Infectious Diseases Affecting the Respiratory Tract

On August 14, 2002, a 39-year-old male oil refinery worker in Crawford County, Illinois, visited the refinery's health unit complaining of a two-week cough. Later that day, the worker's 50-year-old supervisor also visited the unit with a spastic cough, which had started three days earlier. Both patients were advised to see their own health care provider where blood samples indicated a recent infection with *Bordetella pertussis*.

The Crawford County Health Department and Illinois Department of Public Health were contacted because a possible outbreak could be brewing.

In the early parts of the 20th century, one of the most common childhood diseases and causes of death in the United States was pertussis, commonly called whooping cough. Before the introduction of a pertussis vaccine in 1940, *B. pertussis* was responsible for infection and disease in 150 out of every 100,000 people. By 1980, the incidence, or frequency with which the disease occurs, had dropped to one in every 100,000 individuals. The vaccine had almost eliminated the pathogen.
At the oil refinery, active surveillance and case investigations were initiated by the health officials. Those workers with a persistent and spasitic cough were sent to the local hospital for evaluation and interviews. Health department officials needed to know the time of illness onset, where workers worked in the refinery, work schedule, and individuals with whom they had close contacts. Local school officials and health care providers were alerted and given guidelines on ways to recognize pertussis and prevent its spread.

In the course of the epidemiological investigation, 17 cases of pertussis were identified at the refinery, 15 having had close contact with the supervisor originally diagnosed; 7 cases occurred among the community and had no apparent relation to the refinery. In all, 21 of the cases occurred in adults 20 years of age or older. Patients received an antibiotic effective against the pathogen and all recovered.

How the disease was passed from the supervisor remains unclear. *B. pertussis* is spread by airborne droplets (Figure 20.1). Other than an indoor, 5-minute morning meeting each day, work assignments were all outdoors, although workers often congregated in an indoor dining area at lunch.

Every 3 to 4 years, a pertussis outbreak occurs in the United States—and, as indicated above, many of these cases occur in adults. Although nearly all youngsters growing up receive the pertussis vaccine, vaccine-induced protection does not last a lifetime; therefore, adolescents and adults can become susceptible to disease when vaccine-induced immunity wanes, approximately 5 to 10 years after vaccination. As a result, college students and adults (like the refinery workers) may be vulnerable.

Pertussis is but one of a group of infectious diseases affecting the respiratory tract. We will divide these diseases into two general categories. The first category will include diseases of the upper respiratory tract, such as strep throat, diphtheria, and pertussis. The second category will include diseases of the lower respiratory tract: tuberculosis, pneumonia, and influenza. As we proceed, note that antibiotics are available for treating the bacterial diseases while immunizations are used for protecting the community at large.
The respiratory system is composed of a conducting portion that brings oxygen to the lungs and a respiratory portion that exchanges oxygen and carbon-dioxide gasses with the bloodstream. Because air typically contains microbes and viruses carried on dust and droplet nuclei, it should not be surprising that the respiratory system is the most common portal of entry for these infectious agents.

**Upper Respiratory Tract Defenses Limit Microbe Colonization of the Lower Respiratory Tract**

The respiratory system is divided into the upper respiratory tract and the lower respiratory tract (FIGURE 20.3). The upper respiratory tract (URT) is composed of the nose, sinus cavities, and pharynx (throat), while the lower respiratory tract (LRT) is composed of the larynx, trachea, bronchi, and lungs. The lungs contain the alveoli where gas exchange occurs. The average adult inhales and exhales approximately 10,000 liters of air per day. Given that the inspired air contains microbes and microbe-laden particulate matter that could potentially bring microbes that cause infection, the respiratory system has evolved effective defense mechanisms to minimize such possibilities.

During breathing, the URT and bronchi play a critical role in filtering out foreign material, such as bacteria, viruses, and the dust particles that might carry these microbes. A process called mucociliary clearance involves the entrapment of microbes and particulate matter larger than 2 μm in a layer of mucus, which is then moved by ciliated epithelial cells toward the pharynx where it is either swallowed or expectorated (FIGURE 20.4). Mucocil-
primary clearance is supplemented by the presence and activity of several antimicrobial substances, including lysozyme and lactoferrin (see Chapter 19). In addition, an anionic antimicrobial peptide, which is active against gram-positive and gram-negative bacteria, is present, along with IgA and IgG antibodies, and several human defensins (see Chapter 14). Thus, mucociliary clearance and the activity of antimicrobial substances are largely responsible for maintaining much of the LRT virtually free of microbes and particulate matter.

In the nose, large particles present in inhaled air are removed by hairs in the nostrils, while smaller particles and suspended bacteria become trapped in the mucus covering the nasal mucosa. In the posterior two-thirds of the nasal mucosa, the mucociliary clearance also propels the mucus-entrapped particles into the pharynx. However, in the anterior region of the nasal mucosa the disposal of entrapped microbes is largely dependent on microbicidal substances present in nasal fluid. Several antimicrobial agents have been detected, including lysozyme and lactoferrin, and IgA antibodies that block microbial adhesion to epithelial cells. The nasal fluids therefore are capable of killing or inhibiting potential pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Sneezing and coughing are additional mechanical methods to eliminate microbes trapped in the mucus of the respiratory tract.

In the LRT, the epithelial cells lining the alveolar and respiratory bronchioles are not ciliated. However, the region is covered by alveolar fluid, which contains a number of antimicrobial components, including lysozyme and immunoglobulins. The predominant immunoglobulin is IgG (not IgA), which facilitates the phagocytosis of any microbes lining this part of the respiratory tract. It also can activate complement. Should larger numbers of microbes enter the alveoli, the alveolar macrophages recruit neutrophils from the pulmonary capillaries to help clear the invaders.

The constant exposure to the environment means that many different microorganisms can form part of the commensalistic microbiota of URT. Among the microbes identified are species of *Streptococcus*, *Neisseria* (in the nasopharynx), *Haemophilus*, *Staphylococcus* (primarily in the anterior nares of the nose), *Corynebacterium*, and *Propionibacterium*. Several, including *Streptococcus*, *Neisseria*, *Haemophilus*, and *Staphylococcus*, are opportunist species that have the potential to cause serious illnesses in immunocompromised individuals. These members of the microbiota can damage parts of the tract, such as the mucociliary clearance process, if given the opportunity.

As described in Chapter 19 for the skin, host microbiota have the upper hand for space and nutrients, thereby setting the limits on the ability of pathogens to compete for the space and nutrients and thus to colonize and cause infections in the respiratory system.

The indigenous community of microbes will vary depending on the specific part of the tract because of the “environmental differences.” For example, colonization of the external nares primarily involves corynebacteria and propionibacteria, bacteria normally found on the skin surface (see Chapter 19). The anterior nares certainly are a source of *S. aureus*. Interestingly, about 20 percent of the population seldom if ever carries the bacterium, while another 20 percent are persistent carriers. That leaves about 60 percent of the...
The bacterial diseases of the upper respiratory tract (URT) can be severe, as several diseases in this section illustrate. One reason is because the respiratory tract is a portal of entry to the blood, and from there, bacterial pathogens can spread to other sensitive internal organs.

**Pharyngitis Is an Inflammation of the Throat**

**KEY CONCEPT**

- *Streptococcus pyogenes* causes strep throat and scarlet fever.

A sore throat, known medically as pharyngitis, is not a disease itself. Rather, the inflammation usually is a symptom of a viral infection, such as the common cold or the flu. However, sometimes bacteria, especially the streptococci, can be the cause. As described in Chapter 19, group A streptococci (GAS) are bacteria often found on the skin. In particular, *Streptococcus pyogenes*, a facultative, gram-positive coccus, may be carried on the skin of individuals who either have no symptoms of illness or exhibit a relatively mild illness such as impetigo. This gram-positive coccus is also carried in the throat and is the most common cause of tonsillitis, an inflammation of the tonsils. The tonsils help the immune system defend against infection by harmful bacteria and viruses. When tonsillitis occurs, treatment typically involves simple pain relievers or, if indicated, antibiotics. Surgery is seldom necessary, although years ago, surgery was the standard treatment in young children for recurrent tonsillitis.

Another, and sometimes potentially more dangerous, example of pharyngitis is *Streptococcus pharyngitis*, popularly known as strep throat.

The *S. pyogenes* cells are highly contagious and reach the URT within respiratory droplets expelled by infected persons during coughing and sneezing. If the cells grow and secrete toxins, these substances cause damage to surrounding human cells and lead to an inflammation of the oropharynx and tonsils. Besides a sore throat, patients may develop a fever, headache, swollen lymph nodes and tonsils, and a beefy red appearance to pharyngeal tissues owing to tissue damage. More than a million Americans, primarily children, suffer strep throat annually. An oral antibiotic, such as penicillin, is often prescribed to lessen the duration and severity of the inflammation and to prevent possible complications. Hand hygiene is the best prevention.

**Scarlet fever** is a disease arising in about 10 percent of children with streptococcal pharyngitis. Some strains of *S. pyogenes* carry toxin-encoding prophages coding for erythrogenic (*erythro* = “red”) exotoxins that cause a pink-red skin rash on the neck, chest, and soft-skin areas of the arms (Figure 20.5A). The rash, which usually occurs in children under 15 years of age, results from blood leaking through the walls of capillaries damaged by the toxins. Other symptoms include a sore throat, fever, and a strawberry-like inflamed tongue (Figure 20.5B). Normally, an individual experiences only one case of scarlet fever.
otics, such as penicillin or clarithromycin, can shorten the duration of symptoms and prevent serious complications.

A serious complication is rheumatic fever, which is most common in young school-age children. This condition, which is not an infection but rather an inflammation in response to the throat infection, primarily affects the joints and heart. It is characterized by fever and joint pain. The most significant long-range effect is permanent scarring and distortion of the heart valves, a condition called rheumatic heart disease. The damage arises from a response of the body's antibodies to streptococcal M proteins cross reacting with similar proteins on heart muscles. Rheumatic fever cases have been declining in the United States due to antibiotic treatment. In 1994, the last year the Centers for Disease Control and Prevention (CDC) required reporting of rheumatic fever cases, 112 cases were reported versus 10,000 reported cases in 1961. However, in developing nations, rheumatic fever remains a serious problem.

Another complication arising from streptococcal pharyngitis is acute glomerulonephritis, which is a rare inflammatory response to specific types of M proteins. The antigen-antibody complexes formed then accumulate in the glomerulus of the kidney. It is most common in young patients. Progressive, irreversible renal damage may occur in adults.

Infections of the lower respiratory tract, causing streptococcal pneumonia, are described later in this chapter.

**CONCEPT AND REASONING CHECKS**

20.2. What makes *S. pyogenes* such a potentially dangerous pathogen in the upper respiratory tract?

**Diphtheria Is a Life-Threatening Illness**

**KEY CONCEPT**

- *Corynebacterium diphtheriae* secretes a toxin that inhibits protein synthesis in epithelial cells.

Diphtheria is an infection of the URT that is caused by *Corynebacterium diphtheriae* an aerob, club-shaped, gram-positive rod (*coryne* = “club”).

When stained with methylene blue, numerous blue cytoplasmic dots are seen that represent metachromatic granules (see Figure 20.5). Individuals with scarlet fever usually get better within two weeks without treatment (MicroFocus 20.1). Treatment with antibiotics, such as penicillin or clarithromycin, can shorten the duration of symptoms and prevent serious complications.
The bacterial cells remain in clumps after multiplying and form a picket fence-like arrangement called a palisade arrangement. Diphtheria is acquired by inhaling respiratory droplets from an infected person. Initial symptoms include a sore throat and low-grade fever. In epithelial cells, the bacterial cells secrete a potent exotoxin, which is encoded by a corynebacterium-containing prophage gene. The exotoxin inhibits the translation process by ribosomes. The result is the accumulation of dead tissue, mucus, white blood cells, and fibrous material, called a pseudo-membrane (“pseudo” because it does not fit the definition of a true membrane) on the tonsils or pharynx. Mild cases fade after a week while more severe cases can persist for two to six weeks.

Complications can arise if the thickened pseudomembrane results in respiratory blockage. If the exotoxin spreads to the bloodstream, heart and peripheral nerve destruction can lead to cardiac arrhythmia and coma. Left untreated, 5 to 10 percent of respiratory cases result in death.

Treatment requires antibiotics (penicillin or erythromycin) to eradicate the pathogen and antitoxins to neutralize the exotoxins. Immunization against diphtheria may be rendered by an injection of diphtheria toxoid, which, contained in the diphtheria-tetanus-acellular pertussis (DTaP) vaccine, consists of toxin molecules treated with formaldehyde or heat to destroy their toxic qualities. The toxoid induces the immune system to produce antitoxins (antibodies) that circulate in the bloodstream throughout the person’s life. Due to immunization starting in early childhood, the number of cases of diphtheria in the United States is essentially zero (the last confirmed case was in 2003). However, the disease remains a health problem in many regions of the world and booster doses are required. The World Health Organization (WHO) reported 4,190 cases of diphtheria in 2007.

