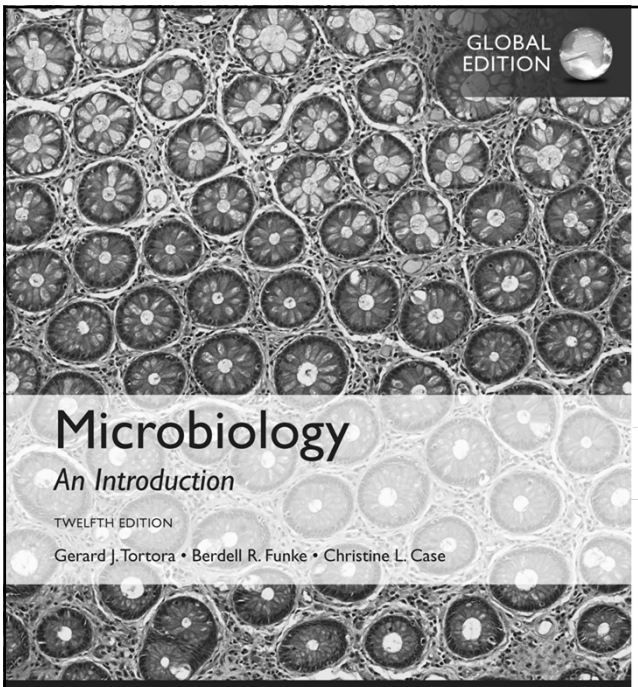
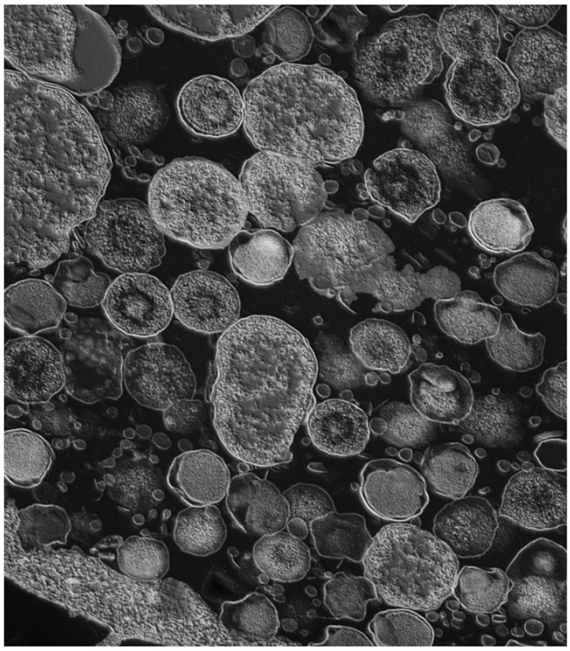



PowerPoint® Lecture Presentations prepared by Bradley W. Christian, McLennan Community College

CHAPTER **24**

# Microbial Diseases of the Respiratory System





# Structure and Function of the Respiratory System

- **Upper respiratory system**
  - Nose, pharynx, middle ear, and eustachian tubes
  - Saliva and tears protect mucosal surfaces
- **Lower respiratory system**
  - Larynx, trachea, bronchial tubes, and alveoli
  - Ciliary escalator moves particles toward the throat via ciliary action
  - Alveolar macrophages destroy microorganisms in the lungs
  - Respiratory mucus protects mucosal surfaces



**Figure 24.1 Structures of the upper respiratory system.**

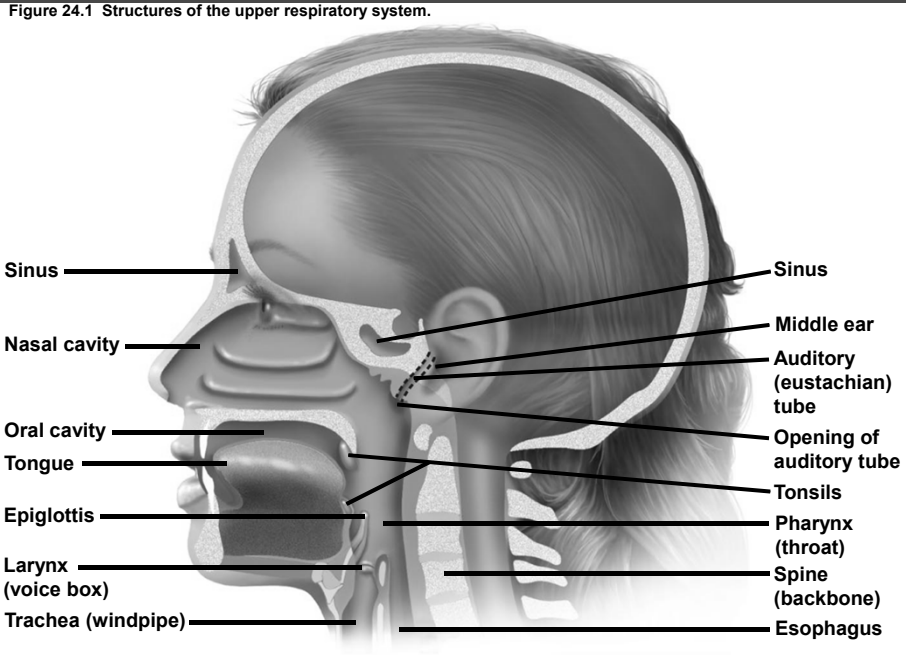
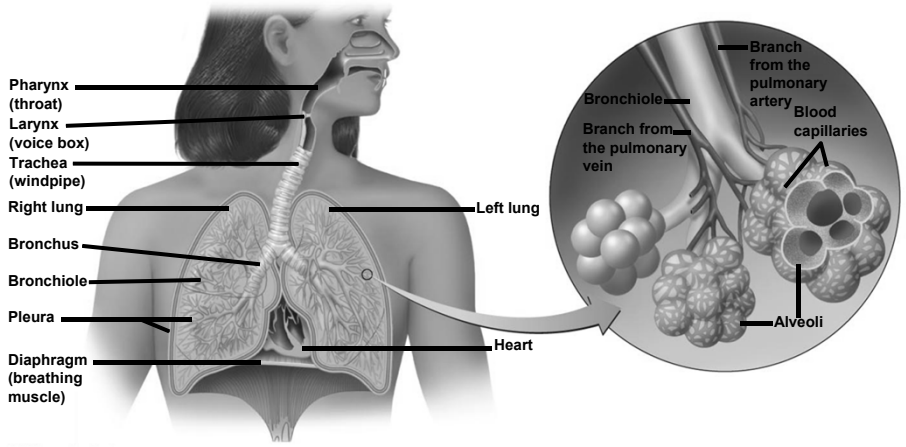


Figure 24.2 Structures of the lower respiratory system.






