mast cell stabilizers, antihistamine drops, and cool compresses.

Complications. Ophthalmia neonatorum can lead to corneal involvement, iridocyclitis, and blindness.

Differential Diagnosis. This includes **dacryostenosis** caused by congenital lacrimal duct obstruction. It is usually unilateral with a clear discharge, although secondary infection can occur. Spontaneous resolution occurs by 1 year of age. Treatment consists of massage, treating secondary infections, and probing.

Subconjunctival Hemorrhage

Subconjunctival hemorrhage is a bright red patch in the bulbar conjunctiva. It can occur with mild trauma, coughing, sneezing, and conjunctivitis. It resolves spontaneously in 1–2 weeks.

ABNORMALITIES OF VISION

Strabismus

Definition. Strabismus is **misalignment** of the eyes. Deviations can be convergent (esotropia) or divergent (exotropia). This results from abnormal innervation of muscles from the supranuclear nerve. Transient strabismus is common up to 4 months of age. **Pseudostrabismus** is caused by the unique facial characteristics of the infant and is not a pathologic condition.

Diagnosis. The **Hirschberg** test, looking for the corneal reflex, and the **cover** test are useful in diagnosing strabismus. Extraocular movements are normal. Visual acuity should always be evaluated.

Treatment. Therapy consists of glasses and surgery to the affected muscles.

Amblyopia

A 5-year-old boy is seen in the office because his left eye turns in. Examination reveals turning in of the left eye. Extraocular movements are intact. Covering the right eye causes the left eye to straighten out. Visual acuity is decreased in the left eye.

Definition. Amblyopia is a decrease in acuity as a result of an unclear image falling on the retina. It is frequently caused by an inwardly deviated eye (**strabismus**) or by an opacity in the visual axis (**deprivation**).

Diagnosis. Frequently, parents bring the matter to the attention of the physician when they see their child's eye deviated inward or during routine screening.

Treatment. This consists of removing any opacity and covering (patching) the good eye to stimulate the affected eye. Early diagnosis is important because these respond better to treatment.

CELLULITIS

A 7-year-old boy presents with swelling around the eye 2 days after suffering an insect bite to the eyelid. There is edema, erythema, and proptosis of the eye. Marked limitation of eye movements are noted. He has a low-grade fever.

Definition. Orbital cellulitis is an inflammatory condition involving the tissues of the orbit.

Risk Factors/Etiology. Orbital cellulitis most commonly occurs as an extension of a paranasal **sinusitis**. Common causative organisms include nontypable *Haemophilus influenzae*, *Staphylococcus aureus*, group A β-hemolytic *Streptococcus*, *Streptococcus pneumoniae*, and anaerobes. Orbital cellulitis can also occur after direct infection from a wound, as a result of bacteremia, or by local spreading from a contiguous site.

Presentation. Patients with orbital cellulitis complain of **orbital pain**, decreased vision, **proptosis**, conjunctival edema (chemosis), and eyelid swelling and may have fever.

Diagnostic Tests. Orbital cellulitis is diagnosed on clinical presentation. Computed tomographic scan of the head and sinuses is helpful in delineating the extent of infection.

Treatment. Treatment consists of systemic **antibiotics** and may require **drainage** of the abscess.

Complications. These include loss of vision from optic nerve involvement, meningitis, cavernous sinus thrombosis, or brain abscesses.

Differential Diagnosis. Orbital cellulitis must be differentiated from **periorbital** cellulitis in which there is no true orbital involvement. Only the eyelids and surrounding tissues are involved. Eye movements are normal. Causes are similar to those of orbital cellulitis. Treatment is with antibiotics.

TRAUMA

Ecchymoses of the eyelids are also known as black eyes and are common after blunt trauma. They absorb spontaneously like any other bruise.

Foreign bodies produce discomfort, tearing, and inflammation. A foreign body under the eyelid can mimic a corneal foreign body. Inspection of the eye usually reveals the foreign body. Most conjunctival foreign bodies can be flushed out. Intraocular foreign bodies necessitate referral to an ophthalmologist.

Corneal abrasions are accompanied by pain, photophobia, tearing, and decreased vision. **Diagnosis** is facilitated by observing the eye under a blue filtered light after instillation of **fluorescein.** Treatment consists of **topical antibiotics.**

Mouth and Teeth

14

TEETHING

A 7-month-old infant is very fussy, is drooling, and grabs at her left ear. Physical exam reveals normal tympanic membranes. There is mild swelling of the gingiva.

Teething begins at approximately 6–8 months of age. **Symptoms** include local discomfort, bluish discoloration of the overlying gums caused by hematoma or eruption cyst, drooling, and irritability. There is **no substantial evidence** relating teething to diarrhea, rashes, rhinorrhea, or fever. **Treatment** consists of teething rings and cool compresses. Below is a table of approximate order of eruption.

Table 14-1

Primary (Deciduous)	Upper (Maxillary)	Lower (Mandibular)
Central incisors	6–8 mo	5–7 mo
Lateral incisors	8–11 mo	7–10 mo
Cuspids (canines)	16–20 mo	16–20 mo
First molars	10–16 mo	10–16 mo
Second molars	20–30 mo	20–30 mo

Table 14-2

Secondary (Permanent)	Upper (Maxillary)	Lower (Mandibular)
Central incisors	7–8 years	6–7 years
Lateral incisors	8–9 years	7–8 years
Cuspids (canines)	11–12 years	9–11 years
First premolars (bicuspids)	10–11 years	10–12 years
Second premolars (bicuspids)	10–12 years	11–13 years
First molars	6–7 years	6–7 years
Second molars	12–13 years	12–13 years
Third molars	17–22 years	17–22 years

CARIES

Etiology. Caries are caused by a combination of **diet** (particularly sticky carbohydrates), oral **bacteria** (*Streptococcus mutans*), and the surface of the tooth.

Presentation. Large lesions are seen on visual inspection as **cavitations. Nursing bottle** caries are easily seen and result from repeated exposure to carbohydrates through bottle feedings. Pain frequently accompanies cavities.

Treatment. Prevention through use of **fluoride**, good hygiene (brushing, flossing), sealants, and proper diet are all useful in preventing cavities. Fillings and crowns as well as pain management and treatment of infections are all indicated.

Complications. Complications of caries include destruction of the tooth, invasion and inflammation of the pulp, and abscess formation.

CLEFT LIP AND PALATE

Cleft lip occurs when the medial nasal and maxillary processes fail to join. It can occur with or without cleft palate. **Cleft palate** results from failure of the palatal shelves to fuse. **Feeding problems** are common with cleft lip or cleft palate. Recurrent **otitis media**, **hearing loss,** and **speech defects** are common complications of cleft palate. Treatment of both cleft lip and cleft palate involves surgical repair.

OTHER

Black hairy tongue is a result of elongation of the filiform papillae. **Geographic tongue** manifests as smooth, sharply demarcated patches with an elevated margin.

Ears, Nose, and Throat

15

EARS

Otitis Media

A 4-year-old child is seen in the office with a 3-day history of fever and cold symptoms, and now complains of right ear pain. Physical examination is remarkable for a bulging tympanic membrane with loss of light reflex and landmarks.

Definition. Otitis media (OM) is inflammation of the middle ear.

Risk Factors/Etiology. Infants and children are at highest risk for otitis media, with the risk decreasing after 6 years of age. Male sex, daycare settings, secondhand smoke, and formula feeding predispose to OM. **Craniofacial anatomy** and **eustachian tube dysfunction** are responsible for development of OM. Patients with craniofacial anomalies are also at increased risk for OM. ***Streptococcus pneumoniae***, nontypable ***Haemophilus influenzae***, and ***Moraxella (Branhamella) catarrhalis*** are the most common bacterial causes of OM. Viruses (respiratory syncytial virus, rhinovirus, influenza, adenovirus) can also cause OM, alone or as copathogens with bacteria.

Presentation. Typical symptoms of acute OM include **otalgia**, fever, irritability, and ear pulling. Fever is seen in up to half the cases. Vomiting and diarrhea are also seen. Older children can complain of hearing loss. Drainage from the ear is not uncommon.

Diagnostic Tests. Pneumatic otoscopy reveals a reddened, bulging tympanic membrane with loss of landmarks and poor mobility. Bullae and otorrhea may be seen.

Treatment. Treatment consists of oral antibiotics. **Amoxicillin** is still the drug of choice for uncomplicated acute otitis media. Otalgia or fever persisting after 72 h of therapy should be considered a treatment failure, and a change in antibiotics is indicated, usually to high-dose amoxicillin and clavulanic acid or cephalosporins. Supportive treatment includes antipyretics and analgesics.

Complications. Complications of OM include the following:

- Persistent middle ear effusion.
- Recurrent OM—treated with myringotomy and ventilating tubes.
- OM with effusion—These patients have persistent fluid but few or no symptoms. It usually clears within 3 months. The tympanic membrane is retracted and poorly mobile. Treatment (antibiotics, decongestants, myringotomy, ventilation tubes) is indicated in those cases of hearing loss or effusion persisting more than 3 months.
- Hearing loss—This is the most common complication.
- Perforation
- Mastoiditis—Symptoms include redness and tenderness over the mastoid bone, with an outward and forward displacement of the outer ear.
- Cholesteatoma—This is a pocket of squamous epithelium in the tympanic membrane. It can spread and destroy other temporal bone structures. Therapy consists of surgical removal.
- Meningitis—This is the most common intracranial complication.
- Labyrinthitis—Symptoms include vertigo, nystagmus, tinnitus, hearing loss, and vomiting.

Otitis Externa

Otitis externa is also known as **swimmer's ear. Repeated wetting** of the ear canal and local trauma can predispose to otitis externa. It is most commonly caused by ***Pseudomonas aeruginosa*** and *Staphylococcus aureus.* **Symptoms** include ear pain exacerbated by moving the ear canal. The ear canal appears inflamed, swollen, and macerated. Clumpy discharge from the canal is seen. **Treatment** consists of topical antibiotics. **Prevention** for frequent swimmers includes instilling dilute alcohol in the ear canal immediately after swimming.

NOSE

Choanal Atresia

> A newborn is noted to be cyanotic in the wellborn nursery. On stimulation, he cries and becomes pink again. The nurse has difficulty passing a catheter through the nose.

Definition. A septum between the nose and pharynx.

Risk Factors. There is a high association with **CHARGE** syndrome—**C**oloboma, **H**eart disease, **A**tresia choanae, **R**etarded growth/development, **G**enital anomalies (hypogonadism), **E**ar anomalies (deafness).

Presentation. Because newborns are basically nose breathers, those with bilateral obstruction present with cyanosis relieved by crying.

Diagnostic Tests. Inability to pass a catheter through the nostril confirms your suspicion. Fiberoptic rhinoscopy reveals the plate.

Treatment. Establishment of an airway is paramount, followed by surgical correction.

Infections

Viral

Upper respiratory infections (URI), or the common cold, are caused by **rhinoviruses**, parainfluenza viruses, respiratory syncytial viruses, and coronaviruses. Children are the major reservoirs. The **incubation** period is 2–5 days. **Transmission** is by large droplets, small aerosol particles, or secretions. **Symptoms** include fever, nasal congestion, rhinorrhea, sneezing, pharyngitis, and malaise. Most symptoms resolve by 5–7 days. **Treatment** is not necessary. **Complications** include otitis media, sinusitis, and pneumonia.

Bacterial

Sinusitis is caused by *S. pneumoniae*, *M. catarrhalis*, and nontypable *H. influenzae*. *S. aureus* and anaerobes are responsible for chronic sinusitis. Also, anything that impairs mucociliary transport or causes nasal obstruction impeding proper drainage can increase the risk of sinusitis. **Symptoms** include purulent nasal discharge and cough in children. Cold symptoms in children persisting longer than 7–10 days are suspicious for sinusitis. Older children and adolescents may complain of headaches, tenderness over the sinuses, and fever. Sinus films show opacification or air fluid levels. Computed tomographic scans demonstrate thickened mucoperiosteum. **Treatment** consists of antibiotics, usually 14–21 days. **Complications** include orbital cellulitis, abscess, or meningitis.

Epistaxis

> An 8-year-old child has repeated episodes of nosebleeds. Past history, family history, and physical examination are unremarkable.

Definition. Epistaxis is a nosebleed, usually from the anterior septum.

Risk Factors/Etiology. The most common cause of epistaxis is as a result of **picking the nose.** Trauma, foreign bodies, and inflammation (from recurrent URI, sinusitis, and allergic rhinitis) can also cause nosebleeds. Rarely, vascular anomalies or bleeding disorders may be responsible. Epistaxis is rare outside of childhood. **Juvenile nasopharyngeal angiofibroma** should be considered in pubertal boys with profuse bleeding and an associated nasal mass. Foreign bodies may cause nosebleeds and are characterized by profuse, purulent, unilateral nasal drainage.

Presentation. Nosebleeds are acute and without warning, usually from one nostril. Episodes may recur when the patient rubs the nose, traumatizing the mucosa further, or dislodging the clot.

Treatment. Most nosebleeds resolve spontaneously. Compression of the nares and upright posture with the head held forward prevents swallowing of the blood. Local vasoconstrictor sprays can also help. Nasal packing and cautery are used for more severe bleeds.

THROAT

Pharyngitis

An 8-year-old girl complains of acute sore throat of 2 day's duration, accompanied by fever and mild abdominal pain. Physical examination reveals enlarged, erythematous tonsils with exudate and enlarged, slightly tender cervical lymph nodes.

Definition. Pharyngitis is inflammation of the throat, usually acute in nature.

Risk Factors/Etiology. Pharyngitis is rare under 1 year of age. The most common bacterial cause of pharyngitis is group A β-hemolytic *Streptococcus* (GABHS). Strep pharyngitis is more common in children 5–15 years of age. Viruses are responsible for the majority of cases of pharyngitis.

Presentation. Viral and bacterial pharyngitis are often difficult differentiate clinically. Erythema, exudate, petechiae, enlarged tonsils, and cervical adenopathy may be common to both. Viral pharyngitis usually has a gradual onset, with moderate throat pain and symptoms of URI. Many times a history of contacts having cold symptoms can be elicited. Vesicles and ulcers are more common with herpes simplex and coxsackievirus. Conjunctivitis is seen with adenovirus. Viral exanthems may be seen. GABHS may present with headache, vomiting, and abdominal pain. URI symptoms are usually absent. Palatal petechiae and diffuse erythema of the tonsils and pillars are highly suggestive. Strep pharyngitis can be associated with a fine, blanching, erythematous, sandpaper rash prominent in inguinal and antecubital areas.

Diagnostic Tests. Rapid Strep antigen detection kits have a high degree of sensitivity and specificity. The gold standard is throat culture, and all negative rapid Strep tests should be backed up with a throat culture.

Treatment. Treatment of viral pharyngitis is symptomatic. Throat lozenges, cool fluids, and saline gargles all help. Streptococcal pharyngitis is treated with antibiotics. Penicillin is the antibiotic of choice; amoxicillin is an acceptable alternative.

Complications. Complications of Strep pharyngitis include the following:

- Rheumatic fever.
- Glomerulonephritis.
- Peritonsillar abscess—This courses with fever and severe sore throat. The patient usually drools, and the tonsil bulges medially. The uvula deviates to the noninvolved side, and the patient has a "hot potato" voice. Treatment is with intravenous antibiotics, and surgical drainage may be necessary.
- Retropharyngeal abscess—This can also be caused by *S. aureus*. Retropharyngeal abscess can cause airway obstruction. Lateral films of the neck reveal a soft tissue mass. Treatment is with IV antibiotics and drainage.

Cervical Lymphadenitis

This is any condition that causes inflammation and enlargement of the cervical lymph nodes. Patients may have fever, swollen cervical lymph nodes, and torticollis. In children this is usually **infectious** in nature, and causes can include viral or bacterial pharyngitis, tuberculosis or atypical mycobacteria, and cat scratch disease, among others. Tumors, although rare, can cause adenitis. The **differential diagnosis** includes **thyroglossal duct cysts, branchial cleft cysts, cystic hygroma, and mumps**. Because they are usually infectious, treatment consists of antibiotics and compresses. Persistent, unexplained cervical lymphadenopathy should be biopsied.

Indications for tonsillectomy/adenoidectomy include the following:

- Tonsillectomy
  - Persistent oral obstruction
  - Recurrent peritonsillar abscess
  - Recurrent cervical adenitis
  - Suspected tonsillar tumor
- Adenoidectomy
  - Persistent nasal obstruction and mouth breathing
  - Snoring and snorting
  - Hyponasal speech
  - Repeated/chronic OM
- Tonsillectomy/adenoidectomy
  - Cor pulmonale
  - Sleep apnea
  - Recurrent aspiration pneumonia
- Invalid reasons
  - Recurrent colds
  - Recurrent Strep pharyngitis (unless >7/y, 5/y for 2 years, 3/y for 3 years)
  - Parents

Respiratory 16

FOREIGN BODY ASPIRATION

A toddler presents to the emergency center after choking on some coins. The child's mother believes that the child swallowed a quarter. On physical examination the patient is noted to be drooling and in moderate respiratory distress. There are decreased breath sounds on the right with intercostal retractions.

Definition. Foreign bodies include items such as hot dogs, peanuts, beans, coins, buttons, nuts, uninflated balloons, etc. These items when aspirated may go to the esophagus or to the airway. If the foreign body enters the airway, it may lodge at the level of the larynx, trachea, or bronchioles. When a foreign body is lodged in the airway, respiratory distress may occur.

Risk Factors/Etiology. Children less than 4 years of age are at risk for foreign body aspiration because of the size of their trachea and also because they have a tendency to put things in their mouths.

The **most commonly aspirated** food is the **peanut. Hot dogs** and **bread** are two of the most common causes of **death** from food aspiration.

Presentation. The patient may present in a variety of ways depending on where the foreign body is located and for how long the foreign body has been present. Symptoms may be minor if the object is small or may include choking. Factors involved include size of the foreign body and location. The **larynx** is the **most common** site for a foreign body if the child is **less than 1 year.** The **trachea** and **bronchi** are the **most common** sites for foreign body aspirations in children **older than 1 year**, especially the **right main stem** bronchus. The patient will exhibit stridor if the foreign body lodges in the pharynx. The history may be highly suggestive of foreign body aspiration even if the aspiration was not witnessed. There may be a sudden onset of respiratory distress. The patient may have cough, hoarseness, shortness of breath, or cyanosis.

Physical Examination. The patient who has a foreign body in the airway may have localized wheezing, stridor, or bloody sputum. The patient may have unilateral absence of breath sounds. Fever may be present if the foreign body has been present in the airway for a period of time.

However, a nonobstructing and nonirritating foreign body may cause minimal symptoms even after an extended period of time.

Diagnostic Tests. Inspiratory and expiratory chest roentgenogram may demonstrate the **ball-valve mechanism.** This mechanism causes the lung with the foreign body to remain overaerated in expiration. Visualization with a **rigid bronchoscope** is the **definitive diagnosis.** The otolaryngologist usually performs this procedure.

Treatment. Removal of the foreign body with a rigid open-tube bronchoscope should be performed. If a secondary infection is present, appropriate antibiotics should be given.

Complications. Serious problems such as aspiration pneumonia may develop. Foreign bodies lodged in the airway must be removed. Complete recovery is expected if the patient with foreign body is diagnosed and treated quickly.

Prevention. Foreign body aspiration can be prevented. Anticipatory guidance should be given to parents to keep small objects out of the reach of young children. Hot dogs, peanuts, grapes, popcorn, and peanut butter should **not** be given to young children.

Differential Diagnosis. Sometimes a patient with foreign body ingestion is thought to have asthma because he or she is wheezing. If fever is present, the patient may be thought to have pneumonia. The patient may be treated with a β-agonist or antibiotic and sent home. The patient may return to the physician and be retreated many times for "asthma" or "pneumonia" before the diagnosis of foreign body aspiration.

LARYNGOTRACHEOBRONCHITIS/CROUP

A 12-month-old child is brought to your office because of a barky cough. The mother states that over the past 3 days the child has developed a runny nose, fever, and a cough. The symptoms are getting worse, and the child seems to have difficulty breathing. He sounds like a seal when he coughs.

Definition. Laryngotracheobronchitis caused by viruses is the most common syndrome of infectious upper airway obstruction.

Risk Factors/Etiology. Parainfluenza virus is the predominant cause of croup. However, adenovirus, respiratory syncytial, influenza, and measles viruses have also been implicated. Other family members may have a mild respiratory illness, i.e., cold symptoms.

Presentation. The child with viral croup is usually between 3 months and 5 years. The patient may have a slightly elevated temperature and a mild respiratory illness, i.e., cold symptoms. These cold symptoms may be present for several days before the patient exhibits a brassy, barking cough.

Physical Examination. The patient may have low-grade fever, barking cough, and intermittent inspiratory stridor. As upper airway obstruction increases, the patient exhibits stridor at rest, nasal flaring, and suprasternal, infrasternal, and intercostal retractions. Most patients with croup will exhibit only the symptoms of stridor and slight dyspnea before recovery. However, those with more severe obstruction are at risk for hypoxia, hypercapnia, tachycardia, and eventual death from hypoventilation.

Diagnostic Tests. At times the patient's presentation for croup may be difficult to differentiate from epiglottitis. In these instances roentgenograms of the nasopharynx and upper airway may be helpful. A **"steeple"** sign indicates a narrow subglottic space.

Treatment. Children with mild laryngotracheobronchitis can be managed at home. Parents should be instructed to keep the child calm and to watch for signs of respiratory distress. Steam from a vaporizer or steam from a shower in a closed bathroom may terminate acute laryngeal spasm. "Cold steam" from a nebulizer may do the same. Using continuous humidification (either hot or cold) for a few days may prevent laryngeal spasm from recurring.

If a patient has **stridor at rest, racemic epinephrine** and **corticosteroid (dexamethasone IM)** treatment is used. The patient should be observed for 2–4 hours for rebound. If the patient improves and does not have worsening symptoms, the patient may be discharged home. Children should be hospitalized if they have worsening stridor, respiratory distress, cyanosis, restlessness, depressed sensorium, or toxic appearance, or if the parent is not reliable.

Complications/Follow-up. Complications of viral croup include middle ear and lung infections from the virus. Also, bacterial tracheitis is considered a complication of viral croup rather than a separate disease.

Differential Diagnosis. Some diseases that should be included in the differential diagnosis of laryngotracheobronchitis are spasmodic croup, bacterial tracheitis, diphtheritic croup, measles croup, and epiglottitis. **Spasmodic croup** has a presentation similar to laryngotracheobronchitis; however, there is usually no history of infection in the patient or their family. Although viruses may cause spasmodic croup, it is more often associated with triggers, such as gastroesophageal reflux, or allergic and psychological factors. **Bacterial tracheitis** usually begins as a viral laryngotracheobronchitis, which becomes a bacterial complication of a viral disease. The patient usually has thick, purulent airway secretions. *Staphylococcus aureus* is the primary cause, although parainfluenza virus type 1, *Moraxella* (*Branhamella*) *catarrhalis*, nontypable *Haemophilus influenzae*, and anaerobic organisms may also cause this entity. **Diphtheritic croup** is rare in North America but like laryngotracheobronchitis begins with "cold" symptoms. The patient may have a serous nasal discharge and a gray-white pharyngeal membrane. Children with **epiglottitis** usually have a toxic appearance, high fever, hoarseness, acute onset of symptoms, and dyspnea. Inspiratory stridor and a brassy cough (not common) may occur, causing it to be confused with laryngotracheobronchitis (see next section for more on epiglottitis).

EPIGLOTTITIS

A 2-year-old child presents to the emergency center with her parents because of high fever and difficulty swallowing. The parents state that the child had been in her usual state of health but awoke with fever of 104°F, a hoarse voice, and difficulty swallowing. On physical examination, the patient is sitting in a tripod position. The child is drooling, has expiratory stridor, nasal flaring, and retractions of the suprasternal notch and supraclavicular and intercostal spaces.

Definition. Epiglottitis is an acute inflammation of the epiglottis causing respiratory distress from airway obstruction.

Risk Factors/Etiology. *H. influenzae* type B is the most common pathogen. Although epiglotittis may occur at any age, this disease is seen more frequently in children ages 2–7 years old.

There appears to be a decrease in the prevalence of this disease as a result of the widespread use of immunization against *H. influenzae* type B. Unlike croup, family members do not usually have upper respiratory infections.

Presentation. Sudden onset of high fever, dysphagia, drooling, muffled voice, and respiratory distress may be seen on presentation. The younger patient may sit in a tripod position with the neck hyperextended.

Physical Examination. The patient is usually in respiratory distress on physical examination with the presence of stridor, nasal flaring, and retractions. The patient may have air hunger that progresses to cyanosis, coma, and death.

Diagnostic Tests. The diagnosis is made on clinical and physical findings as well as the **visualization** of an enlarged, inflamed epiglottis by direct examination or laryngoscopy by physicians who are expert in endotracheal intubation and tracheostomy. The airway is usually obtained in the operating room under controlled conditions. A lateral roentgenogram of the neck will show the "thumb print" sign in patients with epiglotittis. *H. influenzae* type B can be recovered from the blood and the epiglottis.

Treatment. An airway should be secured regardless of the degree of respiratory distress. An airway expert such as an anesthesiologist or otolaryngologist should perform intubation. Intubation is usually performed under general anesthesia in the operating room. When intubation cannot be performed, a tracheostomy should be done. After intubation a blood culture should be drawn, and IV fluids and antibiotics should be started. Third-generation cephalosporin (cefotaxime, ceftriaxone) or ampicillin with sulbactam (Unasyn) should be administered parenterally before having the culture results. The duration of intubation depends on the clinical course and patient response; however, nasotracheal intubation is usually required for an average of 1–3 days.

Complications/Follow-up. A tongue blade should never be used to examine the pharynx in a patient with suspected epiglottitis because these patients may have reflex laryngospasm and cardiorespiratory arrest during or immediately after the examination. Unless treatment is obtained, death may ensue from complete obstruction of the airway. On rare occasions meningitis, pneumonia, or otitis media may occur with epiglotittis.

Differential Diagnosis. Laryngotracheobronchitis may be difficult to differentiate from epiglottitis (see previous section). A foreign body may cause sudden onset of respiratory distress, but these children usually do not have evidence of infection, and may present with choking or coughing. Peritonsillar abscesses and retropharyngeal abscesses may also cause respiratory obstruction.

ASTHMA

A 6-year-old boy presents to his physician with end-expiratory wheezing scattered throughout the lung fields. He is noted to have nasal flaring, tachypnea, and intercostal retractions. These symptoms are triggered by changes in the weather. He has a family history of asthma and atopic dermatitis. He has never been intubated or admitted to the pediatric ICU. His last hospitalization for asthma was 6 months ago. He takes medication for asthma only when he starts to wheeze.

Definition. Asthma is a reversible obstructive airway disease that affects both small and large airways. There are three components of an asthma attack: (*1*) bronchospasm, (*2*) mucus production, and (*3*) airway edema. The obstruction caused during the asthma attack causes increased airway resistance and decreased forced expiratory volumes and flow rates. In addition, the lungs are hyperinflated; there is premature airway closure, increased work of breathing, and changes in the elastic properties of the lungs.

Risk Factors/Etiology. The etiology is not known but is believed to be genetic, environmental, or a combination. Factors such as immunologic, endocrine, infectious, autonomic, and psychologic may contribute in various degrees to different individuals.

Presentation. The presentation of individuals with asthma varies. The attack may be acute or insidious. There may be a tight nonproductive cough early.

Physical Examination. The primary manifestations of asthma include wheezing, dyspnea, a prolonged expiratory phase of respiration, accessory muscle use, and retractions. The patient may have abdominal pain from use of the abdominal muscles. The liver and spleen may be palpable secondary to hyperinflation. Because asthma is a reversible respiratory illness, **clubbing** is not seen.

Diagnostic Tests. Patients may have a family history of asthma or atopy. A history of recurrent coughs and wheezing, especially with exposure to "triggers"(exercise, viral infection, weather changes, allergens, and emotions), suggests a diagnosis of asthma. Physical examination during an episode of severe symptoms may be helpful in making the diagnosis of asthma if the patient responds to treatment with bronchodilators.

- **Eosinophilia** may be present in the blood and sputum of patients with asthma. However, sputum cultures are not helpful in asthmatic children because children rarely have bacterial superinfection. Also, obtaining an uncontaminated sputum sample from a child is very difficult.
- **Allergy skin testing** helps identify environmental allergens. **Exercise testing** may be done to demonstrate the response of an asthmatic patient. **Pulmonary function tests** before and after administration of an aerosol brochodilator are helpful in the evaluation of a patient with suspected asthma.
- **Roentgenograms of the chest** are not always required for every patient with **suspected asthma** but may be helpful to exclude other diagnoses such as pneumonia or foreign body aspiration. A roentgenogram of an asthmatic patient will show increased lung markings. The lungs may be hyperinflated. Atelectasis, especially in the right middle lobe, may be present. The ribs may appear horizontal, and there may be increased intercostal spaces.
- Roentgenograms of the chest need **not** be obtained in **every asthma exacerbation**. However, roentgenograms of the chest may be indicated in the patient with fever or suspicion of pneumothorax, if the patient's condition is not responding to therapy, or if the patient's condition is worsening.
- **Arterial blood gases** are not routinely done on the asthmatic patient. However, indications for performing arterial blood gases on these patients include (*1*) clinical deterioration, (*2*) inability to maintain oxygen saturation above 95%, and (*3*) suspicion of a pneumothorax. Obstruction during an asthma attack is nonuniform, and patients may get a ventilation–perfusion mismatch, resulting in abnormal blood gases.

  Early, P_{CO_2} decreases (hyperventilation).
  Then, P_{CO_2} increases (patient tires).
  Late, pH decreases (no buffer left).

Treatment. Avoidance of triggers is the best therapy.

Short-acting β_2-agonists:

- Most effective drugs for acute bronchospasm
- Careful instruction for proper use critical
- May need spacer/Aerochamber
- *Regularly scheduled daily use not recommended*
- Prophylactic use—exercise

Long-acting inhaled β-agonists (LABA):

- Routine *daily controller and not for acute relief*
- Dosing is every 12 hours (not BID)
- Advair—combined long-acting salmeterol + fluticasone

Daily management of an asthmatic child varies. However, based on history, physical examination, laboratory data, and need for medication, patients with asthma may be classified as having (*1*) mild intermittent, (*2*) mild persistent, (*3*) moderate persistent, or (*4*) severe persistent asthma.

- *Mild intermittent asthma*—Symptoms occur less than or equal to twice a week. Nocturnal symptoms may occur less than or equal to twice a month. Daily medication is not needed. However, PRN use of inhaled, short-acting β_2-agonists should be used when the patient is symptomatic. Treat flares with inhaled or systemic steriods if necessary.

- *Mild persistent*—Symptoms occur more than twice a week. Nocturnal symptoms occur more than twice a month. Long-term control is achieved with daily antiinflammatory drugs:
  - Inhaled steroid (low dose)
  - Alternative therapy—cromolyn-nebulizer preferred.
  - Short-acting inhaled β_2-agonists may be added when the patient is symptomatic. The intensity of therapy depends on the severity of the exacerbation.

- *Moderate persistent*—Daily symptoms plus exacerbation more than or equal to twice a week. Preferred therapy:
  - Low-dose inhaled corticosteroids (ICS) and long-acting β-agonist (LABA), or
  - Medium-dose ICS
  - Alternative therapy—low-dose ICS with leukotriene-receptor antagonist

- *Severe persistent*—Continual symptoms with frequent exacerbations. Daily medication includes:
  - High-dose ICS and LABA
  - Consider leukotriene antagonist
  - If needed, may add systemic steroids
  - Make repeated efforts to reduce systemic steroids and maintain control with high-dose inhaled steroids

Exercise-induced asthma is best prevented by inhalation of a β_2-agonist immediately before exercise.

Quick-Relief Medications: Acute Rescue

- Short acting beta-2-agonists (minutes)
- Anticholinergic agents
- Systemic corticosteroids (hours)

Long-Term Control Medications: Maintenance

- Inhaled corticosteroids
- Long-acting beta-2-agonists
- Leukotriene modifiers
- Mast-cell stabilizers
- Methylxanthines

Complications/Follow-up. Patients with asthma may develop a pneumothorax. Although rare, the numbers of deaths from asthma in children has increased. Although reasons for this increase in mortality are unknown, it is suspected that treatment may be delayed because of an overreliance on bronchodilator inhalers.

Differential Diagnosis. There is a saying "All that wheezes isn't asthma!" When assessing a patient, one should consider other causes of wheezing.

Differential Diagnosis of Wheezing

- Cystic fibrosis
- Postinfectious
- Infectious
- CHD—increased pulmonary circulation
- Ciliary dyskinesia
- Chronic aspiration
- Foreign body
- Immunodeficiency
- Congenital airway anomaly
- Extrinsic airway compression

BRONCHIOLITIS

A 6-month-old infant presents to the physician with a 3-day history of upper respiratory tract infection, wheezy cough, and dyspnea. On physical examination, the patient has a temperature of 39°C, respirations of 60 breaths/min, alae nasi flare, and accessory muscle usage. The patient appears to be air hungry, and the oxygen saturation is 92%.

Definition. Bronchiolitis is a lower respiratory infection in infants caused by inflammatory obstruction of the small airways of the lower respiratory tract.

Risk Factors/Etiology. Bronchiolitis occurs in children younger than 2 years of age with a peak incidence at approximately 6 months of age. A virus, usually **respiratory syncytial virus (RSV)**, invades the bronchioles causing obstruction from mucus, cellular debris, and edema. Other viruses that may cause bronchiolitis in infants include parainfluenza type 3 viruses, mycoplasma, and adenovirus. Infants with mothers who smoke cigarettes are at increased risk for contracting bronchiolitis.

Presentation. The patient usually has a history of upper respiratory tract infection, rhinnorhea, and sneezing. In addition, the patient develops fever of 38.5–39°C and gradually develops respiratory distress evidenced by tachypnea, wheezing, and cough. The patient may have difficulty feeding because of the rate of breathing. Mild cases resolve in 1–3 days. However, in severe cases the course is lengthened.

Physical Examination. The patient presents with rapid breathing, usually 60–80 breaths/min. The patient may have wheezing, rales, and intercostal and subcostal retractions. In severe cases the patient may be restless and irritable from air hunger. Cyanosis may be present.

Diagnostic Tests. Chest roentgenogram reveals hyperinflation of the lungs. Air trapping and peribronchial thickening may be present. Some patients will have atelectasis present. Early bacterial pneumonia cannot be excluded on radiographic grounds alone.