**A Wakeup Call**

In life, sometimes the best way to move past a roadblock is to simply face it head on—or attack the defensive team by running right at them. Often in the microbial world, bacterial species may have the same idea—but with a twist.

One of the most common host responses to a group A streptococci (GAS) infection in humans is to try to contain the infection by forming a blood clot around the infected area (see figure)—in other words, the host attempts to entomb the bacterial cells in the clot. Unfortunately, one of the abilities GAS possess is to simply break through the defensive wall set up to contain the infection. How do they do this?

Normally a blood clot stays as a clot because the protein plasmin that would dissolve the clot stays in an inactive form called plasminogen. What *Streptococcus pyogenes* does is “wake up” or activate plasminogen.

Trapped within a clot, the *S. pyogenes* cells secrete an enzyme called streptokinase. What streptokinase does is to catalyze the conversion of inactive plasminogen into active plasmin—in other words, it wakes the protein up. As plasmin, the protein triggers a series of reactions leading to the dissolving of the clot. Now the bacteria can escape and perhaps cause a serious infection elsewhere in the body.

**Arrhythmia:** An irregular heart beat.

**Epithelial cells:** Cube-like cells lining the skin and body cavities such as the respiratory tract.
The skin (cellulitis) at the tip of the nose. Because this part of the face contains veins that lead to the brain, venous spread of bacteria can lead to a life-threatening condition called cavernous sinus thrombosis.

Sinusitis is inflammation of the sinuses, the air-filled hollow cavities around the nose and nasal passages. The inflammation is most commonly caused by an allergy or infection and represents one of the most common medical conditions. About 10 to 15 million people each year develop a so-called “sinus infection.” It can occur in any of the four groups of sinuses: maxillary, ethmoid, frontal, or sphenoid. Sinusitis nearly always occurs in connection with inflammation of the nasal passages (rhinitis), and some doctors refer to the disorder as rhinosinusitis. It may be acute or chronic.

Acute sinusitis may be caused by a variety of indigenous microbiota of the URT. The condition often develops from a blockage at the openings to the sinuses, resulting from a common cold infection of the URT. Fluid trapped in the sinuses then becomes a nutrient medium for bacterial growth. In addition, white blood cells and more fluid enter the sinuses to fight the bacteria and this only increases the pressure in the sinuses and causes more pain. Acute sinusitis usually
Ear Infections Are Common Illnesses in Early Childhood

KEY CONCEPT
• Infections can occur in the outer and middle ear.

As part of the URT, the ears, nose, and throat are located near each other and, as such, allow infections to spread from one to the other. The ear, which is the organ of hearing and balance, consists of the outer, middle, and inner ear (Figure 20.6). The Eustachian tube vents the middle ear to the nasopharynx, which explains why URT infections (such as the common cold) often result in infections to the middle ear.

A few ear infections can occur in the outer ear. Such an inflammation, referred to as otitis externa (oti = “ear”), can affect the entire ear canal or just one small area, as in a boil (furuncle) or pimple. Normally, the ceruminous glands in the ear canal produce cerumen (earwax) that has antibacterial activity. However, outer ear infections commonly occur in children especially after extended swimming in fresh water pools. This can result in excessive moisture in the ear canal, which irritates and breaks down the skin in the canal, allowing bacteria to penetrate—such infections often are called swimmer’s ear. A bacterial infection is most often caused by species of Streptococcus, Staphylococcus, or Pseudomonas. Fungi also can be the cause of otitis externa.

Results in pain, tenderness, and swelling over the affected sinuses. Yellow or green pus may be discharged from the nose. Fever and chills also can occur, but their presence is a likely indication that the infection has spread beyond the sinuses. Treatment of acute sinusitis is aimed at improving sinus drainage and curing the infection. Nasal sprays can be used for a short time, and antibiotics, such as amoxicillin or trimethoprim-sulfamethoxazole, can be prescribed for a bacterial infection.

If untreated, acute sinusitis may develop into a chronic condition. Chronic sinusitis is defined as an infection that has been ongoing for 8 to 12 weeks. Doctors do not understand exactly what causes chronic sinusitis but it may follow a viral infection. The symptoms of chronic sinusitis are more subtle and pain occurs less often. The most common symptoms are nasal obstruction, nasal congestion, and post-nasal drip. The treatment is the same as with acute sinusitis, except antibiotic use, if bacterial, may be for a longer period of time. Preventing or reducing the risk of developing chronic sinusitis can be accomplished by good hygiene and frequent hand washing, and avoiding contracting viral, bacterial, or fungal infections. Treating cold symptoms immediately and using decongestants also may help prevent the development of a chronic condition.

CONCEPT AND REASONING CHECKS
20.5 How do acute and chronic sinusitis differ?
The primary symptoms of otitis externa are itching followed by ear pain. Treatment involves the application of antibiotic ear drops to the ear several times a day for about one week. Swimmer’s ear can be prevented by not swimming in polluted water and using ear plugs to keep the canal dry when swimming, showering, or bathing.

Short-term infections of the middle ear are called **acute otitis media** \((\text{media} = \text{“middle”})\). Such infections are among the most common illnesses of early childhood. The National Institute on Deafness and Other Communication Disorders reports that three out of four children contract at least one ear infection by age 3. Bacteria typically responsible for middle ear infections include *Streptococcus pneumoniae* and *H. influenzae*.

Middle ear infections usually start with a common cold infection of the URT. Inflammation of the Eustachian tube allows bacteria to infect the sterile environment of the middle ear. Fluid buildup then provides an environment for bacterial growth, which results in the middle ear becoming inflamed. This is followed by ear pain with a red, bulging eardrum. Children with ear infections may develop a fever, produce a fluid that drains from the ears, or have headaches. They also may have trouble sleeping and be unusually irritable.

Most individuals get better without treatment. The American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP) suggest that children older than 6 months who are otherwise healthy and have only mild signs and symptoms not be given antibiotics at least for the first 72 hours, as most cases of otitis media resolve on their own in a few days. In fact, the AAP and AAFP report that about 80 percent of children with otitis media recover without antibiotics. For chronic bacterial infections, a physician may decide to administer an antibiotic such as amoxicillin. Prevention can be difficult due to the behaviors of young children interacting with one another. Limiting the time a child spends in group child care may help prevent common colds and ensuing middle ear infections.

**Chronic otitis media** (COM) is a condition involving long-term infection, inflammation, and damage to the middle ear. Children have persistent fluid in the ears that lasts for months in the absence of any other symptoms except hearing impairment. COM is a major global cause of hearing impairment and can have serious long-term effects on language, auditory and cognitive development, and educational progress; it is a major public health problem in many populations around the world, and a significant cause of morbidity and mortality.

It is now recognized that COM is not the result of re-infection, but rather stems from a persistent biofilm that has colonized the middle ear tissue. As described in Chapter 3, biofilms are antibiotic-resistant colonizations of bacteria that attach to surfaces and form a slime-like defensive barrier, protecting the bacteria from immune attack or antibiotic therapy.

Treatment of COM depends upon the stage of the disease. Efforts are made to control the causes of Eustachian tube obstruction. If active infection is present in the form of ear drainage, antibiotic ear drops are prescribed, which may be supplemented with oral antibiotics. Once the active infection is controlled, surgery is usually recommended to clear the obstruction.
As mentioned earlier in this chapter, the prominent position of the nose in the URT makes it the most commonly infected part of the URT. Rhinitis is an inflammation and swelling of the mucous membranes of the nose, characterized by a runny nose and stuffiness, and usually caused by a common cold virus.

Rhinoviruses and adenoviruses are often responsible for the common cold syndrome. Rhinoviruses, "rhino" = "nose"), are a broad group of over 100 different naked, single-stranded (+ strand), RNA viruses with icosahedral symmetry ( ). They belong to the family Picornaviridae (pico = "small"; hence, small-RNA-viruses).

Rhinoviruses thrive in the human nose, where the temperature is a few degrees cooler (33°C) than in the rest of the body. They are transmitted through respiratory droplets or by contact with an infected person or contaminated fomites. Rhinoviruses account for 30 to 50 percent of common colds, also called head colds. Adults typically suffer two or three colds and children six to eight colds per year. The rhinoviruses are most common in the fall and spring ( ).

A common cold is a viral infection of the lining of the nose, sinuses, throat, and upper airways. One to three days after infection, a sequence of symptoms (common-cold syndrome) begins. These include sneezing, a sore throat, runny or stuffy nose, mild aches and pains, and a mild-to-moderate hacking cough. Some children suffer from croup. The illness usually is of short duration of 7 to 10 days. One of the old wives tales was that becoming chilled could cause colds (MicroFocus 20.2).

So, why cannot scientists find a cure for the common cold? The answer is quite simple. There are more than 120 viruses and strains involved. More than 100 rhinovirus strains alone can cause common colds. In addition to these, common colds can be caused by adenoviruses, respiratory syncytial viruses, coronaviruses, and enteroviruses. Therefore, it would be impractical to develop a vaccine to immunize people against all different types of cold viruses.

Antibiotics will not prevent or cure a cold. Antihistamines can sometimes be used to treat the symptoms of a cold; however, they do not shorten the length of the illness. For other remedies, such as vitamin C, zinc, and herbs like echinacea, there is no verified scientific evidence these substances limit or prevent colds. Since rhinoviruses spread by respiratory droplets, washing hands and sneezing into a handkerchief are important to decrease transmission of the viruses.

Adenoviruses. The adenoviruses (family Adenoviridae) are a group of over 50 antigenic types (serotypes) of nonenveloped, icosahedral virions having double-stranded DNA ( ). They multiply in the nuclei of several human host tissues and induce the for-
20.3 Viral Infections Affecting the Upper Respiratory Tract

Infection of inclusion bodies, which are a series of bodies composed of numerous virions arranged in a crystalline pattern (see Chapter 12). The viruses take their name from the adenoid tissue from which they were first isolated.

Adenoviruses can be highly infectious and are frequent causes of URT diseases often symptomatic of a common cold in infants and young children. Transmitted through respiratory droplets, the viruses most often cause distinctive symptoms because the fever is substantial, the throat is very sore (acute febrile pharyngitis), and the cough is usually severe. In addition, the lymph nodes of the

![Image of inclusion bodies]

**Adenoid tissue:** Refers to the pharyngeal tonsil located in the upper rear of the pharynx.

**Febrile:** Relates to fever.

---

**Hypothesize why different cold viruses cause diseases at different times of the year.**

**FIGURE 20.10** The Seasonal Variation and Estimated Annual Proportion of Viral Respiratory Diseases. This chart shows the seasons associated with various viral diseases of the respiratory tract (and their annual percentage).

**MICROFOCUS 20.2: Being Skeptical**

**Catching a Chill: Can It Cause a Cold?**

How many times can you remember your mom or a family member saying to you, “Bundle up or you will catch a cold!” Can you actually “catch” a cold from a body chill?

During the last 50 years of research, scientists have claimed that one cannot get a cold from a chill. Rather, colds result from more people being cooped up indoors during the winter months, making virus transmission from person-to-person very likely. At least, that was the scientific dogma until 2005.

In the November 2005 issue of *Family Practice*, British researchers Claire Johnson and Professor Ron Eccles at Cardiff University’s Common Cold Center announced that a drop in body temperature can allow a cold to develop.

The researchers signed up 180 volunteers between October and March to participate in the study. Split into two groups, one group put their bare feet into bowls of ice cold water for 20 minutes. The other group put their bare feet in similar but empty bowls.

Over the next five days, 29 percent of individuals who had their feet chilled developed cold symptoms, while just 9 percent of the control group developed symptoms.

Professor Eccles suggests that colds may develop not because the volunteers actually “caught” a cold virus, but rather that they harbored the virus all along. Chilling causes a constriction of blood vessels in the nose, limiting the warm blood flow supplying white blood cells to eliminate or control the cold viruses present. Professor Eccles states that, “A cold nose may be one of the major factors that causes common colds to be seasonal.”

The verdict: Well, the results of one study do not make for a general consensus. More definitive studies may help verify or refute the “cold nose” claim.
neck swell and a whitish-gray material appears over the throat surface. Some adenoviruses may produce a form of conjunctivitis called pharyngoconjunctival fever, which is most commonly contracted by swimming in virus-contaminated water. There were more than 42,000 cases reported in Japan in 2006. New military recruits may suffer acute respiratory disease (ARD) as a result of adenovirus transmission in crowded conditions. Any of these conditions can progress to viral pneumonia.