# Normal Microbiota of the Respiratory System

- Normal microbiota suppress pathogens by competing for nutrients and producing inhibitory substances
- Lower respiratory system is nearly sterile

## Microbial Diseases of the Upper Respiratory System

- **Pharyngitis**
  - Sore throat
- **Laryngitis**
- **Tonsillitis**
- **Sinusitis**
  - Usually self-limiting
- **Epiglottitis**
  - Most life-threatening disease of the upper respiratory system



## Bacterial Diseases of the Upper Respiratory System

- **Streptococcal pharyngitis (strep throat)**
  - Caused by group A streptococci (GAS)
    - *Streptococcus pyogenes*
      - Resistant to phagocytosis
      - Streptokinases lyse clots
      - Streptolysins are cytotoxic
  - Local inflammation, fever, tonsillitis, enlarged lymph nodes
  - Diagnosis by **enzyme immunoassay (EIA)** tests
- **Scarlet fever**
  - Erythrogenic toxin produced by lysogenized *S. pyogenes*

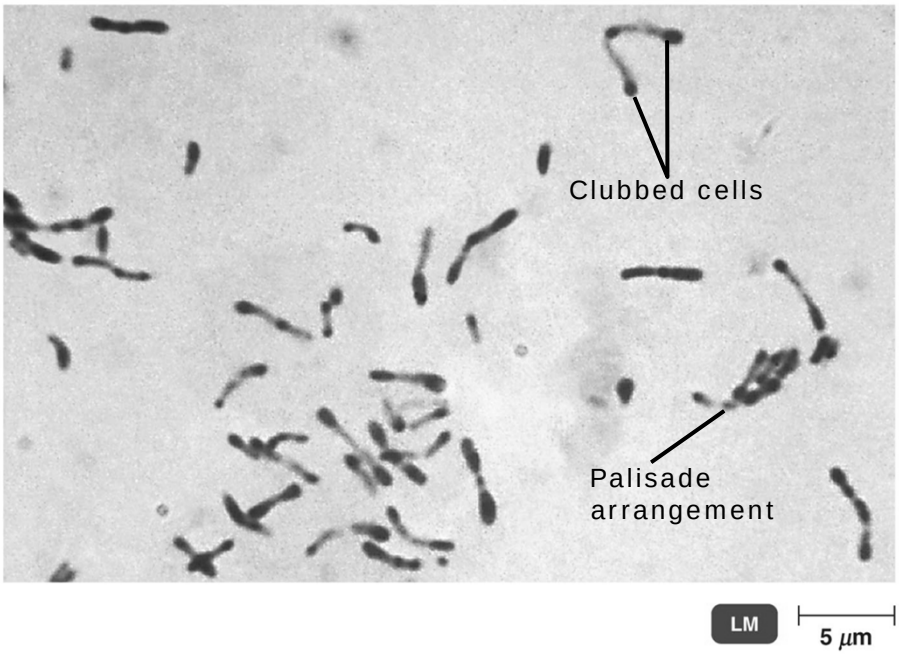
**Figure 24.3 Streptococcal pharyngitis.**



## Diphtheria

- Caused by *Corynebacterium diphtheriae*
  - Gram-positive rod; pleomorphic
- Forms a tough grayish membrane in the throat
  - Fibrin and dead tissue
  - Blocks passage of air to the lungs
- Exotoxin produced by lysogenized bacteria
  - Circulates in the blood; damages the heart and kidneys
- **Cutaneous diphtheria**
  - Forms skin ulcer
- Prevented by **DTaP vaccine**
  - Diphtheria toxoid

**Figure 24.4** ***Corynebacterium diphtheriae*****, the cause of diphtheria.**

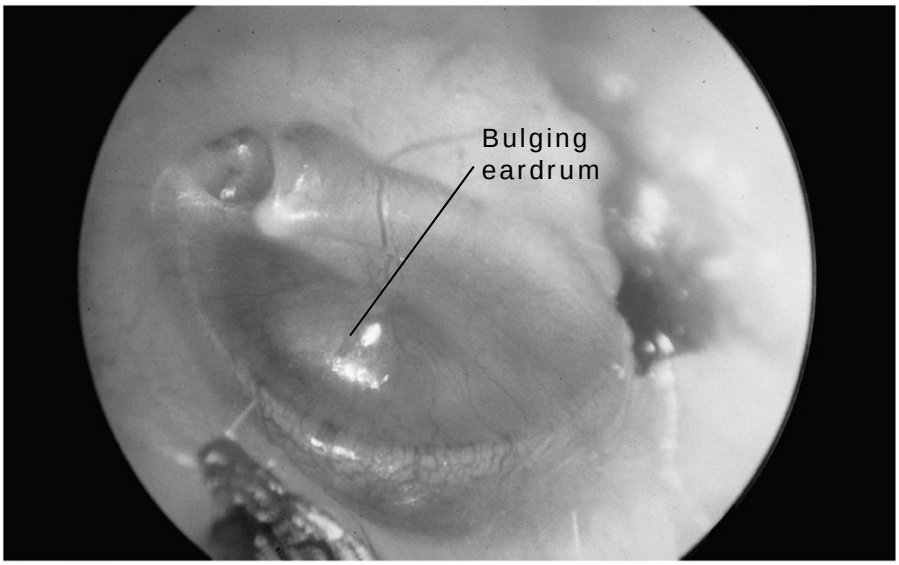





## Otitis Media

- Infection of the middle ear
  - Formation of pus puts pressure on the eardrum
- Causes
  - *Streptococcus pneumoniae* (35%)
  - Nonencapsulated *Haemophilus influenzae* (20–30%)
  - *Moraxella catarrhalis* (10–15%)
  - *S. pyogenes* (8–10%)
  - *Staphylococcus aureus* (1–2%)
- Common in childhood due to smaller auditory tube
- Treated with broad-spectrum penicillins

**Figure 24.5 Acute otitis media, with bulging eardrum.**






## The Common Cold

- Over 200 different viruses
  - Rhinoviruses (30–50%)
    - Thrive in temperatures lower than body temperature
  - Coronaviruses (10–15%)
- Sneezing, nasal secretion, congestion
  - Can lead to laryngitis and otitis media
  - Not accompanied by fever
- Antibiotics are of no use
  - Relief via cough suppressants and antihistamines

## Diseases in Focus: Microbial Diseases of the Upper Respiratory System

- A patient presents with fever and a red, sore throat. Later, a grayish membrane appears in the throat. Gram-positive rods are cultured from the membrane.
- Can you identify infections that could cause these symptoms?