A complete blood count and differential are usually within normal limits. Virus may be detected in **nasopharyngeal secretions** with antigen detection, polymerase chain reaction, or culture.

Treatment. Treatment depends on the severity of the bronchiolitis. In uncomplicated cases of bronchiolitis, treatment is **symptomatic** and includes fluids, antipyretics, and humidified air or oxygen. A trial of a **bronchodilator** to relieve wheezing may be administered and should be continued if a response is obtained. **Aerosolized epinephrine** may be helpful in reducing airway edema. **Corticosteroids** are not indicated and may be harmful. **Antibiotics** are not useful unless there is a secondary bacterial infection.

Some criteria for **hospitalization** of the child with bronchiolitis include high-risk infants (e.g., premature, infants younger than 3 months, immunodeficiency, and chronic lung and congenital heart diseases), a respiratory rate greater than 60 breaths/min, Po_2 less than 60 mm Hg on room air, apnea, feeding difficulties, or if the parent is not reliable.

Ribavirin (Vibrazole), an aerosolized antiviral agent, may be considered for infants with impending respiratory failure, immunodeficiency, bronchopulmonary dysplasia, neuromuscular weakness, or congenital heart disease. Some patients may need **mechanical ventilation** if their illness progresses to respiratory failure.

Complications/Follow-up. Apneic spells may occur in infants. Mortality is less than 1%. Death may occur from prolonged apneic spells, dehydration secondary to inability to feed and loss of water vapor from rapid breathing, and uncompensated respiratory acidosis. Infants with immunodeficiency or heart or lung diseases have a poorer prognosis. A large number of children with bronchiolitis have reactive airway disease in later childhood.

At-risk infants for bronchiolitis (infants younger than 2 years with chronic lung disease or prematurity) should be given RSV immune globulin intravenous (RSV-IGIV) or monoclonal antibody (palivizumab) to RSV before and during RSV season to prevent severe RSV. Children with symptomatic congenital heart disease should not receive these because of complications, including death.

Differential Diagnosis. Bronchiolitis is often confused with asthma. In addition, cystic fibrosis, airway foreign body, heart failure, and bacterial bronchopneumonia should also be in the differential diagnosis of bronchiolitis.

CYSTIC FIBROSIS

A 3-year-old white girl presents with rectal prolapse. She is noted to be in the less than 5 percentile for weight and height. The parents also note that she has a foul-smelling bulky stool each day that "floats." They also state that the child has developed a repetitive cough over the last few months.

Definition. Cystic fibrosis is a multisystem autosomal recessive disease (found on chromosome 7) that is characterized by chronic airway obstruction and infection, malabsorption, and failure to thrive.

Risk Factors/Etiology. Cystic fibrosis is the most common fatal inherited disease of whites. Cystic fibrosis occurs in 1:3,500 white live births and 1/17,000 black infants in the United States.

The cystic fibrosis gene codes for a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). When there is a defect in the CFTR, an abnormality of chloride transport that produces abnormal mucus may occur. Should this result, problems of the lungs, gastrointestinal tract, sweat glands, and genitourinary systems may be seen. Patients with cystic fibrosis have an elevated salt content in their sweat and other secretions, difficulty clearing mucous secretions that are viscous, and chronic lung infections.

Presentation. The presentation of cystic fibrosis is variable. Meconium ileus may be the initial manifestation. Children may also present because they have a **"salty"** taste when their parents kiss them. Others have recurrent respiratory infections, initially with *S. aureus* and *H. influenzae*, and later with *Pseudomonas* and *Aspergillus*. Some children may have malabsorption secondary to pancreatic insufficiency with history of steatorrhea and fat-soluble vitamin deficiency (A, D, K, and E). Still others may present with **nasal polyps**, or **rectal prolapse**.

Physical Examination. Below are some of the physical findings that may be present in a patient with cystic fibrosis.

Respiratory—There may be an increase in the anteroposterior diameter of the chest.

The patient may have cough, tachpnea, wheezing, rales, and exercise intolerance. Nasal polyps may be present.

Meconium ileus—gastrointestinal—In approximately 20% of infants born with cystic fibrosis, the ileum is obstructed by meconium, causing abdominal distention and emesis and failure to pass meconium in the first 24–48 hours of life.

Patients with cystic fibrosis have malabsorption secondary to exocrine pancreatic insufficiency. As a result, these patients will have frequent, greasy, bulky stools and may present with failure to thrive.

On physical examination, the patient may have a protuberant abdomen and decreased muscle mass. The patient may show evidence of vitamin deficiency, especially the fat-soluble vitamins. Children with undiagnosed cystic fibrosis may present with rectal prolapse. Therefore, it is imperative to perform a sweat chloride on children with rectal prolapse to determine whether they have cystic fibrosis.

Biliary Tract—Only 2–3% of patients with cystic fibrosis will develop biliary cirrhosis. In these instances icterus, ascites, and hematemesis may be present.

Pancreas—Approximately 8% of patients with cystic fibrosis will develop insulin-dependent diabetes mellitus, causing weight loss, polyuria, hyperglycemia, and glycosuria.

Genitourinary—There is delayed sexual development in patients with cystic fibrosis. Ninety-five percent of boys will be sterile, and girls have a decreased fertility rate.

Sweat Glands—Excessive sweat loss leads to "frosting" of the skin or a salty taste when the child is kissed. **Hypochloremic alkalosis** occurs in patients with cystic fibrosis who have dehydration from warm weather or gastroenteritis.

Diagnostic Tests. The diagnosis is made by a sweat chloride test. For diagnosis, the patient must have a sweat chloride greater than 60 mEq/L.

Treatment. Therapy is important to prevent complications, and the patient should be evaluated frequently. The goal of therapy for the pulmonary system is to clear the secretions and control infections. This can be done with the use of inhalation therapy, chest physiotherapy, antibiotics, and antiinflamatories. The patient may inhale DNAse to thin secretions. Nutritional therapy is also important because the majority of these patients will lose exocrine pancreatic function and have difficulty digesting fats and proteins. Therefore, these patients should be given pancreatic enzyme replacement and vitamin supplementation, especially for vitamins A, D, K, and E. Electrolyte losses may be corrected by adding salt to the diet, although regimented salt supplements are no longer prescribed.

Complications should be treated as they arise.

Early diagnosis and treatment improve survival, but the average survival is approximately 30 years.

Complications/Follow-up. Initially the patient should be hospitalized for baseline assessment, treatment, and education. The patient should have follow-up outpatient visits every 2–3 months to allow the physician to monitor the patient and the various sequelae.

The patient may develop severe chronic lung disease and recurrent pneumonias. Complications such as atelectasis and pneumothorax should be treated. Colonization of the respiratory tract with *Burkholderia cepacia* may be associated with poor outcomes. The morbidity and mortality of cystic fibrosis is dependent on the rate of progression of lung disease. Patients with cystic fibrosis may also exhibit an exocrine pancreatic insufficiency during early life. Pancreatitis may occur in these patients as well as insulin-dependent diabetes. In addition, a hypochloremic alkalosis can be present when these patients are exposed to hot weather. Patients with cystic fibrosis may have failure to thrive.

Differential Diagnosis. Cystic fibrosis enters into the differential diagnosis of many pediatric disorders because of its multiple-system effect.

APNEA

A 5-year-old child is brought to the physician because her mother states that the child snores and keeps the other family members awake at night. She also stops breathing each night for approximately 20 s and then wakes from sleep. In addition, the mother states that the child is not growing well and has poor school performance. On physical examination the patient is pleasant and in no apparent distress. Pertinent physical findings include mouth breathing, a hyponasal voice, and 4+ tonsils without exudates.

Definition. Apnea is the cessation of breathing for greater than 20 s. **Obstructive sleep apnea** is a combination of prolonged partial upper airway obstruction and intermittent cessation of breathing resulting in disruption of sleep and breathing patterns.

Risk Factors/Etiology. Adenotonsillar hypertrophy, trisomy 21, cleft palate, macroglossia, nasal obstruction, and neuromuscular disease are risk factors for obstructive sleep apnea.

Presentation. The patient will usually present with the chief complaint of **snoring.** The child may also have restless sleep, stop breathing, and wake up frequently.

Physical Examination. The child may mouth breathe and have large tonsils and a hyponasal voice. The child may have an associated craniofacial syndrome, trisomy 21, or neuromuscular disease.

Diagnostic Tests. The diagnosis is suggested by the clinical presentation and physical examination. However, the **gold standard** for the diagnosis of obstructive sleep apnea is **polysomnography** (a sleep study test).

Treatment. Adenotonsillectomy is the treatment.

Complications. Some complications include poor growth, cor pulmonale, poor school performance, and death.

Differential Diagnosis. There are three types of apnea: (1) **central**—lack of respiratory effort, (2) **obstructive**—total airway obstruction, and (3) **mixed.** Some problems that may present as **apnea** include the following:

- **Apnea of prematurity** that occurs in premature infants less than 36 weeks of gestational age. In these patients apnea and bradycardia are seen. The **treatment** includes **theophylline** or **caffeine,** or **intubation**.
- **Cyanotic breath-holding**, i.e., breath-holding spells, are caused by prolonged expiratory apnea and cerebral anoxia. Patients exhibiting this entity are usually younger than 3 years of age and hold their breath because of anger, etc. Fainting (that is self-limited) may be associated with the event. The **treatment** is **reassurance.** If this problem persists, a seizure disorder should be ruled out.
- **Pallid breath-holding** usually occurs after a painful stimulus. During this episode, the patient will turn pale, i.e., "white," and have asystole and a seizure. The **treatment** is **atropine.** A seizure disorder needs to be ruled out.
- **Obesity hypoventilation (morbid obesity, Prader-Willi syndrome)** is usually caused by airway obstruction. It may also involve central control. Obesity, somnolence, polycythemia, and cor pulmonale are clinical features that may be seen. The **treatment** is **weight loss.**

SUDDEN INFANT DEATH SYNDROME

A 2-month-old term infant born without any complications via spontaneous vaginal delivery is brought to the emergency center via ambulance with CPR in progress. According to the mother, the patient was in his usual state of good health until 4 AM when she found the patient cyanotic and not breathing. The mother states that at midnight the infant was fed 4 ounces of formula without any difficulty. After the feeding, the child was placed to sleep in a crib. At 4 AM the mother returned to check on the infant and found the child unresponsive. She immediately called Emergency Medical Services and began CPR. The child was pronounced dead on arrival to the emergency department.

Definition. Sudden infant death syndrome (SIDS) is an unexplained death by history or by thorough postmortem examination of an infant less than 1 year old. The postmortem examination includes autopsy, investigation of the scene of death, and medical history review. It is the **most common cause of death** in infants 1–12 months of age.

Risk Factors/Etiology. There is no clear etiology for SIDS because many factors may contribute, including respiratory pattern, chemoreceptor sensitivity, arousal responses, temperature regulation, and cardiac control. The peak incidence of SIDS is at 2–3 months of age. Most deaths occur between midnight and 9 AM, and more cases occur in the winter. Some other risk factors include prematurity, lack of prenatal care, maternal smoking during pregnancy, and lower socioeconomic conditions. Prone and side sleep positions have also been considered risk factors. Infants with **apparent life-threatening events (ALTE)** have a 3–5 times increased risk of SIDS, as do infants exposed to drugs in utero. Siblings of SIDS victims have a 4–5 times increased risk of being a SIDS victim themselves.

Presentation/Physical Examination. The presentation and physical examination may vary; however, in all cases the child is less than 1 year of age, and the death is unexplainable either by history or by thorough postmortem examination.

Diagnostic Studies. There are no diagnostic studies that determine which children are at risk for SIDS.

On autopsy, mild pulmonary edema and diffuse intrathoracic petechiae may be found. There may be tissue markers of chronic asphyxia.

Treatment/Prevention. Sleep position, i.e., placing the infant on his or her **back** during sleep (unless medically contraindicated) may decrease occurrences of SIDS. Patients who have experienced **ALTE** may need home electronic monitoring of heart rate, respiratory pattern, and oxygenation.

PNEUMONIA

A 3-year-old child presents to the physician with a temperature of 104°F, tachypnea, and a wet cough. The patient's sibling has similar symptoms. The child attends daycare but has no history of travel or pet exposure. The child has a decreased appetite but is able to take fluids and has good urine output. Immunizations are up to date.

Definition. Pneumonia is an inflammation of pulmonary tissue, associated with consolidation of the alveolar spaces. It may be classified by location:

- **Pneumonitis**—lung inflammation with or without consolidation. Interstitial pneumonitis consists of inflammation of the interstitium, i.e., walls of the alveoli, alveolar sacs and ducts, or bronchioles.
- **Lobar pneumonia**—inflammation localized to one or more lobes of the lung with complete consolidation.
- **Bronchopneumonia**—inflammation centered in the bronchioles with mucopurulent exudate.

Risk Factors/Etiology. Infectious agents such as viruses, bacteria, fungi, and parasites may cause pneumonia. Inhaled toxins may cause aspiration pneumonia. Viral pneumonia is the most common pneumonia in childhood.

Presentation/Physical Examination. The clinical triad for pneumonia consists of **fever, tachypnea,** and **cough** (Table 16-1).

- Patients with **viral pneumonia** may exhibit cough, wheezing, and stridor.
- Patients with **bacterial pneumonia** have cough, high fever, and shortness of breath. There are decreased breath sounds and dullness to percussion over the consolidation on physical examination.
- Patients with **mycoplasma pneumonia** or **"walking" pneumonia** usually appear to be less ill than their chest roentgenogram demonstrates. They may complain of a nonproductive cough.
- Infants with **chlamydia pneumonia caused by** *Chlamydia trachomatis* have a **"staccato"** cough and may have a history of eye discharge during day 5–14 of life. These patients usually have a low-grade or no fever. The mother may give the history of having a vaginal infection during pregnancy. Patients with chlamydia pneumonia are usually 6 weeks to 6 months of age.
- Patients with **aspiration pneumonia** may have a history of inhaling a toxin or aspirating food. Wheezing may be heard on auscultation. Cyanosis may be present.

Diagnostic Tests. The **chest roentgenogram** in patients with

- **Viral pneumonia** shows diffuse streaky infiltrates.
- **Bacterial pneumonia** shows lobar consolidation.
- **Mycoplasma pneumonia** shows an interstitial pattern found most commonly in the lower lobes.
- **Chlamydia pneumonia** shows hyperinflation or a ground glass appearance.
- **Aspiration pneumonia** shows alveolar and rarely reticular infiltrates that are usually localized but oftentimes bilateral.

The **complete blood count** in **viral pneumonia** will have a normal white blood cell count with a predominance of lymphocytes. In **bacterial pneumonia,** patients have an increased white blood cell count with neutrophilia. Patients with **chlamydia pneumonia** have normal white blood cell counts, but eosinophilia may be present.

Isolation of an organism from **blood** or **pleural fluid** is diagnostic. A **sputum** culture identifies the organism; however, sputum cultures are difficult to obtain in children and are rarely done. **Nasopharyngeal swabs** may be performed to detect viral agents. **Serum cold hemagglutinins** in a 1:64 titer or a positive **IgM *Mycoplasma pneumoniae*** support the diagnosis of *M. pneumoniae.*

Treatment. When **appropriate**, antibiotics should be given. The choice of antibiotic depends on the organism suspected and the age of the child. Suggested treatments are as follows:

- **Chlamydia pneumonia**—usually seen in patients 6 weeks to 6 months old, erythromycin ethyl succinate drops (EES) by mouth for 14 days. Mothers and their sexual partners also need to be treated.
- **Group B Streptococcus, *Escherichia coli,* Listeria**—usually seen in patients from birth to 2 months, ampicillin plus an aminoglycoside or ampicillin plus a third-generation cephalosporin via intravenous administration. A full septic workup including lumbar puncture should be performed.
- ***S. pneumoniae, H. influenzae,* and Staphylococcus**—usually seen in patients 2 months old to 5 years old. For in-patient therapy, a cephalosporin such as cefuroxime or ceftriaxone may be given intravenously. Remember that if you suspect bacteremia or sepsis in a patient younger than 2 years of age, then cefuroxime should not be used because it does not cross the blood–brain barrier until after an extended period of time. For outpatient therapy one might consider amoxicillin, amoxicillin-clavulinate, or erythromycin plus sulfasoxazole.
- ***M. pneumoniae***—usually seen in patients older than 5 years old along with *S. pneumoniae.* The treatment of *Mycoplasma* pneumonia is erythromycin, azithromycin, or clarithromycin.

Complications. Empyema may be a complication of pneumococcal and staphylococcal pneumonia. This complication is seen more commonly in infants than in older children.

Table 16-1. Pneumonia in Young Infants

Age	Organism	Clinical Features
0–28 d	GBS, Gram– organisms	Severe, sepsis
	Listeria monocytogenes	
3 wk–3 mo	*Chlamydia trachomatis*	Afebrile, subacute
	Respiratory syncytial virus (RSV)	Winter to early spring
	Parainfluenza	Like RSV
	Streptococcus pneumoniae	Most common bacterial cause
	S. aureus	Severe complications
	Bordetella pertussis	Severe cough, apnea

Table 16-2. Pneumonia in Older Infants and Children

Age	Organisms	Clinical Features
4 mo–4 y	Viruses	Most common cause
	S. pneumoniae	Most common—focal infiltrate
	Haemophilus influenzae	Rare in developed countries
	Mycoplasma pneumoniae	Older children
5–15 y	*M. pneumoniae*	Most common cause
	S. pneumoniae	Focal infiltrate

Cardiovascular

17

INTRODUCTION

History. As always, a history is extremely important in arriving at any diagnosis. Children, however, do not present with the typical features of congestive heart failure that are seen in adults. Consequently, the age is very important when assessing a child in possible heart failure. **Infants present with feeding difficulties, easy fatigability, sweating while feeding, and rapid respirations.** An **older child** may have **shortness of breath and dyspnea on exertion.** Orthopnea, edema, and nocturnal dyspnea are uncommon.

Physical Examination. One has to know normal heart rates for ages to determine tachycardia. Height and weight should be assessed to determine proper growth. Upper and lower extremity blood pressures should always be obtained, as well as palpation of upper and lower extremity pulses. **Rales** on auscultation may indicate pulmonary edema and left-sided heart failure. **Hepatomegaly** is suggestive for right-sided heart failure. **Cyanosis and clubbing** result from hypoxia. A prominent precordium is seen with cardiomegaly. Palpation may reveal cardiac impulses and thrills. **Murmurs** may be auscultated and are graded on the following scale:

Table 17-1. Heart Murmur Gradation

Grade	Quality
1	Soft, difficult to hear
2	Easily heard
3	Louder but no thrill
4	Associated with thrill
5	Thrill + audible with edge of stethoscope
6	Thrill + audible with stethoscope just off chest

Features of the Cardiac Exam

Apical heave	Left ventricular enlargement
Substernal thrust	Right ventricular enlargement
Hyperdynamic precordium	Volume overload
Silent precordium	Pericardial effusion or cardiomyopathy
Thrill	Palpable equivalent of murmur at area of maximum auscultation

Ejection click	Early-to-mid systole; associated with pulmonary artery (PA) or aortic stenosis or dilatation
S_3	May be normal in older children and adolescents with slow heart rate
Gallop	S_4 always abnormal; poor compliance of ventricle; atrial kick during ventricular filling
Systolic ejection murmur	Usually implies increased flow or stenosis across one of the ventricular outflow tracts
Pansystolic murmur	Related to blood exiting contracting ventricle via an abnormal opening or atrioventricular (AV) valve insufficiency
Continuous murmur	Systolic murmur that spills into diastole and indicates continuous flow
To-and-fro murmur	Systolic component ends before S_2, and diastolic murmur begins after semilunar valve closure (e.g., aortic stenosis [AS] and aortic insufficiency)
Late systolic murmur	May be heard after a midsystolic click; hallmark is mitral valve prolapse
Diastolic murmur	Blowing, left sternal border, decrescendo
Venous hum	Turbulence of blood flow in jugular venous system; hear in anterior upper chest and neck in systole and diastole
Wide pulse pressure (>40 mm Hg)	Thyrotoxicosis, patent ductus arteriosis (PDA), AI, AV fistula
Narrow pulse pressure	Pericarditis, pericardial effusion, tamponade, significant tachycardia, AS
Narrow split S_2	Conditions that delay aortic valve closure or accelerate PV closure; PA, hypertension, AS, left bundle branch block (LBBB)

Location of murmurs

Upper right sternal border

- AS

Upper left sternal border

- Pulmonic stenosis (PS), pulmonary ejection murmur
- Acute stress disorder (ASD), PDA
- Coarctation
- Total anomalous pulmonary venous return (TAPRV)

Lower left sternum border

- Ventricular septal defect (VSD), AV canal
- Still murmur
- Tetralogy of Fallot
- Tricuspid atresia

Apex

- Still murmur
- Mitral valve prolapse
- Idiopathic, hypertrophic subaortic stenosis (IHSS), asymmetric septal hypertrophy

Diagnostic Tests. These include the chest radiograph (to evaluate heart size, lung fields, ribs for notching, and the position of the aorta and pulmonary arteries), the electrocardiogram, echocardiography (Doppler and color flow), magnetic resonance imaging, cardiac catheterization, angiography, and exercise testing.

Embryology. Knowledge of cardiac embryology is helpful in understanding congenital cardiac lesions, their presentation, symptoms and treatment. Please refer to the figure.

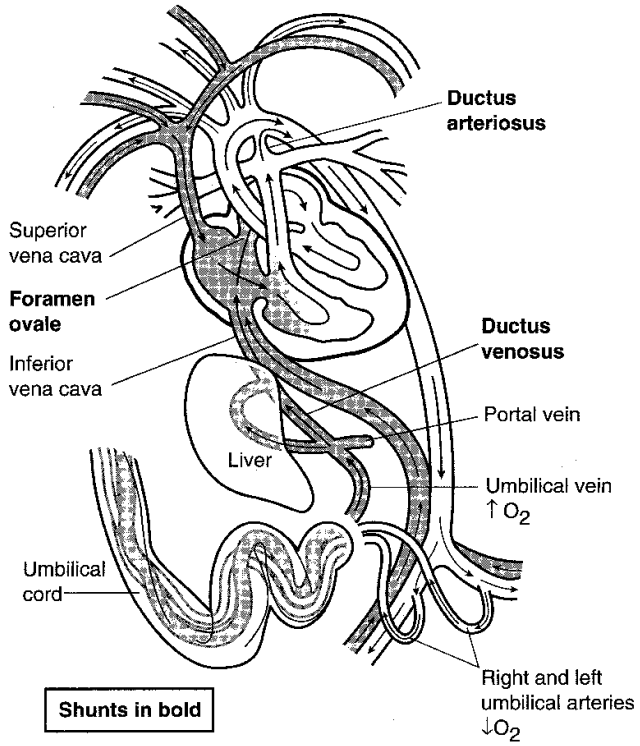


Figure 17-1. Fetal Circulation

INNOCENT MURMURS

A 5-year-old boy is seen for routine physical examination. Parents voice no concerns. Weight and height are at the 75th percentile. Vital signs are normal. Physical examination is remarkable for a soft musical 2/6 murmur best heard at the left lower sternal border.

Definition. Innocent murmurs are also known as **functional, normal, insignificant, or flow** murmurs. These result from flow through a normal heart, vessels, and valves.

Risk Factors/Etiology. Most innocent murmurs are heard between **3 and 7 years** of age. More than 30% of children may have an innocent murmur heard at some time in their lives.

Presentation. Innocent murmurs are usually heard on routine physical examination. They are also easily heard during times of increased cardiac output such as during fever, infection, or anxiety. An innocent murmur is **never diastolic**, is a soft, vibratory or musical systolic ejection murmur best heard at the **left lower to midsternal** border. Innocent murmurs are never greater than **grade 2/6**.

Diagnostic Tests. Innocent murmurs do not require further evaluation.

Treatment. No treatment is necessary, as they have no hemodynamic significance. Only reassurance of parents and patient is recommended.

Differential Diagnosis. Pulmonary flow murmurs are also innocent murmurs. These are higher pitched, blowing, early systolic murmurs best heard in the second left parasternal space with the patient lying down. A **venous hum** is heard in the neck or anterior chest. It is heard in systole and diastole but can disappear with compression of the jugular vein.

CONGENITAL HEART DISEASE

Introduction

Congenital heart disease occurs in about 0.5–0.8/100 live births. Most lesions occur between 15 and 80 days of gestation. The diagnosis is usually made early in life: 50–60% of patients are diagnosed by 1 month of age. Murmurs may not be heard initially in life, and symptoms may not be present until pulmonary vascular resistance falls. Thirty percent of patients with congenital heart disease have other anatomic abnormalities. Although the cause of congenital heart disease is unknown in most cases, there are associations with teratogens such as alcohol and rubella, as well as genetic predispositions (trisomies, Marfan, Noonan, DiGeorge). The recurrence risk of congenital heart disease is 2–6%. Congenital heart disease can be classified according to the following table.

Table 17-2. Congenital Heart Disease

	Shunting		
Stenotic	**Right → Left**	**Left → Right**	**Mixing**
Aortic stenosis	Tetralogy of Fallot	Patent ductus	Truncus
Pulmonic stenosis	Transposition	VSD	TAPVR
Coarctation	Tricuspid atresia	ASD	HLH

Acyanotic Heart Disease

Ventricular septal defect (VSD)

A 3-month-old child presents with poor feeding, poor weight gain, and tachypnea. Physical examination reveals a harsh, pansystolic 3/6 murmur at the left lower sternal border, and hepatomegaly.

Definition. VSD is the most common congenital cardiac malformation. It accounts for 25% of congenital heart disease, and is found in association with other heart defects.

Presentation. Manifestations depend on the **size of the defect**, and the **pulmonary flow** and pressure. **Small defects** limit the size of the shunting. **Large defects** allow for more left to right shunting, which is determined by differences in systemic and pulmonary vascular resistances. Persistently **high pulmonary blood flow** leads to development of increased pulmonary vascular resistance secondary to **medial hypertrophy** of the pulmonary vessels. When the pulmonary vascular resistance equals the systemic vascular resistance, the previously left to right shunt becomes bidirectional or right to left, leading to cyanosis, a condition known as **Eisenmenger** physiology. Small defects are usually asymptomatic. The VSD murmur is typically a harsh holosystolic murmur at the left lower sternal border. A thrill is frequently associated. Large defects can cause dyspnea, feeding difficulties, poor growth, and sweating.

Diagnostic Tests. Chest radiographs reveal a large heart, although it may be normal in small defects. **ECG** can suggest left ventricular hypertrophy. **Biventricular hypertrophy** and notched peaked P waves are seen in large defects. Echocardiography reveals the defect and estimates shunt size.

Treatment. Small defects close spontaneously in 30–50% of cases by 2 years of age and require no therapy. Antibiotic prophylaxis for endocarditis is required. **Medical management** includes controlling heart failure, promoting normal growth, and preventing pulmonary vascular disease. **Surgical closure** is recommended for failure of medical management, or large defects with pulmonary hypertension that has not yet become severe. Patients with small VSDs and those having undergone surgical repair without residua have an excellent long-term prognosis.

Complications. Large defects can result in heart failure and failure to thrive. All patients with unrepaired VSD are at risk for **endocarditis**. Pulmonary hypertension is another complication.

Atrial septal defect (ASD)

Definition. ASDs occur anywhere along the atrial septum. **Ostium secundum** defects are the most common.

Presentation. Many patients are **asymptomatic**. **Exercise intolerance** may develop in older children. A systolic ejection murmur is heard in the left mid and upper sternal border; usually there is no thrill. A **wide fixed split of S2** is characteristic.

Diagnostic Tests. Chest radiograph shows an **enlarged right atrium and ventricle**, depending on the size of the shunt. **Right atrial enlargement** and **right ventricular conduction delay** (**rSR'**) may be evident on ECG. **Echocardiography** shows right ventricular volume overload and demonstrates the ASD.

Treatment. Surgical closure with open heart surgery or occlusion devices is recommended.

Complications. Symptoms do not appear until the third decade. Endocarditis is rare and prophylaxis is not recommended. **Atrial dysrhythmias, valvular insufficiency** (mitral, tricuspid), and heart failure may occur.

Patent ductus arteriosus (PDA)

Definition. PDA results from failure of closure of the ductus arteriosus. This leads to blood flow from the aorta to the pulmonary artery.

Risk Factors/Etiology. PDA is more common in girls by a 2:1 margin. It is also associated with **maternal rubella** infection. It is common in **premature infants.** PDA can be beneficial in providing pulmonary blood flow when there is an associated right ventricular outflow tract obstruction, or in supplying systemic flow in coarctation of the aorta.

Presentation. A small PDA presents no symptoms. Large PDAs can cause heart failure similar to large VSDs. Large PDAs cause a **wide pulse pressure** and **bounding arterial pulses.** An apical heave may be observed, and a thrill may be heard at the second left intercostal space. The characteristic murmur is described as a **machinery** or **to and fro murmur** heard in both systole and diastole. It can be less prominent or not heard in diastole in infants or in the presence of increased pulmonary vascular resistance.

Diagnostic Tests. Chest radiographs show a prominent pulmonary artery and increased pulmonary vascular markings. Heart size may be normal or slightly enlarged. Echocardiogram shows the PDA.

Treatment. PDA in premature infants may close spontaneously or respond well to indomethacin. They rarely close spontaneously after infancy, and surgical or catheter closure is recommended.

Complications. Complications include congestive heart failure and infective endarteritis.

Endocardial cushion defects (A-V Canal)

Definition. This occurs when both ASDs and VSDs occur which are contiguous, and the atrioventricular valves are also abnormal.

Risk Factors/Etiology. Patients with trisomy 21 are at higher risk.

Presentation. Patients with large AV defects tend towards **heart failure early in infancy,** with hepatomegaly and failure to thrive. Increased pulmonary blood flow over time leads to pulmonary vascular disease and **Eisenmenger physiology.** A systolic thrill is appreciable on physical examination. With increased pulmonary blood flow, S2 becomes widely split. A low-pitched diastolic murmur may be heard. The first heart sound may be accentuated.

Diagnostic Tests. Chest radiographs show a markedly enlarged heart, reflecting enlargement of all chambers. **Electrocardiogram** reveals left-axis deviation, biventricular hypertrophy, right ventricular conduction delay, and tall P waves. **Echocardiogram** shows right ventricular enlargement; a common AV valve is seen. Color flow reveals **shunting at both atrial and ventricular levels.**

Treatment. Surgery is performed during infancy because of the high risk of early development of pulmonary hypertension. The defects are patched, and the cleft mitral valve is repaired.

Complications. Complications and prognosis depend on the size of the shunt and the amount of pulmonary vascular resistance. Without surgery, **death** from heart failure will result. Complications from surgery include **heart block,** which may require a pacemaker.

Coarctation of the aorta

Definition. Coarctation of the aorta is a constriction of the aorta arising at any point. The majority (98%) occur just below the origin of the **left subclavian artery.**

Risk Factors/Etiology. Coarctation is more common in boys 2:1. There is an increased incidence in **Turner syndrome,** which is associated with bicuspid aortic valve.

Presentation. A coarctation may be missed in a newborn while the ductus is open. Severe coarctation in infancy presents with congestive heart failure, metabolic acidosis, and lower body hypoperfusion. Upper or lower extremity pulse delay is a classic sign, as is hypertension in the upper extremities and hypotension in the lower extremities. Hypertension in the right upper extremity versus the left upper extremity suggests a coarctation around the left subclavian. A short systolic murmur may be heard along the left sternal border at the third to fourth intercostal space.

Diagnostic Tests. Chest radiographic findings depend on the age of the patient and the severity of the obstruction. **Severe coarctation in infancy reveals cardiac enlargement** and increased pulmonary vascular markings. Older patients show **rib notching** from enlargement of the intercostals providing collateral blood flow. **ECG** in infancy shows right ventricular hypertrophy. Left ventricular hypertrophy is seen in later childhood. **Echocardiography** shows the narrowed segment and a hypopulsatile descending aorta.

Treatment. Surgical correction should be performed as soon as the patient is stable. In neonates, the ductus is kept open with an infusion of prostaglandin E_1.

Complications. Patients with coarctation may develop hypertension, which can lead to premature coronary artery disease, heart failure, encephalopathy, and intracranial hemorrhage. Adults are at higher risk for endocarditis.

Cyanotic Heart Disease

Tetralogy of Fallot (TOF)

> A 6-month-old infant is prone to episodes of restlessness, cyanosis, and gasping respirations. Symptoms resolve when he is placed in the knee chest position. Physical examination reveals an underweight infant, with a harsh holosystolic murmur and a single second heart sound.

Definition. TOF is defined as pulmonary stenosis, VSD, dextroposition of the aorta (overriding), and right ventricular hypertrophy. It is the most common cyanotic congenital heart disease.

Presentation. Symptoms depend on the size of the VSD and the degree of right ventricular outflow tract obstruction. **Acyanotic (pink) tetralogy** occurs when there is sufficient pulmonary blood flow caused by mild obstruction and the shunting across the VSD is balanced. Typically, however, **patients present with cyanosis,** delayed growth and development, and dyspnea. **Paroxysmal hypercyanotic attacks** (hypoxic, blue, or tet spells) are described in the question. **Clubbing** of fingers and toes occurs with chronic hypoxia. A loud, harsh systolic ejection murmur is heard. **S2 is single** or very soft because of the pulmonary stenosis.

Diagnostic Tests. Chest radiographs reveal a **boot-shaped heart (coeur en sabot)** with uptilted apex. **Lung fields are clear** reflecting decreased pulmonary blood flow. ECG shows right ventricular hypertrophy and right-axis deviation. Echocardiogram reveals the anatomic abnormalities.

Treatment. Medical management includes maintaining the ductus open in severe right-sided obstructive lesions, but **surgical correction** is the definitive treatment. Blue spells are treated with knee chest position, sedation, oxygen, and avoiding acidosis. β-Blockade with propranolol, appropriate fluid status, and maintaining the hematocrit at 55–65% are also helpful.

Complications. With earlier surgical correction, complications have become less common. **Cerebral thrombosis** occurs more commonly with extreme polycythemia and dehydration. Patients are usually **less than 2** years of age. **Brain abscess**, while less common than thrombosis, is more common in patients older than 2 years. Tet patients are at higher risk for bacterial **endocarditis.**

Transposition of the great vessels

Definition. Transposition occurs when the aorta arises from the right ventricle and the pulmonary artery from the left ventricle, resulting in a parallel circulation. By definition there is some communication at the atrial, septal, or ductal level.

Risk Factors. Transposition is more common in infants of diabetic mothers and in boys.