No antiviral agents currently available treat adenoviral infections.

Although bacterial infections of the larynx are extremely rare, the most common cause of laryngitis is a viral infection of the URT caused by a common cold or flu virus. Symptoms are an unnatural change of voice, such as hoarseness, or even loss of voice that develops within hours to a day or so after infection. The throat may tickle or feel raw, and a person may have a constant urge to clear the throat. Fever, malaise, difficulty swallowing, and a sore throat may accompany severe infections. Treatment of viral laryngitis depends on the symptoms. Resting the voice (by not speaking), drinking extra fluids, and inhaling steam relieve symptoms and help healing. The bacterial and viral diseases of the URT are summarized in Table 20.1.

20.4 Bacterial Diseases of the Lower Respiratory Tract

In the lower respiratory tract (LRT), a number of bacterial diseases affect the lung tissues. As injury occurs, fluid builds up in the lung cavity, and the space for obtaining oxygen and eliminating carbon dioxide is reduced. This is the basis for a possibly fatal pneumonia.

Pertussis (Whooping Cough) Is Highly Contagious

KEY CONCEPT

- Bordetella pertussis secretes toxins that destroy cells of the ciliated epithelium.

Pertussis (per = “through”; tussi = “cough”), also known as whooping cough, is caused by Bordetella pertussis, a small, aerobic, gram-negative rod. The bacilli are spread by respiratory droplets that adhere to and aggregate on the cilia of epithelial cells in the mouth and throat. Exotoxin production paralyzes the ciliated cells and impairs mucus movement, potentially causing pneumonia.

Pertussis is one of the more dangerous and highly contagious diseases of childhood years. Typical cases of pertussis occur in two stages. The initial (catarrhal) stage is marked by general malaise, low-grade fever, and increasingly severe cough. During the second (paroxysmal) stage, disintegrating cells and mucus accumulate in the airways and cause labored breathing. Patients experience multiple paroxysms, which consist of rapid-fire staccato coughs all in one exhalation, followed by a forced inhalation over a partially closed glottis. The rapid inhalation results in the characteristic “whoop” (hence, the name whooping cough). Ten to fifteen paroxysms may occur daily, and exhaustion usually follows each. Sporadic coughing continues during several weeks of convalescence, even after the pathogen has vanished. (Doctors call it the
“100-day cough.”). Convalescence depends on the speed at which the ciliated epithelium regenerates.

Eradication of the bacterial cells is generally successful when erythromycin is administered before the respiratory passageways become blocked. However, antibiotic treatment only reduces the duration and severity of the illness.

As with diphtheria, the low incidence of pertussis stems partly from use of a pertussis vaccine. The older vaccine (diphtheria-pertussis-tetanus, or DPT) contained merthiolate (Thimerosal)-killed \textit{B. pertussis} cells and was considered risky because about 1 in 300,000 vaccinees suffered high fevers and seizures. Now, public health officials recommended the newer acellular pertussis (aP) vaccine prepared from \textit{B. pertussis} chemical extracts. Combined with diphtheria and tetanus toxoids, the triple vaccine has the acronym DTaP; commercially, it is known as Tripedia.

Although the incidence of pertussis has declined substantially since introduction of an effective vaccine in 1949, the number of cases in the United States has been rising since 1981. In fact, the CDC recorded 15,632 cases in 2006. The majority of reported cases occur in adolescents because adolescents (and adults) lose vaccine-induced immunity 5 to 10 years after vaccination (see chapter opener). In 2005, the US Food and Drug

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|l|l|}
\hline
\textbf{Disease} & \textbf{Causative Agent} & \textbf{Signs and Symptoms} & \textbf{Transmission} & \textbf{Treatment} & \textbf{Prevention} \\
\hline
Streptococcal pharyngitis & \textit{Streptococcus pyogenes} & Sore throat, fever, headache, swollen lymph nodes and tonsils & Respiratory droplets & Penicillin & Practicing good hand hygiene \\
\hline
Scarlet fever & \textit{Streptococcus pyogenes} & Pink-red rash on neck, chest, arms, strawberry-like tongue & Respiratory droplets & Penicillin, Clarithromycin & Practicing good hygiene \\
\hline
Diphtheria & \textit{Corynebacterium diphtheriae} & Sore throat and low-grade fever & Respiratory droplets & Penicillin, Erythromycin & Vaccinating with Hib \\
\hline
Epiglottitis & \textit{Haemophilus influenzae} & Severe throat pain, fever, muffled voice & Respiratory droplets & Intravenous antibiotics & Vaccinating with Hib \\
\hline
Sinusitis & Indigenous microbiota & Pain, tenderness, and swelling & — & Nasal sprays, Antibiotics & Minimizing contact with individuals with colds \\
\hline
Otitis externa & \textit{Streptococcus, Staphylococcus, Pseudomonas} species & Itching and ear pain & Contaminated water & Lifestyle modifications, Topical and oral medications & Keeping ears dry \\
\hline
Acute otitis media & \textit{Streptococcus pneumoniae, Haemophilus influenzae} & Ear pain, Red, bulging eardrum & Airborne Contact & Wait and see, Antibiotics & Limiting time in childcare \\
\hline
Common colds (rhinitis) & Rhinoviruses, Adenoviruses, Other viruses & Sneezing, sore throat, runny and stuffy nose, hacking cough & Respiratory droplets & Pain relievers, Decongestants & Practicing good hygiene \\
\hline
Laryngitis & Cold viruses & Hoarseness, Loss of voice & Respiratory droplets & Rest voice, Drinking plenty of water & \\
\hline
\end{tabular}
\caption{A Summary of the Major Bacterial and Viral URT Diseases}
\end{table}

\textbf{Merthiolate:} A mercury derivative compound formerly used in vaccines as a disinfectant and preservative.
consumption” or “white plague” and it con-
tinued to be the world’s leading cause of death
from all causes, accounting for one fatality in
every seven cases.

Today’s statistics, though improved, are
still threatening. Although the CDC reported
that in 2005 there was an all-time low of
13,779 cases in the United States, in develop-
ing nations health officials report more deaths
from TB than from any other infectious dis-
ease. In fact, today there are more people with
TB than ever in history. The WHO estimates
that some 2 billion individuals, one-third of
the world’s population, are infected with the
TB bacillus; 2 million die of TB every year;
and unless control measures are strengthened,
another one billion people globally will
become infected and 36 million will die of
tuberculosis by 2020.

Tuberculosis is caused by Mycobacterium
tuberculosis, the “tubercle” bacillus first iso-
lated by Robert Koch in 1882. It is a small,
aerobic, nonmotile rod whose cell wall forms
a waxy cell surface that greatly enhances
resistance to drying, chemical disinfectants,
and many antibiotics. In the laboratory, Gram
staining will not penetrate the waxy layer, so,
when processing a sputum sample, the stain-
ing must be accompanied by heat to penetrate
this barrier, or a lipid-dissolving material must
be used. Once stained, however, the organisms
resist decolorization, even when subjected to a
5 percent acid-alcohol solution. Thus, the
bacilli are said to be acid-resistant or
acid-fast (see Chapter 4).

Epidemiology. Tuberculosis is primarily an
airborne disease and, as such, the bacilli are
transmitted from person to person in small,
aerosolized droplets when a person with
active pulmonary disease sneezes, coughs,
spits, or even sings. The infectious dose is
quite small and the inhalation of even a single
M. tuberculosis cell can lead to a new infection.
However, individuals with prolonged, fre-
frequent, or intense contact with a diseased indi-
vidual are at most risk of becoming infected,
with an estimated 30 percent infection rate.
Thus, crowded conditions and poor ventila-
tion often contribute to disease spread and
people who live in overcrowded, urban ghet-
toes often contract TB. Malnutrition and a
generally poor quality of life also contribute to the establishment of disease.

Pathogenesis. Unlike many other infectious diseases where an individual becomes ill after several days or a week, the incubation period for TB is much longer. In addition, the illness has two separate stages: an infection stage and a disease stage (Figure 20.13). If a person has a pulmonary infection (85 percent of infections are respiratory), the bacterial cells enter the alveoli where pathogen interactions occur (Figure 20.14). This individual is now said to have a primary TB infection. If tested, the person would have a positive tuberculin reaction, but a chest x-ray and sputum test would be negative (see Disease Detection, below).

In the alveoli, macrophages respond to the infection by ingesting the bacilli. Unfortunately, the bacilli are not killed in the macrophages and as more macrophages arrive, they too phagocytize bacilli but are incapable of destroying them. An inflammatory condition ensues. After about four weeks, some macrophages gain the ability to kill some bacilli, forming a central area of large, multicellular giant cells. Recruited lymphocytes and fibroblasts surround the mass in the lung, forming a hard nodule called a tubercle (hence the name tuberculosis), which may be visible in a chest X-ray. In 90 percent of primary TB infections, the infection becomes arrested; the tubercles heal and undergo fibrosis and calcification. These individuals often are never aware they are infected, although they may now have a positive chest X-ray. This dormant form of TB is referred to as a latent TB infection and is carried by 2 billion people worldwide. Of these, 90 percent will never develop active disease and will not be infectious.
Mycobacterium tuberculosis is inhaled as airborne droplets into the lungs. The bacilli enter the alveolus. The bacilli are taken up and multiply within alveolar macrophages, and soon the body's immune system dispatches other specialized macrophages and T lymphocytes to the site. Multinucleated giant cells develop as the cells join together. A wall of cells, calcium salts, and fibrous materials eventually form around the giant cell. This is the tubercle.

**FIGURE 20.14 The Progress of Tuberculosis.** Following invasion of the alveoli, the tubercle bacilli are taken up by macrophages and "walled off." What is the immune system attempting to do by forming tubercles?
Up to 10 percent of individuals who have a primary or latent TB infection will develop the second stage of the illness: a clinical disease. Primary TB infections can develop into primary active TB disease and latent TB infections can have a reactivation of the bacilli, which develop into secondary active TB disease. Individuals in both groups will become ill within three months, experience chronic cough, chest pain, and high fever, and they continue to expel sputum that accumulates in the LRT. (Often the sputum is rust colored, indicating that blood has entered the lung cavity.) In these individuals, the immune defenses were unable to keep the tubercle bacilli in check. Many of the infected macrophages die, releasing bacilli and producing a caseous (cheese-like) center in the tubercle. Live bacterial cells rupture from the tubercles, and spread and multiply throughout the LRT as well as other body systems. These individuals will now have a positive tuberculin reaction, chest X ray, and sputum test; these individuals can transmit the disease to others. (Figure 20.15).

Because the bacilli in individuals with active TB disease are not killed, the bacterial cells can spread through the blood and lymph to other organs such as the liver, kidney, meninges, and bone. If active tubercles develop throughout the body, the disease is called miliary (disseminated) tuberculosis (milium = "seed," in reference to the tiny lesions resembling the millet seeds in bird food). Tubercle bacilli produce no known toxins, but growth is so unrelenting that the respiratory and other body tissues are literally consumed, a factor that gave tuberculosis its alternate name of "consumption."

**Disease Detection.** Early detection of tuberculosis is aided by the tuberculin reaction, a delayed hypersensitivity test that begins with the application of a purified protein derivative (PPD) of *M. tuberculosis* to the skin. One method of application, called the Mantoux test, uses an injection of PPD intradermally into the forearm. Depending on the patient’s risk of exposure, the skin becomes thick, and a raised, red welt, termed an induration, of a defined diameter develops (Figure 20.16). For an individual never before exposed to *M. tuberculosis*, an induration greater than 15 mm is interpreted as a positive test. However, a positive test does not necessarily reflect the presence of active TB disease, but may indicate a recent immunization, previous tuberculin test, or past exposure to *M. tuberculosis*. It suggests...
a need for further tests, such as a chest X ray or acid-fast staining of a sputum sample.

**Treatment.** Tuberculosis is an extremely stubborn disease especially with the development of antibiotic resistance. TB has been traditionally treated with such first-line drugs as isoniazid and rifampin. Ethambutol, pyrazinamide, and streptomycin also are used to help delay the emergence of resistant strains. Still, the appearance of multidrug-resistant tuberculosis (MDR-TB) has necessitated a switch to a group of second-line drugs, including fluoroquinolones and kanamycin. If drug therapy is effective for pulmonary TB, patients usually become noninfectious within three weeks as determined by bacteria-free sputum samples. Still, for such individuals, antimicrobial drug therapy is intensive and must be extended over a period of six to nine months or more, partly because the organism multiplies at a very slow rate (its generation time is about 18 hours). Early relief, boredom, and forgetfulness often cause the patient to stop taking the medication, and the disease flares anew. What basic immunological process is responsible for the red and thickened swelling typical of an induration?