**Diseases in Focus 24.1 (1 of 2)**

**Diseases in Focus 24.1 (2 of 2)**

| Disease | Pathogen | Symptoms | Treatment |
|---|---|---|---|
| BACTERIAL DISEASES | | | |
| **Epiglottitis** | *Haemophilus influenzae* | Inflammation of the epiglottis | Antibiotics; maintain airway<br>Prevention: Hib vaccine |
| **Streptococcal Pharyngitis** (strep throat) | Streptococci, especially *Streptococcus pyogenes* | Inflamed mucous membranes of the throat | Penicillin |
| **Scarlet Fever** | Erythrogenic toxin-producing strains of *Streptococcus pyogenes* | Streptococcal exotoxin causes reddening of skin and tongue and peeling of affected skin | Penicillin |
| **Diphtheria** | *Corynebacterium diphtheriae* | Grayish membrane forms in throat; cutaneous form also occurs | Penicillin and antitoxin<br>Prevention: DTaP vaccine |
| **Otitis Media** | Several agents, especially *Staphylococcus aureus, Streptococcus pneumoniae,* and *Haemophilus influenzae* | Accumulations of pus in middle ear cause painful pressure on eardrum | Broad-spectum antibiotics<br>Prevention: pneumococcal vaccine |
| VIRAL DISEASE | | | |
| **Common Cold** | Rhinoviruses, coronaviruses | Familiar symptoms of coughing, sneezing, runny nose | Supportive |



# Microbial Diseases of the Lower Respiratory System

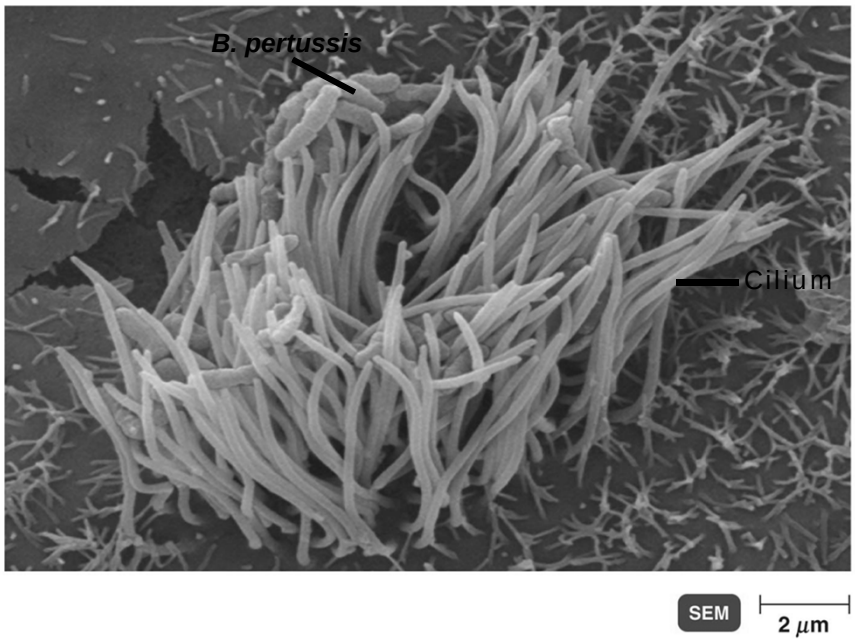
- Caused by many of the same bacteria and viruses as the upper respiratory system
  - **Bronchitis**
  - **Bronchiolitis**
  - **Pneumonia**
    - Pulmonary alveoli are involved

## Pertussis (Whooping Cough)

- Caused by *Bordetella pertussis*
  - Gram-negative coccobacillus
- Produces a capsule
  - Allows attachment to ciliated cells in the trachea
    - Destroys ciliated cells and shuts down the ciliary escalator
- Tracheal cytotoxin of cell wall damages ciliated cells
- Pertussis toxin enters the bloodstream



**Figure 24.6 Ciliated cells of the respiratory system infected with *Bordetella pertussis*.**



## Pertussis (Whooping Cough)

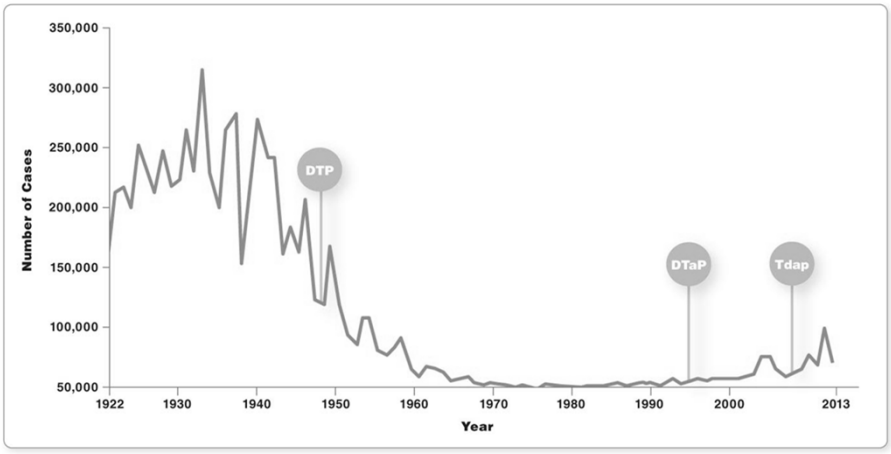
- Stage 1: catarrhal stage, like the common cold
- Stage 2: paroxysmal stage, violent coughing, gasping for air
- Stage 3: convalescence stage, may last for months
- Prevented by **DTaP** vaccine
- Treated with erythromycin or other macrolides



## Big Picture: Pertussis

- Before vaccines, 6000 people died annually in the United States from pertussis
- Today the acellular pertussis vaccine (DTaP) is given

Big Picture pg. 708 (4 of 5).