Presentation. Transposition is the most common congenital heart disease to present with cyanosis in the first 24 h of life. Symptoms of cyanosis and heart failure present within hours to days after birth. The second heart sound may be single and loud. A murmur may or may not be present.

Diagnostic Tests. Chest radiographs demonstrate increased pulmonary blood flow as the pulmonary vascular resistance decreases. The appearance of an **egg on a string** is caused by the change in relationship of the great vessels as they exit the heart. Arterial oxygenation is low and does not respond appreciably to supplemental oxygen. Echocardiograph shows the transposition.

Treatment. Prostaglandin E_1 to maintain the ductus open is imperative until **surgical correction** is performed.

Pulmonary atresia

In pulmonary atresia, right ventricular blood backs up to the right atrium and is shunted across the foramen ovale. Cyanosis occurs after 2–3 days when the ductus closes. There is usually no murmur, but a **single second heart sound** is heard. ECG shows the **tall spiked P waves of right atrial enlargement** and also shows **left ventricular hypertrophy**. Treatment consists of maintaining the ductus open until corrective surgery is performed.

Tricuspid atresia

Tricuspid atresia also causes right ventricular outflow tract obstruction. In this case, there is no outlet from the right atrium to the right ventricle, and blood shunts across the foramen ovale. Pulmonary blood flow is determined by a VSD or PDA. Patients present with **cyanosis usually at birth**. A pansystolic murmur is heard along the left sternal border, and **S2 is single**. Chest radiograph shows **decreased pulmonary blood flow**. ECG shows left-axis deviation and left ventricular hypertrophy. Definitive treatment is **surgical correction.**

Total anomalous pulmonary venous return (TAPVR)

In TAPVR all the pulmonary veins drain back into the systemic venous circulation through a circuitous route. These veins have a high risk of obstruction, leading to pulmonary congestion and pulmonary hypertension. **Mixed blood reaches the left atrium through an ASD or foramen ovale.** With mild obstruction of the veins, a large left to right shunt exists, which leads to pulmonary

artery hypertension. With no obstruction, cyanosis is usually absent. Chest radiograph shows the characteristic **"snowman" pattern or figure 8**. ECG shows right ventricular hypertrophy.

Truncus arteriosus (TA)

In TA, **a single vessel arises from the ventricles**, supplying systemic, pulmonary, and coronary blood flow. **A VSD is always present**. Cyanosis does not present initially because of the somewhat high pulmonary vascular resistance at birth causing normal pulmonary blood flow. As the resistance drops, blood flow increases and if left untreated results in increased pulmonary vascular resistance and Eisenmenger physiology with cyanosis. Clinically, infants can present with **dyspnea and heart failure**. A systolic ejection murmur with thrill is found along the left sternal border. Treatment consists of surgical correction.

Hypoplastic left heart (HLH)

HLH includes all the anomalies related to underdevelopment of the left heart. This results in a **small left heart,** and the right ventricle is forced to do all the work, which it, of course, was not designed to do. This results in **inadequate systemic circulation** and pulmonary venous hypertension. Infants quickly develop **cyanosis, dyspnea, and hepatomegaly. Cardiomegaly** develops rapidly on chest radiograph. **ECG shows right ventricular hypertrophy**. Treatment is surgical correction.

MYOCARDIAL DISEASES

Myocarditis

> A 7-year-old girl presents to the office with a 3-week history of progressive dyspnea, malaise, and fatigue. She has recently recovered from a viral syndrome. Physical examination is remarkable for a holosystolic murmur and hepatomegaly.

Definition. Myocarditis is an **inflammation of the myocardium.**

Risk Factors/Etiology. Myocarditis has multiple etiologies. **Viral causes are the most common and include adenovirus and Coxsackievirus B.** Bacteria (diphtheria), rickettsia, fungi, and parasites are also infectious causes of myocarditis. Connective tissue and granulomatous diseases, as well as toxins, are also responsible for causing myocarditis.

Presentation. Heart failure is the most common presentation. Arrhythmias and sudden death are less common. Patient age influences the presentation, with infants having a more acute and fulminant presentation. **Viral myocarditis is usually preceded by a viral infection**. Patients can present with fever, heart failure, respiratory distress, and cyanosis.

Diagnostic Tests. Erythrocyte sedimentation rate, creatine kinase, and lactate dehydrogenase may all be elevated. **Serum viral titers** are helpful only if positive. **Polymerase chain reaction** can identify specific viruses. **Chest radiograph** shows a large heart and pulmonary edema. **ECG** shows sinus tachycardia, reduced QRS complex, and abnormal S and ST waves. **Echocardiography** shows poor ventricular function and possible pericardial effusions, as well as absence of congenital heart disease and of coronary involvement. **Endomyocardial biopsy confirms the diagnosis of myocarditis.**

Treatment. Treatment includes management of heart failure and arrhythmias. Pericardiocentesis is performed to alleviate the tamponade if present. The role of steroids is controversial. Refractory heart failure is ultimately treated with heart transplantation.

Prognosis. Most patients do very poorly without therapy. Spontaneous resolution can occur.

Endocardial Fibroelastosis (EFE)

Definition. EFE is characterized by a thickened, white, fibroelastic endocardium. It is divided into **primary EFE**, in which there is no predisposing valvular lesion or congenital anomaly, and **secondary EFE**, in which severe left-sided obstructive heart disease is present. Primary EFE shows a dilated left ventricle whereas secondary EFE has a contracted ventricular cavity.

Presentation. Clinical manifestations include **congestive heart failure**; dyspnea and poor feeding are seen in infants.

Diagnostic Tests. Chest radiograph shows an enlarged heart. **ECG** shows left ventricular enlargement and left ventricular strain. **Echocardiograph** shows a poorly functioning ventricle.

Treatment. Heart transplantation is indicated after failure of medical management of congestive heart failure.

ACUTE RHEUMATIC FEVER

A 6-year-old girl complains of severe joint pains of her elbows and wrists. She has had fever for the past 4 days. Past history reveals a sore throat 1 month ago. Physical examination is remarkable for swollen, painful joints and a heart murmur. Laboratory tests show an elevated erythrocyte sedimentation rate and high antistreptolysin (ASO) titers.

Risk Factors/Etiology. Acute rheumatic fever is caused by infection with **group A β-hemolytic streptococci** (GABHS). It is most commonly seen in those who are susceptible to infections by GABHS, namely, **5- to 15-year-olds**. Skin infections with GABHS do not predispose to rheumatic fever; however, upper respiratory infections do.

Presentation. Acute rheumatic fever usually presents 1–3 (2–6) weeks after a **preceding streptococcal pharyngitis.** The **Jones criteria** for diagnosis include the clinical signs and symptoms.

Diagnosis. The diagnosis is based on the Jones criteria.

Table 17-3

Major	Minor
Carditis	Fever
Polyarthritis (migratory)	Arthralgia
Erythema marginatum	Elevated acute phase reactants (ESR < CRP)
Chorea	Prolonged PR interval on ECG
Subcutaneous nodules	*Plus* evidence of preceding streptococci infection

Acute rheumatic fever is diagnosed if there are **two major criteria, one major and two minor plus preceding streptococci infection, and chorea without any other explanation.**

If arthritis is one of the presenting major criteria, then arthralgia cannot be one of the presenting minor criteria.

A useful mnemonic for the major Jones criteria is the word **JONES:** Joints, ♥ (carditis), Nodules, Erythema, and Sydenham chorea; or **ACCES:** Arthritis, Chorea, Carditis, Erythema, Subcutaneous nodules.

Treatment. Management of acute rheumatic fever begins with treatment of the streptococcal infection and monthly penicillin prophylaxis. **Salicylates** help control the arthritis and also treat carditis without failure. **Steroids** are used when there is carditis with heart failure. **Heart failure** is treated conventionally.

Complications. Valvular disease is the most important complication of rheumatic fever. In order of frequency, the mitral, aortic, tricuspid, and pulmonary valves may be involved.

ENDOCARDITIS

A 6-year-old boy has had high intermittent fevers for 3 weeks, accompanied by chills. He has a past history of bicuspid aortic valves and recently had dental work.

Risk Factors/Etiology. ***Streptococcus viridans*** is the most common cause of endocarditis, although in some series ***Staphylococcus aureus*** is more common, certainly if there is no underlying heart disease. ***S. viridans* is more common after dental procedures.** ***Pseudomonas aeruginosa*** and ***Serratia marcescens*** are seen more commonly in intravenous drug abusers. Fungal causes are seen after open-heart surgery. Endocarditis is most often associated with **congenital or rheumatic heart disease. Surgical or dental procedures** are often the predisposing incident. The highest risk occurs in patients with high-velocity blood flow, i.e., VSD and left-sided obstructive lesions.

Presentation. Onset of symptoms may be acute or insidious. They include persistent **fever, chills**, arthralgias, myalgias, **development of new murmurs**, splenomegaly, and petechiae. Neurologic complications are associated with *S. aureus.* Skin manifestations occur later in the disease and probably represent a vasculitis. These include **Osler nodes** (tender nodules on the finger and toe pads), **Janeway lesions** (painless hemorrhagic lesions on palms and soles), and **splinter hemorrhages** (linear lesions beneath the nails).

Diagnosis. A positive blood culture is the most important piece of information in establishing the diagnosis. Leukocytosis, increased sedimentation rate, and anemia are helpful but secondary to the blood culture. Echocardiography may reveal vegetations on the valves.

Treatment. Antibiotics are the mainstay in the treatment of endocarditis. Therapy should continue for 4–6 weeks. Congestive heart failure if present should also be treated. Prevention is with antibiotic prophylaxis before and after dental or surgical procedures.

Complications. Mortality is 20–25%. Complications include heart failure and systemic embolisms.

Endocarditis Prophylaxis

Table 17-4. Prophylaxis and Cardiac Conditions

Recommended for Prophylaxis	
High risk	Prosthetic valves
	Previous endocarditis
	Complex congenital heart disease (CHD)
	Pulmonary shunts or conduits
Moderate risk	Most other CHD
	Acquired valvular disease
	Idiopathic hypertrophic subaortic stenosis
	Mitral valve prolapse (MVP) with regurgitation or thickened valves
***Not* Recommended for Prophylaxis**	
Isolated secundum ASD	
Surgical repair of ASD, VSD, PDA	
Coronary artery bypass	
MVP without regurgitation or thickened valves	
Kawasaki without valvular dysfunction	
Rheumatic fever without valve dysfunction	
Pacemakers and defibrillators	

Table 17-5. Procedures Recommended for Prophylaxis

Respiratory	Tonsil/adenoidectomy
	Surgery of respiratory mucosa
	Rigid bronchoscopy
Gastrointestinal	Esophageal varices, sclerosis
	Dilation of esophageal strictures
	ERCP
	Biliary surgery
	Any surgery of intestinal mucosa
Genitourinary	Prostatic surgery
	Cystoscopy
	Urethral dilatation
Dental Procedures	

Table 17-6. Antibiotics Used for Prophylaxis

	Dental, Oral, Respiratory, or Esophageal Procedures	Gastrointestinal or Genitourinary Procedures
Standard	Amoxicillin No PO—ampicillin	—
High risk	—	Ampicillin and gentamicin
Moderate risk	—	Amoxicillin or ampicillin
Alternative(s), if patient is allergic	Clindamycin Cephalosporin Macrolide	High risk—vancomycin and gentamicin Moderate risk—vancomycin

HYPERTENSION

A 5-year-old girl is noted to have blood pressure above the 95th percentile on routine physical examination. The rest of the examination is unremarkable. Her blood pressure remains elevated on repeat measurement over the next few weeks. Past history is remarkable for a treated urinary tract infection 1 year ago. Complete blood cell count is normal; urinalysis is normal. Blood urea nitrogen is 24 mg/dl and creatinine is 1.8 mg/dl.

Definition. Systemic hypertension is defined as blood pressure above the 95th percentile for age on repeated measurements over a 6-week period.

Risk Factors/Etiology. Hypertension can be divided into primary (essential) or secondary types. **Primary hypertension** usually has no known underlying cause. Predisposing factors include **heredity, salt intake, stress, and obesity**. It is more commonly seen in adolescents and adults. **Secondary hypertension** is caused by an associated disease. It is more common in **infants and younger children.** Secondary hypertension in children is most commonly caused by **renal disease (75–80%)**. A prior urinary tract infection is seen in 25–50% of cases, often related to an obstructive lesion of the urinary tract. In newborns, a history of **umbilical artery catheterization** may be elicited, with resultant thrombus of the renal artery.

Presentation. Hypertension usually presents no symptoms, especially in adolescents with essential hypertension, and is diagnosed on routine examination. Headaches, dizziness, vision changes, and seizures may be present.

Diagnostic Tests. Blood pressure should be measured over several visits and compared with normal values for age. Blood pressure should be taken in all extremities to **rule out coarctation** of the aorta. All children with secondary hypertension should have a **renal evaluation,** including culture, ultrasound, renin levels, blood urea nitrogen, and creatinine. Echocardiography assesses ventricular function and size.

Treatment. Therapy of hypertension in children is the same as in adults: diet, exercise, and medications. Pharmacologic management includes angiotensin-converting enzyme inhibitors, calcium-channel blockers, β-blockers, and diuretics.

Gastroenterology

18

ABDOMINAL PAIN

Abdominal pain is a common childhood complaint. It is divided into two types, acute and chronic.

Acute Abdominal Pain

Risk Factors/Etiology. Acute gastroenteritis is the most common cause of acute abdominal pain. The age of the patient helps in the differential diagnosis.

Presentation. Abdominal pain can be diffuse or localized. Descriptions vary, and include sharp, cramping, and colicky. Nausea, vomiting, diarrhea, and fever may accompany the pain.

Diagnostic Tests. Helpful tests include complete blood cell count (CBC), urine analysis, pregnancy test if applicable, serum amylase, chest radiograph, abdominal radiographs, and computed tomographic (CT) scan of the abdomen.

Differential Diagnosis. A good history and physical is important in establishing the diagnosis. In children **less than 2 years of age, trauma, intussusception, incarcerated hernia, volvulus, and urinary tract infection** are causes of acute abdominal pain. In the 2- **to 5-year-old age group, sickle cell anemia, lower lobe pneumonia, and urinary tract infection** should be considered. **Meckel diverticulum** is a possibility in infants and children. Any older child or adolescent with **appendicitis** can present with acute abdominal pain. Adolescent girls may have **mittelschmerz, ectopic pregnancy, or pelvic inflammatory disease**. Other causes include pancreatitis, Henoch-Schönlein purpura, mesenteric adenitis, lead poisoning, diabetic ketoacidosis, renal stones, and cholecystitis.

Table 18-1. Some Causes and Symptoms of Acute Gastrointestinal Abdominal Pain

Pancreatitis	Epigastric, LUQ Acute onset Referral—back Constant, sharp, boring Nausea and vomiting, tenderness
Intestinal obstruction	Acute or gradual Periumbilical—lower abdomen Referral—back Alternating cramping and painless periods Distension, emesis

(continued)

Table 18-1. Causes and Symptoms of Acute Gastrointestinal Abdominal Pain *(cont'd)*

Appendicitis	Acute Periumbilical, then localized to RLQ; generalized with peritonitis Referral—back or pelvis if retrocecal Sharp, steady Anorexia, nausea, emesis, fever, local tenderness
Intussusception	Acute Periumbilical, lower abdomen No referral Cramping with painless periods Hematochezia, knees pulled up

Chronic Abdominal Pain

Definition. Chronic abdominal pain is defined as three or more episodes of abdominal pain, severe enough to affect activities, occurring over a 3-month period.

Risk Factors/Etiology. Recurrent abdominal pain (RAP) occurs in about 10–15% of children between 5 and 15 years of age. **Organic causes** include diseases of the GI tract such as constipation, lactose intolerance, parasites (*Giardia* sp), inflammatory bowel disease, and peptic ulcer disease. Pancreatitis and cholelithiasis are pancreatic causes of RAP. Urinary tract infections, abdominal epilepsy, porphyria, sickle cell anemia, and lead poisoning are non-GI causes. In contrast to younger children (<2 years), only 5–10% of children with RAP have an organic cause. **Nonorganic causes** include functional abdominal pain (irritable bowel syndrome and nonulcer dyspepsia).

Presentation. Patients with functional RAP have **nonspecific symptoms.** It is difficult to obtain a pattern of occurrence of the pain. Most frequently, the pain is described as periumbilical. **Stressors** such as school or exams may produce a predictable pattern. **Social factors** such as relocating, family illness, and sibling rivalry may account for abdominal pain. **Irritable bowel syndrome** may produce pallor, nausea, vomiting, lethargy, and diarrhea. Thirty percent of patients have nocturnal enuresis, fears, and sleep disturbances. Parents may have suffered from abdominal pain.

RAP features:

- Characteristic presentation of chronic functional pain
- Onset >6 years old
- Midline paroxysmal pain
- Pain interrupts normal activity, but usually has with no relationship to meals
- Typically relieved by stooling

Consider organic cause with the following:

- Onset <6 years old
- Fever
- Weight loss
- Abnormal growth
- Joint symptoms
- Localized away from umbilicus

- Patient awakens from sleep
- Vomiting, diarrhea, blood in stool

Diagnostic Tests. After a thorough history and physical, **most patients with RAP do not require further evaluation.** Useful studies, however, include CBC, sedimentation rate, urine analysis, stool studies, ultrasound, radiographic studies, breath hydrogen, and endoscopy. Screen CBC, ESR (IBD), urinalysis, and stool for parasites (*Giardia*).

Consider:

- Abdominal/pelvic ultrasound
- Upper gastrointestinal endoscopy

Treatment. The most important treatment for the functional RAP patient is reassurance; stress that there is no evidence of an underlying disorder. Advise patient to return to regular activities. Avoid reinforcing the symptoms with secondary gain. Biofeedback and relaxation techniques can be beneficial; medicine, however, is not.

DIARRHEA

A 13-month-old child has had a 3-day history of green watery stools. She has also been vomiting for 1 day. Physical examination reveals a febrile, irritable baby with dry mucous membranes and sunken eyes.

Definition. Diarrhea is defined as increased stool output, with excess loss of fluid and electrolytes. It can be classified as **acute or chronic.** Several mechanisms exist to cause diarrhea, of which more than one may be present.

Mechanisms

Secretory

- Secretogogue—binds to receptor on epithelium
- **Watery, large volume**
- **Normal osmolarity**—electrolyte loss
- Persists when no feeds given by mouth
- *Cholera* toxin, toxigenic *E. coli*, neuroblastoma, *C. difficile*, cryptosporidiosis

Osmotic diarrhea

- Ingestion of poorly absorbed solute (laxatives) or one not absorbed due to defect—**lactase deficiency**
- **Lesser volume, decreases with fasting**
- **Increased osmolarity**—free fatty acids (FFA) released from CHO fermentation

Motility disorders

- Increased motility—decreased transit time
- Loose-to-normal appearing stool
- **Irritable bowel, thyrotoxicosis, infection**

Mucosal inflammation

- Decreased mucosal surface area and colonic reabsorption, increased motility
- Blood and increased WBCs in stool (dysentery)
- Celiac disease, *Salmonella*, *Shigella*, amebiasis, rotavirus

Risk Factors/Etiology. Causes of acute and chronic diarrhea are **age dependent. Acute diarrhea is almost always infectious**, with gastroenteritis the most common cause in any age group. Food poisoning, systemic infections, parasitic infections, and antibiotics are other causes. Chronic diarrhea is commonly caused by lactase deficiency, irritable bowel syndrome, inflammatory bowel disease, and parasitic infections. Below is a table of causes.

Table 18-2. Causes of Diarrhea

	Infant	Child	Adolescent
Acute	Gastroenteritis	Gastroenteritis	Gastroenteritis
	Systemic infection	Food poisoning	Food poisoning
	Antibiotic	Systemic infection	Systemic infection
Chronic	Postinfectious lactase deficiency	Postinfectious lactase deficiency	Irritable bowel Inflammatory bowel
	Milk/soy intolerance	Irritable bowel	Lactose intolerance
	Chronic diarrhea infancy	Celiac disease	*Giardia*
	Celiac disease	Lactose intolerance	Laxative abuse
	Cystic fibrosis	*Giardia*	
		Inflammatory bowel	

Table 18-3. Common Agents of Gastroenteritis

Viruses	• **Rotavirus** • Enteric adenoviruses • CMV, HSV, astrovirus
Bacteria	• *Salmonella* • *Shigella* • *Campylobacter jejuni* • *Yersinia enterocolitica* • *Escherichia coli*
Parasites	• *Cryptosporidium parvum* • *Entamoeba histolytica* • *Giardia lamblia* • *Trichuris trichiura* • *Strongyloides stercoralis*

Presentation. Rotavirus presents with watery diarrhea, which can last for up to 7–10 days. It can be accompanied by 3–4 days of vomiting. Fever may be present. **Enteropathogenic *E. coli*** can be seen in nurseries and day care. **Enterotoxigenic *E. coli*** is responsible for traveler's diarrhea, whereas **enterohemorrhagic *E. coli*** can cause hemorrhagic colitis and **hemolytic uremic syndrome (HUS)**. ***Salmonella*** is contracted from infected animals and contaminated foods such as eggs, milk, and poultry. ***Shigella*** and ***Campylobacter*** are by person-to-person spread or from contaminated food. ***Yersinia enterocolitica*** is transmitted by pets and contaminated foods. Patients may develop arthritis and a rash. In patients with ***Clostridium difficile***, look for a history of prior antibiotic use. Food poisoning by ***Staphylococcus aureus*** is characterized by onset within 12 h of ingestion and a common source for the outbreak. ***E. histolytica*** infects the colon, causing an acute bloody diarrhea. ***Giardia*** causes anorexia, nausea, abdominal distention, watery diarrhea, and weight loss. Cysts are ingested from an infected individual or from contaminated food or water. ***Cryptosporidium*** causes a mild diarrhea in immunocompetent infants, but causes severe diarrhea in AIDS patients.

Diagnostic Tests. Diagnosis is made by **recovering the organism from the stool. Enzyme immunoassays** detect rotavirus and enteric adenovirus. ***C. difficile* toxin** can be detected in the stool. ***Giardia*** can be recovered from stool, duodenal aspirate, or small bowel biopsy.

Treatment. Therapy of viral diarrhea is supportive. Treatment of ***Salmonella* prolongs the carrier state** and is **indicated only for ≤3 months of age, a toxic patient, disseminated disease, or *Salmonella typhi*. *Shigella*** is treated with trimethoprim/sulfamethoxazole. ***Campylobacter*** is usually self-limited. Treatment with erythromycin speeds recovery and reduces the carrier state. It is recommended in severe disease or in dysentery. **Yersinia** usually does not require antibiotic therapy. Aminoglycosides plus a third-generation cephalosporin is recommended for infants ≤3 months of age, or culture-proven septicemia. ***C. difficile*** is treated with metronidazole or vancomycin along with discontinuation of other antibiotics. ***Entamoeba*** is treated with metronidazole. ***Giardia*** can also be treated with metronidazole, or furazolidone.

Table 18-4. Some Common Causes of Chronic Diarrhea

- Postinfection secondary to lactase deficiency
- Cow's milk/soy protein intolerance
- Irritable bowel syndrome
- Inflammatory bowel disease
- Giardiasis
- Cystic fibrosis
- Celiac disease
- Lactose intolerance

Table 18-5. Evaluation of Chronic Diarrhea

First tests:	Clinical history Physical exam with nutritional assessment Stool exam (pH, reducing substances, osmolarity, WBCs, blood, fat, ova and parasites) Stool culture Stool for *C. difficile* toxin CBC, ESR, electrolytes, BUN, creatinine
Then:	Sweat chloride 72-hour fecal fat ?Laxatives—stool phenolphthalein, $MgSO_4$, phosphate Breath hydrogen test
Then:	Endoscopic studies Sigmoidoscopy or colonoscopy with biopsies Barium studies Small bowel biopsy
Then:	Hormonal studies Neurohormonal and neurotransmitter studies

CONSTIPATION

A 6-year-old boy complains of hard bowel movements every fifth day. Physical examination reveals normal weight and height. Abdomen is soft, and hard stool is palpable on rectal examination.

Definition. Constipation is the infrequent passage of hard, dry stools. **Obstipation** is the absence of bowel movements.

The definition depends on stool consistency, frequency, and difficulty in passing.

Table 18-6. Common Causes of Constipation

Anatomic	• Anal stenosis, imperforate anus • Intestinal stricture • Abnormal musculature • Prune belly • Gastroschisis
Intestinal nerve or muscle abnormalities	• Hirschsprung disease
Spinal cord defects	• Tethered cord • Trauma • Spina bifida
Drugs	• Anticholinergics • Narcotics • Antidepressants • Lead
Metabolic disorders	• Hypokalemia • Hypercalcemia • Hypothyroidism • *Hypomagnesemia*

Risk Factors/Etiology. Functional constipation (voluntary withholding) is the most common cause of constipation outside of infancy. Constipation occurs secondary to defects in filling or emptying the rectal vault. **Other causes** of constipation include imperforate anus, cystic fibrosis with meconium ileus at birth, an anteriorly displaced anus, and Hirschsprung disease. **Infantile botulism** can also cause constipation.

Presentation. Hard stools are passed infrequently, sometimes after several days and with difficulty. Occasionally, liquid stool can pass around the obstruction and give the false impression of **diarrhea and encopresis. Constipation in the neonate should be considered Hirschsprung until proven otherwise.** The aganglionic segment is in the colon, usually rectosigmoid. Infants may have failure to thrive and abdominal distension. In older children with Hirschsprung, the rectal vault is empty of stool.

Diagnostic Tools. Hirschsprung is diagnosed by **biopsy** showing areas devoid of ganglion cells. Barium enema shows a megacolon.

Treatment. Treatment of **Hirschsprung is surgical.** Treatment of functional constipation includes initial cleaning out, and may involve dietary manipulation, stool softeners, and counseling.

Table 18-7. Features of Hirschsprung versus Functional Constipation

	Hirschsprung	Functional
History		
Onset	Birth	>2 years
Encopresis	—	+
Failure to thrive	+/–	–
Enterocolitis	+/–	—
Forced bowel training	—	+++
Physical examination		
Abdominal distension	++	—
Poor weight gain	++	—
Anal tone	N	N
Rectal (stool present)	—	++
Malnutrition	0	+/–
Diagnostic tests		
Manometry (sphincter relaxation)	0	+++
Biopsy (ganglion cells)	0	+++
Barium enema (transition zone)	+++	—

N = normal.

VOMITING

Causes of vomiting in children are age related:

- Neonates—GI obstruction secondary to congenital malformations
- Infants—Gastroenteritis, gastroesophageal reflux, food allergy, milk protein intolerance, overfeeding, inborn errors of metabolism
- Children/adolescents—Gastroenteritis, systemic infections, toxic ingestions, appendicitis, ulcers, pancreatitis

Duodenal Atresia

A newborn presents with bilious vomiting with every feed. Abdominal film reveals a double bubble.

Definition. Duodenal atresia is an obstruction resulting from a failure of recanalization of the duodenal lumen.

Risk Factors/Etiology. Duodenal atresia occurs in 1/10,000 live births. Twenty to thirty percent of patients with duodenal atresia have trisomy 21.

Presentation. Duodenal atresia presents early, usually in the first day of life. Vomiting is bilious, and there is no abdominal distension. There may be a history of polyhydramnios.

Diagnostic Tests. Abdominal films reveal the characteristic "double bubble" of the stomach and proximal duodenum.

Treatment. Therapy involves surgical correction. The patient should be evaluated for associated anomalies.

Gastroesophageal Reflux (GER)

A 4-month-old is admitted with episodes of apnea occurring 20–30 min after feeds. The mother states the baby has been spitting up since birth. She is at the fifth percentile for weight.

Definition. GER occurs when the lower esophageal sphincter (LES) pressure is reduced, or from inappropriate LES relaxation, hiatal hernia, or delayed gastric emptying.

Risk Factors. GER is relatively common, but usually is only minor and of no consequence. GER is more common in patients with developmental delay and cerebral palsy.

Presentation. Patients present with a wide array of symptoms. Most patients have some form of spitting up and may have forceful vomiting. Apnea can be a presenting sign. Chronic cough and wheezing may signal aspiration. Some patients exhibit poor weight gain and failure to thrive. Sandifer syndrome presents with GER and opisthotonus, presumably to avoid aspiration or decrease pain.

Diagnostic Tests. A pH probe is the standard for diagnosing GER. Other imaging studies include technetium scanning and barium swallow.

Treatment. Therapy consists of antireflux measures such as elevating the head of the bed and thickening of feeds. Medical management includes antacids, prokinetics, H_2-receptor blockers, and proton pump inhibitors. Failure of medical management results in surgical correction with a Nissen fundoplication. The majority of patients, however, have resolution of symptoms without any treatment.

Hypertrophic Pyloric Stenosis (HPS)

A 4-week-old boy has nonbilious projectile vomiting. Physical examination is remarkable for a small mass palpated in the abdomen.

Definition. Hypertrophic pyloric stenosis is a gastric outlet obstruction.

Risk Factors/Etiology. HPS occurs in about 3/1000 live births. Boys are more frequently affected, 4:1, especially first-born males. It recurs in about 5% of siblings, 25% if the mother had HPS.

Presentation. Nonbilious projectile vomiting is the hallmark of HPS. Vomiting usually begins after 3 weeks of age. The baby remains hungry after the vomiting. An olive may be palpated in the abdomen. Occasionally, a peristaltic wave may be seen. Jaundice and weight loss, as well as signs of dehydration, may be present.

Diagnostic Tests. Abdominal ultrasound reveals a thickened (>4 mm doughnut), elongated (>14 mm) pylorus. Barium swallow shows a dilated stomach with elongated pylorus (string sign), a release of barium into the duodenum (mushroom cap), and parallel streaks of barium in the channel (double tract or railroad tracks). Laboratory tests show a hypokalemic, hypochloremic metabolic alkalosis.

Treatment. After fluid rehydration and correction of electrolyte imbalance, surgical correction resolves the problem.

GASTROINTESTINAL BLEEDING

Definitions

Gastrointestinal bleeding can be described as one of the following:

- Hematemesis—this is bloodstained vomitus and usually indicates bleeding proximal to the ligament of Treitz.
- Melena—these are soft, black, tarry stools and can represent bleeding anywhere from the oropharynx to the colon.
- Hematochezia—these are bright red stools and are usually from the colon but can reflect upper GI bleeding if the transit time is fast enough.

Causes of gastrointestinal bleeding are divided by site of bleeding and age group. Specific entities will be addressed in subsequent sections.

Table 18-8. Differential Diagnosis of Gastrointestinal Bleeding

Infant	
Common	Bacterial enteritis
	Milk protein allergy
	Intussusception
	Neonate-swallowed maternal blood
	Anal fissure
	Volvulus
	Meckel diverticulum
	Coagulation disorder
Child	
Common	Bacterial enteritis
	Anal fissure
	Intussusception
	Swallowed epistaxis
	Varices
	Esophagitis
	Meckel diverticulum
	Henoch-Schönlein purpura (HSP)
	Hemolytic uremic syndrome
Adolescent	
Common	Bacterial enteritis
	Inflammatory bowel disease
	Ulcer/gastritis
	Mallory-Weiss
	Polyps
	Hemorrhoids
	Varices
	Esophagitis

INFLAMMATORY BOWEL DISEASE (IBD)

A 13-year-old girl complains of chronic, cramping abdominal pain and diarrhea. She has noticed occasional blood in her stools. She has had fever off and on for 3 months and has complained of persistent right wrist pain. CBC shows anemia, and her sedimentation rate is elevated.

General

IBD includes **Crohn disease and ulcerative colitis**. Both are characterized by **exacerbations and remissions. Onset is usually during adolescence**. Although a specific etiology is unknown, it is **more common in Jews and whites, and tends to run in families**, indicating a genetic influence.

Crohn Disease (Regional Enteritis, Granulomatous Colitis)

Presentation. Crohn disease can have an insidious presentation and has **more extraintestinal manifestations than ulcerative colitis**. Patients may have persistent **fever of unknown origin, arthritis**, skin manifestations (erythema nodosum), **weight loss**, malaise, and growth retardation to name a few. **Abdominal pain** is cramping in nature; **diarrhea** may at times be bloody. **Perianal disease** is very common, including abscesses and fistulas. **Crohn disease can occur anywhere along the GI tract.**

Diagnostic Tests. Diagnosis may take years owing to the nonspecific symptoms. **Sedimentation rate** may be elevated. Platelet count is usually high. **Plain abdominal films** may show partial small bowel obstruction. **Upper GI** with small bowel followthrough can show thickened folds and narrowing of the GI tract **(string sign). Skip lesions** may be seen when there are normal areas between affected areas. **Fistulas** may be seen. **Colonoscopy and biopsy** are useful when the diagnosis is uncertain.

Treatment. Therapy is aimed at relief of symptoms and includes **steroids, aminosalicylates (including enemas), azathioprine and metronidazole for fistulas, cyclosporine, tacrolimus, and tumor necrosis factor-α. Antibiotics** are commonly used because it is difficult to rule out an infectious process. **Hyperalimentation** provides calories for appropriate growth as well as resting the bowel. **Surgical management** is reserved for failure of medical management, fistula formation, intestinal obstruction, and growth failure.

Complications. Crohn disease is characterized by remissions and exacerbations. GI obstruction requiring surgery, malabsorption, anemia, weight loss, and growth failure are all complications.

Differential Diagnosis. Differential diagnosis includes infectious enteropathies, recurrent abdominal pain, arthritis, and leukemia.

Ulcerative Colitis (UC)

Presentation. UC involves only the colon. Presentation can be insidious or fulminant. Symptoms typically include **bloody diarrhea with mucus. Abdominal pain and tenesmus** may also be present. **Mild to moderate disease** is present in about 90% of cases. These patients have fewer than six stools per day, no fever, and no anemia. **Moderate disease** presents with greater than six stools per day, fever, anemia, and hypoalbuminemia. **Severe, fulminant disease** courses with severe anemia, high fever, leukocytosis, and tachycardia.

Diagnostic Tests. UC is a diagnosis of exclusion. Symptoms should be present for at least 3–4 weeks. Sedimentation rate may be elevated or normal. **Anemia is present with severe or chronic blood loss. Endoscopy** with biopsy is very helpful, particularly in mild disease. **No skip lesions** are seen. The mucosa is friable and bleeds easily. Diffuse superficial ulcerations are seen.

Treatment. Therapy is also aimed at symptom relief. **Aminosalicylates and sulfasalazine** are commonly used. **Steroids, oral or as enemas,** are also used. **Surgical treatment** is total colectomy. The chance of progressing to colectomy is directly related to severity of disease at presentation.