**Prevention.** Vaccination against TB may be rendered by intradermal injections of an attenuated strain of *Mycobacterium bovis*, a species that causes tuberculosis in cows as well as humans. The attenuated strain is called Bacille Calmette-Guérin (BCG), after Albert Calmette and Camille Guérin, the two French investigators who developed it in the 1920s. Though the vaccine is used in parts of the world where the disease causes significant mortality and morbidity, health officials in the United States generally do not recommend the BCG vaccine because it has limited effectiveness for preventing TB in adults and produces occasional side effects. New vaccines consisting of subunits, molecules of DNA, and attenuated strains of mycobacteria are currently being developed.

**Other Mycobacterium Species.** Several other species of *Mycobacterium* deserve a brief mention. *M. chelonae* is another pathogenic species frequently found in soil and water and can cause lung diseases, wound infections, arthritis, and skin abscesses. *M. haemophilum* is a slow-growing pathogen often found in immunocompromised individuals including those with AIDS. Cutaneous ulcerating lesions and respiratory symptoms are typical in the patients. *M. kansasii* causes infections that are indistinguishable from tuberculosis and, in the United...
20.10 Explain how a primary or latent tuberculosis infection is different from a primary or secondary tuberculosis disease.

Infectious Bronchitis Is an Inflammation of the Bronchi

**KEY CONCEPT**
- Bronchitis produces excessive mucus and a narrowing of the bronchi.
Infectious bronchitis occurs most often during the winter and can be caused by bacteria following a URT viral infection, such as the common cold. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* often cause bacterial bronchitis in young adults, while *Streptococcus pneumoniae* and *Haemophilus influenzae* are the primary agents among middle-aged and older individuals. Influenza viruses also can cause a form of viral bronchitis.

Infectious bronchitis generally begins with the symptoms of a common cold: runny nose, sore throat, chills, general malaise, and perhaps a slight fever. The onset of a dry cough usually signals the beginning of acute bronchitis, a condition that occurs when the inner walls lining the main airways of the lungs become infected and inflamed. Inflammation increases the production of mucus, which then narrows the air passages. Bacteria or viruses are present in the mucus. If the condition persists for more than three months, it is referred to as chronic bronchitis. The changing of the clear or white mucus to a yellow or green color usually indicates a bacterial infection.

Most cases of acute bronchitis disappear within a few days without any adverse effects, although a cough can linger for several weeks. Antibiotics may be prescribed if the bronchitis is caused by a bacterial infection. Because many cases of acute bronchitis result from influenza, getting a yearly flu vaccination may reduce the risk of bronchitis. Other preventative measures include good hygiene, including hand washing, to reduce the chance of transmission.

**CONCEPT AND REASONING CHECKS**

20.11 Why does acute bronchitis often produce symptoms of breathlessness and wheezing?

**Pneumonia Can Be Caused by Several Bacteria**

**KEY CONCEPT**

- Bacterial pneumonia can be community or hospital acquired.

The term *pneumonia* refers to microbial disease of the bronchial tubes and lungs. A wide spectrum of organisms, including viruses, fungi, and bacterial species, may cause pneumonia.

“Typical” pneumonia refers to patients complaining of a cough, fever, and chest pain. Over 80 percent of bacterial cases of typical pneumonia are due to *S. pneumoniae*; however, several other species also can cause the lung infection. *Streptococcus Pneumoniae*. Besides being the second leading cause of bacterial meningitis,
S. pneumoniae also causes pneumococcal pneumonia.

As already described, S. pneumoniae is a gram-positive, encapsulated chain of diplococci. Pneumococcal pneumonia is community acquired. Although it exists in all age groups, the mortality rate is highest among infants, the elderly, and those with underlying medical conditions. More than 500,000 cases are reported each year in the United States, resulting in approximately 40,000 deaths.

S. pneumoniae is usually acquired by aerosolized droplets or contact, and the pneumococci exist as a part of the normal microbiota in the URT of many individuals. However, the natural resistance of the body is high, and disease usually does not develop until the defenses are compromised. Malnutrition, smoking, viral infections, and treatment with immune-suppressing drugs most often predispose one to S. pneumoniae infections.

Patients with pneumococcal pneumonia experience high fever, sharp chest pains, difficulty breathing, and rust-colored sputum. The color results from blood seeping into the alveolar sacs of the lung as bacterial cells multiply and cause the tissues to deteriorate. The involvement of an entire lobe of the lung is called lobar pneumonia. If both left and right lungs are involved, the condition is called double pneumonia. Scattered patches of infection in the respiratory passageways are referred to as bronchopneumonia.

The antibiotic for pneumococcal pneumonia has been penicillin. However, increasing penicillin resistance has shifted antibiotic drug choice to cefotaxime or ceftriaxone.

Unfortunately, recovery from one serotype does not confer immunity to another serotype (over 90 capsular serotypes are known). A polyvalent antipneumococcal capsular polysaccharide vaccine immunizes against the 23 serotypes that are responsible for almost 90 percent of pneumococcal pneumonia cases.

Haemophilus Influenzae. Some 10 percent of “typical” pneumonia cases, especially in the elderly and compromised individuals, are caused by inhaling respiratory droplets containing unencapsulated H. influenzae strains. As described, the infection can become systemic and cause otitis media and sinusitis. These URT infections are treated with trimethoprim-sulfamethoxazole.

Staphylococcus Aureus. One of the most common causes of hospital-acquired pneumonia results from an infection by Staphylococcus aureus, a facultatively anaerobic, gram-positive coccus. If bacterial cells infect the lungs, a severe, necrotizing pneumonia may occur.

Klebsiella Pneumoniae. Klebsiella pneumoniae is a nonmotile, gram-negative rod with a prominent capsule. The bacillus is acquired by droplets, and often it occurs naturally in the URT of humans. The K. pneumoniae may be a primary disease or a secondary disease in alcoholics or people with impaired pulmonary function. As a primary lobar pneumonia, it is characterized by sudden onset and gelatinous reddish-brown sputum. The organisms grow over the lung surface and rapidly destroy the tissue, often causing death. In its secondary form, K. pneumoniae occurs in already ill individuals and is a hospital-acquired disease spread by such routes as clothing, intravenous solutions, foods, and the hands of health-care workers.

“Atypical” pneumonia is more insidious than “typical” pneumonia. Patient complaints include fever, cough, headache, and myalgia. Several bacterial species can cause this form of pneumonia.

Mycoplasma Pneumoniae. Mycoplasma pneumoniae causes an illness known as primary atypical pneumonia—“primary” because it
occurs in previously healthy individuals (pneumococcal pneumonia is usually a secondary disease); “atypical” because the organism differs from the typical pneumococcus and symptoms are unlike those in lobar pneumonia. Today, this community-acquired disease causes about 20 percent of pneumonias.

*M. pneumoniae* is recognized as one of the smallest bacterial species causing human disease. Mycoplasmas measure about 0.2 μm in size and are pleomorphic; that is, they assume a variety of shapes (Figure 20.19A). Because they have no cell wall, they have no Gram reaction or sensitivity to penicillin. *M. pneumoniae* cells are very fragile and do not survive for long outside the human or animal host. Therefore, they must be maintained in nature by passage in droplets from host to host.

Most patients, who are usually between 6 and 20 years old, first experience a URT infection. Symptoms include headache, fever, fatigue, and a characteristic dry, hacking cough. The infection then progresses to pneumonia in 30 percent of the infections. Blood invasion does not occur, and the disease is rarely fatal. Often it is called walking pneumonia (even though the term has no clinical significance). Epidemics are common where crowded conditions exist, such as in college dormitories, military bases, and urban ghettos. Erythromycin and tetracycline are commonly used as treatments.

Research in the 1940s established that antibodies produced against *M. pneumoniae* agglutinate type O human red blood cells at 4°C but not at 37°C. This observation was used to develop the cold agglutinin screening test (CAST): A patient's serum is combined with red blood cells at cold temperatures, and the red cells are observed for clumping. Diagnosis is assisted also by isolation of the organism on blood agar and observation of a distinctive “fried-egg” colony appearance (Figure 20.19B).

**MicroFocus 20.4** describes an interesting application for another bacterial species known to cause respiratory infections. *Legionella Pneumophila*. From July 21 to July 24, 1976, the Bellevue-Stratford Hotel in Philadelphia was the site of the 58th annual convention of Pennsylvania's chapter of the American Legion. Toward the end of the convention, 140 conventioneers and 72 other people in or near the hotel became ill with headaches, fever, coughing, and pneumonia. Eventually, 34 individuals died of the disease and its complications. In January 1977, investigators from the CDC announced the isolation of the infecting bacterial species from the lung tissue of one of the patients. The organism appeared responsible not only for the Legionnaires' disease (as the disease had come to be known), but also for a number of other unresolved pneumonia-like diseases.
Legionnaires’ disease (also called legionellosis) is caused by an aerobic, gram-negative rod named *Legionella pneumophila*. The bacillus exists where water collects, and apparently it becomes airborne in wind gusts and breezes. Cooling towers, industrial air-conditioning cooling water, lakes, stagnant pools, and puddles of water have been identified as sources of the pathogen. Older adults are most susceptible. After breathing the contaminated aerosolized droplets into the respiratory tract, the disease develops within a week. Human-to-human transmission does not occur.

Legionnaires’ disease usually causes a severe atypical pneumonia characterized by headache, fever, a dry cough with little sputum, and some diarrhea and vomiting. In
occurs primarily by inhaling the organisms in dust particles or handling infected animals. In addition, humans may acquire the disease by consuming raw milk or cheese infected with \textit{C. burnetii} or milk that has been improperly pasteurized. Patients experience a bronchopneumonia characterized by severe headache, high fever, a dry cough, and occasionally, lesions on the lung surface. The mortality rate is low, and treatment with doxycycline is effective for chronic infections. A vaccine is available for workers in high-risk occupations.

\textit{Chlamydia Psittaci}. Psittacosis is a zoonotic disease caused by \textit{Chlamydia} (formerly \textit{Chlamydia} \textit{psittaci}). These obligate, intracellular pathogens are transmitted to humans by infected parrots, parakeets, canaries, and other members of the psittacine family of birds (\textit{psittakos} = "parrot"). The disease also occurs in pigeons, chickens, turkeys, and seagulls, and some microbiologists prefer to call it ornithosis (\textit{ornith} = "bird") to reflect the more widespread occurrence in bird species. Humans acquire \textit{C. psittaci} by inhaling airborne dust or dried droppings from contaminated bird feces. Sometimes the disease is transmitted by a bite from a bird or via the respiratory droplets from another human. The symptoms of psittacosis resemble those of primary atypical pneumonia. Fever is accompanied by headaches, dry cough, and scattered patches of lung infection. Doxycycline is commonly used in therapy.
In 2006, the CDC reported 21 cases based on reports from less than 40 states. The incidence of psittacosis in the United States remains low, partly because federal law requires a 30-day quarantine for imported psittacine birds. In addition, birds are given water treated with chlortetracycline hydrochloride (CTC) and CTC-impregnated feed.

**Chlamydophila pneumoniae.** Chlamydial pneumonia is caused by *Chlamydophila pneumoniae*. The organism is transmitted by respiratory droplets and causes a mild community-acquired pneumonia, principally in young adults and college students. The disease is clinically similar to psittacosis and primary atypical pneumonia, and is characterized by fever, headache, and nonproductive cough. Treatment with doxycycline or erythromycin hastens recovery from the infection. *C. pneumoniae’s* relationship to cardiovascular disease is explored in **MICROFOCUS 20.5**.

### Concept and Reasoning Checks

**20.13** Summarize (1) the unique characteristics and (2) the mode of transmission of the rickettsiae and chlamydiae.

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**MICROFOCUS 20.5: Being Skeptical**

**Can Heart Disease Be Caused by an Infection?**

Here’s one to startle the senses: the “germ theory of cardiovascular diseases.” Skeptical? Let’s look deeper.

Coronary artery disease (CAD) remains a leading cause of death even with current medications and laser, angioplasty, or other innovative devices that are available. Perhaps antimicrobial drugs would help.

But, antibiotics for what? Why not start, scientists say, with *Chlamydophila pneumoniae*? In several studies, *C. pneumoniae* has been associated with heart attack patients and in numerous males with CAD. Researchers suggest the chlamydiae could injure the blood vessels, triggering an inflammatory response where immune system cells attack the vessel walls and induce the formation of large, fibrous lesions, or plaques. When pieces of plaque break free, they start blood clots that clog the arteries and cause heart attacks (the condition is known as atherosclerosis). Also, inoculation of mice and rabbits with *C. pneumoniae* accelerates atherosclerosis, even more so if the animals are fed cholesterol-enriched diets.