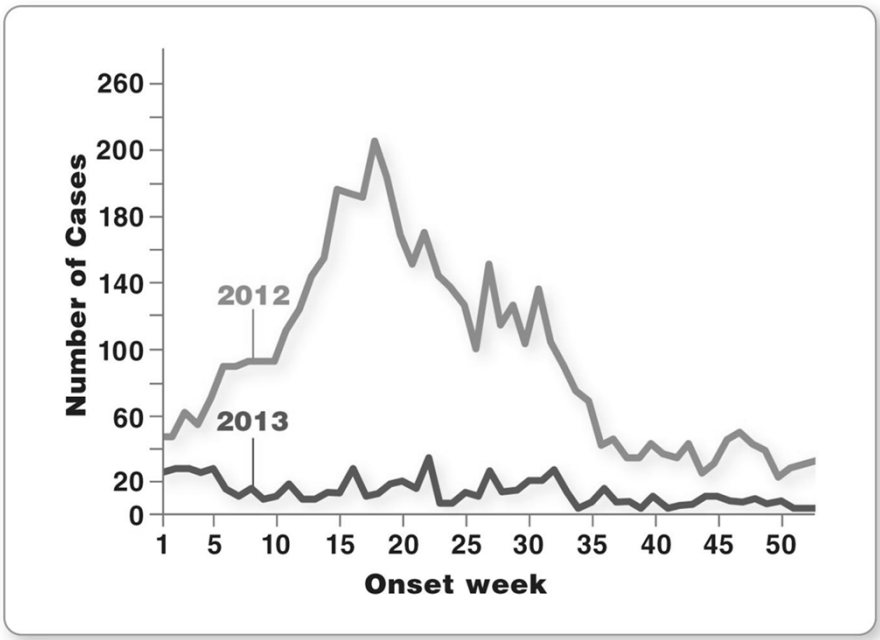





## Big Picture: Pertussis

- Increasing pertussis cases due to:
  - Breakdown in herd immunity
  - Mutation of the organism
  - Better diagnostic test leading to more reporting
  - Acellular vaccine having lower long-term immunity
- New strategies for fighting pertussis
  - New booster for teens, adults, and pregnant women
  - Additional vaccination requirements for students
  - More government health campaigns

Big Picture pg. 709 (3 of 3).

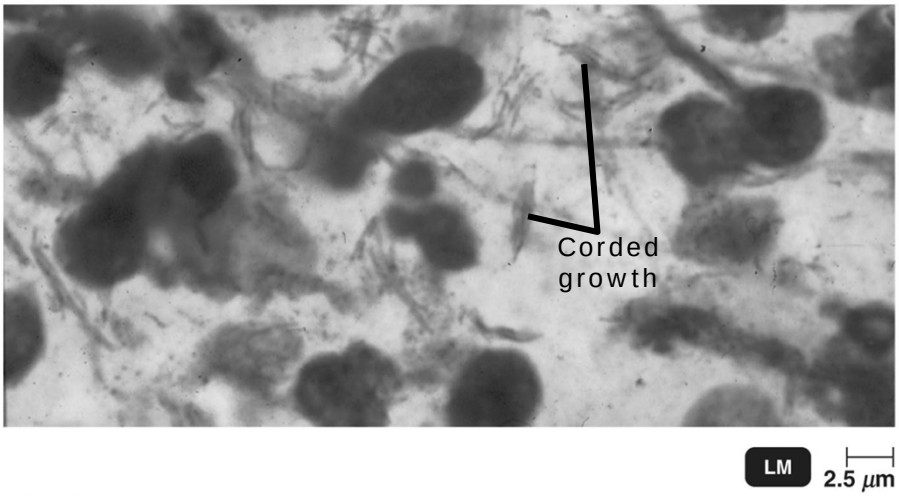





## Tuberculosis

- Caused by *Mycobacterium tuberculosis*
  - Acid-fast rod; obligate aerobe
  - 20-hour generation time
  - Lipids in the cell wall make it resistant to drying and antimicrobials
- Other causes
  - *Mycobacterium bovis*
    - **Bovine tuberculosis;** <1% of U.S. cases
  - *Mycobacterium avium-intracellulare* complex
    - Infects people with late-stage HIV infection

**Figure 24.7** ***Mycobacterium tuberculosis*.**

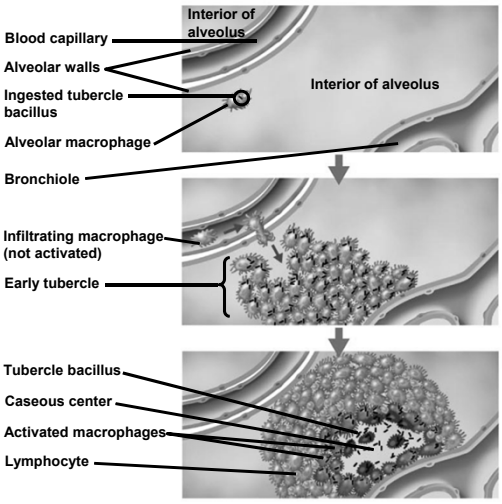





## Pathogenesis of Tuberculosis

- Inhaled organisms are phagocytized by alveolar macrophages
- Mycolic acids in the cell wall stimulate an inflammatory response
- Organisms are isolated in the walled-off tubercle
- Tubercles heal and become calcified (Ghon's complexes)
- Tubercle breaks down, releasing bacteria into the lungs and cardiovascular and lymphatic systems
  - Miliary tuberculosis: disseminated infection

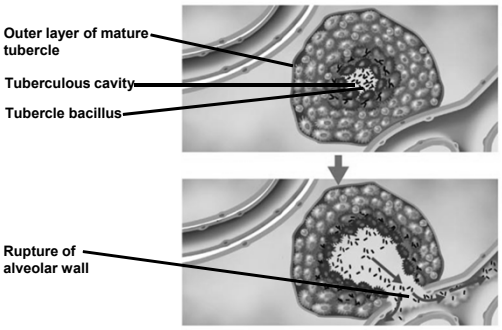
**Figure 24.8 The pathogenesis of tuberculosis (2 of 3).**




1. Tubercle bacilli that reach the alveoli of the lung are ingested by macrophages, but often some survive. Infection is present, but no symptoms of disease.
2. Tubercle bacilli multiplying in macrophages cause a chemotactic response that brings additional macrophages and other defensive cells to the area. These form a surrounding layer and, in turn, an early tubercle. Most of the surrounding macrophages are not successful in destroying bacteria but release enzymes and cytokines that cause a lung-damaging inflammation.
3. After a few weeks, disease symptoms appear as many of the macrophages die, releasing tubercle bacilli and forming a *caseous center* in the tubercle. The aerobic tubercle bacilli do not grow well in this location. However, many remain dormant (latent TB) and serve as a basis for later reactivation of the disease. The disease may be arrested at this stage, and the lesions become calcified.