Complications. Patients with UC are at higher risk for developing **colon cancer.**

Differential Diagnosis. Infectious colitis and Crohn disease must be ruled out.

Table 18-9. Features of Crohn Disease Versus Ulcerative Colitis

Features	Crohn Disease	Ulcerative Colitis
Rectal bleeding	Sometimes	Common
Diarrhea	Variable	Common
Abdominal pain	Common	Variable
Abdominal mass	Common	No
Growth failure	Common	Variable
Perianal disease	Common	Unusual
Rectal disease	Occasional	Universal
Pyoderma gangrenosum	Rare	Present
Erythema nodosum	Common	Less common
Mouth ulceration	Common	Rare
Colonic disease	Common	Universal
Ileal disease	Common	Backwash ileitis
Strictures	Common	Unusual
Fissures	Common	None
Fistulas	Common	Unusual
Toxic megacolon	None	Present
Risk for cancer	Increased	Greatly increased
Skip lesions	Common	No
Transmural	Common	Unusual
Crypt abscesses	Less common	Common
Granulomas	Common	Unusual
Linear ulcerations	Uncommon	Common
Thrombosis	Less common	Present
Stomach-esophageal disease	Uncommon	None

INTUSSUSCEPTION

A 15-month-old child is seen for cramping, colicky abdominal pain of 12 h duration. He has had two episodes of vomiting and a fever. Physical examination is remarkable for a lethargic child; abdomen is tender to palpation. Leukocytosis is present. During examination, the patient passes a bloody stool with mucus.

Definition. Intussusception occurs when a portion of the GI tract slips or telescopes into the portion just distal to it. Most intussusceptions are **ileocolic.**

Risk Factors/Etiology. The majority of intussusceptions have no known cause. Most occur between **6 and 24 months** of age, although it has been reported in children 3 months to 6 years of age. **Associations** have been made with lymphoid hyperplasia, Meckel diverticulum, lymphosarcoma, polyps, cystic fibrosis, and Henoch-Schönlein purpura, as well as a preceding viral enteritis. Recently there has been an association with the now discontinued **rotavirus vaccine.**

Presentation. Acute onset of cramping, colicky abdominal pain is the hallmark of intussusception. Patients may have vomiting. As the obstruction progresses, the patient may develop fever and become lethargic. The classic **currant jelly stool** is a late finding. Passing a stool may temporarily relieve pain. A **sausage-shaped mass** may be palpated in the upper abdomen on physical examination. A shocklike state may occur.

Diagnostic Tests. Barium enema is both diagnostic and therapeutic. A coil-spring sign is seen as the barium fills the obstruction. **Air enemas** may also diagnose and treat and are safer. **Ultrasound** is also helpful.

Treatment. Intussusception is an emergency and should be reduced as quickly as possible. **Hydrostatic reduction** is successful about 50% of the time for symptoms >48 h and 75–80% for symptoms <48 h. It should not be done in the face of prolonged intussusception, peritonitis, or perforation. **Surgery** is recommended in those cases or after failure of hydrostatic reduction. Untreated intussusception is almost uniformly fatal.

Differential Diagnosis. Gastroenteritis presents similarly to the initial stages of intussusception. Meckel diverticulum produces GI bleeding but it is usually painless. Henoch-Schönlein purpura produces bloody stools and may cause intussusception.

MECKEL DIVERTICULUM

A 2-year-old boy presents with a 1-week history of painless rectal bleeding. Physical examination is unremarkable. The abdomen is soft and nontender. Rectal examination is unremarkable.

Definition. Meckel diverticulum is the most frequent congenital anomaly of the GI tract. It is a vestigial remnant of the omphalomesenteric duct.

Risk Factors/Etiology. Meckel diverticulum is known as the **disease of two's.** It presents in about **2%** of infants, the peak incidence is by **2 years of age,** it contains **two types of tissue** (ectopic gastric mucosa), it is about **2 cm** in size, and it is located about **2 feet from the ileocecal valve.**

Presentation. Painless rectal bleeding is the most common manifestation of a Meckel diverticulum. Stools are sometimes described as **currant jelly.** Occasionally, Meckel diverticulum can

cause obstruction or be the lead point for an intussusception. It can become inflamed and mimic appendicitis, or it can perforate and cause peritonitis.

Diagnostic Tests. The **technetium scan (Meckel scan)** is the most sensitive way to diagnose Meckel diverticulum.

Treatment. Treatment is **surgical** removal.

REYE SYNDROME

An 8-year-old is seen in the emergency department with persistent vomiting and mental status changes. On examination he is combative and has a seizure, becomes apneic, and requires intubation. Laboratory tests are remarkable for hypoglycemia and elevated ammonia. The patient had recently recovered from a viral upper respiratory infection.

Definition. Reye syndrome is an **encephalopathy** with fatty degeneration of the liver.

Risk Factors/Etiology. Many patients have a history of a **recent viral upper respiratory tract infection or varicella.** Concomitant use of **aspirin** is also related to development of Reye syndrome and elimination of aspirin use in children has led to a decrease in the incidence of Reye syndrome. The peak age for Reye syndrome is 6 years with a range of 4–12 years.

Presentation. Patients have typically recovered from a viral illness. **After 5–7 days they then present with abrupt onset of protracted vomiting.** Delirium, combative behavior, and stupor quickly ensue. The patient can progress to seizures, coma, and death. Focal neurologic signs are absent.

Diagnostic Tests. Reye syndrome can be **staged by symptoms.** A table is shown below. Laboratory tests are remarkable for normal cerebrospinal fluid. **Ammonia, transaminases, creatine kinase, and lactic dehydrogenase are markedly elevated. Hypoglycemia may be present.** Prothrombin time is elevated. The liver is yellow to white in color owing to high triglyceride content. **Liver biopsy** shows a diffuse noninflammatory fatty infiltration, with the mitochondria being the major site of injury.

Table 18-10. Reye Syndrome

Stage	Symptoms
I	Lethargy, vomiting, sleepy
II	Confused, lethargic
III	Light coma, decorticate
IV	Deep coma, decerebrate
V	Flaccid, apneic, reactive pupils

Treatment. Treatment of Reye syndrome is **supportive.** Intracranial pressure elevations need to be treated, and hypoglycemia should be avoided.

Differential Diagnosis. Encephalitis, toxic and drug encephalopathies, and metabolic diseases all can mimic the presenting signs and symptoms of Reye syndrome.

Renal

URINARY TRACT INFECTION

A 12-day-old infant presents with fever of 39°C, vomiting, and diarrhea. On physical examination the infant appears to be ill and mildly dehydrated.

Definition. There are three basic forms of urinary tract infection (UTI): (*1*) **pyelonephritis** (involvement of the upper urinary tract), (*2*) **cystitis** (infection involving the bladder), and (*3*) **asymptomatic bacteriuria** (positive urine culture with no associated clinical findings and no renal injury, except in pregnant women).

Risk Factors/Etiology. UTIs result from fecal flora, especially coliform bacteria (e.g., *E. coli*), *Klebsiella*, and *Proteus*, which has ascended up the urethra to the bladder. *Staphylococcus saprophyticus* may also cause UTIs in both sexes. Viral infections such as adenovirus may be responsible for infection, especially cystitis. UTIs are seen more commonly in boys as infants and are more common in uncircumcised boys. However, after 2 years of age, this infection is more common in girls. Patients who are sexually active are at a higher risk.

Presentation. The classic symptoms of cystitis (dysuria, urgency, frequency) are often absent in children, making it difficult to recognize infection. Infants with UTIs may present with unexplained fever, failure to thrive, weight loss, vomiting, and diarrhea. Older children may have fever, abdominal pain, hematuria, or enuresis. An infant or child with pyelonephritis may not have the classic symptoms of flank pain or shaking chills. Asymptomatic bacteriuria (positive urine culture and no symptoms) may also occur but is more prevalent in girls.

Diagnostic Tests. The **urine culture** is the **gold standard**. Urinalysis, blood urea nitrogen (BUN)/creatinine, and a blood culture are other tests that may be helpful in the diagnosis.

Treatment. The neonate should be hospitalized and treated with intravenous ampicillin and gentamicin. Older children who need hospitalization should be treated with intravenous ceftriaxone or ampicillin with an aminoglycoside. Children with dehydration, emesis, or possible sepsis should be admitted to the hospital for rehydration and intravenous antibiotics. Outpatient therapy for children with UTIs includes trimethoprim-sulfamethoxazole, or amoxicillin.

A repeat urinalysis should be obtained 1 week after completion of therapy of any UTI. Follow-up urine cultures should be performed periodically for 1–2 years even in the asymptomatic child. Once-a-day prophylaxis with trimethoprim-sulfamethoxazole or nitrofurantoin at one third of the normal therapeutic dose may be effective against recurrent UTI.

Complications/Follow-up. Children with UTIs are at risk for developing renal insufficiency and end-stage renal disease. Follow-up is necessary in children with UTI. A workup should include renal ultrasound to rule out hydronephrosis, or renal or perirenal abscesses. In addition, all children younger than 5 years of age with a UTI, children with a febrile UTI, school-aged

girls with more than two UTI, and any boy with a UTI should have a VCUG. This VCUG is performed to investigate the presence of valves, reflux, and diverticulum. Cultures should be repeated at intervals. If reflux is suspected, then a renal scan with technetium-labeled dimercaptosuccinic acid (DMSA) should be performed to assess for renal scarring.

VESICOURETERAL REFLUX

A 2-year-old girl presents with urinary tract infection. She has had multiple urinary tract infections since birth but has never had any follow-up studies to evaluate these infections. Physical examination is remarkable for an ill-appearing child who has a temperature of 40°C and is vomiting.

Definition. Vesicoureteral reflux is abnormal back flow of the urine from the bladder to the kidney.

Risk Factors/Etiology. Vesicoureteral reflux is caused by congenital incompetence of the vesicoureteral junction and may be familial. Urinary tract infections are more common in uncircumcised boys.

There is incompetence of the junction from infection and obstruction. This incompetence exposes the kidney to increased pressure during voiding and predisposes the patient to urinary tract infections. Vesicoureteral reflux is a common cause of hypertension in children and may lead to renal scarring. Reflux is seen in 50% of boys with posterior urethral valves.

Presentation. Vesicoureteral reflux is usually found during an evaluation for urinary tract infection.

Of these children, 80% are girls ages 2–3 years. Primary reflux is usually found in prenatal hydronephrosis, and of these children 80% are boys.

Diagnostic Tests. Reflux is graded using the International Study Classification of I to V. These gradings are based on the appearance of the urinary tract on a contrast cystourethrogram (VCUG).

Classification

- Grade I—reflux into a nondilated distal ureter
- Grade II—reflux into the upper collecting system (ureter, pelvis, calyces) without dilatation of the kidney
- Grade III—reflux into the dilated ureter and/or blunting of the calyceal fornices
- Grade IV—reflux into a grossly dilated ureter with moderate dilatation of the pelvis, calyces
- Grade V—massive reflux, with gross dilatation/tortuosity of the ureter, pelvis, calyces

After reflux is diagnosed and grading is assigned, it is important to assess the upper urinary tract. This can be done using renal ultrasound, an intravenous pyelogram, or renal scintigraphy. If there is renal scarring, then serum creatinine should be measured. A urinalysis should be completed to determine whether infection or proteinuria is present.

Treatment. Vesicoureteral reflux may resolve with time. Antibiotic prophylaxis with trimethoprim-sulfamethoxazole, trimethoprim alone, or nitrofurantoin is the most important therapy in the management of these children with vesicoureteral reflux. Surgical repair is usually done for grade IV or V reflux and unresolving reflux or persistent urinary tract infections.

Complications/Follow-up. Renal scarring and reflux nephropathy may develop as complications of vesicoureteral reflux.

ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

A 10-year-old boy presents with Coca-Cola–colored urine and edema of his lower extremities. On physical examination the patient has a blood pressure of 185/100. He does not appear to be in any distress. His lungs are clear to auscultation, and his heart has a regular rate and rhythm without any murmurs, gallops, or rubs. His past medical history is remarkable for a sore throat that was presumed viral by his physician 2 weeks before.

Definition. Acute poststreptococcal glomerulonephritis follows infection of the throat or skin with "nephritogenic" strains of group A β-hemolytic streptococci.

Risk Factors/Etiology. This problem may manifest 1–2 weeks after a streptococcal infection of the throat or skin (impetigo). This illness is seen commonly in children but is rare before 3 years of age.

Presentation. Acute glomerulonephritis follows infection with nephritogenic group A β-hemolytic streptococci by 1 to 2 weeks. The patient may exhibit gross hematuria, edema, hypertension, and renal insufficiency. The severity of the illness varies with the patient.

Patients may also complain of fever, malaise, and abdominal or flank pain.

Diagnostic Tests. Red blood cell casts and protein may be found on urinalysis. There should be evidence of a past infection with **group A β-hemolytic streptococcus**. The best method for determining this is the **deoxyribonuclease (DNase) B antigen**. In addition, the patient may have mild anemia and a decreased serum C3. An antinuclear antibodies **(ANA) test** may be obtained to rule out systemic lupus erythematosus. A renal biopsy is usually not needed in **classic cases** (acute nephritic syndrome plus evidence of streptococcal infection plus low C3 level).

Treatment. Antibiotics may be given to curtail the spread of the nephritogenic strain; however, there is no evidence to demonstrate that they will eliminate the risks or change the natural course of the disease. Antihypertensive medications should be used for hypertension. If present, renal failure should be treated promptly to avoid morbidity and mortality.

Complications/Follow-up. The patient may experience hypertension and acute renal failure. Some other problems include seizures, hyperkalemia, and hypocalcemia. However, 95% of patients with acute poststreptococcal glomerulonephritis will have complete recovery.

Differential Diagnosis. Systemic lupus erythematosus should be considered in the differential diagnosis and an ANA may be obtained to rule it out. Entities that cause hematuria (hemolytic uremic syndrome, membranous glomerulopathy, etc.) should also be considered in the differential diagnosis.

ALPORT SYNDROME

The school nurse refers a 7-year-old boy because he failed his hearing test at school. The men in this patient's family have a history of renal problems, and a few of his maternal uncles are deaf. A urinalysis is obtained from the patient, which shows microscopic hematuria.

Definition. Alport syndrome is the most common type of hereditary nephritis.

Risk Factors/Etiology. It is an X-linked dominant disorder. Autosomal transmissions as well as spontaneous mutations have also been described.

Presentation. The clinical presentation of this disease is variable. However, presentation with asymptomatic hematuria is common. A sensorineural hearing loss or deafness may be present. Eye abnormalities (e.g., cataracts) may also be seen in a small number of patients.

Physical Examination. This is described under presentation.

Diagnostic Tests. In patients with microscopic hematuria and proteinuria, a **renal biopsy** should be performed. Biopsy shows glomerular sclerosis and a thickened basement membrane. As the disease progresses, tubular atrophy, fibrosis, and **foam cells** arise.

Treatment. There is no specific therapy; however, men with Alport syndrome usually develop end-stage renal failure in the second or third decade of life. These patients need dialysis and renal transplantation. Women usually have a normal life span with subclinical hearing loss.

Complications/Follow-up. Hypertension, urinary tract infections, and chronic renal failure develop as problems with renal function occur. Genetic counseling should be given.

HEMOLYTIC-UREMIC SYNDROME

A 3-year-old child presents to the emergency center with history of bloody diarrhea and decreased urination. The mother states that the child's symptoms began 5 days ago after the family ate at a fast-food restaurant. At that time the patient developed fever, vomiting, abdominal pain, and diarrhea. On physical examination the patient appears ill. He is pale and lethargic.

Definition. Hemolytic uremic syndrome is a systemic disease that causes acute renal failure in young children, as well as hematologic manifestations.

Risk Factors/Etiology. Hemolytic uremic syndrome is most commonly caused by *Escherichia coli* (O157:H7). This organism may be transmitted by undercooked meat and unpasteurized milk. It has also been associated with other bacterial and viral infections. In addition, bathing in contaminated swimming pools, drinking contaminated apple cider, and oral contraceptives have also been associated with hemolytic uremic syndrome. *E. coli* (O157:H7) produces a verotoxin that is absorbed from the intestines and causes endothelial cell injury of the infected individual. Endothelial injury of the kidney results in localized clotting. Red blood cell and intrarenal platelet damage causes microangiopathic anemia and thrombocytopenia.

Presentation. This syndrome usually occurs in children younger than 4 years of age. The patient may have had gastroenteritis before onset with bloody diarrhea or upper respiratory infection symptoms. Approximately 1 week after these symptoms the patient may develop oliguria and may be pale, weak, and lethargic.

Physical Examination. In addition to the physical findings described above in the Presentation, the patient may be dehydrated and have hepatosplenomegaly and petechiae. The patient may appear ill tempered.

Diagnostic Tests. This syndrome should be suspected in patients with acute renal failure and microangiopathic hemolytic anemia. The diagnosis is made on history and clinical and laboratory findings. The complete blood count may show the white blood cell count to be 30,000/mm^3, hemoglobin to be 5–9 g/dL, and platelets to be 20,000–100,000/mm^3. Helmet and burr cells may be seen on peripheral smear. The Coombs test is negative. Hematuria and proteinuria may be seen on urinalysis. The renal involvement varies from mild renal insufficiency to severe renal failure requiring dialysis.

Treatment. Management of renal failure and hematologic problems should be the goal of therapy. Peritoneal dialysis is essential to control the uremic state and to remove an inhibitor of fibrinolysis. Ninety percent of patients survive the acute phase of the disease, and most regain normal renal function. Corticosteroids are not helpful as therapy for hemolytic uremic syndrome.

Complications/Follow-up. Anemia, hypertension, acidosis, heart failure, diabetes mellitus, seizures, and colitis are some of the complications of hemolytic uremic syndrome. The pathogenesis of these complications is unknown. Patients with hemolytic uremic syndrome should be monitored for late onset of hypertension and chronic renal disease.

Differential Diagnosis. Hemolytic uremic syndrome looks similar to thrombotic thrombocytopenic purpura (TTP), but TTP occurs in young women and affects the central nervous system. Patients with TTP also have fever, decreased platelets, and cutaneous symptoms. Lupus and malignant hypertension should also be considered in the differential because both may have acute renal failure and anemia. Bilateral renal vein thrombosis has a similar presentation to hemolytic uremic syndrome (gastroenteritis, pallor, dehydration), but children with renal vein thrombosis have large kidneys.

NEPHROTIC SYNDROME

> A 3-year-old child presents to the physician with a chief complaint of puffy eyes. On physical examination there is no erythema or evidence of trauma, insect bite, cellulitis conjunctival injection, or discharge.

Definition. Nephrotic syndrome is characterized by **proteinuria, hypoalbuminemia, edema,** and **hyperlipidemia**. Nephrotic syndrome may be classified as (*1*) **idiopathic** (minimal change disease, 85%; focal sclerosis, 10%; and mesangial proliferation, 5%) and (*2*) **glomerulonephritis** (membranous and membranoproliferative). Ninety percent of patients will have the idiopathic form, and 10% will have nephrotic syndrome caused by some form of glomerulonephritis.

Risk Factors/Etiology. Nil disease (minimal change) has an unknown etiology. It is not a common disease, but it accounts for 85% of all children's nephrotic syndrome. The male-to-female ratio is 2:1, and it appears to be more common in children ages 2 to 6 years. The pathophysiology of nephrotic syndrome includes

- Increased glomerular capillary wall permeability
- Proteinuria
- Edema secondary to decreased oncotic pressure
- Hyperlipidemia
  - Decreased protein stimulates protein synthesis, including lipoproteins
  - Decreased lipoprotein lipase

Presentation. Nephrotic syndrome usually follows a viral upper respiratory infection. There may be **generalized** or **pitting edema**. The patient may have complaints of fatigue, anorexia, abdominal pain, or diarrhea. **Hypertension** is **not common**. The patient may have weight gain.

Physical Examination. On physical examination the patient may have **edema** (pretibial, pedal, sacral, scrotal, labial, or periorbital). The patient may have evidence of dehydration or respiratory distress (pleural effusion). Ascites may be present.

Diagnostic Tests. The patient with idiopathic nephrotic syndrome will have heavy **proteinuria**, and **microscopic hematuria** may be present. The patient will have a **decreased serum protein**, an **elevated cholesterol**, and **normal C3**. A trial of **steroid** therapy for 4–8 weeks should precede **renal needle biopsy**.

Treatment. Therapy for nephrotic syndrome may include (*1*) **diuretics** and **salt restriction**, (*2*) **albumin**, (*3*) **steroid**, i.e., prednisone, and (*4*) **alkylating agents**, i.e., cyclophosphamide. The patient may use salt after the edema resolves. **Renal transplantation** is indicated for end-stage renal failure secondary to steroid-resistant focal and segmental glomerulosclerosis.

Complications/Follow-up. Infection is a major complication of nephrotic syndrome. These patients are susceptible to developing a **spontaneous peritonitis**, usually caused by *Streptococcus pneumoniae*. All patients with nephrotic syndrome should receive **polyvalent pneumococcal vaccine**. **Arterial** and **venous thrombosis** may also occur in patients with nephrotic syndrome. Most children with steroid-responsive nephrotic syndrome have relapses until the second decade, when they have a spontaneous remission. These children should have no long-term renal problems.

Rheumatology

20

JUVENILE RHEUMATOID ARTHRITIS (JRA)

A 7-year-old girl has been complaining of pain and swelling of the left wrist and right knee off and on for the past 3 months. She has been previously healthy. The pain is worse in the morning and improves throughout the day. Physical examination is remarkable for swelling and effusion of the right knee, with decreased range of motion.

Definition. JRA is a **chronic nonsuppurative inflammation of the synovium of the joints.** It is characterized by **joint effusions, destruction of joint cartilage, and bone deformity, destruction, and fusion.**

Risk Factors/Etiology. Although a **specific etiology is not known,** a preexisting susceptibility followed by an environmental trigger are believed to result in development of JRA. Infectious triggers include viruses, *Borrelia,* and *Mycoplasma.* An autoimmune origin is also suggested.

Presentation. Initial presentation includes **morning stiffness, joint pain, and swelling.** The joint is warm and has **decreased range of motion.** Erythema is rare. Low-grade fever may be present, as well as malaise. JRA is subclassified according to presentation of symptoms. These are listed below.

- **Polyarticular (polyarthritis)**—this involves **many small joints**, especially of the hands, and accounts for 35% of all JRA. Onset can be insidious or fulminant. Polyarticular JRA can be further subdivided into
  - **RF+**—older age of onset, association with nodules, erosions, predilection for hands and wrists, and more common in females
  - **ANA+**—also in females, but with onset at a younger age and with a good prognosis
  - **Seronegative**
- **Pauciarticular (oligoarthritis)**—this affects **fewer but larger joints** in an asymmetric distribution. It can also be subclassified into
  - **ANA+**—most common form of JRA; presentation usually before the fourth birthday; affects the knees, ankles, and elbows; more common in girls; high risk for eye involvement such as **iridocyclitis;** prognosis excellent
  - **RF+**—with erosions, polyarthritis, and a poor prognosis
  - **HLA B27+**—more common in males and with a high risk for **ankylosing spondylitis**
  - **Seronegative**

- **Systemic JRA** is known for its initial **extraarticular manifestations** such as **fever, rash** (especially with fever), hepatosplenomegaly, **pleuritis, and pericarditis.** Joint manifestations appear within a few months of the fever and are similar to polyarticular JRA, although a pauciarticular form also exists.

Diagnostic Tests. Diagnosis is mostly clinical with the help of some laboratory tests. **Clinical criteria** are listed below:

- Onset <16 years of age
- Arthritis or two or more of the following: limited range of motion, tenderness or pain on motion, increased heat in one or more joints
- Duration 6 weeks or more
- Onset type of disease in first 6 months
  - Polyarthritis: five or more inflamed joints
  - Oligoarthritis: fewer than five inflamed joints
  - Systemic: arthritis with fever
- Exclusion of other forms of juvenile arthritis

Sedimentation rate and C-reactive protein are elevated during the active phases of the disease. **Anemia** of chronic disease is common. **Leukocytosis and thrombocytosis** are also seen. **Radiographs** show soft tissue swelling early in the course of the disease, bone and joint changes later. **ANA** is rare in systemic onset disease, but can be seen in pauciarticular and polyarticular disease. **Rheumatoid factor** may or may not be positive.

Treatment. The **goals** of treatment are to **preserve joint function and approximate normal lifestyle** with the fewest side effects possible. **Nonsteroidals,** including aspirin, are the first-line drugs used. **Methotrexate** is the safest second-line drug and has replaced gold salts. **Antimalarials** are occasionally used. **Corticosteroids** have few indications for use. **Physical therapy** and **ophthalmologic follow-up** are extremely important.

Differential Diagnosis. Diseases that mimic JRA include rheumatic fever, systemic lupus erythematosus, ankylosing spondylitis, osteomyelitis, Lyme disease, and leukemia.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

A 10-year-old girl presents with fever, fatigue, and joint pains. Physical examination is remarkable for a rash on the cheeks, swelling of the right knee, and a pericardial friction rub. Initial laboratory tests reveal anemia and an elevated blood urea nitrogen and creatinine.

Definition. SLE is an autoimmune inflammatory rheumatoid disease affecting multiple organ systems.

Risk Factors/Etiology. The etiology is unknown, but is believed to be **multifactorial.** Autoantibodies are produced against self-antigens, especially DNA and other nuclear antigens. **Sunlight** and some infections can exacerbate episodes of lupus. Some **drugs** (anticonvulsants, sulfonamides, antiarrhythmics) are associated with causing a milder, reversible, lupuslike disease. Onset is usually after 8 years of age, and **the incidence is much higher in females** (4:1 before puberty, 8:1 afterward).

Presentation. SLE can **mimic many diseases** and should be considered in the differential of many diseases. Onset may be acute or insidious. **Fever, malaise, arthritis, and arthralgia** are common. A variety of **skin manifestations** may be present: the classic malar **butterfly rash**, vasculitic rashes, erythematous macules, and oral ulcers. Rashes may be **photosensitive**. Pleural or pericardial rubs may be heard from a **serositis**. GI manifestations from the vasculitis include pain and diarrhea. Cardiac involvement includes **Libman-Sacks endocarditis**, cardiomegaly, and heart failure. Most children have **renal involvement** including hypertension and acute renal failure. **CNS involvement** includes seizures, stroke, and aseptic meningitis. Vasculitis can manifest as **Raynaud phenomenon**.

Diagnostic Tests. Diagnosis is made from the following criteria and mnemonic. **Four** of the criteria must be present at some time.

Malar rash
Discoid rash
Serositis
Oral ulcers
Arthritis—nonerosive, ≥2 peripheral joints
Photosensitivity
Neurologic—seizures
Hematologic—hemolytic anemia, leukopenia <4000, lymphopenia <1500, platelets =100K
Antinuclear antibody
Immunologic—LE prep, anti-DNA antibodies, anti-Smith antibodies
Renal—proteinuria, casts

ANA is the best screening lab test. Antibodies to **double-stranded DNA** is much more specific, and is present during active disease. **C_3, C_4, and CH_{50}** are all decreased in active disease. **Anti-Smith** antibodies, although not measuring disease activity, are found only in patients with SLE. Renal biopsy confirms lupus nephritis.

Treatment. Nonsteroidal drugs are used to treat arthritis and arthralgia if there is no nephritis. Patients with thrombosis and antiphospholipid antibodies should be on **anticoagulants**. **Corticosteroids** are the mainstay of therapy. **Cyclophosphamide** has been used for nephritis, vasculitis, pulmonary hemorrhage, and CNS disease. **Five-year survival is now >90%. Death is usually because of nephritis, CNS complications, and infections.**

Neonatal Lupus. This may occur in newborns of mothers with lupus, as a result of transfer of IgG autoantibodies (anti-Ro) at 12–16 weeks' gestation. Manifestations (liver, skin, thrombocytopenia) resolve, except for **congenital heart block**.

MUCOCUTANEOUS LYMPH NODE SYNDROME (MCLNS, KAWASAKI DISEASE)

> An 18-month-old has had fever for 10 days. He now has conjunctival injection, a very red tongue and cracked lips, edema of the hands, and a truncal rash.

Definition. Kawasaki disease is a febrile disease with vasculitis, especially of the coronary vessels.

Risk Factors/Etiology. The etiology is unknown, although it is believed to be **infectious, probably viral**. Incidence is higher in Asian children. Patients are <5 years old.

Presentation. Fever is present in all cases, for ≥5 days, usually 1–2 weeks, and does not respond to antibiotics. Other important clinical findings are listed in the next section. Patients may be irritable and have diarrhea or signs or symptoms of aseptic meningitis. **Cardiac involvement is very common and is the most important manifestation.** Myocarditis and pericarditis with small effusions are common. **Coronary artery aneurysms** develop during the second to third week of illness. Kawasaki disease is divided into three stages:

- **Acute**—fever, acute signs. Lasts 1–2 weeks.
- **Subacute**—fever resolves, desquamation, thrombocytosis, coronary aneurysms, highest risk of death. Lasts until fourth week.
- **Convalescent**—all clinical signs resolved, erythrocyte sedimentation rate (ESR) normal. Occurs 6–8 weeks after onset.

Diagnostic Tests. Diagnosis is based on the following criteria:

- **Fever** for ≥5 days, and four of the following five.
- **Bilateral nonpurulent conjunctival injection.**
- **Mucous membrane changes**—injected pharynx, injected, dry, cracked lips, strawberry tongue
- **Peripheral extremity changes**—edema or erythema of hands or feet, periungual desquamation
- **Rash**—truncal, polymorphous, nonvesicular
- **Cervical lymphadenopathy**—>1.5 cm, usually unilateral

There are no specific tests for Kawasaki disease. ESR and C-reactive protein are elevated. **Thrombocytosis occurs in the second to third week. Sterile pyuria and anemia** may be seen. **Echocardiography** should be performed on every patient suspected of having Kawasaki disease.

Treatment. Therapy is with **intravenous immunoglobulin (IVIG) and high-dose aspirin.**

HENOCH-SCHÖNLEIN PURPURA (HSP, ANAPHYLACTOID PURPURA)

A 5-year-old boy is seen with maculopapular lesions on the legs and buttocks. He complains of abdominal pain. He has recently recovered from a viral upper respiratory infection. Complete blood cell count, coagulation studies, and electrolytes are normal. Microscopic hematuria is present on urine analysis.

Definition. HSP is an **IgA-mediated vasculitis of small vessels** and is the most common cause of nonthrombocytopenic purpura in children. Capillaries are most frequently involved. It affects the skin, synovium, GI tract, and CNS.

Risk Factors/Etiology. The etiology of HSP is unknown. Allergies and drug sensitivity have been implicated. **It commonly follows an upper respiratory infection.** Boys are more commonly affected, and the peak age is usually **4–8 years old.**

Presentation. Onset may be acute or insidious. **There is usually a preceding upper respiratory infection. Skin lesions** are the hallmark of the disease. They start out as a macule or wheal, and blanch on pressure. The rash progresses to petechiae, and the vasculitis causes a palpable purpuric rash. Typically the rash is distributed on the buttocks and legs, but may occur anywhere. **Edema and arthritis (in two thirds of patients) may be present. GI symptoms** include colicky abdominal pain, gross or occult blood in the stool, and, rarely, intussusception. **Renal manifestations** occur in 25–50% of patients, and include hematuria, proteinuria, and hypertension. **CNS involvement** is rare, but can include seizures.

Diagnostic Tests. There is no specific diagnostic test. **Most laboratory tests are normal.** Sedimentation rate may be elevated, and anemia may be seen. Urine may show red blood cells, white blood cells, casts, or albumin. Coagulation studies are normal.

Treatment. Therapy is supportive, as this is a self-limited disease. **Corticosteroids** are used for GI and CNS complications.

Table 20-1. Pediatric Arthritis Syndromes: Differential Diagnosis

Feature	Systemic Lupus Erythematosis	Juvenile Rheumatoid Arthritis	Kawasaki Disease	Rheumatic Fever	Lyme Disease
1. Age	10–20 years	5–10 years	<4 years	5–15 years	5–20 years
2. Predominant Sex	Female	Varies with type	Male & female	Male & female	Male & female
3. Arthralgia	+	+	+	+	+
4. Rash	Butterfly, discoid	Salmon pink macules	Diffuse, maculopapular	Erythema marginatum	Erythema chronicum migrans
5. Pauciarticular or polyarticular	Polyarticular	May be either	Polyarticular	Polyarticular	Pauciarticular
6. Small joint involvement	+	+	+	–	–
7. Eye involvement	Uveitis and retinits	Iridocyclitis	Conjunctivits uveitis	–	–
8. Antinuclear antibody	+	+ in 50%	–	–	–
9. Rheumatoid factor	+/–	+ in 10%	–	–	–
10. Characteristic lab results	↓ Complement	____	Thrombocytosis ↑ Immune complexes	↑ ASO titre	↑ Cryoglobulin ↑ Immune complex
11. Other manifestations	Proteinuria, serositis	Fever, serositis	Fever, swelling of hands and feet, cracked lips	Carditis, chorea, nodules	Carditis, neuropathy
12. Mechanism	Autoimmune	Autoimmune	Unknown	Group A streptococci	*Borrelia burgdorferi*
13. Treatment	NSAIDs and steroids	NSAIDs	Aspirin, I.V. immunoglobulin	Penicillin prophylaxis, aspirin, steroids	Penicillin, tetracyclin, ceftriaxone

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DIABETES MELLITUS (DM)

An 8-year-old boy is seen in the emergency department with vomiting and abdominal pain of 2 days' duration. His mother states he has been drinking a lot of fluids for the past month, and reports weight loss during that time. Physical examination reveals a low-grade fever, and a moderately dehydrated boy who appears acutely ill. He is somnolent but asks for water. Respirations are rapid and deep. Laboratory tests reveal a metabolic acidosis and hyperglycemia.

Definition. DM results from a **deficiency in insulin**, or a defect in its action, or both. This results in abnormal metabolism of carbohydrate, protein, and fat. The two major classifications of diabetes are **type I** diabetes, also known as insulin-dependent DM (IDDM), in which there is a severe lack of insulin. This is more common in children and is also known as juvenile DM. **Type II** diabetes, also known as adult-onset, maturity-onset, or non–insulin-dependent DM (NIDDM), is characterized by insulin resistance.