A second suspect is cytomegalovirus (CMV), an animal virus of the herpes family. In fact, more than 70 percent of the CAD population is CMV-positive. Scientists have known that people infected with CMV respond very poorly to arterial cleaning, the technique of angioplasty, and the arteries quickly close up. CMV also accelerates atherosclerosis in mice and rats.

A weaker association with CAD is seen with *Streptococcus sanguis*, an agent of periodontal disease. Some microbiologists suggest that poor oral hygiene and bleeding gums give the bacterial species access to the blood, where it produces blood-clotting proteins. It’s no coincidence, they maintain, that people with unhealthy teeth and gums tend to have more heart trouble. Unfortunately, such groups also have other lifestyle factors that confound the association.

The final suspect is *Helicobacter pylori*, the cause of most peptic ulcers. Italian scientists have linked a virulent strain of *H. pylori* with increased incidence of heart disease. However, other trials do not find the organism as significant in predicting CAD as the other agents.

To account for these observations and research findings, many medical researchers and microbiologists are proposing the concept of a total pathogen burden. First proposed in 2000, the concept suggests that while a single infectious agent may only minimally increase the risk of atherosclerosis, the burden of several agents could greatly increase the risk. In fact, several recent studies suggest that exposure to several microbial suspects does correlate with increased risk for CAD and, in established CAD cases, incident death. The studies propose that *C. pneumoniae* and CMV probably play a direct role in atherosclerosis while other agents, like *S. sanguis* and *H. pylori*, contribute indirectly to inflammation. The concept does not prove causality, but suggests avenues for further study, including the possible use of antibiotics, antivirals, or vaccines to prevent or cure CAD.

Still skeptical? Many scientists are too but they keep an open mind to new evidence. So, for now, stick with the more likely anti-inflammatory factors of diet, exercise, and not smoking.
Viruses are the most common cause of disease in the LRT of infants and young children. In addition, LRT diseases, such as influenza, cause substantial morbidity and mortality in the elderly and immunocompromised patients.

Influenza is a highly communicable acute respiratory infection

KEY CONCEPT

• Influenza A and B viruses evolve through antigenic drift and antigenic shift.

Influenza is a highly contagious acute disease of the respiratory tract that is transmitted by airborne respiratory droplets. The disease is believed to take its name from the Italian word for “influence,” a reference either to the influence of heavenly bodies, or to the influenza di freddo, “influence of the cold.” Since the first recorded epidemic in 1510, scientists have described 31 pandemics. The most notable pandemic of the twentieth century was the “Spanish” flu in 1918–1919; others took place in 1957 (the “Asian” flu) and in 1968 (the “Hong Kong” flu). Today, there are about 35,000 deaths in the United States and 250,000 to 500,000 deaths worldwide annually related to influenza infections.

The enveloped influenza virion belongs to the Orthomyxoviridae family. It is composed of eight single-stranded (– strand) segments of RNA, each wound helically and surrounded by a nucleocapsid (\(\text{N}\)). An additional structural protein, the matrix protein, surrounds the core of RNA segments. An envelope covers the matrix protein.

Projecting through the envelope are two types of spikes. One type contains the enzyme hemagglutinin (H), a substance facilitating the attachment and penetration of influenza viruses into host cells. Its shape determines the virus’ host range and tropism. The second type contains another enzyme, neuraminidase (N), a protein assisting in the release of the virions from the host cell when replication is complete.

Three types of influenza viruses are recognized.

Influenza A strikes every year and causes most “flu” epidemics. It circulates in many animals, including birds, pigs, and humans. Type A is divided into subtypes based on the H and N surface glycoproteins. There are 15
known H subtypes and 9 different N subtypes. The current subtypes in humans are A(H1N1) and A(H3N2).

Influenza B also strikes every year but is less widespread than type A. It only circulates between humans and is not divided into subtypes. Each year's flu vaccine is a mixture of the most prevalent A and B subtypes.

Influenza C causes a mild respiratory illness but not epidemics.

Each year a slightly different flu strain evolves, based, in part, on changes to H and/or N spike proteins; thus, there is a need for a new flu vaccine each year. Sometimes the new strain is quite mild, while in other years, a predominant strain will be more dangerous, such as the Spanish flu. How do new flu strains arise? MicroInquiry 20 examines their evolution.

The onset of influenza A is abrupt after an incubation period of one to four days. The individual with an uncomplicated illness develops sudden chills, fatigue, headache, and pain most pronounced in the chest, back, and legs. Over a 24-hour period, body temperature can rise to 40°C, and a severe cough develops. Individuals may experience sore throat, nasal congestion, sneezing, and tight chest, the latter a probable reflection of viral invasion of tissues of the trachea and bronchi. Despite these severe symptoms, influenza is normally short-lived and has a favorable prognosis. The disease is self-limiting and usually resolves in seven to ten days.

Most of the annual deaths from influenza A are due to pneumonia caused by the virus spreading into the lungs. Secondary complications in unvaccinated individuals, especially those over 65 years, infants, or with underlying medical conditions (immunocompromised), may lead to bacterial pneumonia if Staphylococcus aureus or Haemophilus influenzae invade the damaged respiratory tissue. MicroFocus 20.6 describes the role of preschoolers in driving flu outbreaks that can lead to pneumonia deaths in the community.

Influenza infection in rare cases is associated with two serious complications. Guillain-Barré syndrome (GBS) occurs when the body mistargets the infection and instead damages its own peripheral nerve cells, causing muscle weakness and sometimes paralysis. Reye syndrome usually makes its appearance in young people after they are given aspirin to treat fever or pain associated with influenza. It begins with nausea and vomiting, but the progressive mental changes (such as confusion or delirium) may occur. Very few children develop Reye syndrome (less than 0.03–1 case per 100,000 persons younger than 18 years).

Because influenza-like symptoms can be caused by bacterial and other viral infections, a diagnosis of influenza, if necessary, is based on several factors. This includes the pattern of spread in the community, observation of disease symptoms, laboratory isolation of viruses, or hemagglutination of red blood cells (see Chapter 12).

The best prevention for the flu is an annual flu vaccination. Each year's batch of vaccine (see MicroFocus 16.1) is based on the previous year's predominant influenza A and B viruses and is about 75 percent effective. Because the viruses are grown in chicken embryos (see Chapter 12), people who are allergic to chickens or eggs should not be given the vaccine.

Treatment of uncomplicated cases of influenza requires bed rest, adequate fluid intake, and aspirin (or acetaminophen in children) for fever and muscle pain. Two antiviral
INQUIRY

Influenza viruses evolve in two different ways. Both involve antigenic variation, a process in which chemical and structural changes occur periodically in hemagglutinin (H) and neuraminidase (N) spike proteins (antigens), thereby yielding new virus strains.

Antigenic drift involves small changes to the virus. These changes involve minor point mutations resulting from RNA replication errors. The mutations will be expressed in the new virions produced. Although such mutations may be detrimental, on occasion one might confer an advantage to the virus, such as being resistant to a host’s immune system. For example, a spike protein might have a subtle change in shape (that is, the structural shape has “drifted”) so they are not recognized by the host’s immune system. This is what happens prior to most flu seasons. The virus spikes are different enough from the previous season that the host’s antibodies fail to recognize the new strain. Both influenza A and B viruses can undergo antigenic drift.

Antigenic shift is an abrupt, major change in structure to influenza A viruses. Antigenic shift may give rise to new strains with completely new hemagglutinin and neuraminidase spike proteins (that is, the spike structure has “shifted”) to which everyone is totally defenseless, and from which a pandemic may ensue (see figure, next page).

Two mechanisms account for antigenic shift:

The “Spanish” flu was the introduction of a completely new flu strain (H1N1) into the human population from birds. The H1N1 strain jumped directly to humans and adapted quickly to replicate efficiently in humans (Panel A).

The second mechanism involves “gene swapping” or reassortment between different flu viruses (Panel B). The 1957 influenza virus (“Asian” influenza; H2N2), for example, was a reassortment, where the human H1N1 virus acquired new spike genetic segments (H2 and N2) from an avian species. The 1968 influenza virus (“Hong Kong” influenza; H3N2) was the result of another reassortment; the human H2N2 strain acquired a new hemagglutinin genetic segment (H3) from another avian species (Panel C).

Pigs usually are the reassortment “vessels” (or intermediate host) because they can be infected by both avian and human flu viruses.

Future pandemic strains could arise through either antigenic drift or shift (Panel D). The 2005 H5N1 avian flu strain could mutate further or recombine with H3N2 to produce a potentially deadly new strain in humans.

Discussion Point

The current avian (or bird) flu (H5N1 strain) is lethal to domestic fowl and can be transmitted to humans. As mentioned in the chapter introduction, as of late October 2006, at least 151 of the 256 people infected have died (see map).

If a human pandemic should occur, health care providers would play a crucial role in minimizing the pandemic. Therefore, planning for pandemic influenza is crucial.

Discuss the specific steps that should be taken by individuals, colleges and universities, and communities in planning for a pandemic outbreak.

Once you have come up with a plan, check out what the CDC suggests (http://www.pandemicflu.gov/) and what your state is doing.
20.5 Viral Infections of the Lower Respiratory Tract

Viral Infections of the Lower Respiratory Tract

The Major Influenza Pandemics. These three pandemics were the result of antigenic shifts.

(A) H1N1 influenza virus
- Bird-to-human transmission of H1N1 virus
- All 8 genetic segments thought to have originated from avian influenza virus

(B) H2N2 influenza virus
- Reassortment human H2N2
- Three new genetic segments from avian influenza virus introduced, including H and N; containing 5 RNA segments from 1918

(C) H3N2 influenza virus
- Reassortment human H3N2
- Two new genetic segments from avian influenza virus introduced, including H; containing 5 RNA segments from 1918

(D) Next pandemic virus?
- All eight genes new or further derivative of 1918 virus

Relative number of influenza cases (not to scale)

First virus isolation from humans

“Spanish” influenza

“Asian” influenza

“Hong Kong” influenza

Reappearance of H1N1


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Preschoolers Drive Flu Outbreaks

Every October to November in the Northern Hemisphere, we brace for another outbreak or epidemic spread of the flu. Many people go to their physician, clinic, or even grocery store for a flu shot. Others of us will “catch” the flu and suffer through several days of agony. For some 35,000, especially the elderly and immunocompromised, contracting the flu will lead to pneumonia and death. Wouldn’t it be great if there was some way to predict pneumonia and flu deaths in a population? That now may be possible.

Researchers at the Children’s Hospital of Boston and Harvard Medical School reported biosurveillance data suggesting that otherwise healthy preschoolers (3- to 4-year-olds) drive flu epidemics. The researchers found that by late September, kids in this age group were the first to develop flu symptoms.

Why is this group most vulnerable? Current immunization policies suggest that infants 6 to 23 months old be vaccinated against the flu. Policy also suggests that older children, including those preschoolers, only be vaccinated if they have high medical-risk conditions. That means they will be vulnerable to the flu. And with many being in daycare and preschool, close contact makes spreading the flu effortless as those exposed bring the infection home.

The data also demonstrate that when preschoolers start sneezing, the unvaccinated elderly become ill. Thus, the research suggests vaccinating those individuals who are driving and transmitting flu to others—the preschoolers. They are the sentinels by which an ensuing flu outbreak or epidemic can be identified. Immunizing preschoolers will decrease flu transmission and limit adult mortality in the unvaccinated.

Paramyxovirus Infections Affect the Lower Respiratory Tract

A number of viruses, primarily in the Paramyxoviridae, are associated with the LRT. The respiratory syncytial virus (RSV) is the most common lower respiratory tract disease affecting children. The measles virus, which affects the skin, was discussed in Chapter 19 and the mumps virus will be discussed in Chapter 21.

Respiratory syncytial (RS) disease is caused by the respiratory syncytial virus (RSV). Since 1985, RS disease has been the most common lower respiratory tract disease affecting
Bronchioles:
The narrow tubes inside of the lungs that branch off of the main air passages (bronchi).

20.5 Viral Infections of the Lower Respiratory Tract

Infants and young children. RSV is transmitted by respiratory droplets or virus-contaminated hands.

Infection takes place in the bronchioles and air sacs of the lungs, and the disease is often described as viral pneumonia. When the virus infects tissue cells, the latter tend to fuse together, forming giant multinucleate cells called syncytia (see Chapter 12).