**Figure 24.8 The pathogenesis of tuberculosis (3 of 3).**



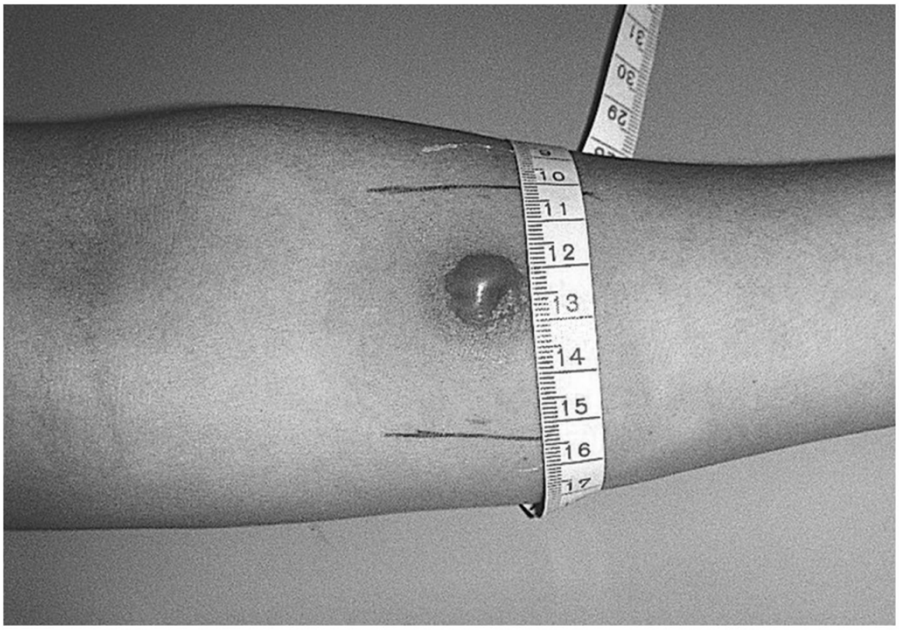

4. In some individuals, disease symptoms appear as a mature tubercle is formed. The disease progresses as the caseous center enlarges in the process called *liquefaction*. The caseous center now enlarges and forms an air-filled t*uberculous cavity* in which the aerobic bacilli multiply outside the macrophages.
5. Liquefaction continues until the tubercle ruptures, allowing bacilli to spill into a bronchiole and thus be disseminated throughout the lung and then to the circulatory and lymphatic systems.

## Diagnosis of Tuberculosis

- **Tuberculin skin test**
  - Positive reaction means a current or previous infection
  - T cells react with purified protein derivative from the TB bacterium
    - Delayed hypersensitivity induration
- Followed by an X-ray or CT exam, acid-fast staining of sputum, and culturing of bacteria
- New rapid blood test for IFN-γ and PCR test
  - Higher specificity and less cross-reactivity



**Figure 24.9 A positive tuberculin skin test on an arm.**



## Treatment of Tuberculosis

- Minimum of 6 months of drug therapy due to slow growth and dormancy
- **First-line drugs:** isoniazid, ethambutol, pyrazinamide, rifampin
- **Second-line drugs:** aminoglycosides, fluoroquinolones, para-aminoslicyclic acid (PAS)
- **Multi-drug-resistant (MDR)** strains: resistant to first-line drugs
- **Extensively drug-resistant (XDR)** strains: resistant to second-line drugs



## Tuberculosis

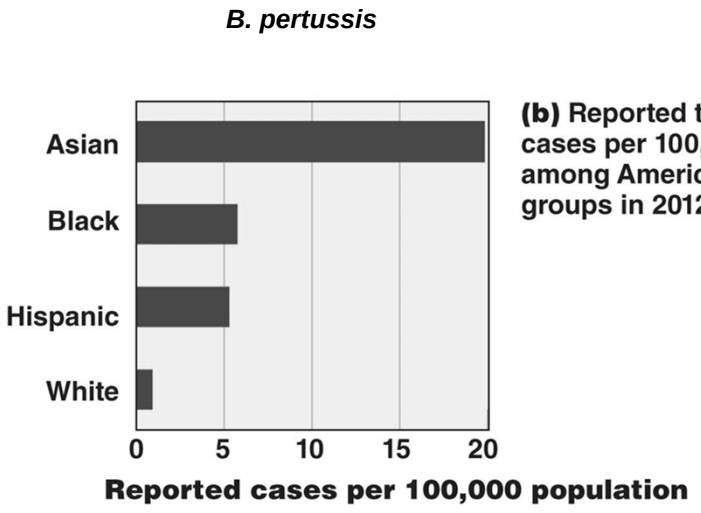
- 9 million develop TB annually; 2 million die
- 1/3 of the world's population infected
- Leading cause of death for those with HIV
- **BCG vaccine:** live culture of avirulent *M. bovis*
  - Not widely used in the United States due to questionable effectiveness

**Figure 24.10a Distribution of tuberculosis.**


**(a)** Estimated tuberculosis incidence worldwide, per 100,000 population



**Figure 24.10b Distribution of tuberculosis.**




**(b)** Reported tuberculosis cases per 100,000 population among American ethnic groups in 2012

## Bacterial Pneumonias

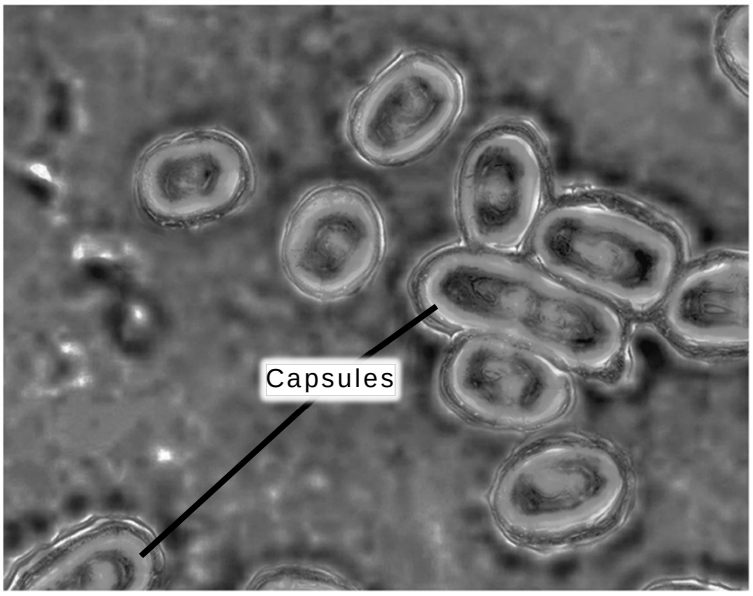
- Typical pneumonia
  - Caused by *S. pneumoniae*
- Atypical pneumonia
  - Caused by other microorganisms
- Lobar pneumonia
  - Infects the lobes of the lungs
- Bronchopneumonia
  - Infects the alveoli adjacent to the lungs
- Pleurisy
  - Pleural membranes inflamed