Risk Factors/Etiology. Type I DM is has a very strong correlation with an **autoimmune etiology**. It is more common in persons with other autoimmune diseases, and there is an association with certain HLAs. Islet cell antibodies are present in most newly diagnosed patients. IDDM also tends to run in families. **Preceding viral infections may serve as a trigger.**

Presentation. Many children present with the classic symptoms of **polyuria, polydipsia, polyphagia, and weight loss. Up to 25% present in diabetic ketoacidosis**, with vomiting, abdominal pain, dehydration, **Kussmaul respirations**, and cerebral obtundation.

Diagnostic Tests. Diabetic ketoacidosis (DKA) occurs when **the glucose is >300 mg/dl and there is ketonemia**, acidosis (pH <7.30; bicarbonate, 15 mEq/L), glucosuria, and ketonuria. DM can also be diagnosed in patients with milder symptoms. The new criteria are symptoms of diabetes with a **random plasma glucose ≥200 mg/dl**, or **fasting glucose ≥126 mg/dl**, or **2-h glucose tolerance ≥200 mg/dl.** In all cases, hyperglycemia and glucosuria are necessary.

Treatment. Treatment of DKA consists of correction of dehydration and electrolytes, and insulin. Treatment of IDDM consists of **insulin, diet, and exercise.**

Complications. Complications of diabetes include retinopathy, cataracts, nephropathy, neuropathy, and atherosclerosis. Most diabetic complications occur in adults.

CONGENITAL HYPOTHYROIDISM

A 2-month-old patient appears to be having inadequate weight gain. His mother states he is constipated. On examination, he has decreased muscle tone, a large fontanel, a large tongue, and an umbilical hernia.

Definition. Congenital hypothyroidism results from a **deficiency of thyroid hormone.**

Risk Factors/Etiology. Congenital hypothyroidism occurs in about 1/4000 births. The majority of cases occur because of **thyroid dysgenesis**. This is either caused by complete absence of or ectopic thyroid tissue. Congenital hypothyroidism is twice as common in females.

Presentation. Symptoms appear gradually. Prolonged **jaundice** may be the earliest sign. **Poor feeding**, somnolence, a **large tongue, constipation,** and an **umbilical hernia** may be present. The skin may be cold and **mottled.** The full clinical picture develops by 3–6 months. Growth and development are retarded. The **fontanels stay widely open.** Hair is coarse and brittle. There is a generalized muscle **hypotonia.**

Diagnostic Tests. Serum levels of T_4 **are low, whereas thyrotropin (TSH) levels are elevated.** Newborn screening tests detect most cases of congenital hypothyroidism. Retardation of osseous development can be shown on radiographs. **Thyroid scans** with technetium or radiolabeled iodine detect absence of or ectopic thyroid tissue.

Treatment. Replacement of thyroid hormone with **thyroxine** is the therapy. Thyroxine should not be mixed with soy formula or iron.

Complications. Early diagnosis and treatment has greatly reduced the incidence of complications. Overtreatment with thyroxine can result in temperament problems. Early diagnosis and replacement therapy are crucial in preventing severe developmental delays.

ACQUIRED HYPOTHYROIDISM

Etiology/Risk Factors. **Thyroiditis** is the most common cause of acquired hypothyroidism. Down, Turner, and Klinefelter syndromes carry a higher risk for **autoimmune** thyroid disease. **Irradiation** and ingestion of iodides can also lead to hypothyroidism.

Presentation. Growth deceleration is usually the first sign, but may be subtle. Patients also develop constipation, **cold intolerance,** and **decreased energy**. Schoolwork and grades do not suffer. Osseous maturation is delayed. In lymphocytic **thyroiditis, growth retardation and goiter are the first signs.**

Diagnostic Tests. Diagnostic tests are the same as for congenital hypothyroidism.

Treatment. Treatment consists of replacement therapy.

HYPERTHYROIDISM/GRAVES DISEASE

A 12-year-old girl has a 6-month history of hyperactivity and declining school performance. Appetite is increased but she shows no weight gain. Physical examination reveals a slight tremor of the fingers, mild exophthalmos, and a neck mass.

Definition. Hyperthyroidism results from overproduction of thyroid hormone.

Risk Factors/Etiology. Hyperthyroidism almost always results **from Graves disease**, a diffuse toxic goiter. **Neonatal hyperthyroidism** results in infants born to mothers with Graves disease. Graves is associated with HLA-B8 and HLA-DR3.

Presentation. Symptoms develop over 6–12 months. Patients may have **emotional disturbances**, motor hyperactivity, emotional lability, and **deterioration in school performance. Tremors** of the fingers may be noticed on extension of the arms. **Voracious appetite** without weight gain may be described. **Exophthalmos** results from binding of antibodies to extraocular muscles, producing a cytotoxic effect. **Sweating and flushing** are common. **Tachycardia and palpitations** are cardiac manifestations. **Thyroid storm** is a severe presentation, which can lead to death, but is rare in children.

Diagnostic Tests. T_4, free T_4, T_3, and free T_3 are elevated, whereas TSH levels are low. Thyroid receptor stimulating antibodies are often present.

Treatment. Medical treatment consists of **propylthiouracil or methimazole. Propranolol** is useful for reversing symptoms in severely toxic patients. **Surgery or radioablation** with iodine are reserved for patients who do not respond to medical management.

CONGENITAL ADRENAL HYPERPLASIA (CAH)

A 1-month-old infant is seen with vomiting and severe dehydration. Physical examination reveals ambiguous genitalia; laboratory tests show hyponatremia.

Definition. CAH results from **cortisol deficiency**, which causes increased corticotropin secretion and subsequent hyperplasia.

Risk Factors/Etiology. CAH is a series of **autosomal recessive** disorders: **21-hydroxylase deficiency** is the most common cause of CAH, followed by 11β-hydroxylase deficiency and 3β-hydroxysteroid dehydrogenase.

Presentation. Clinical presentation depends on the enzyme deficiency. 21-Hydroxylase deficiency with salt losing results in **virilization and ambiguous genitalia** in females. Patients may present with **vomiting and hyponatremic dehydration.** Non–salt-losing boys have **premature sexual development**, whereas girls have pseudohermaphroditism. 11β-Hydroxylase deficiency causes **severe virilization**, and hypertension, but does not cause salt losing.

Diagnostic Tests. Hyponatremia, hypochloremia, elevated potassium, and blood urea nitrogen are seen in salt-losers. **Plasma renin is high, aldosterone is low. 17-OH progesterone levels are elevated** in 21-hydroxylase deficiency. **Urinary 17-ketosteroids** are elevated. **Prenatal diagnosis** can be made by measuring 17-OH progesterone and androstenedione in amniotic fluid. 11-Hydroxyalse deficiency produces elevated deoxycorticosterone and 11-deoxycortisol.

Treatment. Glucocorticoids (hydrocortisone) prevent androgen production and subsequent virilization. Salt-losers require mineralocorticoid and sodium replacement. **Increased doses of hydrocortisone are required during periods of stress.**

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ANEMIA

Iron Deficiency Anemia

An 18-month-old child of Mediterranean origin presents to the physician for routine well-child care. The mother states that the child is a "picky" eater and prefers milk to solids. In fact, the mother states that the patient, who still drinks from a bottle, consumes 64 ounces of cow's milk per day. The child appears pale. A hemoglobin (Hb) and hematocrit (Hct) were measured, and the Hb is 6.5 g/dl and the Hct is 20%. The mean corpuscular volume (MCV) is 65 fl.

Definition. Iron deficiency anemia is a microcytic hypochromic anemia and is commonly seen in children at 6–24 months of age.

Risk Factors/Etiology. It is the most common hematologic disease of infancy and childhood. The etiology includes (*1*) **low birth weight,** (*2*) **inadequate dietary intake,** especially in children 9-24 months old, and, less commonly, (*3*) **blood loss** from peptic ulcer disease, Meckel diverticulum, polyps, hookworms, and ingestion of whole cow's milk in infants. The most common cause is the inadequate intake of iron.

Presentation. The typical patient is on a diet consisting mainly of milk. Mild anemia is relatively asymptomatic. The parent may complain that the patient is lethargic, anorexic, irritable, and easily fatigued. High-output cardiac failure may be present when the Hb is <3 g/dl.

Physical Examination. The patient may appear pale, have tachycardia, and have a systolic murmur on physical examination. Koilonychia (spoon nails) may also be present. Splenomegaly is seen in 10–15% of patients.

Diagnostic Tests. A reticulocyte count will be minimal (0–1%) and should be performed before beginning ferrous sulfate. A complete blood count with differential and platelets should be obtained. The red blood cells will be small because Hb is decreased. Thrombocytosis may be present. The serum iron and serum ferritin levels are decreased. The iron-binding capacity and free erythrocyte protoporphyrin level are increased.

Treatment. Oral iron in the form of **ferrous sulfate** (6 mg/kg/d of elemental iron) should be prescribed. Iron replacement and a dramatic response to therapy is a good diagnostic tool. Reticulocytosis should be seen within 72 h of initiation. Hb will increase in 3–4 weeks. Iron replacement should continue for 4–5 months after the Hb level has returned to normal, allowing the tissues to replenish tissue iron stores. Dietary counseling should simultaneously be given to assure the patient gets adequate amounts of iron in the diet. Severe iron deficiency may

require transfusion therapy or parenteral iron; however, these treatments should be given in consultation with a hematologist.

Complications/Follow-up. A repeat reticulocyte count should be done 5 days after starting iron. An Hct level should be checked 1 month after initiating therapy. If iron therapy does not work, consider blood loss from a Meckel diverticulum.

Differential Diagnosis. The differential diagnosis for microcytic hypochromic anemia includes lead poisoning, thalassemia, and chronic disease.

Hemolytic Anemia

A 2-year-old boy presents to the physician's office for an ear check. The child had an ear infection that was treated with trimethaprim-sulfamethoxazole 3 weeks earlier. On physical examination the patient is noted to be extremely pale. Hb and Hct were obtained and are noted to be 7.0 g/dl and 22%, respectively.

Definition. Hemolytic anemia results from a decrease in red blood cell survival.

Risk Factors/Etiology. There are two types of hemolytic anemia: (*1*) **premature destruction** caused by intrinsic red blood cell abnormalities, e.g., hereditary **spherocytosis**, and (*2*) **enzymatic defects**, e.g., **glucose-6-phosphate dehydrogenase (G-6-PD)**. Hereditary spherocytosis is the most common inherited (usually autosomal dominant) hemolytic anemia. **Spherocytosis** has a defect in the skeletal proteins of the red blood cells causing the shape of the cell to be altered. In **G-6-PD** there is a structural variant in the normal enzyme causing low enzyme activity.

Presentation. Patients with spherocytosis may have slight jaundice, and gallstones.

Physical Examination. The patient with spherocytosis may have splenomegaly.

Diagnostic Tests. Patients with **spherocytosis** have **spherocytes** in the peripheral blood. There is also an increased reticulocyte count, indirect bilirubin, and lactate dehydrogenase. Haptoglobin is decreased. The Coombs test is negative. The **osmotic fragility** test should be performed to test for spherocytosis. Gallstones may be seen on ultrasound.

In **G-6-PD blister cells** may be seen on peripheral smear, and reticulocytosis is present. Enzyme assays may be done.

Treatment. Spherocytosis: Patients with mild spherocytosis should receive folate therapy. **Splenectomy** is the treatment for severe spherocytosis, but should not be performed until after 5 years of age. Before splenectomy the patient needs to receive the *Pneumococcus, Meningococcus,* and *Haemophilus influenzae* vaccines. Splenectomized patients should receive oral penicillin daily.

G-6-PD: Avoidance of triggers such as sulfa drugs, fava beans, high-dose aspirin, and antimalarials is the treatment for G-6-PD. Administration of oral folic acid daily is recommended. Splenectomy may be considered in patients with chronic disease.

Complications/Follow-up. Splenectomized patients have a risk of sepsis from encapsulated organisms.

HEMOGLOBINOPATHIES

A 6-month-old African American infant presents to the pediatrician with painful swollen hands and swollen feet.

Sickle Cell Disease (Hemoglobin SS)

Definition. Sickle cell disease is a blood disorder that occurs when valine is substituted for glutamic acid at the sixth position of the β chain. This change results in the formation of rigid crystals when the oxygen levels are low.

Risk Factors/Etiology. The incidence of sickle cell disease is higher in areas where *Plasmodium falciparum* malaria is epidemic. There is a 0.2% incidence of the disease in American blacks; however, approximately 10% of American blacks have sickle cell trait (Hb AS).

Presentation. In the **newborn** period there are **no clinical features** as there is still Hb F and not much Hb S. During the first 2–4 months, hemolytic anemia develops, and by **5–6 months** patients develop the **hand-foot syndrome, i.e., dactylitis.** Dactylitis is usually the first manifestation of sickle cell disease, and infants present with painful symmetric swelling of the hands and feet secondary to poor blood flow to the expanding marrow spaces. From **6 months to 5 years** the **spleen "auto infarcts,"** predisposing the patient to **encapsulated organisms** such as *Streptococcus pneumoniae* and *H. influenzae.* Splenic sequestration, i.e., acute splenic engorgement, can lead to shock and death. From **6 months to a lifetime vasoocclusive episodes** precipitated by intercurrent illness is the most frequent manifestation. Young children may complain of painful extremities. Older children may present with chest pain, back pain, and abdominal pain that mimics a surgical abdomen.

Physical Examination. Vasoocclusive episodes may cause ischemic damage, bone infarcts, splenic infarcts, pulmonary infarcts, and stroke. There may be splenic sequestration.

Diagnostic Tests. Laboratory tests include a complete blood count, reticulocyte count, sickle prep, and Hb electrophoresis. Gallstones (secondary to increased bile production from chronic hemolysis) may be visualized on ultrasound. A blood culture and chest roentgenogram should be performed on febrile patients.

Treatment. The patient should be **immunized** to prevent disease, especially against pneumococcal and *H. influenzae* infection. Patients with sickle cell disease should receive prophylaxis with **penicillin** and **folic acid supplement. High fevers** in young children require **parenteral antibiotics** such as ceftriaxone. **Painful episodes** should be managed with **analgesics, rest,** and **hydration. Transfusion** and oxygen therapy are not indicated for uncomplicated painful crisis. However, **transfusion** should be given in consultation with a hematologist to patients with aplastic crisis, splenic sequestration, major surgery, acute chest syndrome, cerebrovascular accident, and priaprism.

Complications/Follow-up. Patients with sickle cell disease have an increased susceptibility to **infections,** particularly sepsis, meningitis, and **salmonella osteomyelitis.** Infection is a leading cause of death. Other problems that may occur in the patient with sickle cell disease include aplastic crisis. This aplastic crisis often occurs after an acute illness such as parvovirus, causing reticulocytes to fall and a profound anemia. Patients are also susceptible to delayed growth and puberty. Leg ulcers may occur.

Thalassemia Major (Cooley, Homozygous B)

A 9-year-old has a greenish-brown complexion, maxillary hyperplasia, splenomegaly, and gallstones. Her Hb level is 5.0 g/dl, and she has an MCV of 65 ml.

Definition. Thalassemia major is a severe blood disorder resulting from an imbalance of α- and β-globin chains. There is a surplus of α-globin chains, causing ineffective erythropoiesis and hemolysis.

Risk Factors/Etiology. Reduced oxygen carrying ability, ineffective increase in iron absorption, and red marrow expansion are present.

Presentation. The patient becomes symptomatic in the second 6 months and develops severe progressive hemolytic anemia.

Physical Examination. The patients may have pallor or a greenish-brown complexion (jaundice). Facial deformities are present from expansion of the marrow. Splenomegaly is present. Heart failure may be present secondary to high urine output. Gallstones may be present.

Diagnostic Tests. A complete blood count will usually have Hb in the range of 2.0–6.5 g/dl. The peripheral blood smear shows a hypochromic, microcytic anemia. Patients develop hemosiderosis. On peripheral smear hypochromia and microcytosis are found, as well as bizarre, fragmented cells. Unconjugated bilirubin is increased. The diagnosis is made with Hb electrophoresis. The patient has high levels of fetal Hb, with Hb A <3%.

Treatment. The treatment is transfusion therapy and chelation therapy. Hematopoietic stem cell transplantation is also used.

Complications/Follow-up. If the patient develops hemochromatosis, deferoxamine should be administered.

CONGENITAL PURE RED BLOOD CELL ANEMIA

Diamond-Blackfan Syndrome

A 2-week-old on routine physical examination is noted to have pallor. The birth history was uncomplicated. The patient has been doing well according to the mother.

Definition. Diamond-Blackfan syndrome is a congenital pure red blood cell anemia.

Risk Factors/Etiology. This syndrome appears to be genetic, as there are familial occurrences.

Presentation. Half of the affected infants appear pale in the first few days. Patients have profound anemia by 2–6 months.

Physical Diagnosis. There may be associated congenital anomalies in 25% of patients.

Laboratory Tests. Laboratory evaluation should include complete blood count with MCV as these patients have a **macrocytic** anemia. A bone-marrow aspiration shows reduced red-cell precursors. Serum or urine erythropoietin levels are elevated.

Treatment. Transfusions and corticosteroids are used as therapy for the illness. Androgens, immunosuppressive agents, and hematopoietic growth factors have variable success. Bone marrow transplantation may be an option for some patients.

Complication/Follow-up. Iron overload from chronic red blood cell transfusion may occur.

PANCYTOPENIAS

Constitutional (Fanconi)

A 2-year-old presents to the physician with aplastic anemia. The patient has microcephaly, microphthalmia, and absent radii and thumbs.

Definition. Fanconi pancytopenia is an autosomal recessive blood disorder characterized by bone marrow failure.

Risk Factors/Etiology. Fanconi anemia is associated with aplastic anemia and congenital musculoskeletal and cutaneous abnormalities.

Presentation/Physical Diagnosis. There are associated physical abnormalities with this illness, including microcephaly, microphthalmia, hearing loss, and absent radii and thumbs. Short stature is present in two thirds of patients. There is generalized hyperpigmentation.

Laboratory Tests. Severe pancytopenia is seen, and the red blood cells are macrocytic. The bone marrow is hypocellular. The diagnosis is confirmed by cytogenetic analysis (increased chromosomal breakage) in the presence of diepoxybutane. Diagnosis is possible during the prenatal period.

Treatment. Therapy includes transfusions, antibiotics, androgenic steroids, low-dose corticosteroids, and bone marrow transplantation.

Complication/Follow-up. Acute myelogenous leukemia may be a complication of Fanconi.

Acquired Aplastic Anemia

Definition. Aplastic anemia is characterized by a decrease in production of red blood cells, white blood cells, and platelets.

Etiology/Risk Factors. Causes of acquired aplastic anemia include (*1*) **physical-ionizing radiation,** (*2*) **drugs,** e.g., chemotherapeutic, chloramphenicol, sulfonamides, anticonvulsants, (*3*) **infections,** i.e., parvovirus and mononucleosis, and (*4*) **no prior history (50%).**

Presentation/Physical Examination. The first sign of acquired aplastic anemia is usually hemorrhage secondary to thrombocytopenia. The patient may have signs of anemia.

Diagnostic Studies. Laboratory studies show a profound decrease in platelets, red blood cells, and white blood cells and scanty bone marrow. Diagnosis is confirmed by pancytopenia of the **bone marrow.**

Treatment. The patient should be removed from the source if possible. If hemorrhage is present then transfuse. Antibiotics should be prescribed for infection. A bone marrow transplant may be helpful. A bone marrow transplant offers the best chance for survival. Androgens and hematopoietic growth factors may be helpful to some patients.

Complications/Follow-up. Approximately two thirds of patients with acquired aplastic anemia will die within 6 months. Approximately 10–20% will recover. Death occurs from hemorrhage or infection.

THROMBOCYTOPENIA

Idiopathic Thrombocytopenic Purpura (ITP)

A 4-year-old child previously healthy presents with petechiae, purpura, and excessive bleeding after falling from his bicycle.

Definition. ITP is the most common cause of thrombocytopenic purpura of childhood. There is no apparent exogenous cause for platelet destruction, and it is immune-mediated.

Etiology/Risk Factors. The etiology is thought to be autoimmune but is uncertain. Approximately 70% of cases have antecedent viral infection. The acute form usually occurs in children between the ages of 2 and 6 years after a nonspecific viral illness. There is no difference in prevalence between boys and girls.

Presentation. Clinical features (acute form) usually present as an acute onset. Bruising and petechial rash occur 1–4 weeks after viral infection. The patient appears clinically well, but intracranial hemorrhage may be present in <1%. The patient may also present with petechiae, purpura, and excessive bleeding after trauma. Joint bleeding is rare.

Physical Examination. The physical examination is normal except for the skin manifestations of bruising and petechiae. The spleen is **not** enlarged.

Diagnosis. All ITP patients show varying degrees of thrombocytopenia, which is sometimes very severe (platelet count <1,000/mm^3). Hemorrhage secondary to thrombocytopenia is usually the first sign. There is an abnormal bleeding time. Bone marrow shows **normal** or **increased megakaryocytes,** and all other findings and cell lines are normal. Signs of anemia are present.

Treatment. Patients have an excellent prognosis even without treatment. Seventy-five percent of patients will recover in 8 weeks. Intravenous immunoglobulin causes a rapid rise in platelet count. Because most of the cases resolve spontaneously, the use of corticosteroids are controversial. In severe cases, short courses of corticosteroids may be useful. Patients need to be protected from trauma.

Complications/Follow-up. The acute childhood variant runs its course and resolves within 4–8 weeks.

Other entities associated with **thrombocytopenia** include the following:

- **Wiskott-Aldrich:** This is an X-linked syndrome involving the **triad** of (*1*) **recurrent infections** (all classes of microorganisms), (*2*) **hemorrhage** secondary to thrombocytopenia, and (*3*) **eczema.** For a more detailed explanation of Wiskott-Aldrich, see Chapter 12, **Allergies/Immunology.**
- **Kasabach-Merritt:** Kasabach Merritt syndrome is characterized by a rapidly enlarging **cavernous hemangioma,** and a consumption coagulopathy resulting in **thrombocytopenia.** The lesion is usually cutaneous and rarely found in viscera. The platelet count is depressed. Anemia may be present. Bone marrow megakaryocytes are increased but normal. The treatment is surgical removal (if possible), laser therapy,

high-dose corticosteroids, and interferon. A trial of ε-aminocaproic acid (Amicar) may be used for the coagulopathy.

- **TAR:** TAR syndrome is associated with thrombocytopenia absent radius.

HEMOPHILIA

Hemophilia A (Factor VIII Deficiency)

A newborn infant has prolonged bleeding after circumcision. There is no family history of bleeding disorders.

Definition. Hemophilia A is an X-linked recessive deficiency of factor VIII activity.

Etiology/Risk Factors. Hemophilia A accounts for 80% of all hemophilias. Approximately, 1 in 5,000 to 10,000 males are affected. Family history is usually positive for hemophilia A.

Presentation. Bleeding can be seen in neonatal period hematomas after injection or circumcision. Ninety percent of patients have increased bleeding by 1 year of age. Patients may have bruising with ambulation, resulting in hemarthrosis.

Physical Examination. Excessive bruising may be visible. The physical examination should focus on areas of past and acute bleeding.

Diagnostic Studies. Bleeding history is important in the evaluation of hemophilia. The diagnosis of hemophilia can be established in one of four ways: (*1*) prenatal evaluation with a family history of hemophilia, (*2*) prolonged bleeding after circumcision, (*3*) toddlers with excessive bruising from falls, and (*4*) at times, prolonged partial thromboplastin time (PTT) that is discovered preoperatively in the mild hemophiliac.

Laboratory tests include a decreased factor VIII activity, and normal von Willebrand factor (vWF) assay. The PTT is prolonged; the platelet count is normal, as is the prothrombin and bleeding time.

Treatment. Bleeds must be treated immediately with factor VIII. 1-Desamino-8-D-arginine vasopressin (DDAVP) may be used to increase factor VIII levels in some patients with mild hemophilia. Trauma prevention should be a goal of therapy. Aspirin and other antiplatelet medications should be avoided.

Follow-up/Complications. Inhibitors to clotting factors may result and are more common in hemophilia A. Transfusion-transmitted disease is possible but uncommon.

Hemophilia B (Factor IX Deficiency, Christmas Disease)

A 2-year-old presents to the pediatrician and is noted to have excessive bruising during physical examination. The mother says that the child's skin is very sensitive to bruising. She also notes that the child has epistaxis. There is a family history of bleeding.

Definition. Hemophilia B is an X-linked recessive deficiency of factor IX. It is less common than hemophilia A.

Etiology/Risk Factors. This is a vitamin K-dependent factor. Hemophilia B is clinically indistinguishable from hemophilia A

Presentation/Physical Examination. The presentation and physical examination are the same as in hemophilia A.

Diagnostic Studies. Evaluation is the same as described for hemophilia A. Low levels of factor IX confirm the diagnosis. Vitamin K deficiency should also be ruled out.

Treatment. Therapy includes replacement with factor IX.

Follow-up/Complications. Some complications include multiple hemarthrosis and life-threatening bleeding problems. Transfusion-transmitted disease is possible but uncommon.

von Willebrand

Definition. von Willebrand disease (vWD) is the most common inherited (autosomal dominant) bleeding tendency.

Etiology/Risk Factors. There is an underproduction of von Willebrand protein. von Willebrand factor (vWF) has three main functions: (*1*) adhesion of platelets, (*2*) platelet to platelet aggregation, and (*3*) carrier for factor VIII.

Presentation/Physical Examination. Clinically patients may present with nosebleeds, bleeding from gums, menorrhagia, and prolonged bleeding from cuts. Spontaneous hemarthrosis is rare, and may be seen in those patients with a more severe form of vWD.

Diagnostic Studies. The patient's bleeding history and the bleeding history of the patient's family members are critical to making the diagnosis. The patient will have a prolonged bleeding time. The platelet count and prothrombin time are normal. PTT is mildly elevated. There are reduced levels of vWF. Platelets will have decreased adhesiveness.

Treatment. The treatment for vWD is replacement using fresh-frozen plasma or cryoprecipitate, and DDAVP.

SUMMARY

Table 22-1. Blood Disorders According to Reticulocyte Count Changes

Low Reticulocyte Count	
Microcytic	Iron deficiency Lead poisoning Chronic disease
Normocytic	Chronic disease RBC aplasias: transient erythroblastopenia of childhood (TEC), drugs, infection
Macrocytic	Folate deficiency B_{12} deficiency Aplastic anemia Congenital marrow dysfunction: Blackfan-Diamond, Fanconi
Normal Reticulocyte Count	
Microcytic	Thalassemia trait
Normocytic	Acute bleeding Hypersplenism
Macrocytic	—
High Reticulocyte Count	
Microcytic	Thalassemia syndromes HbC disorders
Normocytic	Ab-mediated hemolysis Microangiopathic Membrane defects Enzyme defects Hemoglobinopathies
Macrocytic	Active hemolysis

Table 22-2. Coagulation Labs

Lab	Function	Increases with/in	Notes
Bleeding time	Assesses platelet function and interaction with vessel wall	Qualitative platelet disorders von Willebrand disease (VWD)	
PTT	Measures initiation of clotting at level of factor 12 through final clot endpoint Intrinsic	VIII, IX, XI, and XII deficiencies VWD, heparin, factor-inhibitor	Does *not* measure VII, XIII, or anticoagulants
PT	Measures extrinsic system after activation of clotting by thromboplastin with calcium	Coumadin, VII deficiency	*Not* prolonged with deficiencies of VIII, IX, XI, and XII
PT and PTT	Measures extrinsic and intrinsic systems	Deficiencies of II, V, X Acquired liver disease Vitamin K deficiency	
Thrombin time	Measures final step in which fibrinogen is converted to fibrin	Hypo- or dysfibrinogenemia Heparin Fibrin split products (FSP)	
Mixing studies	Correction of coagulation studies—indicates deficiency of clotting factor(s); rules out presence of an inhibitor No correction of coagulation studies—indicates the presence of an coagulation factor inhibitor	No bleeding: lupus-like anticoagulant	
Clotting factor assays			
Platelet aggregation	Qualitative platelet function defect		
Decrease of anticoagulant factors	Functional assays for proteins C, S, and AT-III Thrombotic disposition		

Oncology

23

ACUTE LYMPHOCYTIC LEUKEMIA (ALL)

A 5-year-old patient is brought to the physician's office with chief complaint of limp. The patient on physical examination has a low-grade fever, URI symptoms, hepatosplenomegaly, and petechiae.

Definition. Leukemia is the most common childhood cancer. It is characterized by large numbers of lymphoblasts in the bone marrow and on peripheral smear.

Risk Factors/Etiology. The peak incidence for acute lymphocytic leukemia (ALL) is 3–4 years of age. It is more prevalent in white children than in black children. Children with conditions such as Down syndrome, ataxia telangiectasia, von Recklinghausen, and sideroblastic anemia are at risk for developing ALL. Being a twin sibling of a leukemic patient younger than 4 years of age also increases the chances of a child to develop ALL. Children with solid tumors, such as Hodgkin disease and Wilms tumor, or those who have undergone intense treatment may develop leukemia as a secondary malignancy (more commonly AML [acute myelogenous leukemia]).

Presentation. Patients present with a nonspecific viral illness initially. They may complain of anorexia, irritability, and lethargy. Bone marrow failure leads to pallor, bleeding, and fever. The presenting clinical features of leukemia are similar to those of aplastic anemia (anemia, bruising, frequent infection), but they also include lymphadenopathy, splenomegaly, and bone pain. Many of the patients have had signs or symptoms less than 4 weeks.

Physical Examination. As described above the patient appears pale and may have splenomegaly, petechiae (secondary to thrombocytopenia), or mucous membrane bleeding.

Diagnostic Tests. The white blood cell (**WBC**) count may be increased or decreased. Blast cells may be seen on the peripheral blood smear. The **bone marrow** shows leukemic lymphoblasts. The patient may have anemia and thrombocytopenia. A **chest radiograph** should be completed to look for mediastinal mass. The **cerebrospinal fluid** should be evaluated for leukemic cells.

There is no anatomic staging system because the disease is usually disseminated at the time of diagnosis.

Treatment. Therapy for ALL begins with **remission induction**. Patients receive vincristine, prednisone, and L-asparaginase over 6 weeks. In addition, either prophylactic **CNS radiation** or **intrathecal methotrexate**, and **cytosine arabinoside** with **hydrocortisone** is given. After remission is attained the **consolidation phase** begins using several chemotherapeutic agents to improve outcome. **Maintenance therapy** is given for 2–3 years. If transfusion is necessary, use irradiated blood products to decrease the risk of graft-versus-host disease.

Complications/Follow-up. The **bone marrow** is the most common site of **relapse**, although **relapses** also occur in the **CNS** and **testes**.

Prognosis for ALL is **least favorable** in children younger than 2 years of age or older than 10 years of age. A WBC count greater than 100,000 is **not favorable**. Other **poor prognostic indicators** include being a boy or black, and having CNS leukemia and mediastinal masses.

Survival without therapy is less than 6 months. With treatment the overall cure rate for childhood ALL is approximately 80%.

Tumor lysis syndrome can occur with initiation of chemotherapy. Hyperuricemia occurs and is treated by vigorous hydration of the patient and alkalization of the urine. Administration of allopurinol, a xanthine oxidase inhibitor, will block uric acid formation. Hyperkalemia may also develop and cause serious arrhythmias if not corrected. Hyperphosphatemia causes a fall in serum Ca^{2+} that may result in (*1*) tetany, (*2*) potentiation of the effect of hyperkalemia on the heart, and (*3*) precipitation of calcium phosphate in the renal tubules.

Differential Diagnosis. Aplastic anemia, mononucleosis, rheumatoid arthritis, pertussis, and other types of malignant tumors that can cause pancytopenia (e.g., neuroblastoma, retinoblastoma, rhabdomyosarcoma) should be considered in the differential diagnosis of ALL.

LYMPHOMA

Lymphoma is the third most common cancer in children in the United States and is divided into two groups: (1) Hodgkin disease and (2) non-Hodgkin lymphoma.

Hodgkin Disease

> A 16-year-old boy presents with complaints of weight loss, fever, and night sweats. On physical examination he is noted to have a nontender cervical lymph node that is 4 × 5 cm.

Definition. Hodgkin disease is a lymphoma that causes approximately 5% of cancers in children and adolescents in the United States.

Risk Factors/Etiology. Hodgkin disease occurs in older children and adolescents. It is more prevalent in younger boys but appears to have an equal gender rate in adolescents. A preexisting immunodeficiency increases a person's chances of acquiring Hodgkin disease. Although uncertain, it is thought that Epstein-Barr virus (EBV) plays a role in Hodgkin disease. The **Reed-Sternberg cell** is the central histologic feature of Hodgkin disease. There are four major histologic subtypes classified on the basis of histopathology: (*1*) **lymphocyte predominant,** (*2*) **nodular sclerosing,** (*3*) **mixed cellularity,** and (*4*) **lymphocytic depleted.** Previously, lymphocyte predominant had the best prognosis and lymphocytic depleted the least favorable prognosis. However, curative therapy has lessened the importance of these different histologic types.

Presentation. Localized adenopathy, especially in the cervical or supraclavicular region, is the **most common** presenting symptom. A mediastinal mass is often present. The presentation varies with the extent of the disease. Manifestations may include night sweats, fever, weight loss, lethargy, anorexia, and pruritus.

Physical Examination. A firm, nontender enlarged cervical or supraclavicular lymph node is usually present.

Diagnostic Tests. The **diagnosis** should be suspected in a patient who has persistent unexplained lymphadenopathy without evidence of inflammation or infection. An **excisional biopsy** of the node should be performed; however, a chest roentgenogram should be done to identify mediastinal mass before the excision. After Hodgkin disease is diagnosed it is important to stage the disease. Surgical staging is no longer routinely performed.

Studies that are necessary for clinical staging of Hodgkin disease include a **complete blood count** to look for anemia and thrombocytopenia. **Erythrocyte sedimentation rate, serum ferritin,** and **serum copper** serve as a baseline to evaluate the effects of treatment. **Chest radiograph, chest and abdominal CT with contrast,** and a **gallium scan** help to identify mediastinal mass, liver and spleen enlargement, and subdiaphragmatic nodal involvement. A **bone marrow** is indicated in patients who have stage III or stage IV disease and in patients with B symptoms (fever or weight loss).

Staging for Hodgkin disease is performed according to the Ann Arbor classification.