RS disease can occur in adults as an influenza-like syndrome and as severe bronchitis with pneumonia in the elderly. Outbreaks occur yearly throughout the United States, but most cases are misdiagnosed or unreported. Some virologists believe that up to 95 percent of all children have been exposed to the disease by the age of five, and CDC epidemiologists estimate there are 51,000 to 82,000 hospitalizations and 4,500 deaths in infants and children each year in the United States as a result of RS disease.

Maternal antibodies passed from mother to child probably provide protection during the first few months of life, but the risk of infection increases as these antibodies disappear. Indeed, researchers have successfully used preparations of antibodies to lessen the severity of established cases of RS disease. Aerosolized ribavirin also has been used with success.

Parainfluenza (para = “near”) infections are caused primarily by human parainfluenza viruses 1 and 3 (FIGURE 20.24). They account for 40 percent of acute respiratory infections in children. Although as widespread as influenza, parainfluenza is a much milder disease and is transmitted by direct contact or aerosolized droplets. It is characterized by minor upper respiratory illness, often referred to as a cold. Bronchiolitis and croup may

FIGURE 20.23 The Relationships between the Human Paramyxoviruses. This concept map illustrates the relationships between the paramyxoviruses that cause human respiratory and skin diseases. Note the relationship between measles and mumps (skin diseases). Which virus is most closely related to the respiratory syncytial virus?

FIGURE 20.24 The Parainfluenza Virus. False-color transmission electron micrograph of a parainfluenza virus. The envelope of individual virions often gives the virus a pleomorphic shape, although they do have a helical capsid. (Bar = 50 nm.) Why is the virus referred to as parainfluenza?
accompany the disease, which is most often seen in children under the age of six. The disease predominates in the late fall and early spring, and is seasonal, as Figure 20.10 indicated. No specific therapy exists. RSV-like illnesses may be caused by the human metapneumovirus (hMPV). Just about every child in the world has been infected by the virus by age 5. Human MPV is responsible for 12 percent of LRT infections and 15 percent of common colds in children. It appears to be milder than RS disease and, like RS disease, can be treated with ribavirin.

**CONCEPT AND REASONING CHECKS**

20.16 Identify the common relationships between the paramyxoviruses. Other Viruses Also Produce Pneumonia

**KEY CONCEPT**

- The SARS coronavirus and Hantaviruses cause unique forms of pneumonia.

Several other viruses can cause LRT infections in adults. These include the SARS coronavirus and the Hantaviruses. **SARS Coronavirus.** Severe acute respiratory syndrome (SARS), an emerging infectious disease of the LRT, was first reported in China in spring 2003, and quickly spread through Southeast Asia and to Canada. It is an example of how fast an emerging disease can spread (Textbook Case 20).

Scientists at the CDC and other laboratories identified in SARS patients a previously unrecognized coronavirus, which they named the SARS coronavirus (SARS-CoV). Being a member of the *Coronaviridae*, it is a single-stranded (+ strand) RNA virus with helical symmetry and a spiked envelope (Figure 20.25). The mortality rate from SARS appears to be about 10 percent. During the 2002 to 2003 epidemic, the WHO identified 8,098 cases from 29 countries. There were 774 deaths, the majority being in China, Taiwan, Vietnam, Singapore, and Canada.

SARS-CoV can be spread through close person-to-person contact by touching one’s eyes, nose, or mouth after contact with the skin of someone with SARS. Spreading also comes from contact with objects contaminated through coughing or sneezing with infectious droplets by a SARS-infected individual. Whether SARS can spread through the air or in other ways remains to be discovered. Bats are the natural host of SARS-CoV.

Many people remain asymptomatic after contacting SARS-CoV. However, in affected individuals, moderate URT illness may occur and include fever (greater than 38°C), headache, an overall feeling of discomfort, and body aches. After two to seven days, SARS patients may develop a dry cough and have trouble breathing. In those patients progressing to a severe respiratory illness, pneumonia develops with insufficient oxygen reaching the blood. In 10 to 20 percent of cases, patients require mechanical ventilation.

Most of the cases of SARS in the United States in 2003 occurred among travelers returning from other parts of the world where SARS was present. Transmission of SARS to health care workers appears to have occurred after close contact with sick people before recommended infection control precautions were put into place.

Because this is a newly emerging disease, treatment options remain unclear. **Hantaviruses.** In the autumn of 1992, the El Niño oscillation of the ocean-atmosphere system caused heavy precipitation in the Four Corners region of the United States (New Mexico, Arizona, Colorado, and Utah), resulting in
the increased growth of berries, seeds, and nuts in the spring of 1993. The increased food supply brought an explosion in the rodent population in this area. Then, a cluster of sudden and unexplained deaths in previously healthy young adults occurred in rural New Mexico and the Four Corners region. The CDC identified a Hantavirus, now called Sin Nombre virus, as the infectious agent and termed the pulmonary disease Hantavirus pulmonary syndrome (HPS). Between 1993 and 2008, there have been some 500 cases of HPS and about 35 percent of reported cases have resulted in death.

The Hantaviruses are members of the Bunyaviridae. Their name is derived from the Hantaan River in South Korea where the virus was first isolated in 1978. These are enveloped, single-stranded, (− strand) RNA
viruses with helical symmetry. The genome consists of three segments.

The deer mouse is the host for the Sin Nombre virus, and it sheds the virus in saliva, urine, and feces. Humans usually are infected by breathing the infectious aerosolized dried urine or feces.

In one to five weeks after exposure, early symptoms of infection include fatigue, fever, and muscle aches. About half of all HPS patients experience headaches, dizziness, difficulty breathing, and low blood pressure that can lead to respiratory failure as the lungs fill with fluid.

Prevention consists of eliminating rodent nests and minimizing contact with them. There is no vaccine for hantavirus infection.

HPS has now become an established disease in the lexicon of medicine not only in the United States but throughout much of the Americas. summarizes the bacterial and viral diseases affecting the LRT.

### Concept and Reasoning Checks

20.17 How do the SARS coronavirus and the Hantavirus differ in their spread between individuals?

### Table 20.2

**A Summary of the Major Bacterial and Viral LRT Diseases**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Causative Agent</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Treatment</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial Pertussis</td>
<td><em>Bordetella pertussis</em></td>
<td>Malaise, low-grade fever, severe cough</td>
<td>Respiratory droplets</td>
<td>Erythromycin</td>
<td>Vaccinating with DTaP, Tdap</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td><em>Mycobacterium tuberculosis</em></td>
<td>Active TB: Cough, weight loss, fatigue, fever, night sweats, chills, breathing pain</td>
<td>Respiratory droplets</td>
<td>Antibiotics</td>
<td>Preventing exposure to active TB patients, BCG vaccine</td>
</tr>
<tr>
<td>Infectious bronchitis</td>
<td><em>Mycoplasma pneumoniae</em></td>
<td>Runny nose, sore throat, chills, general malaise, slight fever, and dry cough</td>
<td>Respiratory droplets</td>
<td>Antibiotics</td>
<td>Annual flu vaccination, Good hygiene</td>
</tr>
<tr>
<td>Pneumococcal pneumonia</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>High fever, sharp chest pains, difficulty breathing, rust-colored sputum</td>
<td>Respiratory droplets</td>
<td>Penicillin</td>
<td>Vaccinating, Hand hygiene</td>
</tr>
<tr>
<td>Disease</td>
<td>Causative Agent</td>
<td>Signs and Symptoms</td>
<td>Transmission</td>
<td>Treatment</td>
<td>Prevention</td>
</tr>
<tr>
<td>----------------------------------</td>
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<td>-------------------------------------------------</td>
</tr>
<tr>
<td>Other “typical” pneumonias</td>
<td><em>Haemophilus influenzae</em> <em>Staphylococcus aureus</em> <em>Klebsiella pneumoniae</em></td>
<td>Chills, high fever, sweating, shortness of breath, chest pain, cough with thick, greenish or yellow sputum</td>
<td>Respiratory droplets</td>
<td>Antibiotics</td>
<td>Practicing good hand hygiene</td>
</tr>
<tr>
<td>“Atypical” pneumonia</td>
<td><em>Mycoplasma pneumoniae</em> <em>Legionella pneumophila</em></td>
<td>Headache, fever, fatigue, dry hacking cough</td>
<td>Respiratory droplets</td>
<td>Antibiotics</td>
<td>Extreme cleaning and disinfecting of water systems, pools, and spas</td>
</tr>
<tr>
<td>Q fever</td>
<td><em>Coxiella burnetii</em></td>
<td>Headache, fever, dry cough</td>
<td>Dust particles</td>
<td>Doxycycline</td>
<td>Vaccine for high risk occupations</td>
</tr>
<tr>
<td>Psittacosis</td>
<td><em>Chlamydia psittaci</em></td>
<td>Headache, fever, dry cough</td>
<td>Contact with infected psittacine birds</td>
<td>Doxycycline</td>
<td>Keeping susceptible birds away from the infecting agent</td>
</tr>
<tr>
<td>Chlamydial pneumonia</td>
<td><em>Chlamydia pneumoniae</em></td>
<td>Headache, fever, dry cough</td>
<td>Respiratory droplets</td>
<td>Doxycycline</td>
<td>Practicing good hygiene</td>
</tr>
<tr>
<td>Inhalational anthrax</td>
<td><em>Bacillus anthracis</em></td>
<td>Fever, chills, cough, chest pain, headache, and malaise</td>
<td>Airborne endospores</td>
<td>Penicillin</td>
<td>Avoiding contact with infected livestock and animal products</td>
</tr>
<tr>
<td>Viral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td><em>Influenza A, B, and C viruses</em></td>
<td>Chills, fatigue, headache Chest, back, and leg pain</td>
<td>Respiratory droplets</td>
<td>Bed rest and fluids</td>
<td>Getting annual flu vaccination</td>
</tr>
<tr>
<td>Respiratory syncytial (RS) disease</td>
<td><em>Respiratory syncytial virus (RSV)</em></td>
<td>Influenza-like</td>
<td>Respiratory droplets</td>
<td>Fever-reducing</td>
<td>Practicing good hygiene</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td><em>Human parainfluenza viruses 1 and 3</em></td>
<td>Cold-like</td>
<td>Respiratory droplets</td>
<td>Hand contact</td>
<td></td>
</tr>
<tr>
<td>RSV-like illness</td>
<td><em>Human metapneumovirus</em></td>
<td>Cold-like</td>
<td>Respiratory droplets</td>
<td>No specific therapy</td>
<td>Practicing good hygiene</td>
</tr>
<tr>
<td>SARS</td>
<td><em>SARS coronavirus</em></td>
<td>Fever, headache, body aches, dry cough, and breathing difficulty</td>
<td>Respiratory droplets and airborne particles</td>
<td>Ribavirin for severe cases</td>
<td>Practicing good hygiene</td>
</tr>
<tr>
<td>Hantavirus pulmonary syndrome</td>
<td><em>Hantavirus (Sin Nombre virus)</em></td>
<td>Fatigue, fever, muscle aches, headache, dizziness, breathing difficulty</td>
<td>Aerosolized droplets of rodent saliva, urine, feces</td>
<td>Supportive care</td>
<td>Eliminating rodent nests Minimizing contact</td>
</tr>
</tbody>
</table>
Several fungi can affect the respiratory system, often with a primary infection in the lungs that can spread to other body areas. These systemic or opportunistic mycotic infections often cause life-threatening disease in individuals with a weakened immune system.

**Systemic Mycoses Can Affect Healthy and Immunocompromised Individuals**

**KEY CONCEPT**

- Histoplasmosis, blastomycosis, and coccidioidomycosis affect otherwise healthy individuals.

**Histoplasmosis**

Histoplasmosis is a worldwide lung disease. In 2008, three American mission groups consisting of 33 individuals traveled to El Salvador to renovate a church. Within two weeks, 20 travelers developed fever, headache, cough, and severe chest pains. Seven of the 20 tested positive for *Histoplasma capsulatum*, and all 20 were treated for histoplasmosis.

In the United States, histoplasmosis is most prevalent in the Ohio and the Mississippi River valleys where it is often called summer flu. The causative agent is *H. capsulatum*. Infection usually occurs from the inhalation of spores (conidia) present in dry, dusty soil or found in the air of chicken coops and bat caves. Sweeping and cleaning the church, and working within a bird or bat roost area were associated with increased risk in the El Salvador cases. Being a dimorphic fungus, it grows as a yeast form at 37°C. Most otherwise healthy people experience mild influenza-like illness and recover without treatment. However, in immunocompromised people histoplasmosis causes a systemic infection, forming tuberculosis-like lesions in the lungs and other internal organs, making AIDS patients especially vulnerable. Amphotericin B or ketoconazole may be used in treatment.