## Pneumococcal Pneumonia

- Caused by *S. pneumoniae*
  - Gram-positive; encapsulated diplococci
  - 90 serotypes
- Infected alveoli of the lung fill with fluids and RBCs; interferes with oxygen uptake
- Diagnosis: optochin-inhibition test, bile solubility test, or antigen in urine
- Treated with macrolides and fluoroquinolones
- Prevented with conjugated pneumococcal vaccine

**Figure 24.11** ***Streptococcus pneumoniae*****, the cause of pneumococcal pneumonia.**






## *Haemophilus influenzae* Pneumonia

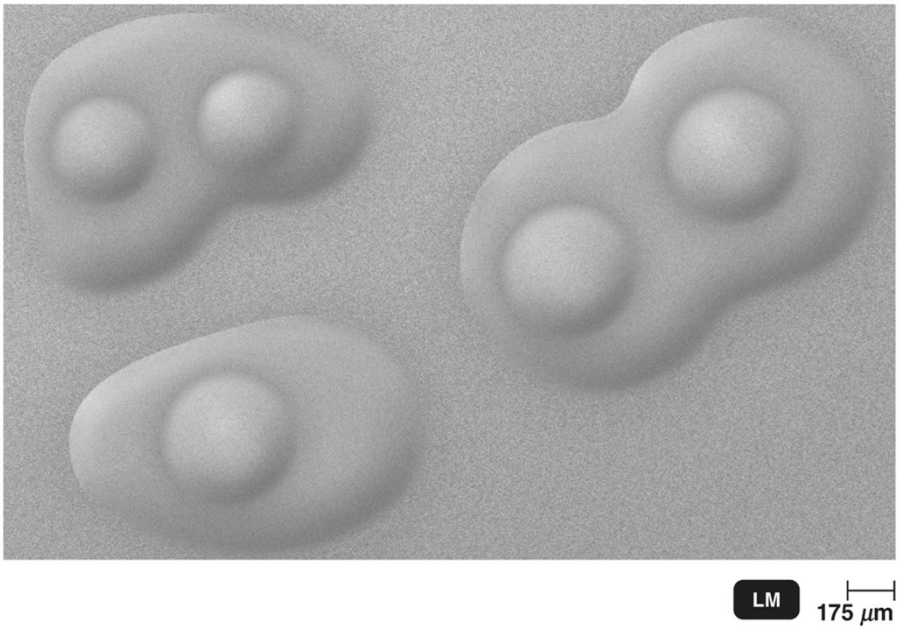
- Gram-negative coccobacillus
- Predisposing factors: alcoholism, poor nutrition, cancer, or diabetes
- Symptoms resemble those of pneumococcal pneumonia
- Diagnosis: isolation on special media for nutritional requirements (X and V factors)
- Treated with cephalosporins

## Mycoplasmal Pneumonia

- Also called primary atypical pneumonia or walking pneumonia
- Caused by *Mycoplasma pneumoniae*
  - No cell wall
- Mild but persistent respiratory symptoms; low fever, cough, headache
  - Common in children and young adults
- "Fried-egg" appearance on media
- Diagnosis: PCR and serological testing
- Treated with tetracyclines



**Figure 24.12 Colonies of *Mycoplasma pneumoniae*, the cause of mycoplasmal pneumonia.**



## Legionellosis

- Also called **Legionnaires' disease**
- Caused by *Legionella pneumophila*
  - Aerobic, gram-negative rod
  - Grows in water and air conditioning, biofilms, and waterborne amebae
- Transmitted by inhaling aerosols; not transmitted person to person
- Symptoms: high fever and cough
  - Similar to symptoms of **Pontiac fever**
- Treated with erythromycin and macrolides



## Psittacosis (Ornithosis)

- Caused by *Chlamydophila psittaci*
  - Gram-negative intracellular bacterium
- Transmitted to humans by **elementary bodies** from bird droppings transmitted through air
- Fever, headache, chills, disorientation
- Diagnosis: growth of bacteria in eggs or cell culture
- Treated with tetracyclines

## Chlamydial Pneumonia

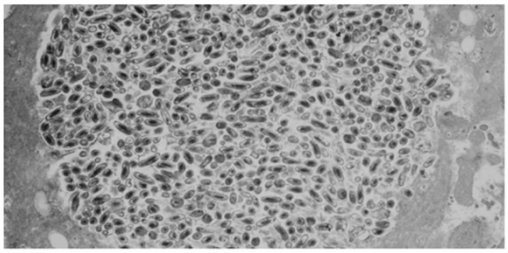
- Caused by *Chlamydophila pneumoniae*
- Transmitted person to person
- Mild respiratory illness common in young people; resembles mycoplasmal pneumonia
- Possible association with artherosclerosis
- Diagnosis: serological tests
- Treated with tetracyclines



## Q Fever

- Caused by *Coxiella burnetii*
  - Obligately parasitic, intracellular gamma proteobacteria
- Acute Q fever
  - High fever, muscle aches, headache, coughing
- Chronic Q fever
  - Endocarditis (may occur years after infection)
- Transmitted to farm animals from tick bites
  - Transmitted to humans from the inhalation of aerosols from animals and unpasteurized milk
- Treated with doxycycline; chloroquine for chronic infections

**Figure 24.13** ***Coxiella burnetii*****, the cause of Q fever.**



**(a) Masses of *Coxiella burnetii* growing in a placental cell** TEM 2 μm


**(b) This cell has just divided; notice the endospore-like body (E), which is probably responsible for the relative resistance of the organism.** TEM 0.5 μm