- Stage I—Involves single lymph node region or single extralymphatic organ
- Stage II—Two or more lymph node regions, same side of the diaphragm, or localized involvement of an extralymphatic organ and one or more lymph node regions on the same side of the diaphragm
- Stage III—Lymph nodes on both sides of the diaphragm are involved, may have local involvement of an extralymphatic organ or spleen
- Stage IV—Disseminated involvement of one or more extralymphatic organs, with or without associated lymph node involvement

Systemic or "B" symptoms occur in 30% of children and consist of the following:

- Temperature exceeding 38°C (100.4°F)
- Night sweating
- Weight loss of more than 10% in 6 months

Treatment. Treatment is determined by **disease stage, patient's age,** and **presence** or **absence of "B" symptoms**. Many centers treating children use **combined** radiotherapy and chemotherapy or chemotherapy alone. **Chemotherapy** includes the MOPP (mechlorethamine hydrochloride, vincristine sulfate, procarbazine, and prednisone) or ABVD (doxorubicin hydrochloride, bleomycin, vinblastine, and dacarbazine) regimen. **Radiotherapy** is given to the involved lymph node and to the next lymph node group to which the tumor may spread. More aggressive regimens for advanced disease (stages IIIB and IV) are in clinical trials.

Complications/Follow-up. The prognosis is good with cure rates of 90% in patients with early disease and 70% in patients with more advanced cases.

Non-Hodgkin Lymphoma

A 6-year-old boy presents to his primary care provider (PCP) with a nonproductive cough. The PCP makes the diagnosis of an upper respiratory infection. However, the patient's symptoms persist, and he returns to his PCP. At this visit the patient is wheezing, and the PCP makes the diagnosis of reactive airway disease and prescribes an inhaled β_2-agonist. The medication does not improve the symptoms, and the patient returns to the PCP for a third time. The patient is now complaining of cough and has a low-grade fever. The patient is diagnosed with clinical pneumonia, and an antibiotic is prescribed. Two days later the patient presents to the emergency center in respiratory distress. A chest roentgenogram shows a large mediastinal mass.

Definition. Non-Hodgkin lymphoma (NHL) is a heterogeneous group of diseases characterized by neoplastic proliferation of immature lymphoid cells that, unlike the malignant lymphoid cells of ALL, accumulate primarily outside the bone marrow.

Risk Factors/Etiology. NHL occurs in younger children more commonly than Hodgkin lymphoma, and its incidence increases steadily throughout life. Patients with preexisting immunodeficiency are at risk for developing NHL. Childhood NHLs differ from adult cases in that they are predominantly extranodal in presentation and are as likely to be T-cell lymphomas as B-cell lymphomas.

There are three histologic subtypes of NHL: (*1*) **lymphoblastic** (usually of T-cell origin); (*2*) **large cell** (of T-, B-, or indeterminate cell origin); and (*3*) **small noncleaved cell lymphoma** (SNCCL, B-cell, Burkitt, and non-Burkitt subtypes). Although its contribution is unclear, EBV plays a role in the pathogenesis of Burkitt lymphoma.

Presentation. The clinical presentation depends on the site of the primary tumor and the extent of the disease. The most common presentation of **lymphoblastic lymphomas** is that of an anterior mediastinal mass, sometimes associated with pleural effusions, which can produce (1) **respiratory distress from airway compromise** and (2) **a superior vena cava syndrome**. The CNS may be involved. The most common presentation of **small noncleaved cell lymphomas** is that of abdominal enlargement from a rapidly growing tumor, sometimes producing pain, ascites, and urinary tract obstruction. These lymphomas may also present as an intestinal obstruction causing an intussusception. The CNS may be involved. **Large cell lymphomas** occur in many sites, such as abdomen, mediastinum, skin, bone, and soft tissues. Involvement of the CNS is rare. Peripheral lymph node enlargement can be seen with any type.

Physical Examination. The physical examination depends on the presentation of the disease.

Diagnostic Tests. NHL is an aggressive disease. Therefore, it is important to make the diagnosis and stage the disease.

Studies for staging pediatric non-Hodgkin disease include **serum** for a complete blood count, serum electrolytes, uric acid, lactate dehydrogenase, creatinine, calcium, and phosphorous. Patients should have a **chest radiograph.** If this is abnormal, the next step should be to obtain a **chest CT scan** and an **abdominal and pelvic ultrasound** or **CT scan,** as well as **gallium** or **bone scan.** A bilateral **bone marrow** aspirate and biopsy as well as **spinal fluid** cytology should be performed.

The St. Jude staging system for NHL of childhood is used.

- Stage I—Disease is localized to a single tumor (extranodal) or single anatomic area (nodal), but not mediastinal tumor abdomen.
- Stage II—A single tumor (extranodal)/regional involvement; two or more nodal areas/same side of diaphragm; two single (extranodal) tumors with or without regional node involvement/same side of diaphragm
- Stage III—Two single tumors (extranodal)/opposite sides of diaphragm; two or more nodal areas above and below the diaphragm; any primary intrathoracic tumor (mediastinal, pleural, thymic); any extensive primary abdominal disease
- Stage IV—Any of above plus CNS or bone marrow involvement

Treatment. Patients with NHL receive extensive **surgical debulking**. In addition, all patients with NHL receive systemic **chemotherapy** because the tumor spreads hematogenously. The **CHOP** (cyclophosphamide, vincristine, methotrexate, and prednisone) criteria are used. **Radiotherapy** may be needed for bulky tumors and for those causing life-threatening airway obstruction. **Treatment** for patients with advanced NHL, **stages III and IV**, is different and **depends on** the **histologic subtype**. Patients with advanced NHL **lymphoblastic** type receive intensive chemotherapy, as well as cranial irradiation, and intrathecal therapy to prevent CNS disease. Patients with advanced NHL **small noncleaved cell lymphoma** type receive intensive chemotherapy. Patients with advanced NHL **large cell** type receive intensive chemotherapy similar to regimens used for lymphoblastic lymphoma, or those used for Burkitt.

Complications/Follow-up. Without therapy rapid and widespread dissemination occurs. Both B-cell and T-cell lymphomas spread to the bone marrow and meninges. Prognosis is good for stages I and II, and approximately 90% of patients are cured.

BRAIN TUMORS

Brain tumors are the most common solid tumors in childhood and the second most common malignancy in this group. Two thirds of these tumors arise below the tentorium and one third arises above the tentorium. CNS tumors may be classified as *(1)* **infratentorial tumors** or *(2)* **supratentorial tumors. Infratentorial** tumors, i.e., cerebellar astrocytomas, medulloblastomas, brain stem gliomas, and ependymomas are more common in children. However, in children younger than 2 years and in adolescents, **supratentorial** tumors, i.e., craniopharyngiomas, optic gliomas, and astrocytomas, are found more frequently. Magnetic resonance imaging (MRI) is the imaging study of choice to detect and delineate brain tumor.

Not all brain tumors are malignant, but special problems arise in the management of pediatric brain cancers. The blood–brain barrier limits the delivery of intravenous chemotherapy. The developing brain of infants and young children is vulnerable to the toxicity of radiotherapy or chemotherapy. The proximity of some brain tumors to important areas of the brain precludes extensive surgical resection. New technology for treating brain tumors, such as the implantation of radiation seeds, i.e., brachytherapy, is promising.

Infratentorial Tumors

Cerebellar astrocytoma

A 10-year-old child presents to the physician because of a new onset seizure. The patient has a 1-month history of severe headache and a progressively worsening wide-based gait.

Definition. Astrocytomas are posterior fossa tumors that are usually cystic with a mural nodule of solid tumor. There are two histologic types: (*1*) **pilocytic astrocytomas** and (*2*) **diffuse or fibrillary astrocytomas.** The majority of astrocytomas are pilocytic astrocytomas and have a benign nature. The diffuse or fibrillary astrocytomas account for approximately 15% of astrocytomas and are more aggressive tumors.

Risk Factors/Etiology. This is the most common posterior fossa tumor of childhood and has the best prognosis. The tumor may be midline or in a hemisphere. This tumor may cause hydrocephalus by increasing the intracranial pressure by obstructing the aqueduct of Sylvius or fourth ventricle.

Presentation. The patient is usually between 5 and 10 years old. The parents may complain of personality changes in the child. The patient may have headache, motor weakness, seizures, and ataxia. Later, the patient develops increased intracranial pressure and may have associated emesis.

Physical Examination. This is described under presentation. The patient may have focal neurologic signs.

Diagnostic Tests. Tumors of the posterior fossa are best evaluated by MRI.

Treatment. Resection is the treatment of choice. Location of the tumor determines whether the patient has surgery or radiotherapy. Anticonvulsants and corticosteroids may be prescribed. Chemotherapy may be initiated depending on the type of astrocytoma, the age of the child, and whether the tumor is recurrent.

Complications/Follow-up. There is a 5-year survival of 90%.

Medulloblastoma

A 6-year-old child presents to the pediatrician because of headache and persistent emesis for the past week that is not associated with fever or abdominal pain.

Definition. Medulloblastoma (primitive neuroectodermal tumor [PNET]) is the second most common posterior fossa tumor, which oftentimes originates from the roof of the fourth ventricle. This tumor is aggressive, grows rapidly to fill the fourth ventricle, and progresses to the adjacent cerebellar hemisphere. Medulloblastomas are capable of metastasizing to extracranial sites.

Risk Factors/Etiology. This tumor is most prevalent in children younger than 7 years of age. This is the second most common brain tumor in childhood and accounts for 25% of all intracranial tumors. The peak incidence is between 2 and 10 years old. Medulloblastomas are more common in boys than in girls. The primary location of these tumors is the midline of the cerebellum (vermis), but they may also arise from the cerebellar hemisphere. Medulloblastomas usually extend to the fourth ventricle, causing hydrocephalus. This tumor can metastasize through the cerebral spinal fluid (CSF).

Presentation. Clinical features depend on the location of the tumor. Patients may complain of slow onset of headache, neurologic impairment, or epilepsy. Increased intracranial pressure and hydrocephalus may occur. Ataxia may be present.

Physical Examination. Please refer to presentation.

Diagnostic Tests. Studies that should be performed include MRI of the spine, chest radiograph, skeletal survey, CSF cytology, liver function tests, and bone marrow examination.

Treatment. The initial therapy is **surgical excision.** If removal of the tumor does not relieve the intracranial pressure, then a ventricular shunt should be placed. **Radiation therapy** has improved the survival of children with medulloblastoma. Adjuvant **chemotherapy** improves the disease-free survival for patients with unfavorable prognostic factors, such as age less than 4 years, positive CSF cytology, and positive MRI of the spine. Adjuvant chemotherapy also improves the disease-free survival (90%) in patients with favorable prognostic factors.

Complications/Follow-up. This tumor can metastasize. The prognosis for medulloblastomas depends on the age of the patient, the size of the tumor, and whether it is disseminated. There is a poor prognosis for patients younger than 4 years of age.

Brain stem gliomas

> A 9-year-old child is brought to the physician by her parents because of personality change. The parents state that over the past month the child has become very aggressive, i.e., arguing, hitting, and biting other children. Her grades have dropped from straight *A*s to failing. This is quite out of character for their intelligent, outgoing, and friendly daughter.

Definition. Brain stem gliomas are the third most frequent posterior fossa tumor in children. They comprise two types, which infiltrate the pons and extend throughout the brainstem: (*1*) anaplastic astrocytomas and (*2*) low-grade focal tumors.

Risk Factors/Etiology. The anaplastic astrocytomas have a poor prognosis. The low-grade focal tumors (midbrain and medulla) have good prognosis with surgery alone.

Presentation. Half of patients with brain stem gliomas present with cranial nerve and long tract signs. Changes in personality are seen commonly with brain stem gliomas.

Physical Examination. Patients may have diplopia and facial weakness. The patient may also have speech and gait disturbances. Until the tumor becomes massive, increased intracranial pressure and papilledema occur late, if at all.

Diagnostic Tests. The diagnosis is usually made on the **MRI** results. **Biopsy is unnecessary** unless there is uncertainty after neuroimaging.

Treatment. Surgery is not usually possible for the brain stem glioma. **Limited radiotherapy** is used in the management of these patients. During radiotherapy the addition of high-dose steroids may help to reduce brain stem edema. **Chemotherapy** plays a palliative role and has not improved outcome. If the patient has a low-grade focal tumor, then **surgery** alone offers an excellent prognosis.

Complications/Follow-up. These tumors have a poor prognosis unless they are of the low-grade focal tumor type.

Ependymoma

A 5-year-old child presents to the emergency center because of neck stiffness and torticollis for the past 3 days. The patient also has vomiting, headache, and papilledema.

Definition. These tumors may occur either infratentorially or supratentorially. The fourth ventricle is the most common location.

Risk Factors/Etiology. Fifty percent of all ependymomas occur during childhood and adolescence.

Presentation/Physical Examination. Ependymomas commonly present as obstructive hydrocephalus. These tumors may occur in the spinal cord.

Treatment. Surgery rarely removes the tumor completely, and the addition of **radiotherapy** increases survival. **Cyclic chemotherapy** is also used for the treatment of ependymoma.

Complications/Follow-up. Prognosis depends on the histologic grade. Low-grade lesions have a 5-year survival of approximately 70% and a 10-year survival of 50–70%. High-grade tumors have a poor prognosis, with a 5-year survival of about 15–20%.

Supratentorial Tumors

Craniopharyngioma

A 14-year-old girl presents to the physicians because of short stature. On physical examination the patient is found to have bitemporal visual field defects. A head CT shows calcification at the sella turcica.

Definition. The craniopharyngioma is a common **supratentorial** tumor in children, consisting of cystic and solid areas that tend to calcify.

Risk Factors/Etiology. This is the most common supratentorial tumor.

Presentation. The patient may present to the physician because of short stature secondary to pituitary-hypothalamic involvement. Peripheral vision loss may occur secondary to pressure or injury to the optic chiasm. If the patient has hydrocephalus, then papilledema is present.

Physical Examination. Many children will present with **short stature**, and others will have **visual problems**.

Diagnostic Tests. An **MRI** or **CT scan** of the **head** will help to make the diagnosis. In 90% of the cases **calcifications** on **plain skull films** or CT of the head are visualized. The patient with craniopharyngioma should undergo **baseline endocrine studies.** If there is an endocrine deficiency, replacement therapy with growth hormone, cortisone, thyroxine, or sex hormones may be necessary.

Treatment. The **treatment** is to **surgically** remove the tumor. **Radiation** therapy is controversial, but it is used at some centers if tumor removal is incomplete and the craniopharyngioma reoccurs.

Complications/Follow-up. The patient needs close follow-up because endocrine disorders such as hypothyroidism, diabetes insipidus, and adrenal insufficiency may develop after surgery. Growth should be monitored in these children.

Optic gliomas

A 4-year-old boy with neurofibromatosis presents to the ophthalmologist with complaints of decreased visual acuity according to his parents. On physical examination the patient has proptosis and papilledema.

Definition. Optic gliomas are low-grade astrocytomas that cause decreased visual acuity and pallor of the discs.

Risk Factors/Etiology. Patients with **neurofibromatosis** and **chiasmal** tumors tend to develop optic gliomas. In children the majority of these tumors are diagnosed by 5 years of age.

Presentation. Patients with optic gliomas may present with papilledema, decreased visual acuity, proptosis, and optic atrophy. If a child has a **chiasmatic** tumor, **asymmetric nystagmus** may be the presenting sign.

Physical Examination. Findings on physical examination will vary with the presentation.

Diagnostic Tests. The **MRI** and **CT (head)** should be used to make the diagnosis of an optic glioma because tumor biopsy may damage vision.

Treatment. Treatment is delayed until the tumor progresses, and the decision for therapy is based on radiographic findings and vision changes. The recommended treatment plan is (*1*) **no treatment** if there is an optic nerve tumor but normal vision. In these cases reevaluation should be performed every 6 months with CT scan and a vision examination; (*2*) **chemotherapy** for patients with a tumor extending into the optic canal and progression of visual changes; and (*3*) **chemotherapy** for patients who do not have tumor extension into the optic canal but still have progression of visual changes.

Complications/Follow-up. Progression-free survival rates with carboplatin and vincristine are 75% at 2 years.

WILMS TUMOR

A mother brings her 3-year-old child to the physician because she found an abdominal mass while bathing the child. The child has been in her usual state of health according to the mother. However, on review of the vital signs the patient is noted to have an elevated blood pressure.

Definition. Wilms tumor is a **renal neoplasm** that occurs in childhood. The neoplastic embryonal renal cells of the metanephros cause the tumor, which is composed of an admixture of cells that originate in the blastema, epithelium, and stroma. **Histologically**, spindle-shaped cells, anaplasia, and fibrillar inclusions with the presence of striated muscle are characteristic.

Risk Factors/Etiology. Wilms tumor accounts for almost all renal neoplasms in childhood. It is seen equally in boys and girls and in all races. It is important to know that Wilms tumor may

be associated with **congenital anomalies** of the genitourinary tract, hemihypertrophy, and aniridia.

Presentation. Wilms tumors usually manifest around 3 years of age. They most frequently appear as an asymptomatic abdominal mass. Oftentimes, the tumor is detected by the parent or discovered on routine physical examination. Fifty percent of the patients will have abdominal pain and vomiting. Hypertension will be seen in up to 60% of patients with Wilms tumor.

Physical Examination. An abdominal mass may be palpated on physical examination.

Diagnostic Tests. A **urinalysis** may show microscopic or gross hematuria. Appropriate imaging studies are necessary to define the site of origin within the kidney and to evaluate the contralateral kidney. **Ultrasound** is the imaging study of choice to determine whether the mass is intrarenal. Once a Wilms tumor is suspected on ultrasound, a **CT scan** of the abdomen is obtained to better define the tumor and its extension. There should be a search for distant metastases to the lungs, liver, bones, and brain. A tumor **biopsy** is essential to stage the disease. Most patients have localized disease, and only 10–15% of the patients have distant metastases at diagnosis.

- Stage I—Tumor is in one kidney and the capsule is intact.
- Stage II—Tumor is in one kidney and the capsule is involved.
- Stage III—Capsule is ruptured but there is no hematogenous metastasis.
- Stage IV—Hematogenous metastasis
- Stage V—Involvement of both kidneys

Treatment. Therapy includes (*1*) **surgical resection** to remove the primary tumor, (*2*) **radiotherapy** to treat residual local disease, and (*3*) **chemotherapy** with actinomycin D and vincristine sulfate.

Prognosis. Ninety percent of patients have favorable histology, and most, in the absence of distant metastases, do well. However, 10% have unfavorable histologic findings and often do poorly, even if the disease is localized. These unfavorable tumors are anaplastic Wilms tumor and sarcomatous Wilms tumor.

Differential Diagnosis. Another abdominal mass, neuroblastoma, should be high on the list for differential diagnosis of a Wilms tumor. Therefore, for your examination and in practice you must be able to differentiate between these two tumors. Remember a tumor of renal origin usually rules out neuroblastoma. Other disease entities to be included in the differential diagnosis of Wilms tumor may be hydronephrosis, renal cysts, and other renal cancers.

NEUROBLASTOMA

A 2-year-old child is brought to the physician because of bluish skin nodules, periorbital proptosis, and periorbital ecchymosis that has developed over the last few days. On physical examination a hard smooth abdominal mass is palpated.

Definition. Neuroblastoma is a malignancy of neural crest cells. These cells in the course of their normal development give rise to the paraspinal sympathetic ganglia (chromaffin) and the adrenal medulla. Tumors may arise anywhere neural crest cells are present (adrenal glands, sympathetic ganglia). They appear as rosettes with a central fibrillar material (dendrites) and mature ganglion cells.

Risk Factors/Etiology. Neuroblastoma represents 8% of all childhood tumors and occurs at a rate of 10:1,000,000 per year. This is the most common solid malignancy in children outside of the CNS. It occurs predominantly in preschool children, and 90% of diagnoses will be made before 5 years of age. It is slightly more common in boys and in whites. There appears to be an association with Beckwith-Wiedemann syndrome. It arises anywhere there are neural crest cells.

Presentation. The clinical manifestations of neuroblastoma vary owing to the number of sites at which the primary tumor is able to appear. Seventy percent of neuroblastomas are in the abdomen, and half of these are in the adrenal. There is hematogenous spread to the liver and bone marrow. The patient may present with an abdominal (usually flank) mass that is hard, smooth, and nontender. Hypertension may be caused by catecholamines or by compression of the renal vasculature. Thoracic tumors are located in the posterior mediastinum and may cause the patient to have respiratory distress. This thoracic tumor may be detected as an incidental finding on a chest radiograph that was obtained for unrelated symptoms. Head and neck tumors present as palpable tumors. They are sometimes associated with Horner syndrome. Dumbbell-shaped neuroblastomas are found in the paraspinal area. The patient may present with back pain, limp, lower extremity weakness, or bladder and anal sphincter dysfunction. Metastasis is commonly found in the bone, liver, or skin. Children with neuroblastoma may have opsoclonus-myoclonus causing the "dancing eyes and dancing feet" syndrome. Patients with this syndrome have chaotic eye movements, myoclonus, and ataxia. They may also have periorbital hemorrhage ("raccoon's eyes"), exophthalmos, ptosis, and papilledema.

Physical Examination. The findings on physical examination depend on the presentation of the patient.

Diagnostic Tests. A **CT scan** of the abdomen will show an extrarenal tumor. Vanillylmandelic acid (VMA) and homovanillic acid (HVA) levels are useful for diagnosis, response to therapy, and detection of recurrence. A **biopsy** of the tumor will make the pathologic diagnosis. A **bone marrow biopsy** and **bone scan** should be performed to look for metastatic disease. Other markers include neuron-specific **enolase**, **ferritin**, and **lactate dehydrogenase**.

Staging of the tumor should be made according to the International Neuroblastoma Staging System.

- Stage I—Tumor is localized in the organ of origin.
- Stage II—A. Tumor extends beyond the structure of origin, without ipsilateral lymph node.
  B. Tumor extends beyond the structure of origin but does not cross midline.
- Stage III—Tumor crosses the midline with or without bilateral nodes.
- Stage IV—Distant metastasis (e.g., cortical bone, liver, other organs)
- Stage IV-S—Tumors are small primary tumors, occurring in infants younger than 1 year, with metastasis limited to the skin, liver, and bone marrow, but not to cortical bone.

Treatment. The role of surgery, radiation, and chemotherapy depends on the stage and age of the child. **Surgical excision** is usually performed in **stages I and II. Chemotherapy** (vincristine, cyclophosphamide, doxorubicin hydrochloride, cis-platinum, etoposide, and daunorubicin) can often produce dramatic tumor regression in **stage III and IV** disease. There is a high rate of **spontaneous regression** without any therapy in infants with **stage IV-S.**

Complications/Follow-up. Infants **younger than 1 year** have the **best prognosis**, and children **older than 2 years** have the **worst prognosis**. Children with **advanced disease** and ***N-myc* amplification** or **1p deletion** in their tumors have **poorer** outcomes. Neuroblastomas metastasize to bone and brain.

Differential Diagnosis. Neuroblastoma is a round cell tumor and may appear similar to other round cell tumors such as rhabdomyosarcoma and NHL.

RHABDOMYOSARCOMA

A mother brings her 3-year-old daughter to the physician for evaluation because the young girl has "grapes" growing out of her vagina.

Definition. Rhabdomyosarcoma, a tumor of striated muscle, is the most common soft tissue sarcoma in children and accounts for 5–8% of childhood cancers.

Risk Factors/Etiology. Rhabdomyosarcoma is a round cell tumor, and it is thought to arise from the same mesenchyme as striated muscle. There are varying histologic subtypes: (*1*) *embryonal type,* responsible for 60% of cases, has an intermediate prognosis; (*2*) *botryoid type,* 6% of cases, grapelike mass extends into a body cavity; (*3*) *alveolar tumors,* 15% of cases, poorest prognosis; (*4*) *undifferentiated sarcomas,* 20% of cases; and (*5*) *pleomorphic type,* adult form, 1% of cases.

Presentation. A **mass** is the most common presenting sign. If the mass is in the nasopharynx, then the patient may have congestion, mouth breathing, and epistaxis. When the tumor involves the face or cheek the patient may have paralysis, swelling, or pain. Rhabdomyosarcoma of the trunk or extremities may look like a hematoma. If the tumor is in the genitourinary tract, the patient may have hematuria and obstruction. Patients with vaginal rhabdomyosarcoma have a vaginal grapelike mass (***sarcoma botryoides***). Tumors in any location may disseminate, causing pulmonary or bone metastasis.

Physical Examination. The physical examination depends on the presentation.

Diagnostic Tests. The diagnostic studies depend on the location of the tumor. Patients with head and neck rhabdomyosarcomas need radiographs of the neck and CT of the head and neck. Patients with suspected abdominal and pelvic tumors should have ultrasound and CT with contrast of the abdomen and pelvis. A cystourethrogram is performed to detect bladder tumors. Tumor tissue should be obtained. However, before surgery the patient should have a bone marrow, bone scan, a chest radiograph, and chest CT to determine the extent of disease.

Treatment. Treatment is dependent on the **primary tumor location** and "clinical group." Rarely is a rhabdomyosarcoma completely resectable. Chemotherapy and radiation may also be required. Patients in ***group I*** receive complete local tumor excision and chemotherapy. Patients in ***groups II and III*** (with residual tumor) receive surgery plus radiation plus chemotherapy. Patients in ***group IV*** (metastatic rhabdomyosarcoma) are treated primarily with systemic chemotherapy and irradiation.

Complications/Follow-up. The primary tumor site, the extent of the disease at diagnosis, and the treatment used determines the prognosis. The best prognosis is in patients with completely resectable tumors. Poorer outcomes are seen in older patients and in those with disseminated disease.

Differential Diagnosis. Rhabdomyosarcoma is a small round cell tumor and should be differentiated from other small round cell tumors such as neuroblastoma, NHL, and Ewing sarcoma.

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CONGENITAL ANOMALIES

Myelomeningocele

The pediatrician is called to the delivery room because an infant is born with a defect in the lumbosacral area.

Definition. Myelomeningocele is a neural tube defect and the most severe form of dysraphism involving the vertebral column.

Risk Factors/Etiology. The etiology is unknown; however, it is thought that agents such as drugs, radiation, malnutrition, and genetics have a role in adversely affecting normal CNS development.

Presentation. The majority of patients will present with the defect in the lumbosacral region. Patients may have bowel and bladder incontinence.

Physical Examination. On physical examination the patient may demonstrate flaccid paralysis of lower extremities, as well as absent deep tendon reflexes, and lack of response to touch or pain. Postural abnormalities, including clubfoot or subluxed hips, may be present. Eighty percent of these patients will develop hydrocephalus associated with type II Chiari defect.

Diagnostic Studies. The biochemical markers for neural tube defects are **α-fetoprotein** and **acetylcholinesterase (AFP).** This substance is excreted from the fetus and leaks into the amniotic fluid when there is failure of the neural tube to close.

Treatment. Attention to nutrition in the prenatal period with **prenatal vitamins** and **folic acid** decreases the risk.

A multidisciplinary (e.g., surgeons, physicians, therapists) approach is needed to care for these patients. Patients will need surgical repair, and children who develop hydrocephalus will need a shunt. These patients are prone to urinary tract infections because of the frequent catheterizations, and urinary tract infections should be treated with antibiotics.

Complications/Follow-up. Prenatal screening at 16 to 18 weeks should be done to detect the presence of **AFP.**

At times infants with the Chiari II malformation develop feeding problems, drooling, and choking, which may lead to death if left untreated. This problem occurs as a result of downward herniation of the medulla and cerebellar tonsils through the foramen magnum.

Other Neural Tube Defects

Other examples of neural tube defects (dysraphism) include spina bifida occulta and meningocele.

Spina bifida occulta is the most benign form of dysraphism. There is a defect of the closure of the posterior vertebral arches and laminae usually at L5 and S1. Most children will be asymptomatic. However, a dermal sinus or patch of hair may be present over the defect. Patients may have recurrent meningitis because of the sinus opening. A spinal roentgenogram shows a defect in closure of the vertebral arches.

Meningocele occurs when the meninges herniate through a defect in the posterior vertebral arches. These patients have a fluctuant midline mass along the vertebral column. This defect may be associated with hydrocephalus. Plain roentgenograms show a defect in the sacrum, and computed tomography (CT) and magnetic resonance imaging (MRI) will show the extent of the lesion.

SEIZURES

Febrile

> An 18-month-old child is brought to the emergency center after having a generalized tonic-clonic seizure that lasted approximately 5 min. The parents say that the child had been previously well but developed cold symptoms earlier today with a temperature of 39°C.

Definition. Febrile seizures are the most common seizure disorder of childhood (incidence 3–4%). Febrile seizures occur between 9 months and 5 years.

Risk Factors/Etiology. A small number of patients develop multiple recurrent seizures. The risk of epilepsy is 9% if there is a family history of febrile seizures, positive family history of seizures, initial febrile seizure <9 months, prolonged or atypical febrile seizure, or abnormal neurologic examination. There is a 1% chance if none of these factors are present.

Presentation. Febrile seizures usually occur with a rapid rise of temperature. The seizure is generalized, tonic-clonic, and usually lasts a few seconds to 10 min. Atypical febrile seizures last more than 15 min, and may be focal and repeat for hours and days.

Physical Examination. The core temperature is usually 39°C or greater when the febrile seizure occurs.

Diagnostic Studies. The electroencephalogram (EEG) is normal and usually is not needed, unless there was an atypical seizure. Appropriate studies should be obtained to rule out the suspected infection. Meningitis should be considered in all cases and needs to be ruled out, especially in children younger than 9 months and older than 5 years of age.

Treatment. The cause of fever needs to be determined (e.g., otitis media, upper respiratory infection). Antipyretics should be given. Parents should be reassured. Anticonvulsants have no effect. Rectal diazepam or lorazepam may be used if the febrile seizure is prolonged.

Complications/Follow-up. Fifty percent of patients have recurrent febrile seizures.

Generalized Seizures

Infantile spasms

A 6-month-old infant is noted to have brief, symmetric contractions (more than 100 times) of the head, neck, and extremities onto the trunk.

Definition. Infantile spasms are characterized by brief, symmetric contractions of neck, trunk, and extremities. They usually begin around 4–8 months of age.

Risk Factors/Etiology. It is hypothesized that corticotropin-releasing hormone is overproduced in patients with infantile spasms causing neuronal hyperexcitability and seizures.

Presentation. The spasm usually occurs during sleep or on initial arousal.

Physical Examination. There are at least three types of infantile spasms: (1) **flexor spasms** consisting of flexion of the head, arms, and neck onto the trunk; (2) **extensor spasms** consisting of extension of the trunk and the extremities; and (3) **mixed spasms** consisting of both flexion and extension.

Diagnostic Studies. The EEG will show hypsarrhythmia.

Treatment. The treatment for infantile spasms is adrenocorticotropic hormone (ACTH) and prednisone.

Complications/Follow-up. Some problems associated with infantile spasms are tuberous sclerosis, inborn errors of metabolism, congenital infections, and prematurity.

Absence (petit mal)

An 8-year-old child is referred to the pediatrician by the school nurse with reports of "spacing out" in class. During provoked hyperventilation in the office the patient has a similar episode.

Definition. Absence seizures are characterized by a sudden cessation of motor activity and are associated with a blank stare.

Risk Factors/Etiology. These seizures are uncommon before the age of 5 years, and are predominant in girls. The seizure lasts less than 30 s, and patients experience no aura and no postictal state.

Presentation. There is a sudden cessation of motor activity or speech.

Physical Examination. Patients have a blank facial expression, and flickering of eyelids. Patients tend to space out. Absence seizures are provoked with hyperventilation.

Diagnostic Studies. The EEG shows a 3/s spike and wave.

Treatment. The treatment for absence seizures is ethosuxamide.

Other generalized seizures

Other types of **generalized** seizures found in children include **generalized tonic-clonic seizures** that may follow a partial seizure, or occur de novo. These seizures are associated with aura and have a postictal period lasting 30 min–2 h.

Pseudoseizures are not true seizures, and patients with these "seizures" exhibit thrashing rather than tonic-clonic movement.

Some patients will have **myoclonic epilepsies** consisting of brief, symmetric contractions with loss of body tone. Patients fall or slump forward. There are different types of myoclonic epilepsies, (e.g., benign, typical, complex, and juvenile). It is important to mention that the **benign myoclonus of infancy** can be confused with infantile spasms. However, the EEG is normal and these seizures resolve by 2 years.

Partial Seizures

There are different types of partial seizures (simple, complex, and benign focal). **Simple partial seizures** last 10–20 s, and may be confused with tics. Motor activity is the most common symptom and there are no automatisms.

The **complex partial seizure** is associated with auras and automatism is common. The EEG shows interictal anterior temporal lobe sharp waves or spikes.

The **benign focal (Rolandic)** are focal motor seizures with generalized spread. They begin by 5–10 years and disappear by adolescence.

CEREBRAL PALSY

Definition. Cerebral palsy (CP) is a disorder of impaired motor functioning and posture with onset before or at birth or during the first year of life. It is a nonprogressive disorder and varies widely in its causes, manifestations, and prognosis. The most obvious manifestation is impaired ability of voluntary muscles.

Risk Factors/Etiology. The incidence of CP is approximately 1.5–5 per 1000 live births. The specific etiology is unknown; but the incidence is high among infants who are small for gestational age. Some other known causes are intrauterine bleeding, infections, congenital malformations, intracranial hemorrhage, neonatal hypoglycemia, and kernicterus. Studies have demonstrated that birth asphyxia is an uncommon cause.

Seizures and abnormalities of speech, vision, and intellect are also associated with CP.

Presentation/Physical Examination. CP may be classified by the predominant motor deficit.

Classification and some patterns that are seen include **spastic forms, extrapyramidal, atonic, and mixed.** The **spastic form** is present in approximately 75% of cases. There are different subtypes of the spastic form (**diplegia, quadriplegia, and hemiplegia**).

- **Spastic diplegia** accounts for 10–33% of cases and usually is seen in low-birth-weight infants. The lower extremities are more involved than the upper. These patients have increased muscle tone (spasticity) and increased deep tendon reflexes, contractures, and seizures.
- **Spastic quadriplegia** accounts for 9–43% of cases, the four extremities are equally involved, and scoliosis is more common with this type of CP. This type of CP is associated with severe asphyxia, low birth weight, mental retardation, and seizures.

- **Spastic hemiplegia** accounts for 25–40% of the cases, and involves one side of the body only. Cognitive function may be spared but seizures are common.

The **extrapyramidal form** accounts for 9–22% of the cases and is characterized by hypotonia, choreoathetosis, and dystonia. It is often associated with rigidity or spastic quadriplegia or diplegia (15% of cases) and can be associated with kernicterus.

The **ataxic (atonic diplegia, congenital cerebellar ataxia) form** accounts for 1–2% of cases of CP. There is marked hypotonia, brisk reflexes, and severe cognitive delays.