**Blastomycosis**

Blastomycosis occurs principally in Canada, the Great Lakes region, and areas of the United States from the Mississippi River to the Carolinas. The pathogen is *Blastomyces dermatitidis* (sexual stage *Ajellomyces dermatitidis*). The fungus is dimorphic and produces conidia that are inhaled. Within the lungs, the conidia germinate as the yeast form.

Acute blastomycosis is associated with dusty soil and bird droppings, particularly in moist soils near barns and sheds. Inhalation leads to lung lesions with persistent cough and chest pains.

Although blastomycosis is rare, it can affect immunocompromised patients, such as those with AIDS. Chronic pneumonia is the most common manifestation. The systemic form of blastomycosis may involve many internal organs (bones, liver, spleen, or nervous system) and may prove fatal. Amphotericin B is used in therapy.

Travelers to the San Joaquin Valley of California and dry regions of the southwestern United States may contract a fungal disease known as *coccidioidomycosis*, known more commonly as valley or desert fever. It is caused by *Coccidioides immitis*, or *C. posadasii*. The ascomycete fungus produces highly infectious arthrospores by a unique process of endospore and spherule formation (Figure 20.28). Coccidioidomycosis is usually transmitted by dust particles laden with fungal spores. Cattle, sheep, and other animals deposit the spores in soil, and they become airborne with gusts of wind.

When inhaled into the human lungs, *C. immitis* induces an influenza-like disease, with a dry, hacking cough, chest pains, and high fever. During most of the 1980s, about 450 annual cases of coccidioidomycosis were
20.6 Fungal Diseases Affecting the Lower Respiratory Tract

Conidia or arthrospores
Spherules
Infective phase (37°C)
Saprobic phase (25°C)
Infective phase (37°C)
Yeast forms
H. capsulatum
B. dermititidis
C. immitis

Systemic Fungal Respiratory Diseases. Inhaled spores germinate and grow as a yeast form (H. capsulatum and B. dermititidis) or as spherules (C. immitis). Why are these diseases considered to be systemic mycoses?

FIGURE 20.28

reported to the CDC. In 1991, that number jumped to over 1,200 cases, and in 2006, the number of reports exceeded 8,900, the majority occurring in California and Arizona.

Although most cases are self-limiting, a small number of cases (1 out of 1,000) become disseminated and involve myriad internal organs and structures, including the meninges of the spinal cord. Recovery brings lifelong immunity. Amphotericin B is prescribed for severe cases, and another drug, nikkomycin, and a vaccine are in the early stages of development.

CONCEPT AND REASONING CHECKS

20.18 Why are histoplasmosis, blastomycosis, and coccidioidomycosis considered systemic mycotic infections?

Opportunistic Mycoses Affect Immunocompromised Individuals

KEY CONCEPT

- Cryptococcosis, Pneumocystis pneumonia, and aspergillosis are escalating fungal diseases.

Cryptococcosis is among the most dangerous fungal diseases in humans. As an opportunistic mycosis, it affects the lungs and the meninges, and is estimated to account for over 25 percent of all deaths from fungal disease.

Cryptococcosis is caused by an oval-shaped yeast known as Cryptococcus neoformans (sexual stage Filobasidiella neoformans) and is a member of the Basidiomycota. The organism is found in the soil of urban environments and grows actively in the droppings of pigeons, but not within the pigeon tissues. Cryptococci may become airborne with gusts of wind, and the organisms subsequently enter the respiratory passageways of humans.

C. neoformans cells, having a diameter of about 5 to 6 μm, are embedded in a thick, gelatinous capsule that provides resistance to phagocytosis. Cryptococcosis usually produces a mild lung infection, but symptoms of infection are generally rare. However, in immunocompromised patients (especially HIV-infected) the cryptococci pass into the bloodstream and localize in the meninges and brain. The patient experiences piercing headaches, stiffness in the neck, and paralysis. Diagnosis is aided by the observation of encapsulated

FIGURE 20.29

Cryptococcus neoformans.

(A) A light microscope photomicrograph of C. neoformans cells. The capsules (white halos) are prominent. (Bar = 20 μm.)

(B) A stained photomicrograph of C. neoformans cells (red) from lung tissue of an AIDS patient. The capsule surrounding the cells provides resistance to phagocytosis and enhances the pathogenic tendency of the fungus. (Bar = 20 μm.) Why would C. neoformans be a serious health threat to AIDS patients?

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yeasts in respiratory secretions or cerebrospinal fluid (CSF) obtained by a spinal tap.

Untreated cryptococcal meningitis may be fatal. However, intravenous treatment with the antifungal drug amphotericin B is usually successful, even in severe cases.

Resistance to cryptococcal meningitis appears to depend upon the proper functioning of the branch of the immune system governed by T lymphocytes (see Chapter 15). When these cells are absent in sufficient quantities, the immune system becomes severely compromised, and cryptococci can invade the tissues as opportunists. In AIDS patients cryptococcosis can be life-threatening.

**Pneumocystis pneumonia (PCP)** currently is the most common cause of nonbacterial pneumonia in Americans with suppressed immune systems. The causative organism, *Pneumocystis jiroveci* (previously called *Pneumocystis carinii*) produces an atypical pneumonia that remained in relative obscurity until the 1980s, when it was recognized as the cause of death in over 50 percent of patients dying from the effects of AIDS.

*P. jiroveci* has a complex life cycle taking place entirely in the alveoli of the lung. A feeding stage, called the **trophozoite**, swells to become a precyst stage, in which up to eight sporozoites develop in forming a cyst. When the cyst is mature, it opens and liberates the sporozoites, which enlarge and undergo further reproduction and maturation to trophozoites.

*P. jiroveci* is transmitted person-to-person by droplets from the respiratory tract, although transmission from the environment also can occur. A wide cross section of individuals harbors the organism without symptoms, mainly because of the control imposed by the immune system.

When the immune system is suppressed, as in AIDS patients, *Pneumocystis* trophozoites and cysts fill the alveoli and occupy all the air spaces. A nonproductive cough develops, with fever and difficult breathing. Progressive deterioration leads to consolidation of the lungs and, eventually, death. The current treatment for PCP is trimethoprim-sulfamethoxazole (co-trimoxazole) and corticosteroid therapy.

**Aspergillosis** is caused by a few species of *Aspergillus*, primarily *A. fumigatus*. These opportunistic molds, which are ubiquitous in soil, air, and decaying vegetation produce spores that can affect the sinuses and ear canals. However, in the lungs, the inhalation of spores can lead to a severe and sometimes fatal disease.

The pulmonary condition begins after immunocompromised people have inhaled *Aspergillus* spores. In these individuals, a pulmonary aspergilloma—a tangled ball of fungal mycelium—forms in the lungs. At first the “fungus ball” may not produce any symptoms. However, eventually symptoms do develop and include a bloody cough, chest pain, and wheezing with a shortness of breath.

The most deadly form of aspergillosis—**invasive aspergillosis**—occurs when the fungal infection spreads beyond the lungs to the other organs, such as the skin, heart, kidneys, or brain. Signs and symptoms depend on which organs are affected, but, in general, include headache, fever with chills, bloody cough, shortness of breath, and chest or joint pain.

Treatment usually involves antifungal drugs such as voriconazole. It can be difficult to avoid *Aspergillus* spores in the environment. Staying away from obvious sources of mold, such as compost piles and damp places, can help prevent infection in susceptible individuals.

**TABLE 20.3** summarizes the fungal diseases of the LRT. The **Summary Map of Infectious Diseases** presents the bacterial, viral, and fungal diseases of the respiratory system.
### Table 20.3: A Summary of the Major Fungal LRT Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Causative Agent</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Treatment</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histoplasmosis</td>
<td><em>Histoplasma capsulatum</em></td>
<td>Mild influenza-like illness, Can disseminate to other organs</td>
<td>Airborne spores</td>
<td>Amphotericin B or ketoconazole for systemic disease</td>
<td>Wearing face mask in contaminated areas</td>
</tr>
<tr>
<td>Blastomycosis</td>
<td><em>Blastomyces dermatitidis</em></td>
<td>Persistent cough, Chest pains, Chronic pneumonia, Dry, hacking cough, Chest pains, High fever</td>
<td>Airborne spores</td>
<td>Amphotericin B</td>
<td>Wearing face mask in contaminated areas</td>
</tr>
<tr>
<td>Coccidioidomycosis</td>
<td><em>Coccidioides immitis</em></td>
<td>Dry, hacking cough, Chest pains, High fever</td>
<td>Airborne arthrospores</td>
<td>Amphotericin B</td>
<td>Limiting exposure where infection is highest</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td><em>Cryptococcus neoformans</em></td>
<td>Asymptomatic, Opportunistic infection leads to severe headache, stiff neck, paralysis</td>
<td>Airborne cells</td>
<td>Amphotericin B</td>
<td>Maintaining strong immune system</td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td><em>Pneumocystis jiroveci</em></td>
<td>Nonproductive cough, Fever, Breathing difficulty</td>
<td>Airborne droplets</td>
<td>Trimethoprim-sulfamethoxazole</td>
<td>Maintaining strong immune system</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td><em>Aspergillus fumigatus</em></td>
<td>Bloody cough, Chest pain, Wheezing, Shortness of breath</td>
<td>Airborne spores</td>
<td>Voriconazole</td>
<td>Staying away from sources of mold</td>
</tr>
</tbody>
</table>
The Summary Map of Infectious Disease: The Respiratory System

**Bacterial URT Diseases**
- Streptococcal pharyngitis
  - *Streptococcus pyogenes*
- Scarlet fever
  - *Streptococcus pyogenes*
- Diphtheria
  - *Corynebacterium diphtheriae*
- Epiglottitis
  - *Haemophilus influenzae*
- Sinusitis
  - Various bacterial species
- Otitis externa
  - *Streptococcus, Staphylococcus, Pseudomonas species*
- Otitis media
  - *Streptococcus pyogenes, Haemophilus influenzae*

**Viral URT Diseases**
- Common colds
  - Rhinoviruses, adenoviruses, and others
- Laryngitis
  - Rhinoviruses

**Bacterial LRT Diseases**
- Pertussis
  - *Bordetella pertussis*
- Tuberculosis
  - *Mycobacterium tuberculosis*
- Infectious bronchitis
  - *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Streptococcus pneumoniae, Haemophilus influenzae*
- "Typical" pneumonia
  - *Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Klebsiella pneumoniae*
- "Atypical" pneumonia
  - *Mycoplasma pneumoniae, Legionella pneumophila*
- Q fever
  - *Coxiella burnetii*
- Psittacosis
  - *Chlamydophila psittaci*
- Chlamydial pneumonia
- *Chlamydophila pneumoniae*
- Inhalational anthrax
  - *Bacillus anthracis*

**Viral LRT Diseases**
- Influenza
  - *Influenza A and B viruses*
- Respiratory syncytial (RS) disease
  - *Respiratory syncytial virus, Parainfluenza*
  - *Human parainfluenza viruses 1 and 3, RSV-like illness*
  - *Human metapneumovirus, SARS*
  - *Hantavirus pulmonary syndrome (HPS)*
  - *Hantavirus*

**Fungal LRT Diseases**
- Histoplasmosis
  - *Histoplasma capsulatum*
  - *Blastomycosis*
  - *Blastomyces dermatitidis*
- Coccidioidomycosis
  - *Coccidioides immitis, Coccidioides posadasii*
- Cryptococcosis
  - *Cryptococcus neoformans*
- Pneumocystis pneumonia
  - *Pneumocystis jiroveci*
- Aspergillosis
  - *Aspergillus fumigatus*
20.2 Bacterial Diseases Affecting the Upper Respiratory Tract

- Streptococcal diseases are caused by *Streptococcus pyogenes*. This includes: streptococcal pharyngitis (strep throat), scarlet fever, and a skin rash.
- Diphtheria is caused by a phage-containing strain of *Corynebacterium diphtheriae*. As dead tissue accumulates, a pseudomembrane forms in the throat or nasopharynx.
- Epiglottitis is an infection of the epiglottis by bacteria such as *Haemophilus influenzae*. Inflammation can cause the epiglottis to swell such that it blocks the flow of air through the trachea and into the lungs.
- The nose is a major portal of entry for infectious organisms and viruses. Sinusitis is inflammation of the sinuses. Acute sinusitis can be caused by a variety of indigenous microbiota of the URT and results in pain, tenderness, and swelling over the affected sinuses. Chronic sinusitis can be caused by a variety of indigenous microbiota of the URT and results in pain, tenderness, and swelling over the affected sinuses. Chronic sinusitis is an ongoing infection that produces nasal obstruction, nasal congestion, and post-nasal drip.
- Ear infections can occur in the outer ear (otitis externa). Extended swimming in fresh water pools can irritate and break down the skin in the canal, allowing bacteria such as *Streptococcus*, *Staphylococcus*, or *Pseudomonas* to penetrate. Middle ear infections (acute otorrhea) involve *Streptococcus pneumoniae* or *Haemophilus influenzae* result from an inflammation of the Eustachian tube and leads to a red, bulging eardrum. Chronic otitis media involves long-term infection, inflammation, and damage to the middle ear due to biofilm development.