## Melioidosis

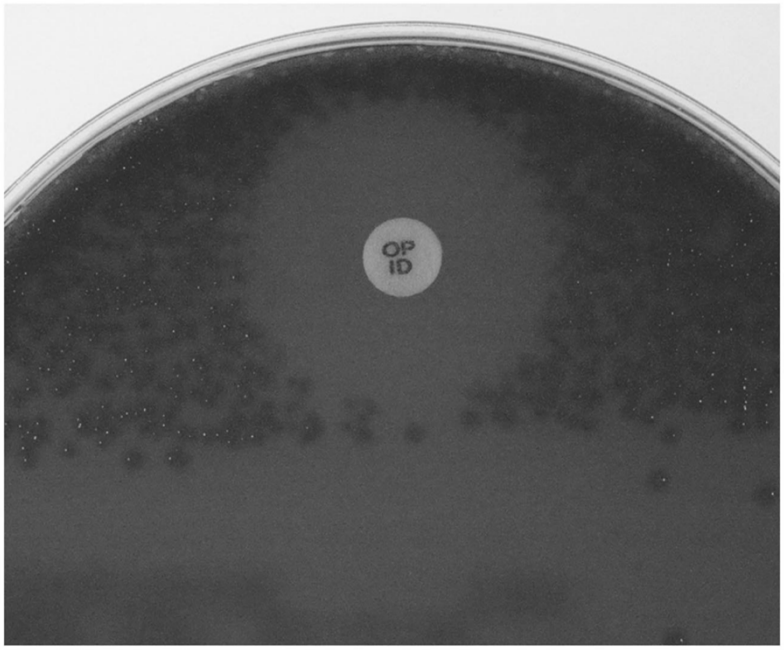
- Caused by *Burkholderia pseudomallei*
  - Gram-negative rod
- Occurs mostly in southeast Asia and northern Australia (in moist soils)
- Commonly affects those with lowered immune systems
  - Pneumonia or tissue abscesses (necrotizing fasciitis) and severe sepsis
- Transmission by inhalation, puncture wounds, and ingestion
- Treated with ceftazidime

## Diseases in Focus: Common Bacterial Pneumonias

- A 27-year-old man with a history of asthma is hospitalized with a 4-day history of progressive cough and 2 days of spiking fevers. Gram-positive cocci in pairs are cultured from a blood sample.
- Can you identify infections that could cause these symptoms?



**Diseases in Focus 24.2 (1 of 2)**



**Diseases in Focus 24.2 (2 of 2)**

| Disease | Pathogen | Symptoms | Reservoir | Diagnosis | Treatment |
|---|---|---|---|---|---|
| **Pneumococcal Pneumonia** | *Streptococcus pneumoniae* | Infected alveoli of lung fill with fluids; interferes with oxygen uptake | Humans | Positive optochin inhibition test or bile solubility test; serological typing of bacteria | Fluoroquinolones Prevention: pneumococcal vaccine |
| ***Haemophilus influenzae* Pneumonia** | *Haemophilus influenzae* | Symptoms resemble pneumococcal pneumonia | Humans | Isolation; special media for nutritional requirements | Cephalosporins |
| **Mycoplasmal Pneumonia** | *Mycoplasma pneumoniae* | Mild but persistent respiratory symptoms; low fever, cough, headache | Humans | PCR and serological tests | Tetracyclines |
| **Legionellosis** | *Legionella pneumophila* | Potentially fatal pneumonia | Water | Culture on selective media; DNA probe | Erythromycin |
| **Psittacosis (Ornithosis)** | *Chlamydophila psittaci* | Symptoms, if any, are fever, headache, chills | Birds | Growth of bacteria in eggs or cell culture | Tetracyclines |
| **Chlamydial Pneumonia** | *Chlamydophila pneumoniae* | Mild respiratory illness; resembles mycoplasmal pneumonia | Humans | Serological tests | Tetracyclines |
| **Q Fever** | *Coxiella burnetii* | Mild respiratory disease lasting 1–2 weeks; occasional complications such as endocarditis occur | Large mammals; can be transmitted via unpasteurized milk | Growth in cell culture | Doxycycline and chloroquine |



## Viral Pneumonia

- **Viral pneumonia** occurs as a complication of influenza, measles, or chickenpox
- Few labs are equipped to test clinical samples properly for viruses
- **SARS-associated coronavirus (SARS)**
  - Emerged in Asia in 2003
- **Middle East respiratory syndrome (MERS-CoV)**
  - Reported in Saudi Arabia in 2012

## Respiratory Syncytial Virus (RSV)

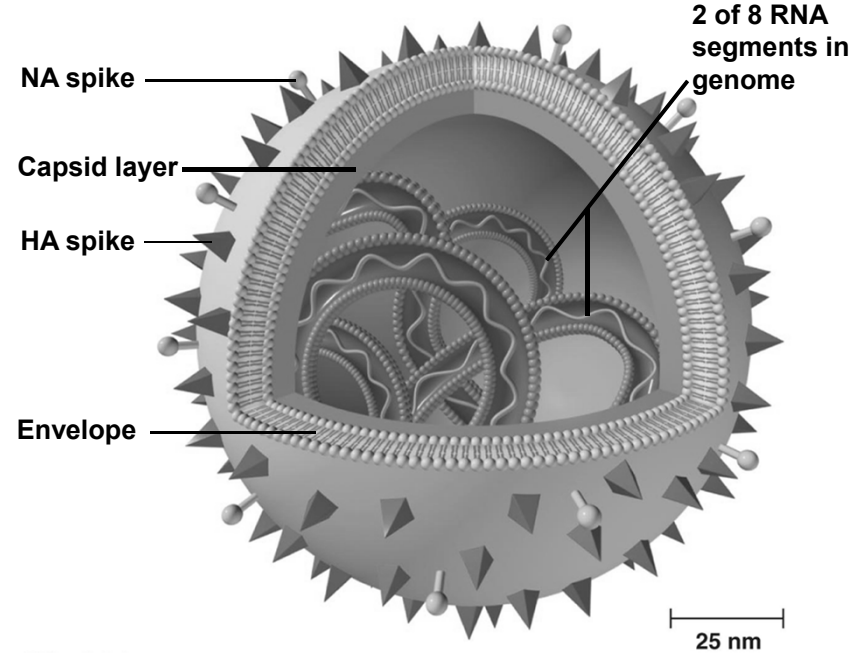
- Most common viral respiratory disease in infants
  - Almost all children are infected by age 2
  - 4500 deaths annually
- Causes cell fusion (syncytium) in cell culture
- Coughing and wheezing for more than a week
- Diagnosis: serological test for viruses and antibodies
- Treated with ribavirin and palivizumab



## Influenza (Flu)

- *Influenzavirus*
  - Contains eight RNA segments and an outer lipid bilayer
- Chills, fever, headache, and muscle aches
  - No intestinal symptoms
  - 30,000 to 50,000 deaths in the United States annually
- Avian, swine, and mammalian strains
  - Swine serve as "mixing vessels" for new strains

Figure 24.14 Detailed structure of the influenza virus.