The **mixed form** results from a combination of insults to multiple cerebral areas and is associated with more complications, such as seizure and sensory deficits.

Laboratory Findings. No routine workup can be outlined.

Therapy. The goal of therapy should be to help patients achieve their maximum potential. This can be done using a multidisciplinary approach. Patients with CP may need occupational therapy, physical therapy, orthotics, and muscle relaxants. Underlying diseases or symptoms, such as seizure management, if necessary, should be addressed. Some patients will need special education.

PROGRESSIVE MENTAL RETARDATION

Acquired

At times mental retardation is acquired. Some causes of this are seizures (if extremely frequent), chronic drug overdose, lead poisoning, vitamin deficiencies, infections, and psychosocial deprivation.

Hereditary/Metabolic

Degenerative diseases with focal manifestations

Friedreich Ataxia

Definition. Friedreich ataxia is caused by expanded GAA triplet repeats in the frataxin gene (9q13–q21.1). Frataxin is a mitochondrial protein involved in iron hemostasis.

Risk Factors/Etiology. It is transmitted as an autosomal recessive or dominant trait.

Presentation. Ataxia usually appears before 10 years of age. The patients have an explosive dysarthric speech and nystagmus.

Physical Examination. Patients with Friedreich ataxia have ataxia, and absent deep tendon reflexes. The lower extremities are usually more involved than the upper extremities, and there is also loss of vibration and position sense. Skeletal deformities, such as high arched foot (pes cavus), hammertoes, or kyphoscoliosis, may be present.

Diagnostic Tests. The diagnosis is dependent on clinical signs and symptoms.

Treatment. There is no treatment.

Complications/Follow-up. Hypertrophic cardiomyopathy may progress to intractable congestive heart failure causing death.

Lesch-Nyhan

Definition. Lesch-Nyhan is an X-linked disorder of purine metabolism deficiency of hypoxanthine-guanine phosphoribosyl transferase (HPRT).

Risk Factors/Etiology. This deficiency leads to excess uric acid.

Presentation. Infants with Lesch-Nyhan have no apparent neurologic dysfunction until a delay in motor development occurs in the first few months. This is usually the first abnormality noted. In addition, patients have self-destructive behavior.

Physical Examination. Patients have self-mutilation, choreoathetosis, spasticity, psychomotor retardation, gouty arthritis, and renal calculi.

Diagnostic Studies. The diagnosis may be made by the presence of dystonia and self-mutilation. The **definitive diagnosis** is made by analysis of the **HPRT enzyme**.

Therapy. Allopurinol should be administered for renal complications. Behavior modification, restraints, and removal of teeth are needed to reduce self-mutilation. Medication should be used to reduce anxiety and stabilize mood.

Wilson Disease

Hepatolenticular degeneration

Definition. Wilson disease is an autosomal recessive degeneration of basal ganglia characterized by increased copper deposition in brain, liver, kidney, and cornea and low serum copper and ceruloplasmin levels.

Risk Factors/Etiology. A family history is often present, and screening asymptomatic homozygous family members identifies 25% of cases.

Presentation. Wilson disease occurs between adolescence and 40 years of age. The clinical presentation varies; however, it has been noted that hepatic failure is more common in children, and psychiatric symptoms are more common in adults.

Physical Examination. Patients may have tremors, drooling, "fixed-smile," dysarthria, and choreoathetosis. Children may have hepatomegaly. Almost all patients with neurologic disease have **Kayser-Fleischer rings,** i.e., a yellow-brown deposit at the limbus of the cornea.

Diagnostic Studies. The diagnosis of Wilson disease is confirmed by low serum copper and ceruloplasmin levels, increased urine copper concentrations after the administration of penicillamine, and a rise in the level of copper in the liver. CT of the brain shows hypodense areas in the region of the basal ganglia, and MRI shows increased T_2 signal intensity in the caudate and putamen.

Treatment. The goal of therapy is to reduce copper intake and to increase excretion of copper in the urine. D-Penicillamine is used to chelate copper. Triethylene tetramine dihydrochloride is approved for patients with Wilson disease who are sensitive to penicillamine. The administration of zinc sulfate may reduce copper absorption.

Complications/Follow-up. Hepatic involvement may be fulminant and progress to postnecrotic cirrhosis. However, if the diagnosis is made early, and dietary and chelating therapy initiated, the progression of liver and neurologic damage can be stopped and even reversed.

Degenerative disease of white matter

Metachromatic Leukodystrophy (MLD). Metachromatic leukodystrophy (MLD) is another neurodegenerative disorder of white matter. It is an autosomal recessive disorder of myelin metabolism, and there is a deficiency of **arylsulfatase A** activity. Prenatal diagnosis of MDL is made by assay of arylsulfatase A in the chorionic villi or cultured amniotic cells. Cresyl violet produces metachromatic staining of tissue specimens. Late infantile MDL, juvenile MDL, and adult leukodystrophies are all a part of the MDL group of diseases.

There are two types of MDL: (*1*) **late infantile**, and (*2*) **juvenile**.

Patients with the **late infantile** type have a gait disturbance by 1–2 years, as well as hypotonia and absent deep tendon reflexes. Patients will exhibit slurred speech, an apathetic appearance, nystagmus, and optic atrophy. Patients with **juvenile MLD** have onset at 5–10 years. Personality changes, dysarthria, and worsening school performance are symptoms manifested in these patients.

Krabbe (Globoid Cell Leukodystrophy). Krabbe is a disorder of myelin destruction. It is an autosomal recessive disorder caused by a deficiency of galactocerebroside β-galactosidase. Symptoms of this disease appear in the first few months and include irritability, crying, feeding problems, seizures, opisthotonus, and optic atrophy.

Adrenoleukodystrophy. Adrenoleukodystrophy is an X-linked recessive disorder with symptoms occurring between 5 and 15 years. Patients will have academic deterioration, behavioral disturbances, gait abnormalities such as ataxia, and seizures. There may be abnormal skin pigmentation.

Degenerative disease of gray matter with visceromegaly

Patients with **mucopolysaccharidoses** have coarse facies, skeletal abnormalities, mental retardation, and visceromegaly. These diseases include Hurler and Sanfilippo that are autosomal recessive, as well as Hunter disease that is X-linked recessive.

Degenerative disease of gray matter without visceromegaly

Rett Syndrome

> The pediatrician examines a 5-year-old girl with hand wringing and autistic behavior.

Definition. Rett syndrome is a neurodegenerative disorder of unknown cause.

Risk Factors/Etiology. Rett syndrome only affects females.

Presentation. The onset usually occurs at 1 year of age with loss of developmental milestones and acquired microcephaly.

Physical Examination. A loss of purposeful movement, social withdrawal, stereotypic hand movements (hand wringing), and acquired microcephaly may be seen on physical examination. The patient may have sighing, intermittent apnea, and autistic behavior.

Diagnostic Tests. There are no diagnostic tests.

Treatment. Therapy consists of supportive care. If the patient has seizures, anticonvulsants should be administered.

Complications/Follow-up. These patients may have generalized tonic-clonic seizures. Death occurs during adolescence or the third decade, and may be caused suddenly from a cardiac arrhythmia.

Tay-Sachs Disease (GM2 Gangliosidosis, Type 1). Tay-Sachs disease is associated with cerebral degeneration secondary to lysosomal storage of GM2 ganglioside in the nervous system. It is autosomal recessive and is prominent in Ashkenazi Jews (1/30 carrier rate). Patients are normal until 6 months, and then begin to lag and lose developmental milestones. These patients develop seizures, hypotonia, and blindness. A **cherry red spot** may be found in the macula. There is a severe deficiency of hexosaminidase A. Most patients die between 3 and 4 years of age. Prenatal diagnosis is possible with amniocentesis or chorionic villi sampling.

HYDROCEPHALUS

A 2-month-old infant is noted to have a head circumference greater than the 95th percentile.

Definition. Hydrocephalus occurs as a result of impaired circulation and absorption of cerebrospinal fluid (CSF), or rarely by increased production of CSF.

Risk Factors/Etiology. There are two types of hydrocephalus: (*1*) **obstructive (noncommunicating)** and (*2*) **nonobstructive (communicating).** The **obstructive (noncommunicating)** type is caused by an obstruction in the ventricular system. There is an abnormality of the aqueduct, and a lesion in the fourth ventricle. The **nonobstructive (communicating)** type results from obliteration of the subarachnoid cisterns or malfunctioning of the arachnoid villi, e.g., after intraventricular hemorrhage or meningitis.

Presentation/Physical Examination. The clinical presentation depends on the age of the patient, the type of lesion, and intracranial pressure.

- **Infants** with hydrocephalus have accelerated head growth, wide-open, bulging fontanelles, dilated scalp veins, and "setting-sun" eyes. **Older** children with hydrocephalus have irritability, lethargy, poor appetite, and vomiting. They may complain of headache, and the "cracked pot" sign (Macewen sign), may be present on percussion of the scalp, indicating separated sutures.
- A foreshortened occiput suggests **Arnold-Chiari malformation I,** which is not associated with hydrocephalus. Symptoms occur at adolescence, and there is an obstruction of the caudal portion of the fourth ventricle. Patients complain of recurrent headache, neck pain, and urinary frequency. Patients with **Arnold-Chiari malformation II** have progressive hydrocephalus and a myelomeningocele. These patients may have stridor and apnea.
- **Dandy-Walker** malformation consists of a cystic expansion of the fourth ventricle of the posterior fossa. These patients have hydrocephalus and a prominent occiput. Papilledema and gait abnormalities such as ataxia are present.

Diagnostic Studies. A thorough history and physical examination are important to making the diagnosis. Ultrasound may be used to look for hydrocephalus, as well as CT and MRI of the head.

Treatment. Therapy depends on the cause of the hydrocephalus. **Medical treatment** includes acetazolamide and furosemide that give temporary relief. A **surgical shunt** is necessary for most cases of hydrocephalus. Treatment should be with a multidisciplinary approach.

Follow-up/Complications. Bacterial infections are the main complications of shunt. The most common organism seen in shunt infections is *Staphylococcus epidermidis.*

ANTERIOR HORN CELL DISEASE

Neuropathies

Werdnig-Hoffmann disease (infantile spinal muscular atrophy [SMA])

A pediatrician examines an infant who is on the examination table in frog-leg position, with subdiaphragmatic retractions and absent tendon reflexes.

Definition. Werdnig-Hoffmann disease is a degenerative disease of motor neurons.

Risk Factors/Etiology. The primary pathology of Werdnig-Hoffmann disease is atrophy of anterior horn cells in the spinal cord and of motor nuclei in the brain stem, with secondary atrophy of motor nerve roots and of muscle. The disease is transmitted as an autosomal recessive trait.

Onset occurs before 2 years of age and often begins in utero.

Presentation. Patients have generalized weakness and severe hypotonia of the proximal and distal limbs, intercostals, and bulbar muscles. The legs tend to lie in **a frog-leg position** with hips abducted and knees flexed.

Physical Examination. Fasciculations are visible in the tongue, and the patient has flaccid quadriplegia.

Tendon stretch reflexes are absent. Infants have normal intelligence.

Diagnostic Studies. The electromyelogram shows fibrillation and evidence of muscle denervation. The serum enzyme determinations (creatine kinase [CK]) are normal or slightly elevated. Specific nerve conduction velocity test shows evidence of denervation; nerve conduction studies reveal normal conduction velocity.

Treatment. There is no medical treatment to stop the progression of the disease; therefore, only supportive care is given.

Complications/Follow-up. Most patients die before 2 years of age from respiratory failure and food aspiration.

PERIPHERAL NEUROPATHY

Guillain-Barré

A 9-year-old child presents to the pediatrician because of muscle pain and weakness in the lower extremities. The parents state that the patient is refusing to walk. The patient was seen approximately 10 days before with gastroenteritis. He has no other significant past medical history.

Definition. Guillain-Barré is a postinfectious polyneuropathy that causes demyelination in motor and sometimes sensory nerves.

Risk Factors/Etiology. This disease affects patients of all ages. *Campylobacter jejuni* and *Mycoplasma pneumoniae* have been associated with Guillain-Barré.

Presentation. An ascending weakness and paralysis beginning in the lower extremities can be seen in patients with Guillain-Barré. This usually occurs 10 days after a nonspecific viral infection.

The onset is gradual and may last days to weeks.

Physical Examination. Tendon reflexes are lost early. Weakness may progress to include the respiratory muscles, causing respiratory insufficiency.

Diagnostic Studies. CSF results are essential for diagnosis. **CSF protein** is **elevated**, and there is normal glucose, with a white blood cell count less than 10 cells (WBCs/mm^3). There is reduced motor nerve conduction, and sensory nerve conduction is slow.

Treatment. Patients with acute symptoms should be admitted to the hospital for observation because the ascending paralysis might involve the respiratory muscles. If the respiratory muscles become involved, supportive care (respiratory support) should be given. In addition, for rapidly progressive ascending paralysis, patients should receive intravenous immunoglobulin (IVIg). Alternatives include steroids, immunosuppressive drugs, and plasmapheresis. However, in most cases there is a spontaneous recovery in 2–3 weeks.

Complications/Follow-up. Involvement of the respiratory muscles may result in respiratory failure. Some patients may develop a chronic relapsing form of Guillain-Barré that does not improve over months to years.

Hereditary Motor-Sensory Neuropathy–HMSN Type I (Charcot-Marie-Tooth)

A teenager presents to the clinic with claw hands and storklike lower extremities.

Definition. Charcot-Marie-Tooth is the most common genetic neuropathy. In this disease patients have peroneal muscular atrophy.

Risk Factors/Etiology. It is transmitted as an autosomal dominant trait. Most patients are asymptomatic until late childhood or early adolescence.

Presentation. Patients have a history of gait disturbance, clumsiness, and tripping over their own feet. By the teenage years patients exhibit pes cavus, tremor, and variable sensory loss (stocking-glove distribution).

Physical Examination. The peroneal and tibial nerves are most frequently affected. There is muscle wasting of the lower legs giving them a storklike appearance. Patients have claw hands with nerves that are palpably enlarged.

Diagnostic Studies. There is decreased motor and sensory conduction. A sural nerve biopsy demonstrates "**onion bulb**" formations that surround the axons. This pathologic finding is called **interstitial hypertrophic neuropathy.** The definitive genetic diagnosis is made in blood.

Treatment. Orthotics are used to brace the feet and the legs. Parents should be examined and nerve conduction studies performed.

NEUROMUSCULAR JUNCTION DISORDER

Myasthenia Gravis

A pediatrician examines an infant with poor sucking and swallowing since birth. The infant is noted to be a floppy baby with poor head control. There is associated ocular ptosis and weak muscles on repeated use.

Definition. Myasthenia gravis is an autoimmune disease of the neuromuscular junction that causes weakness of skeletal muscles and fatigability on exertion.

Risk Factors/Etiology. The pathophysiology is an immune-mediated neuromuscular blockade. The release of ACh into the synaptic cleft is normal, but the motor end plate is less responsive than normal. This is because circulating receptor-binding antibodies decrease the number of available ACh receptors. This disorder is generally considered to be nonhereditary.

Neonatal myasthenia has two forms:

- *Transient.* Found in infants born to mothers with myasthenia. This condition is due to the placental transfer of ACh receptor antibodies. Duration is usually days to weeks.
- *Congenital myasthenia.* Rare condition that is not related to maternal myasthenic disease. Not caused by receptor antibodies and often responds poorly to therapy. May result from a genetic etiology. Always permanent without remission.

Presentation. Ptosis and extraocular muscle weakness is the earliest and most consistent finding. Other features include dysphagia and facial weakness, feeding difficulties, poor head control, weakness of limb-girdle and distal muscles of hands and feet.

Physical Examination. Rapid muscle fatigue (more pronounced when tired and late in day)

Diagnostic Studies:

- EMG is more diagnostic than muscle biopsy.
  - Decremental response to repetitive nerve stimulation
  - Nerve conduction velocity normal
  - Reversed after cholinesterase inhibitor
- Anti-ACh antibody—inconsistent feature
- Hashimoto thyroiditis
- Edrophonium test

Treatment. In mild and transient disease, supportive treatment may be the only treatment necessary. Respiratory assistance may be required, and suctioning of secretions is essential in infants and children with cholinergic crisis.

Primary treatment—cholinesterase-inhibiting drugs

- Neostigmine methylsulfate IM
- Neostigmine bromide PO
- Physostigmine
  - Need 4× greater dose of neostigmine, but has much longer activity
- Long-term steroids—improve muscle strength by suppressing the production of abnormal antibodies
- Thymectomy may provide cure
  - Mostly with high Ab titers and symptoms <2 years
- Plasmapheresis—effective in removing ACh receptor antibodies in severely affected patients
- Intravenous immunoglobulin (IVIG)

Complications. Don't use neuromuscular blocking agents in these patients because they can cause paralysis for weeks after a single dose. Avoid aminoglycosides—potentiates

Prognosis. Some with spontaneous remission; others will have permanent disease into adult life.

MUSCULAR DYSTROPHIES

Duchenne Muscular Dystrophy

A 3-year-old boy is brought to the pediatrician because the patient is very clumsy. According to the young boy's parents, he is having difficulty climbing stairs and frequently falls. On physical examination hypertrophy of the calves is noted.

Definition. Duchenne muscular dystrophy is the most common hereditary neuromuscular disease. There is an association with the genetic locus Xp2.1.

Risk Factors/Etiology. It is X-linked recessive, with approximately 30% new mutations. The incidence is 1:3600 males.

Presentation. Poor head control may be the first sign of the disease. There will be mild, if any, delay in early gross motor skills.

Physical Examination. Patients will have pseudohypertrophy of the calves. **Gower sign** is seen by 3 years of age. Hip girdle weakness and a Trendelenberg gait (5–6 years old) develop. Patients eventually lose ambulation. Patients have a poor cough and pharyngeal weakness. Cardiomyopathy also develops.

Diagnostic Studies. Diagnosis is made by **muscle biopsy** demonstrating necrosis, fat cells, and fibrous tissue. The CK is greatly elevated. Atrophy of the brain may be seen on CT of the head.

Treatment. Treatment is supportive, as there is no cure.

Complications/Follow-up. Death usually occurs by 18 years of age from respiratory problems and, rarely, heart problems.

Becker

Becker is the same as Duchenne muscular dystrophy, but the age of onset is later and the course of the disease is slower. Pseudohypertrophy is prominent, and pes cavus deformities are present. Cardiac and nervous system involvement is unusual.

NEUROCUTANEOUS SYNDROMES

Neurofibromatosis (Von Recklinghausen Disease)

A 6-year-old presents to the pediatrician for a routine evaluation. The child is noted to have 10 café au lait lesions as well as axillary freckling.

Definition. Neurofibromatosis (NF) is an autosomal dominant disorder that occurs as a result of an abnormality of neural crest differentiation during embryogenesis.

Risk Factors/Etiology. There are two forms of NF: NF-1 and NF-2. Patients with NF are at high risk for neurologic complications, as well as malignant neoplasms.

Presentation/Physical Examination. Children may present with **café au lait** spots, which are the hallmark of the disease and are present in almost 100% of patients with NF. Axillary freckling, Lisch nodules, optic nerve gliomas, and scoliosis are other physical findings associated with NF.

Diagnostic Studies. A good history and physical examination are needed to make the diagnosis.

To make the diagnosis of NF-1, two of the following are needed:

- At least five café-au-lait spots >5 mm prepubertal or at least six café-au-lait spots >15 mm postpubertal
- Axillary/inguinal freckling
- >2 iris Lisch nodules (seen on slit lamp only)
- >2 neurofibromas or one plexiform neurofibroma
- Osseous lesion-kyphoscoliosis, sphenoid dysplasia
- Optic gliomas

To make the diagnosis of NF-2, one of the following is needed:

- Bilateral eighth nerve masses (acoustic neuromas)
- Parent, sibling, or child with NF-2
- Bilateral acoustic neuroma most common feature

Treatment. There is no specific therapy for NF. Therefore, genetic counseling should be done. Prenatal testing is available. Therapy should include early identification and treatment of complications. A pediatric ophthalmologist should perform an annual ophthalmology examination.

Tuberous Sclerosis

A 1-month-old infant presents with infantile spasms and has a hypsarrhythmic EEG pattern.

Definition. Tuberous sclerosis is a neurocutaneous syndrome characterized by the triad of mental retardation, facial fibroangiomas, and hypopigmented spots of the skin, and epilepsy. It is an autosomal dominant disease. The gene is located on chromosomes 9 and 16; however, 50% of the cases are the result of new mutations.

Risk Factors/Etiology. Mental retardation is more prevalent in patients who present with symptoms of tuberous sclerosis at a younger age. In addition to the skin and the brain, the heart, lungs, kidney, eyes, and bone can be affected.

Presentation. Infants may present with **infantile spasms**. These patients have a high incidence of mental retardation. Older children may present with generalized seizures and the skin lesions (ash leaf and shagreen spots). Half of the children will have rhabdomyomas of the heart that are able to cause arrhythmias and congestive heart failure. In most cases, however, the rhabdomyomas resolve spontaneously.

Physical Examination. Some of the physical findings of tuberous sclerosis are the typical skin lesions: (*1*) **ash leaf spots** (hypopigmented lesions), (*2*) **shagreen patches** ("orange-peel" lesions), and (*3*) **sebaceous adenomas** (acnelike appearance). The patients may have subungal fibromas beneath the nails of the fingers and toes. Retinal hemartomas or "mulberry lesions" may also be present.

Diagnostic Studies. History and physical examination should point one toward the diagnosis of tuberous sclerosis. **Tubers** are the characteristic lesions, and periventricular calcified tubers may be seen on CT of the head. A head CT or MRI confirms the diagnosis in most cases. An ECHO may be performed to look for rhabdomyomas. Hematuria may be an indication that the kidneys are involved in these patients.

Treatment. The goal of therapy is seizure control. Other studies should include renal ultrasound, chest roentgenogram, and ECHO with periodic follow-up.

Complications/Follow-up. Tubers may differentiate into malignant astrocytomas.

Sturge-Weber

A newborn is examined in the nursery by the pediatrician. The patient is a product of a term spontaneous vaginal delivery without complications. On physical examination the patient is noted to have a facial nevus.

Definition. Sturge-Weber syndrome is a neurocutaneous syndrome that has a facial nevus (**port-wine stain**) in the trigeminal area of the face. It is associated with intracranial calcifications, hemiparesis contralateral to the facial lesion, and in half the cases, mental retardation or developmental delay.

Risk Factors/Etiology. Sturge-Weber is thought to be the result of an anomaly associated with vascularization that occurs sporadically in the embryonic period. Its frequency is approximately 1/50,000. Patients with Sturge-Weber are at risk for glaucoma.

Presentation/Physical Examination. Patients are born with a facial nevus, i.e., **port-wine stain**, consisting of dermal capillaries. In most cases this facial nevus is unilateral and always includes the upper face and eyelids.

Diagnostic Studies. Intracranial calcifications are found on skull radiographs and on CT scan of the head.

Treatment. Therapy is conservative if there is no mental retardation. Seizures should be well controlled. However, in those cases in which seizures are not well controlled, a hemispherectomy and lobectomy may prevent mental retardation. The port-wine stain is permanent; however, it may be covered up with cosmetics. The flashlamp-pulsed laser therapy may be a solution to clearing the port-wine stain.

Complications/Follow-up. Seizures usually develop in the first year, may be refractory to treatment, and are associated with hemiparesis. Patients with mental retardation and developmental delay often require special education.

Child Abuse 25

PHYSICAL ABUSE

A 2-year-old boy presents to the emergency department with a skull fracture that the mother states the child acquired after falling from a sofa onto a carpeted floor. During the physical examination the child is alert. He is noted to have old bruising on the buttocks and back, as well as a cigarette burn on his palm. The mother states that the child "falls a lot" and is always touching things he should not.

Definition. Physical abuse may be defined as an intentional injury to a child younger than 18 years by a parent, guardian, or caregiver that results in bruises, burns, fractures, lacerations, or any bodily harm.

Risk Factors/Etiology. The adult abuser usually is under stress, lonely, and unhappy. Inciting events that may cause the caregiver to physically abuse may be job loss, divorce, a "special needs" child, substance abuse, or exhaustion. Caregivers who are, or were, abused are at high risk for becoming abusers themselves. Although poverty may put a person at higher risk for physical abuse, it occurs at all socioeconomic levels. An increased incidence of physical abuse has been noted on military bases.

Presentation. The child who is physically abused may present with physical findings that are not consistent with the history or the child's developmental stage. The parents may have no explanation for the injury. Head trauma is the most common cause of death from physical abuse, and more than 95% of serious intracranial injuries in the first year of life are from abuse. The parent or guardian may have delayed in seeking appropriate care for the injury.

Physical Examination. On examination the physician should evaluate whether there are fractures or bruises in various stages of healing. Bruises, especially patterned bruises, and those on the buttocks and lower back should make one suspicious of physical abuse. For example, cigarette burns are circular, punched out lesions with uniformity in size. Immersion burns may have a stocking or glove pattern if the child's extremities are immersed in scalding water. Bite marks greater than 3 cm should be attributed to those of an adult. The patient may have alopecia from having the hair pulled and broken at various lengths. The patient with head trauma may present with coma, seizures, apnea, and evidence of increased intracranial pressure. The practitioner should check for retinal hemorrhages that are associated with the shaken baby syndrome.

Intra-abdominal injuries may be associated with a lacerated liver, spleen, or intestine.

Diagnostic Tests. Bleeding tests (platelets, prothrombin time, and partial thromboplastin time) should be done if bruising is present to rule out a bleeding disorder. If physical abuse is suspected, a roentgenologic bone survey should be done in children younger than 2 years old and may be helpful in children younger than 5 years old. This survey is obtained to look for

fractures in various stages of healing. If abdominal trauma is suspected, samples of urine and stool should be tested for blood.

Treatment. It is the physician's responsibility to report all cases suspicious for child abuse. The physician is obligated to report the suspicion to Child Protective Services. The history and physical findings must be documented appropriately. The patient should be hospitalized if necessary.

Complications/Follow-up. Children with central nervous system injuries may develop mental retardation, blindness, seizures, and learning problems. A small number of children returned to parents without any intervention are killed or harmed.

Differential Diagnosis. Impetigo, coining, insect bites, and idiopathic thrombocytic purpura are some of the things that may be confused with physical abuse. Roentgenograms from patients with scurvy and syphilis may appear as nonaccidental bone trauma. Children with osteogenesis imperfecta may have pathologic fractures.

SEXUAL ABUSE

A 3-year-old girl presents with green vaginal discharge. Microscopic examination of the discharge revealed Gram-negative intracellular diplococci.

Definition. Sexual abuse includes any activity with a child, before the age of legal consent, which is for sexual satisfaction of an adult or someone who is significantly older than the child. Sexual abuse may include molestation, sexual intercourse, incest, and rape.

Risk Factors/Etiology. The perpetrator for sexual abuse of children is usually a family member or someone with whom the victim is familiar. Strangers are least likely to be the perpetrator in sexual abuse cases. The majority of cases of reported sexual abuse include girls. It is thought that boys under-report sexual abuse because they feel that they should have protected themselves from the perpetrator. Ninety-seven percent of sexual abuse offenders are men. Approximately one third of the victims are toddlers, one third are school age, and one third are adolescents.

Presentation. To diagnose sexual abuse it is important for the physician to perform a detailed history and physical examination. The patient may present to the physician with any number of complaints. Some examples of complaints that may be associated with sexual abuse are genital infections, genital or anal trauma, recurrent urinary tract infections, enuresis, encopresis, and inappropriate sexual behavior. The child may have other complaints such as sleep disorders, anxiety, phobias, fire setting, drug abuse, and eating disorders. In some instances the child tells her mother or a friend that she has been sexually abused.

Physical Examination. The patient many times has no abnormal physical findings. The physician should look for evidence of trauma and vaginal discharge. The physician should check for bite marks and bruising. The abdominal examination in a girl may show pregnancy. Although not applicable to all cases, the hymenal opening is usually less than 5 mm in girls younger than 5 years of age; thereafter, an additional opening of 1 mm/y may be added, up to 9 years of age. The hymenal opening size is *not* considered diagnostic. In boys, sexual assault is usually associated with a transitory redness of the penis, although bite marks and other evidence of trauma may also be seen.

Diagnostic Studies. The postmenarchal patient should be evaluated for pregnancy. If intercourse occurred, then specimens for acid phosphatase, gonorrhea, chlamydia, and syphilis should be collected, as should those for hepatitis B and HIV. The Wood's lamp may be used to search for evidence of semen if the sexual assault occurred within 72 hours of presentation. In rape cases,

additional specimens, such as samples of the patient's pubic hair and fingernail scrapings, may be needed for evaluation. The presence of *Trichomonas vaginalis* and condyloma acuminatum after age 3 years is highly suggestive of sexual abuse. Meticulous documentation is required in sexual abuse evaluations.

Treatment. The police should investigate all cases of sexual abuse. Both the victim and the offender should be offered counseling. Medication to prevent pregnancy may be offered to girls who are at risk for pregnancy if intercourse occurred within 72 hours of presentation. Antibiotics should be administered to any victim who is known to be at risk for venereal disease and if the victim has any evidence of infection.

Complications/Follow-up. Some adolescent victims may become promiscuous and turn to prostitution. Others may experiment with illicit drugs. These victims may show poor school performance. Still others develop depression and suicidal gestures. They may have difficulties with close relationships.

NONORGANIC FAILURE TO THRIVE

A 4-month-old infant presents to the emergency department because the mother states that the infant has upper respiratory symptoms. The patient is less than the fifth percentile in weight and length. He is 3.5 kg. Birth weight was 4.2 kg. The mother states that the patient takes 16 oz of infant formula per day with cereal added.

Definition. Nonorganic failure to thrive usually occurs when an infant or child is fed insufficient calories.

Risk Factors/Etiology. Factors contributing to nonorganic failure to thrive include the mother not giving adequate nourishment to the child secondary to insufficient knowledge about appropriate feeding, substance abuse, depression, poverty, retardation, or emotional disturbance.

Presentation. The presentation may vary from patient to patient. However, the parent usually does not give an accurate nutritional history.

Physical Examination. The patient may be very thin with prominent ribs and wasted buttocks. In some cases the patient appears very unkempt and expressionless. There may be a torn frenulum in the infant because the mother fed the child with unnecessary force. The patient may have developmental delay, especially with speech and social skills.

Diagnosis. Hospitalization with unlimited feedings (150 calories/kg) with a diet that is age-appropriate is recommended. There should be documentation of input and output, daily weights, and maternal–child interaction. The child may demonstrate a very hearty appetite.

Extensive testing is unnecessary until a trial of dietary management has been done for at least a week and the child fails to gain weight. If physical abuse is suspected, then a skeletal survey should be performed.

Treatment. Cases of nonorganic failure to thrive caused by inadequate caloric intake must be referred to Child Protective Services. Child Protective Services will make a disposition on the child, i.e., home or temporary or permanent foster care.

Complications/Follow-up. If the patient goes home with the parent, then close medical follow-up is necessary, as well as long-term intervention with support services. A small percentage of unidentified infants with caloric deprivation will die of starvation. Physical abuse is also found in some of the children with nonorganic failure to thrive. In addition, some of these children will have learning problems.

Differential Diagnosis. One should always consider organic reasons for failure to thrive such as heart failure, cystic fibrosis, hypothyroidism, diabetes, malabsorption, and psychological and central nervous system problems before assuming that the diagnosis is nonorganic failure to thrive.

MUNCHAUSEN SYNDROME BY PROXY

A 3-year-old child presents to the hospital with severe diarrhea. The mother is a nurse employed by one of the physicians on staff. She is well liked by the hospital team because she is always so willing to "help out," i.e., taking her daughter's vital signs and feeding her. However, after 3 days of extensive therapy, the patient shows no improvement. No one can understand why this child remains ill until a nurse's assistant finds "chocolates" under the sheets while making the patient's bed.

Definition. Munchausen by proxy describes a situation whereby a parent (usually the mother) fabricates or induces illness in a child.

Risk Factors/Etiology. The parent may have a history of Munchausen syndrome (i.e., an adult who falsifies his/her own symptoms). The parent may be in the health care profession and may be regarded as a model parent. He/She may appear unconcerned about the child's illness and may form close bonds with the health care team. The child is usually less than 6 years old.

Presentation. The child usually presents with symptoms that are not compatible with a recognized disease.

Physical Examination. The patient may have chronic diarrhea from laxatives, rashes from caustic substances rubbed into the patient's skin, "foreign" blood or stool discovered in urine and blood samples, seizures from injection of insulin, and apnea from being "suffocated" with a pillow.

Diagnosis. If there is a high index of suspicion for this diagnosis, then unnecessary tests are **not** to be undertaken on the patient. All specimens should be analyzed for harmful and "foreign" agents. Old medical records should be obtained and reviewed, including those of the patient's siblings. Children who are hospitalized should be under strict surveillance, and this may include hidden television monitoring.

Treatment. On establishing the diagnosis, the offending parent should be confronted in a nonjudgmental way and offered help. All cases of Munchausen by proxy syndrome must be reported to Child Protective Services.

Complications/Follow-up. The complications from Munchausen by proxy syndrome include abuse, emotional problems, disability, and death. Other siblings may be, or may have already been, in danger of being victims of this syndrome.

Adolescence

ADOLESCENCE

Definition. Adolescence is the period bridging childhood and adulthood. It begins at approximately 11–12 years and ends at approximately 18–21 years. During this period the adolescent experiences many changes, such as completing puberty and somatic growth; developing socially, emotionally, and cognitively; moving from concrete to abstract thinking; establishing an independent identity; and preparing for a career or vocation. Adolescence includes, but does not correspond with, puberty.

Risk Factors/Etiology. The adolescent is at risk for **mortality** and **morbidity**. Examples of **mortality** in adolescence include accidents (particularly motor vehicle accidents), suicide (boys are more successful), homicide (particularly in blacks), and cancer-leukemia, (Hodgkin, lymphoma, bone, and CNS).

Examples of **morbidity** in adolescence include unintended pregnancy, sexually transmitted diseases, smoking, school dropouts, depression, runaways, physical violence, and crime/juvenile delinquency.

Presentation. There are three stages of adolescence: **early** (10–14 years), **middle** (15–16 years), and **late** (17–20 years).