20.3 Viral Infections Affecting the Upper Respiratory Tract

- Rhinitis is a swelling and inflammation in the mucous membrane of the nose. More than 100 rhinoviruses are transmitted through airborne droplets or by contaminated objects, producing typical head cold symptoms of runny nose and stuffiness. Adenoviruses also cause some types of colds.
- Ear infections can occur in the outer ear (otitis externa).
- The nose is a major portal of entry for infectious organisms.
- Epiglottitis is an infection of the epiglottis by bacteria such as *Streptococcus pyogenes*.
- Diphtheria is caused by a phage-harboring strain of *Streptococcus pyogenes*.
- Commensalistic microbiota of the URT include *Streptococcus*, *Neisseria* (in the nasopharynx), *Haemophilus*, and *Staphylococcus*.
- In the LRT, *Haemophilus* and *Staphylococcus* as well as alveolar macrophages help eliminate any pathogens that may have entered the respiratory system.
- Commensalistic microbiota of the LRT include *Streptococcus*, *Neisseria* (in the nasopharynx), *Haemophilus*, and *Staphylococcus*.
- In the LRT, *Haemophilus* and *Staphylococcus* as well as alveolar macrophages help eliminate any pathogens that may have entered the respiratory system.
20.5 Viral Infections of the Lower Respiratory Tract

- Influenza is caused by three different orthomyxoviruses: types A, B, and C. The spike proteins hemagglutinin and neuraminidase are necessary for viral entry and exit during an infection. Symptoms include sudden chills, headache, fatigue, and chest pain. Influenza A is best prevented with yearly vaccination, although new antiviral drugs can shorten the duration of symptoms. Antigenic drift and antigenic shift account for the yearly differences in flu strains and for flu pandemics.

- Paramyxoviruses cause infections of the LRT. These include respiratory syncytial (RS) disease that leads to a type of viral pneumonia in children and an upper respiratory disease in adults; parainfluenza produces milder symptoms than influenza; and a common respiratory illness in most all children that is milder than RS disease is now thought to be caused by the human metapneumovirus.

- Severe acute respiratory syndrome (SARS) represents a newly emerging viral disease caused by a coronavirus. It is spread by person-to-person contact. Symptoms include fever, headache, feeling of discomfort, and body aches. A dry cough and difficulty breathing often occur.

- Hantavirus infection in a minority of individuals causes Hantavirus pulmonary syndrome. Inhaling the viruses in dried rodent urine or feces can lead to blood hemorrhaging, and renal and respiratory failure.

20.6 Fungal Diseases Affecting the Lower Respiratory Tract

- Fungal mycoses can be responsible for systemic infections. Histoplasmosis develops from the inhalation of spores of **Histoplasma capsulatum**. The infection usually does not require treatment. However, if the disease becomes disseminated, it produces tuberculosis-like lesions that can be fatal. Blastomycosis develops from breathing dusty soil or aerosols in bird droppings containing spores of **Blastomyces dermatitidis**. In humans, the disease can disseminate and produce wart-like lesions on the face, hands, and legs. **Coccidioides immitis** and **C. posadasii** cause coccidioidomycosis, a respiratory infection that develops from breathing the fungal spores. In most infected individuals, it produces flu-like symptoms; in others, the disease becomes disseminated and severe cases can be fatal.

- Some fungi also cause opportunistic infections. **Cryptococcus neoformans** is caused by **Cryptococcus neoformans**. It often infects immunosuppressed individuals, such as AIDS patients, affecting the lungs and spinal cord. **Pneumocystis jiroveci** is an opportunistic fungus that infects the alveoli of the lungs leading to a nonproductive cough and fever. Progressive deterioration is called **Pneumocystis pneumonia** (PCP). Without treatment, infection often leads to death.

- **Aspergillus** is caused by a few species of Aspergillus, primarily **A. fumigatus**. Pulmonary aspergillosis produces a tangled ball of fungal mycelium in the lungs. The most deadly form of aspergillosis is invasive aspergillosis. Here the fungal infection spreads beyond the lungs to the other organs, such as the skin, heart, kidneys, or brain.
SELF-TEST

Answer each of the following questions by selecting the one answer that best fits the question or statement.

1. Which one of the following is not part of the lower respiratory system?
   A. Alveoli
   B. Pharynx
   C. Larynx
   D. Trachea

2. Which one of the following is a complication of streptococcus pharyngitis?
   A. Rheumatic fever
   B. Pseudomembrane blockage
   C. Strawberry tongue
   D. Chest, back, and leg pain

3. Methylene blue staining of metachromatic granules is diagnostic for which of the following bacteria?
   A. Mycobacterium tuberculosis
   B. Corynebacterium diphtheriae
   C. Chlamydia pneumoniae
   D. Bordetella pertussis

4. Which one of the following illnesses is characterized by yellow or green pus discharged from the nose?
   A. Pertussis
   B. Diphtheria
   C. Bronchitis
   D. Acute sinusitis

5. Swimmer’s ear is a common name for a ______ infection of the ______ ear.
   A. bacterial; outer
   B. viral; outer
   C. bacterial; middle
   D. viral; inner

6. There are more than _____ different rhinoviruses, which belong to the ______ family.
   A. 50; Orthomyxoviridae
   B. 100; Adenoviridae
   C. 30; Paramyxoviridae
   D. 100; Picornaviridae

7. Viral pneumonia is a condition associated with
   A. RS disease.
   B. rhinovirus infections.
   C. adenovirus infections.
   D. parainfluenza infections.

8. A catarrhal and paroxysmal stage is typical of which one of the following bacterial diseases?
   A. Tuberculosis
   B. Pneumonia
   C. Pertussis
   D. Q fever

9. Acid-fast staining is typically used to stain which bacterial genus?
   A. Haemophilus
   B. Streptococcus
   C. Klebsiella
   D. Mycobacterium

10. The Mantoux test is used to identify which condition or disease?
    A. TB exposure
    B. Q fever
    C. Pertussis
    D. Pneumococcal pneumonia

11. Which one of the following is a bacterial species commonly causing hospital-acquired pneumonia?
    A. Haemophilus influenzae
    B. Klebsiella pneumoniae
    C. Staphylococcus aureus
    D. Chlamydia pneumoniae

12. This bacillus-shaped organism exists where water collects and is inhaled as aerosolized droplets.
    A. Klebsiella pneumoniae
    B. Legionella pneumophila
    C. Mycoplasma pneumoniae
    D. Chlamydia pneumoniae

13. Humans can acquire which one of the following diseases from the droppings of infected birds?
    A. Q fever
    B. Legionellosis
    C. Tuberculosis
    D. Psittacosis

14. Which one of the following statements is not true of the influenza viruses?
    A. They have a segmented genome.
    B. The genome is double-stranded DNA.
    C. The viruses have an envelope.
    D. Spikes project from the virus surface.

15. Why should aspirin not be given to children for most viral diseases?
    A. The drug leads to viral resistance.
    B. The drug can cause an antigenic shift.
    C. The drug may cause Reye syndrome.
    D. The drug may cause a bacterial infection.

16. Which one of the following is not a member of the Paramyxoviridae? If all are, select (D).
    A. Human metapneumovirus
    B. SARS-CoV
    C. Parainfluenza virus
    D. All the above (A–C) are members.

17. This disease develops after inhaling arthrospores and is commonly called valley fever.
    A. Blastomycosis
    B. Coccidioidomycosis
    C. Cryptococcosis
    D. Histoplasmosis

18. Which one of the following fungi would most likely be found in pigeon droppings?
    A. Histoplasma
    B. Cryptococcus
    C. Coccidioides
    D. Aspergillus
QUESTIONS FOR THOUGHT AND DISCUSSION

1. A bacteriophage is responsible for the ability of the diphtheria bacillus to produce the toxin that leads to disease. Do you believe that having the virus is advantageous to the infecting bacillus? Why or why not?

2. A children’s hospital in Salt Lake City reported a dramatic increase in the number of rheumatic fever cases. Doctors were alerted to start monitoring sore throats more carefully. Why do you suppose this prevention method was recommended?

3. A Boeing 737 bound for Kodiak, Alaska, developed engine trouble and was forced to land. While the airline rounded up another aircraft, the passengers sat for 4 hours in the unventilated cabin. A passenger, it seemed, was in the early stages of influenza and was coughing heavily. By the week's end, 38 of the 54 passengers on the plane had developed influenza. What lessons about infectious disease does this incident teach?

4. In a suburban community, a group of residents obtained a court order preventing another resident from feeding the flocks of pigeons that regularly visited the area. Microbiologically, was this action justified? Explain.

5. Residents of a New York community, unhappy about the smell from a nearby composting facility and concerned about the health hazard posed by such a facility, had the air at a local school tested for the presence of fungal spores. Investigators from the testing laboratory found abnormally high levels of *Aspergillus* spores on many inside building surfaces. Is there any connection between the high spore count and the composting facility? Is there any health hazard involved?

6. On January 17, 1994, a serious earthquake struck the Northridge section of Los Angeles County in California. From that date through March 15, 170 cases of coccidioidomycosis were identified in adjacent Ventura County. This number was almost four times the previous year’s number of cases. What is the connection between the two events?

APPLICATIONS

1. One of the major world health stories of 1995 was the outbreak of diphtheria in the New Independent and Baltic States of the former Soviet Union. If you were in charge of this international public health emergency, what would be your plan to help quell the spread of *Corynebacterium diphtheriae*?

2. The CDC reports that an estimated 40,000 people in the United States die annually from pneumococcal pneumonia. Despite this high statistic, only 30 percent of older adults who could benefit from the pneumococcal vaccine are vaccinated (compared to over 50 percent who receive an influenza vaccine yearly). As an epidemiologist in charge of bringing the pneumonia vaccine to a greater percentage of older Americans, what would you do to convince older adults to be vaccinated?

3. In a Kentucky community, a crew of five workers demolished an abandoned building. Three weeks later, all five required treatment for acute respiratory illness, and three were hospitalized. Cells obtained from the patients by lung biopsy revealed oval bodies and epidemiologists found an accumulation of bat droppings at the demolition site. As the head epidemiologist, what disease did the workers contract?

4. On January 17, 1994, a serious earthquake struck the Northridge section of Los Angeles County in California. From that date through March 15, 170 cases of coccidioidomycosis were identified in adjacent Ventura County. This number was almost four times the previous year’s number of cases. What is the connection between the two events?

5. Scarlet fever is caused by a species of (*Streptococcus, Streptococcus*) that often produces a (strawberry tongue, pseudomembrane) in children.

6. Middle ear infections called (otitis media, otitis externa) are common in children and often are caused by a species of (*Bartolonia, Streptococcus*) following a cold that inflamed the (eustachian tube, larynx).

7. A person with active secondary TB disease would have a positive (sputum, urine) test, while someone with a latent infection might have only a positive (sputum, tuberculin) test. The dissemination of TB bacilli throughout the body is called (latent, miliary) TB.

8. A systemic mycosis is (aspergillosis, blastomycosis) grows in the lungs as a (yeast, filamentous) form and is transmitted by diseased or contaminated (cattle, bird droppings).

REVIEW

On completing your study of viral diseases of the respiratory tract, test your comprehension of the chapter contents by circling the choices that best complete each of the following statements. The answers to even-numbered statements are listed in Appendix C.

1. Rhinoviruses are a collection of (RNA, DNA) viruses having (helical, icosahedral) symmetry and the ability to infect the (air sacs, nose) causing (mild, serious) respiratory symptoms.

2. Respiratory syncytial disease is caused by a (DNA, RNA) virus infecting the (lungs, intestines) of (adults, children) and inducing cells to (fuse together, cluster) and form giant cells called (syncytia, tumors).

3. SARS is caused by a (coronavirus, orthomyxovirus), a/an (naked, enveloped) virus spread by (sexual, person-to-person) contact.

4. Adenoviruses include a collection of (DNA, RNA) viruses and are responsible for (pneumonia, common colds) as well as infections of the (eye, ear).

5. Scarlet fever is caused by a species of (*Staphylococcus, Streptococcus*) that often produces a (strawberry tongue, pseudomembrane) in children.

6. Middle ear infections called (otitis media, otitis externa) are common in children and often are caused by a species of (*Bartolonia, Streptococcus*) following a cold that inflamed the (eustachian tube, larynx).

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