- In **early** adolescence, the patient has physical changes related to puberty. There is rapid growth during this period, and secondary sexual characteristics begin to manifest. During this time adolescents are developing body images and self-esteem, and they are comparing themselves with their peers. They are concrete thinkers during this stage and oftentimes feel awkward. The early adolescent is more comfortable with the same sex, and their allegiance is beginning to shift from family to peers.
- In **middle** adolescence, the patient becomes more independent and has a sense of identity. These adolescents are becoming more comfortable with their new bodies. Mood swings are common, and peers provide emotional support and determine standards. Abstract thinking is beginning to develop. These teens may be dating, and some are experimenting. Their relationships are one-sided and narcissistic.
- In **late** adolescence, the adolescent becomes less self-centered and cares more about others. Their relationships change from group to individual. They begin more intimate dating. These adolescents are contemplating future goals, plans, and careers. They are more independent from the family. They have a sense of right and wrong and are very idealistic.

A 14-year-old girl who has not yet achieved menarche presents to the physician with her concerned mother. The mother is afraid that her daughter is not "normal." On physical examination the patient appears well nourished and is in the 50th percentile for height and weight. Her breast examination shows the areolar diameter to be enlarged, but there is no separation of contours. Her pubic hair is increased in amount and is curled but is not coarse in texture. The mother and her daughter wait anxiously for your opinion.

Physical Examination

See Table 26-1 for the Tanner stages.

Table 26-1. Tanner Stages

	Females		Males	
Stage	**Breast**	**Pubic Hair**	**Genitalia**	**Pubic Hair**
I	Preadolescent—elevation of papilla only	None	Childhood size	None
II	Breast bud stage—small mound formed by elevation of breast and papilla	Sparse, long, generally straight	Enlargement of scrotum and testes	Sparse, straight, slightly pigmented at base
III	Areolar diameter enlarges	Darker, beginning to curl, increased amount	Penis grows in length; scrotum and testes continue to enlarge	Darker, more curled, small amount
IV	Further evaluation of breast and areola with separation of contours	Coarse and curly adult type, not on thighs	Penis increases in breadth; scrotum darkens and testes continue to enlarge	Coarse and curly adult type, not on thighs
V	Mature female—projection of areola and papilla to form a secondary mound	Adult quantity and type, extends onto thighs	Adult shape and size	Adult quantity and type, extends onto thighs

Patterns of development are also seen during adolescence, and these patterns are important for the physician to know.

Table 26-2. Patterns of Development

	Mean Age of Onset (years)	
Pubertal Event	**Boys**	**Girls**
Breast development		11.2
Testicular development	11.6	
Pubic hair development	13.4	11.7
Peak height velocity	14.1	12.1
Menarche		13.5
Adult pubic hair	15.2	14.4
Adult type breast		15.3

Some **normal variants** such as breast asymmetry, gynecomastia (breast development in 50–60% of males during Tanner Stage 3), and irregular menses (secondary to anovulatory cycles) may occur during adolescence causing concern for teenagers and their parents or guardians. The physician should reassure adolescents and their parents or guardians that these differences are normal. Breast asymmetry does not cause any physical problems, and gynecomastia and anovulatory cycles should be transient.

Complications/Follow-up. The complications of adolescence are related to growth and development and to morbidity and mortality. In addition, female patients may also experience primary or secondary amenorrhea, dysfunctional uterine bleeding, or dysmenorrhea. Both boys and girls may contract sexually transmitted diseases and have complications of the diseases as described below.

VAGINAL DISCHARGE

Table 26-3. Key Distinguishing Features of Vaginal Discharge

Feature	Bacterial Vaginosis	*Trichomonas*	*Candida*	Chlamydia/ Gonorrhea
Vaginal discharge	Profuse, malodorous, "fishy" amine odor	Gray-green, frothy, foul-smelling	Normal/ "cottage-cheese"-like	Purulent discharge
Wet prep	(+) Clue cells* (+) WBCs (+) Lactobacilli (+) Amine odor with KOH ("whiff test")	(+) Trichomonads (+) WBCs	(+) Branching hyphae and spores	(+) WBCs (–) Trichomonads (–) Lactobacilli
pH				
STD	No	Yes	No	Yes

*Clue cells are vaginal epithelial cells that are diffusely covered with bacteria.

SEXUALLY TRANSMITTED DISEASES

Gonorrhea

A 16-year-old girl presents to her physician because of fever, chills, pain and swelling in the small joints of her hands, and a maculopapular rash on her upper and lower extremities.

Definition. Gonorrhea is an infection caused by *Neisseria gonorrhoeae.* It affects the mucous membranes of the genitourinary tract and may at times also infect the mucosa of the oropharynx, rectum, and conjunctiva.

Risk Factors/Etiology. The agent is *N. gonorrhoeae.*

Presentation. Clinical presentations of gonorrhea may vary. Some patients with gonorrhea have urethritis, cervicitis, or dysuria. Other patients with gonorrhea may be asymptomatic. These patients are at risk for disseminated disease. Patients with disseminated gonorrhea may present with fever, chills, and polyarthralgias especially involving fingers, hands, and wrists.

Physical Examination. The physical examination will vary according to the clinical presentation. Boys with urethritis may have a purulent discharge and burning on urination. Postpubertal girls with symptomatic cervicitis may have a purulent discharge, suprapubic pain, and dysuria. The cervix may be inflamed and friable. Rectal gonorrhea may be asymptomatic, but at times proctitis, rectal bleeding, anal discharge, and constipation are presenting symptoms.

Diagnostic Tests. A **culture** for gonorrhea should be performed on any discharge from the cervix, urethra, rectum, or eye. If disseminated gonorrhea is suspected, cultures of the blood, pharynx, rectum, urethra, cervix, and synovial fluid (if applicable) should be evaluated. The discharge should also be Gram stained. A **Gram stain** indicative of gonorrhea will show Gram-negative intracellular diplococci in polymorphonuclear cells. All patients with gonorrhea should be **tested** for **syphilis** and **HIV.**

Treatment. Ceftriaxone is the treatment for gonorrhea. In addition, **doxycycline,** or **azithromycin,** should be administered to treat presumed or proven *Chlamydia.* Please remember that pregnant women and children younger than 9 years of age should not receive tetracycline drugs. Also, consider therapy for other sexually transmitted diseases that may be present, such as syphilis and HIV.

Complications. Disseminated gonococcal infection via hematogenous spread is a complication of gonorrhea. Other complications include perineal, perianal, and periprostatic abscesses. Pelvic inflammatory disease may also occur. Patients with Fitz-Hugh-Curtis syndrome as a complication of gonococcal infection complain of right upper quadrant pain, with or without salpingitis. In this syndrome the infection spreads, seeding the liver capsule, resulting in a perihepatitis.

Differential Diagnosis. Gonorrhea must be differentiated from other causes of purulent discharge from the vagina or urethra. Some diagnoses for consideration are group A β-hemolytic streptococci, *Chlamydia trachomatis, Trichomonas vaginalis,* and *Candida albicans.* Gonococcal arthritis needs to be differentiated from problems such as rheumatoid arthritis, rheumatic fever, and inflammatory bowel disease. Pelvic inflammatory disease caused by gonorrhea may mimic appendicitis, ovarian cyst or ovarian tumor, urinary tract infection, and inflammatory bowel disease.

Chlamydia

A 16-year-old boy presents to the emergency center with a persistent penile discharge. The patient states that 1 week ago he saw his family physician for this same problem. At that time the physician gave him an IM shot of penicillin. However, the patient states that the discharge did not resolve with the penicillin therapy. He would like a second opinion.

Definition. *Chlamydia* are intracellular obligate parasites with a cell wall, and they are responsible for a variety of diseases in sexually active adolescents such as nongonococcal urethritis, epididymitis, cervicitis, salpingitis, and Fitz-Hugh-Curtis syndrome.

Risk Factors/Etiology. In developed countries *C. trachomatis* is the most prevalent sexually transmitted disease. Lymphogranuloma venereum is related to *Chlamydia.*

Presentation. Patients with *Chlamydia* infection may be asymptomatic or may present with urethritis, cervicitis, Fitz-Hugh-Curtis syndrome, or pelvic inflammatory disease.

Physical Examination. Girls with genital infection of *Chlamydia* may have a mucoid discharge. Boys may have an asymptomatic urethral infection.

Diagnostic Tests. A *Chlamydia* culture may be performed from tissue culture of the infected genitalia. Rapid presumptive diagnosis may be made with antigen detection kits using monoclonal antibodies, DNA probe, enzyme-linked immunosorbent assay (ELISA), or nucleic acid amplification (NAA) tests.

Treatment. Uncomplicated cervicitis (or urethritis in boys) caused by *C. trachomatis* may be treated with azithromycin or doxycycline. Erythromycin is the treatment of choice for pregnant women. All sexual partners should be treated.

Complication. Fitz-Hugh-Curtis syndrome and salpingitis are complications of *Chlamydia* genital infection in girls. Salpingitis may put the patient at risk for infertility and ectopic pregnancy.

Trichomoniasis (*Trichomonas vaginalis*)

A 15-year-old presents to her physician because she has a yellow, foul-smelling vaginal discharge. On physical examination she is noted to have a "strawberry cervix."

Definition. *Trichomonas vaginalis* is a sexually transmitted protozoan parasite that causes vaginitis in girls.

Risk Factors/Etiology. *T. vaginalis* is more commonly seen in girls with multiple sexual partners or in groups with high instances of other sexually transmitted diseases. *T. vaginalis* may be transmitted to the neonate during the birth process, but this infection is usually self-limited. The presence of *T. vaginalis* in a prepubertal child is rare, and sexual abuse should be suspected if present.

Presentation. The patient may complain of pruritus and a foul-smelling vaginal discharge. Males are usually asymptomatic.

Physical Examination. There is a **frothy vaginal discharge.** Cervical hemorrhages (**"strawberry cervix"**) may be seen.

Diagnostic Tests. Finding motile protozoan in fresh saline preparations of genital secretions makes the diagnosis. However, a negative wet mount does not eliminate the diagnosis. In boys, the diagnosis of trichomoniasis may be made by microscopic review of urine sediment after prostatic massage.

Treatment. Metronidazole is the treatment for trichomoniasis. All sexual partners should be treated to prevent reinfection.

Complications/Follow-up. In girls, trichomoniasis is associated with premature rupture of membranes, low birth-weight infants, and infertility. In boys, epididymitis, prostatic involvement, and penile ulceration may occur as complications of this infection.

Herpes

A 17-year-old sexually active boy presents to the physician because of painful ulcerations on his glans penis and on the shaft of his penis. He has multiple sexual partners and does not use condoms. Fever and inguinal adenopathy are also present.

Definition. Herpes simplex virus is a double-stranded, DNA-containing enveloped virus that causes a number of problems involving the skin, eye, oral mucosa, CNS, and genital tract. There are two types of herpes simplex virus, HSV-1 and HSV-2. HSV-1 may cause genital disease but more commonly causes nongenital infections of the mouth, lips, eyes, and CNS. HSV-2 is responsible for genital infections and neonatal infections and may cause oral lesions.

Risk Factors/Etiology. Genital herpes is usually caused by HSV-2 and is more commonly seen in teenagers and adults. It is transmitted by sexual activity.

Presentation. Fever, regional adenopathy, and dysuria may be present in patients with primary genital herpes infection.

Physical Examination. In girls, the vulva and vagina may have vesicles and ulcers, but the cervix is the primary site of infection. In boys, vesicles and ulcers may be found on the penis.

Diagnostic Tests. The Tzanck stain may be performed on scrapings from the herpetic lesion. If herpes is present, then multinuclear giant cells and intranuclear inclusions will be detected. ELISA and immunofluorescent techniques may be useful. The diagnosis may also be made clinically.

Treatment. Acyclovir is the treatment for herpes. Valacyclovir, a prodrug of acyclovir, and famciclovir, a prodrug of penciclovir, are oral antiherpes drugs used to treat genital herpes.

Complications/Follow-up. Genital herpes is a risk factor for HIV. Genital herpes virus may reoccur without symptoms. During this recurrent infection, herpes virus is being shed and sexual partners are at risk. If the female patient with recurrent genital herpes is pregnant and has active herpes infection, then the infant passing through the birth canal is at risk for acquiring infection.

ACNE VULGARIS

A mother brings her 15-year-old daughter to the dermatologist because she has developed pimples. The mother says that her daughter's face "breaks out" because she drinks soda pop. The daughter is argumentative about this but admits that she does drink soda pop every day at lunch. The mother would like you to tell her daughter to stop drinking soda pop. On physical examination the patient has open and closed comedones and pimples on her forehead, nose, and cheeks.

Definition. Acne is a skin disorder caused by (*1*) *Propionibacterium acnes,* (*2*) abnormal keratinization of the follicular epithelium, (*3*) increased production of sebum, and (*4*) inflammation.

Risk Factors/Etiology. Lesions of acne vulgaris originate in sebaceous follicles. There are four primary pathogenetic changes in acne.

- Keratinized cells become impacted in the follicular lumen.
- There is increased sebaceous gland production of sebum.
- *P. acnes* located within the sebaceous follicle forms free fatty acids.
- Inflammation occurs from lysosomal enzymes that phagocytize the bacteria.

Presentation. Acne vulgaris has four types of lesions. Patients with acne vulgaris may have any or all of the four types of lesions. These lesions are (*1*) open and closed comedones, (*2*) papules, (*3*) pustules, and (*4*) nodulocystic lesions.

Physical Examination. The distribution of acne vulgaris lesions varies from patient to patient. Lesions may occur on the forehead, central area of the face, chest, upper back, and deltoid region. These lesions often heal, leaving temporary erythema and hyperpigmentation. If the acne vulgaris is severe, such as in the nodulocystic type, scarring may result.

Diagnostic Tests. Acne is a clinical diagnosis. There are no diagnostic tests.

Treatment

Therapy must be **individualized.** The skin must be kept **clean.** There is **no special diet** to prevent acne vulgaris because there is little evidence to show that ingestion of particular foods causes acne to become manifest.

Topical preparations are helpful for treatment of comedones and papulopustular acne. These topical agents include **benzoyl peroxide, tretinoin (Retin-A), Adapalene (Differin gel),** and **topical antibiotics** such as clindamycin and erythromycin. It takes 4–8 weeks to assess the effectiveness of topical agents. A regimen that is used frequently is benzoyl peroxide gel in the morning and tretinoin at night.

Systemic therapy such as tetracycline is indicated if a patient does not respond to topical medications. Systemic antibiotics are also used for patients who have moderate to severe acne vulgaris or have a tendency to scar.

A trial of **hormonal therapy** with an antiandrogen may be prescribed for women with acne and hormonal abnormalities who are unresponsive to antibiotic therapy and are not candidates for isotretinoin.

Isotretinoin (13-*cis*-retinoic acid, Accutane) is necessary for cases of moderate to severe nodulocystic acne vulgaris that are resistant to conventional therapy. Isotretinoin decreases *P. acnes* on the skin and also decreases the inflammatory response.

Corticosteroid injections may heal painful nodulocystic lesions faster. **Dermabrasion** may be considered to minimize scarring only after the active process abates.

Complications

Scarring can be a complication of acne. For patients taking systemic tetracycline, side effects of tetracycline (phototoxic reactions, gastrointestinal irritation, staining of growing teeth) may occur. For patients taking isotretinoin, pregnancy must be avoided because of the teratogenicity of this drug to the fetus. Some other side effects from isotretinoin include elevated triglycerides, depression, arthralgias, and scalp folliculitis.

Differential Diagnosis

Flat warts, folliculitis, and other types of acne (drug-induced, halogen, chloracne, tropical, conglobata) are sometimes confused with acne vulgaris.

Genetics/Dysmorphology

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DEFINITIONS

Malformation	Morphologic defect of an organ, part of an organ, or a larger region, resulting from an intrinsically abnormal developmental process
Deformation	Abnormal form or position of a part of the body caused by nondisruptive mechanical forces on normally formed tissues
Disruption	Structural defect of an organ, part of an organ, or larger region, resulting from a breakdown of or interference with an originally normal developmental process
Dysplasia	Structural defect due to abnormal organization of cells into tissues
Syndrome	A pattern of multiple abnormalities thought to be pathogenically related and not known to represent a sequence
Sequence	A pattern of multiple anomalies derived from a single known or presumed prior anomaly or mechanical factor
Association	The nonrandom occurrence in two or more individuals of multiple, idiopathic anomalies of blastogenesis

PATTERNS OF INHERITANCE

Autosomal dominant

- Disorder appears in a vertical pattern in a pedigree.
- Affected individuals present in every generation.
- Any child of an affected parent has a 50% of inheriting the condition.
- Phenotypically normal parents do not transmit to offspring.
- Males and females are equally affected.
- Significant proportion of cases are due to new mutations.
- There is variable expressivity of the gene.
- There is variable penetrance.
- There may be somatic and/or germ cell mosaicism.
- The more severe the disorder, the higher the cases from de novo mutation.
- In severe disorders, reduced reproductive capacity limits transmission.
- Older paternal age is observed in some cases of new mutation.

Autosomal recessive

- Both carriers are heterozygous.
- The child of two heterozygous parents has a 25% chance of inheriting the gene.
- Males and females are affected with equal frequency.
- Affected individuals are almost always born in one generation of the family.
- Children of the affected person are always heterozygous.
- Related parents are more likely to be heterozygous for the same harmful gene.
- Often displays a horizontal pattern in pedigrees.

X-linked recessive

- Incidence of the condition is much higher in males than in females.
- Heterozygous female carriers are usually unaffected.
- The gene is transmitted from an affected male to all of his daughters, and any daughter has a 50% chance of inheriting the gene.
- The gene is transmitted through a series of female carriers. Therefore, all affected males are related through the carrier females.
- A significant proportion of sporadic cases is the result of a new mutation.
- Disorders are more common in females with Turner syndrome.
- Skewed X-inactivation pattern—there will be a few females who, by chance, have one or the other of their X chromosomes inactivated.

X-linked dominant

- The condition is regularly expressed in heterozygous female carriers.
- All of the daughters and none of the sons of an affected male have the condition.
- Both male and female offspring of an affected female have a 50% chance of inheriting the condition.
- For rare, X-linked dominant conditions, affected females are about 2× more common than affected males, but affected females typically have milder manifestations of the phenotype.

Multifactorial inheritance

- It is the product of a number of genetic and environmental factors.
- There is a similar rate of recurrence (3–5%) among all first-degree relatives of the affected case; however, it is unusual to find a significant increase in risk for relatives related more distantly than second-degree to the index case.
- The risk of recurrence is related to the incidence of the disease.
- Some disorders have a sex predilection. When there is an altered ratio, the risk is higher for relatives of an index case in the less commonly affected sex.
- The likelihood that both identical twins will be affected with the same malformation is less than 100%, but much greater than the chance that both members of a nonidentical twin pair will be affected.
- The risk of recurrence is increased when multiple family members are affected.
- The risk of recurrence may be greater when the disorder is more severe.

Mitochondrial inheritance

- Mitochondria contain small circular chromosomes that encode 13 proteins, which function in the respiratory chain of the organelle.
- Mutation of the mitochondrial genome are often deletions and produce specific disease.
- Abnormalities are typically seen in one or more specific organs: brain, eye, skeletal muscle.
- Because mitochondria are inherited virtually exclusively from the mother, conditions are passed from mother to offspring without regard to sex.
- The mitochondria of an individual constitute a heterogeneous mixture of genotypes within and between cells, so the mitochondrial complement passed in the egg is often not representative of the total mitochondrial population of the mother. Therefore, mitochondrial DNA mutations produce disease only in the presence of many mutated mitochondria.
- Mitochondrial populations are not equally distributed to all tissues, so there is great variability of symptoms within a family.
- Rarely, mutations may occur by paternal inheritance. Typically, sperm mitochondria undergo destruction by nuclear encoded proteins.

SEQUENCES

Pierre Robin Sequence

Pierre Robin syndrome may be secondary to **hypoplasia of the mandibular area**. The **tongue becomes posteriorly located, preventing closure of the posterior palatal shelves. Physical findings** include micrognathia, glossoptosis, and a cleft soft palate. Airway obstruction can occur. Thirty percent of patients require tracheostomy until the airway reaches adequate size. The mandible achieves a normal appearance by 4–6 years. **Pierre Robin syndrome can be a feature of other syndromes**, such as Edwards (discussed below) and Stickler (autosomal dominant, early arthritis, ocular problems).

Potter Sequence

Potter syndrome is a **bilateral renal agenesis** and is therefore incompatible with life. Usually there is a history of **oligohydramnios**. Death is not caused by renal failure but rather by **pulmonary hypoplasia**, as there is late development of alveolar sacs. **Potter facies** consists of hypertelorism, epicanthal folds, low-set ears, micrognathia, a compressed, flat nose, and limb anomalies. Parents and siblings may have asymptomatic renal anomalies.

DUE TO TERATOGEN

Fetal Alcohol Syndrome

Alcohol is the most common major teratogen to which the fetus is exposed. The exact amount of alcohol that causes findings is not known. However, the higher the intake, the more severe the findings. Patients **have pre- and postnatal growth deficiency. Mental retardation is present**, with an average IQ of 63. Infants are **irritable**, and patients demonstrate hyperactivity as children. **Fine motor dysfunction** manifests as a weak grasp and fine tremors. **Physical findings** include microcephaly, short palpebral fissures, maxillary hypoplasia, short nose, a smooth philtrum, and a smooth upper lip. Cardiac anomalies are common, specifically **septal defects.**

Occasionally, patients have ptosis, cleft lip, cervical vertebral malformations, tetralogy of Fallot, and coarctation of the aorta. **Infants appear as failure to thrive because of having thin adipose tissue.** Findings may be subtle or full-blown, depending on maternal alcohol intake during pregnancy. Two drinks a day may result only in smaller birth size, 4–6 drinks a day may cause only subtle physical findings, whereas 8–10 drinks a day can result in severe fetal alcohol syndrome. There is no specific therapy.

CHROMOSOMAL

Trisomy 21 (Down Syndrome)

This is the most common pattern of malformation, occurring in 1/660 births. Physical findings are many: **hypotonia,** protruding tongue, **small stature,** awkward gait, hyperflexible joints, and diastasis recti. **Mental retardation** is present to varying degrees. Cranial abnormalities include a **flat occiput,** mild microcephaly, **upslanting palpebral fissures,** late closure of the fontanel, hypoplasia of the frontal sinuses, a small nose, low nasal bridge, and **inner epicanthal folds.** Ocular anomalies include **Brushfield spots** and refractive errors. Patients have small ears, overfolding upper helix, and small or absent earlobes. **Hypoplastic teeth** are common. Hand findings include short metacarpals and fingers, **clinodactyly (60%), simian crease (45%),** and characteristic prints. They exhibit a wide gap between the first and second toes. **Cardiac abnormalities** are present in 49%, with endocardial cushion defects, ventricular septal defects (VSDs), patent ductus arteriosus (PDA), and atrial septal defects (ASDs). Cutaneous manifestations include **dry skin, cutis marmorata,** fine, soft sparse hair, and straight pubic hair. Occasionally, patients have seizures, strabismus, and low-set ears. Patients are at higher risk for **duodenal atresia, atlantoaxial instability,** leukemia, and thyroid disease.

Trisomy 18

This is the second most common multiple malformation syndrome. Findings include feeble fetal activity and a weak cry. Polyhydramnios is common. Patients have growth deficiency and mental retardation. Physical examination shows a prominent occiput, low-set ears, and micrognathia. The hands are held in a typical clenching posture, with overlapping fingers (second over third, fifth over fourth). Rocker bottom feet and hammertoes are seen. The nails are hypoplastic. There is limited hip abduction. Cardiac defects include VSDs, ASDs, and PDA. Thirty percent die by 1 month of age, 50% by 2 months, and only 10% survive to 1 year.

Trisomy 13

Trisomy 13 (Patau syndrome) is a chromosomal disorder resulting in multiple developmental anomalies, including forebrain abnormalities and severe mental retardation. Advanced maternal age increases the risk, and the extra chromosome is often maternally derived. Characteristically, anomalies are located in the midline and include midline clefts, scalp defects (cutis aplasia), microcephaly, and holoprosencephaly (failure of the forebrain to divide properly). Cleft lip and cleft palate are common, and anomalies of the eye include microphthalmia and colobomas of the iris. Fingers are usually flexed, and polydactyly may be seen. Most patients are so severely affected that they die before 6 months of age. Only 10% live beyond 1 year of age.

Turner Syndrome (XO)

Turner syndrome occurs in 1/5000 newborns. It has a sporadic occurrence. Usually it is the paternal X chromosome that is missing. **All patients have short stature and gonadal dysgenesis.**

Findings include a tendency to obesity, **congenital lymphedema, broad (shield) chest, and widely spaced nipples.** Patients have a **low posterior hairline** and a **webbed neck (pterygium coli).** Skeletal manifestations include **cubitus valgus** and hip dislocation. Skin findings include narrow hyperconvex nails, **pigmented nevi,** and a tendency to form keloids. Bicuspid aortic valves, **coarctation of the aorta,** and valvular aortic stenosis are cardiac anomalies. **Horseshoe kidneys** may be seen. Occasionally, patients have **blue sclera,** cataracts, mental retardation, Crohn disease, or thyroid disorders. The congenital lymphedema resolves. Patients do not achieve an adolescent growth spurt, reaching a final height of 55 inches. Estrogen replacement is indicated.

Fragile X Syndrome

This is the most common cause of inherited mental retardation, and is **the most common cause of mental retardation in boys. Clinical findings** are mental retardation, large testicles, prominent jaw, large ears, a wide nasal bridge, and a large head. Stereotypical behavior and speech are also observed.

Klinefelter Syndrome

This is the most common single cause of hypogonadism and infertility, occurring in 1/500–1/1000 newborn boys. **47,XXY** is the most common pattern. Patients tend to have **low IQ. Behavior problems and immaturity** are early manifestations, arising in childhood well before adolescence and hypogonadism. **Fire-setting behavior** has been reported. Patients tend to be **tall and slim with long limbs.** They may be obese as adults. **Hypogonadism** and a small penis are observed; cryptorchidism or hypospadias may occur. **Gynecomastia** occurs in 40% of patients, and there is an increased incidence of breast cancer. The diagnosis is made by demonstrating an X chromatin-positive male. Therapy consists of **testosterone replacement** at 11–12 years.

ASSOCIATED WITH SHORT STATURES

Achondroplasia

Although achondroplasia in an **autosomal dominant** disorder, **90% of cases are fresh mutations.** Patients exhibit **short stature, a large head,** a low nasal bridge, and a **prominent forehead. A lumbar lordosis** is present, and the **limbs are short,** particularly the proximal segments. There is incomplete extension of elbows, and **bowlegs.** Patients have **normal intelligence. Hydrocephalus** may occur secondary to a narrow foramen magnum.

ASSOCIATED WITH PIGMENTED LESIONS

LEOPARD syndrome

Lentigines are benign, dark brown macules, which can be mistaken for nevi. LEOPARD syndrome is an autosomal dominant syndrome consisting of:

Lentigines—multiple, 1–5 mm in size

EKG abnormalities such as prolonged P-R interval, abnormal QRS, abnormal P waves

Ocular hypertelorism

Pulmonic stenosis

Abnormal genitalia—hypogonadism, cryptorchidism
Retarded growth
Deafness

Waardenburg Syndrome

Findings in Waardenburg syndrome include **lateral displacement of the inner canthi, severe bilateral deafness,** and **partial albinism** (white forelock, pale blue eyes). The eyebrows flare medially, and may meet in the middle. Occasionally, patients exhibit the Cupid's bow lips, and may have VSDs or Hirschsprung. It is transmitted in an **autosomal dominant** fashion. Older paternal age is reported in fresh mutations.

Peutz-Jeghers Syndrome

Peutz-Jeghers is **autosomal dominant.** Fifty percent of patients have no family history, implying a **high rate of spontaneous mutation.** This syndrome is known for **pigmentation and polyps.** Vertical bands of epidermal pigment appear as blue-gray or brownish spots on **the lips, oral mucous membranes, and periorally. Polyps can be found in the jejunum,** nasopharynx, and bladder. The spots appear in infancy to early childhood, and fade in adults. Seventy percent of patients have GI problems by age 20. Sixty percent can have colicky abdominal pain, and up to **25% have an intussusception.** The GI polyps have a low rate of malignancy. **Clubbing** of fingers may occasionally be seen.

Ataxia-Telangiectasia

Ataxia-telangiectasia is transmitted as an **autosomal recessive** trait. The defect is found on the long arm of **chromosome 11. Ataxia** begins shortly after children learn to walk. It is progressive, and patients end up in wheelchairs by age 10–12 years. **Telangiectasia** first appears at 3–6 years of age and can occur anywhere, but is typically on the bulbar conjunctiva. Patients have **chronic upper respiratory infections and deficient cellular immunity** (low or absent IgA and IgE, lymphopenia). They are **at higher risk for malignancies** such as Hodgkin, leukemia, and sarcoma. Growth deficiency manifests in infancy or childhood. Patients develop **ataxia, choreoathetosis, drooling, and a masklike facies.** Nystagmus may be seen. Death occurs because of serious pulmonary infections or neurologic deficit.

ASSOCIATED WITH COLLAGEN DISORDERS

Ehlers-Danlos Syndrome

Ehlers-Danlos is an **autosomal dominant** disease, with a wide variance in expression. It has been classified into 10 different types of disease. **Type VI is autosomal recessive.** The problem is a **qualitative collagen deficiency.** Findings include a narrow maxilla, hypermobile ears, and **velvety skin, which is hyperextensible.** The skin is fragile and demonstrates **poor wound healing.** Joints are also hyperextensible and easily dislocated. Patients exhibit easy bruising and flat feet, and may have **mitral valve prolapse.** Occasionally they may have blue sclera, a wide nasal bridge, glaucoma, retinal detachment, small stature, kyphoscoliosis, dissecting aortic aneurysm, ASDs, mental deficiencies, and renal anomalies. Many patients are born prematurely after premature rupture of membranes, a possible sign of tissue friability. Unnecessary surgeries should be avoided because of poor wound healing and prolonged hemorrhage.

Marfan Syndrome

Findings of Marfan include **tall stature**, long limbs, little subcutaneous fat, muscle hypotonia, and **arachnodactyly**. Sixty percent have **kyphosis or scoliosis. Pectus excavatum** or carinatum is very common. Ocular findings include **lens subluxation**, myopia, and retinal detachment. **Cardiac anomalies** are dilatation with or without dissecting aneurysm of the ascending aorta, and mitral valve prolapse. Occasionally, patients have large ears, hemivertebra, learning disorders, and attention deficit hyperactivity disorder. **Patients are of normal intelligence. Vascular complications** can occur at any time and are the chief cause of death. Marfan is inherited in an **autosomal dominant** fashion with wide variability in expression.

MISCELLANEOUS

Prader-Willi Syndrome

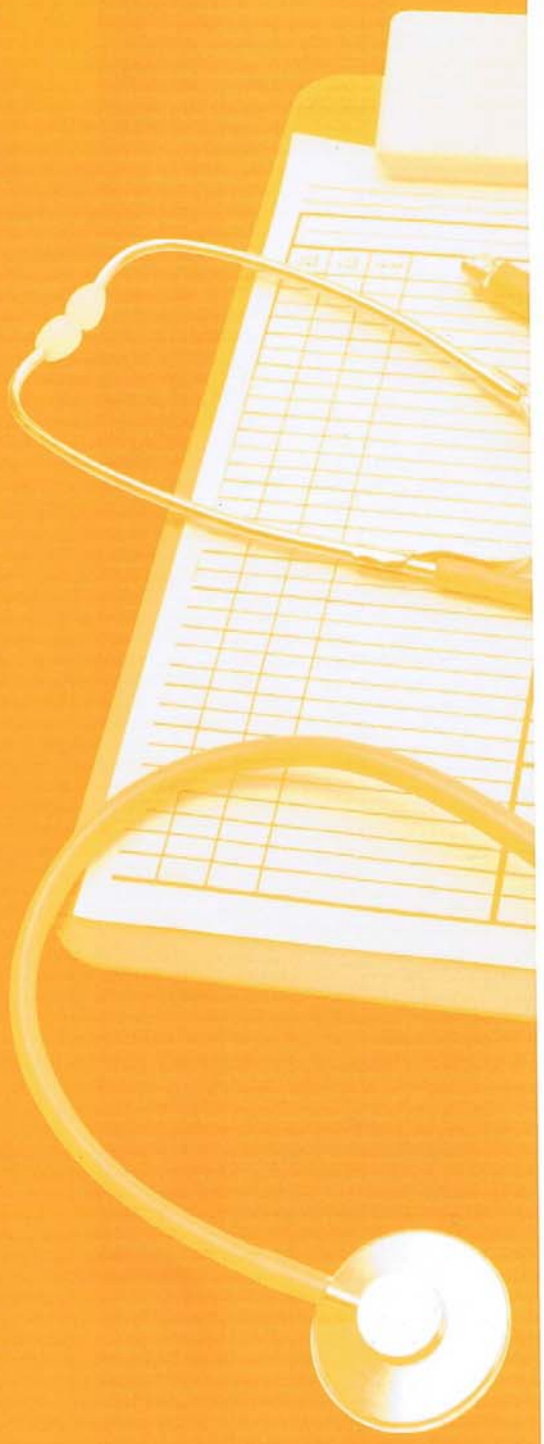
Prader-Willi results from a deletion on **chromosome 15.** Patients have **hypotonia, hypogonadism, hypomentia, and obesity.** Short stature responds to growth hormone replacement. Small hands and feet are seen.

Prune Belly (Eagle-Barrett Syndrome)

Prune belly syndrome results from a congenital absence of the anterior abdominal wall muscles. It consists of the triad of **urinary anomalies** (hypoplastic kidneys, hydronephrosis, hydroureter), **deficiency of abdominal wall muscles**, and **undescended testes.** Intestinal malrotation is common. **Ninety-five percent of patients are males.** One third are stillborn or die early because of pulmonary complications.

Beckwith-Wiedemann Syndrome

Beckwith-Wiedemann syndrome occurs in about 1/14,000 births. It is characterized by **macrosomia and accelerated osseous maturation.** Mild to moderate mental deficiency may be present; patients may have normal intelligence. Physical examination is remarkable for **macroglossia, a large fontanel, a linear fissure in the external ear**, and indentations along the posterior rim of the helix. **Organomegaly** of the pancreas and kidney also occur, as well as **omphalocele. Hypoglycemia** occurs in one third to one half of patients, presenting in early infancy. **In the neonate, apnea cyanosis and feeding problems** may be related to the macroglossia. Neonates also have **seizures and hypoglycemia.** Patients are at higher risk for neonatal polycythemia and **Wilms** and other tumors (gonads, hepatoblastoma). **Routine ultrasound and α-fetoprotein** should be performed every 6 months until 6 years of age. Survivors of infancy tend to do well, and the excessive growth rate slows down.



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