## Influenza (Flu)

- Hemagglutinin (HA) spikes
  - Recognize and attach to host cells
- Neuraminidase (NA) spikes
  - Help the virus separate from the infected cell
- **Antigenic drift**
  - Minor antigenic changes in HA and NA
  - Allow the virus to elude some host immunity
- **Antigenic shifts**
  - Changes great enough to evade most immunity
  - Lead to pandemics
  - Involve the reassortment of the eight RNA segments

Table 24.1 Human Influenza Viruses*

**TABLE 24.1 Human Influenza Viruses***

| Type | Antigenic Subtype | Year | Disease Severity |
|---|---|---|---|
| A | H3N2 (the first "modern" pandemic; originated in southern China) | 1889 | Moderate |
| | H1N1 (Spanish) | 1918 | Severe |
| | H2N2 (Asian) | 1957 | Severe |
| | H3N2 (Hong Kong) | 1968 | Moderate |
| | H1N1 (Russian)† | 1977 | Low |
| | H1N1 (Mexico)‡ | 2009 | Low |
| B | None | 1940 | Moderate |
| C | None | 1947 | Very mild |

*The conventional wisdom is that H1, H2, and H3 are human-infecting strains; H4, H5, H6, and H7 primarily infect animals, especially swine and poultry. (Avian influenza strains H5N1 and H7N7 have caused human fatalities.)
†Probably escaped from a laboratory. At this time persons over age 20 were mostly immune from similar viruses circulating in the 1950s and earlier in the century.
‡The H1N1 virus causing this recent pandemic, the first in more than 40 years, differs significantly from the regular H1N1 virus that had been circulating. There has been confusion concerning a differentiating name for this virus. It has popularly been called the swine flu, and the CDC has referred to it as 2009H1N1, but in 2014 the WHO designed it as A(H1N1) pdm09.

*Source:* Adapted from C. Mims, J. Playfair, I. Roitt, D. Wakelin, and R. Williams, *Medical Microbiology,* 2nd ed. London: Mosby International, 1998.



# Influenza (Flu)

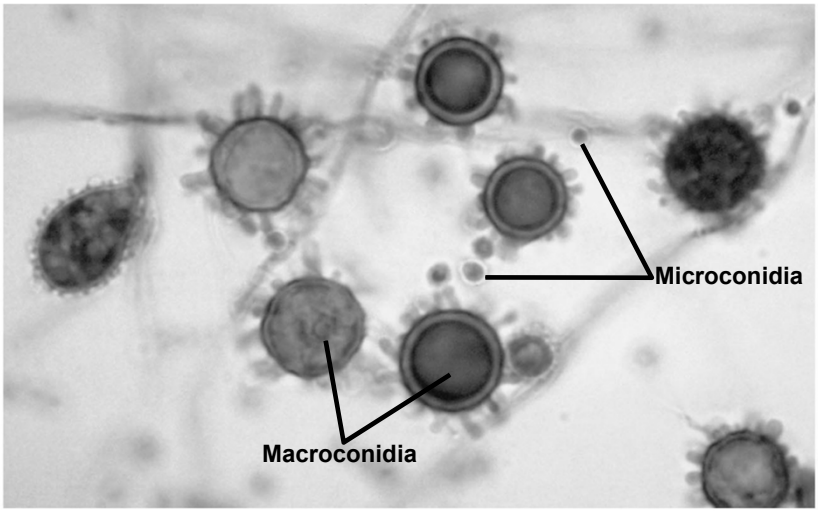
- 1% mortality; usually the very young and very old
- Multivalent vaccine for the most important strains
  - Composition of the vaccine determined annually by the identification of circulating viruses
    - Labor-intensive to produce
    - Does not provide long-term immunity
- Difficult to diagnose from clinical symptoms
- Treated with zanamivir (Relenza) and oseltamivir (Tamiflu)
  - Inhibits neuraminidase

## Histoplasmosis

- Caused by *Histoplasma capsulatum*
  - Dimorphic fungus
  - Yeast-form grows intracellularly in macrophages
- Forms lung lesions; 0.1% of cases become a severe, generalized disease
- Acquired from airborne conidia in areas with bird or bat droppings
  - Limited geographical range in the United States
- Treated with amphotericin B or itraconazole



**Figure 24.15** ***Histoplasma capsulatum*****, a dimorphic fungus that causes histoplasmosis.**




**The macroconidia of *Histoplasma capsulatum* are especially useful for diagnostic purposes. Microconidia bud off from hyphae and are the infectious form. At 37°C in tissues, the organism converts to a yeast phase composed of oval, budding yeasts.**

**Figure 24.16 Histoplasmosis distribution.**



## Coccidioidomycosis

- Also known as Valley fever or San Joaquin fever
- Caused by *Coccidioides immitis*
  - Dimorphic fungus
- Arthroconidia found in alkaline desert soils of the American Southwest
- Form a spherule filled with endospores in tissues
- Most infections are not apparent; fever, coughing, weight loss
  - <1% of cases resemble tuberculosis
- Treated with amphotericin B or imidazole drugs

Figure 24.17 The life cycle of *Coccidioides immitis*, the cause of coccidioidomycosis.

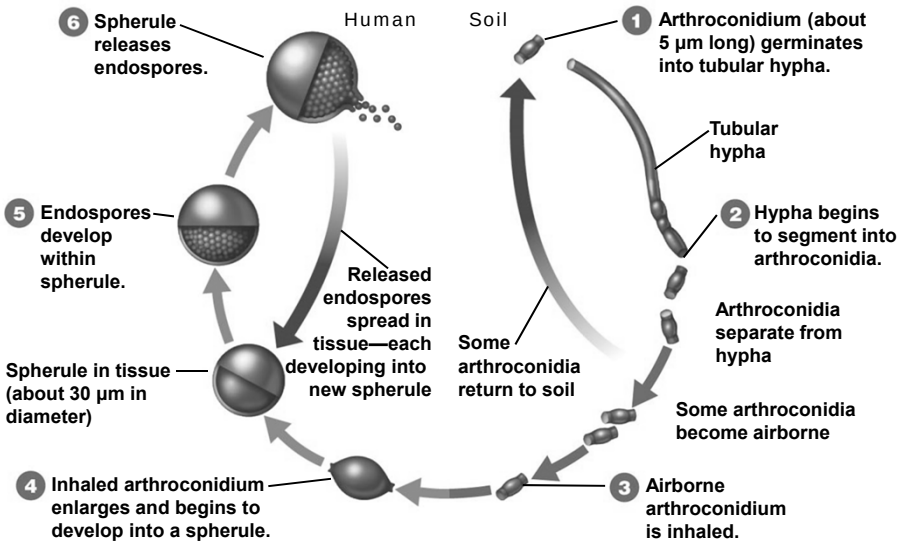
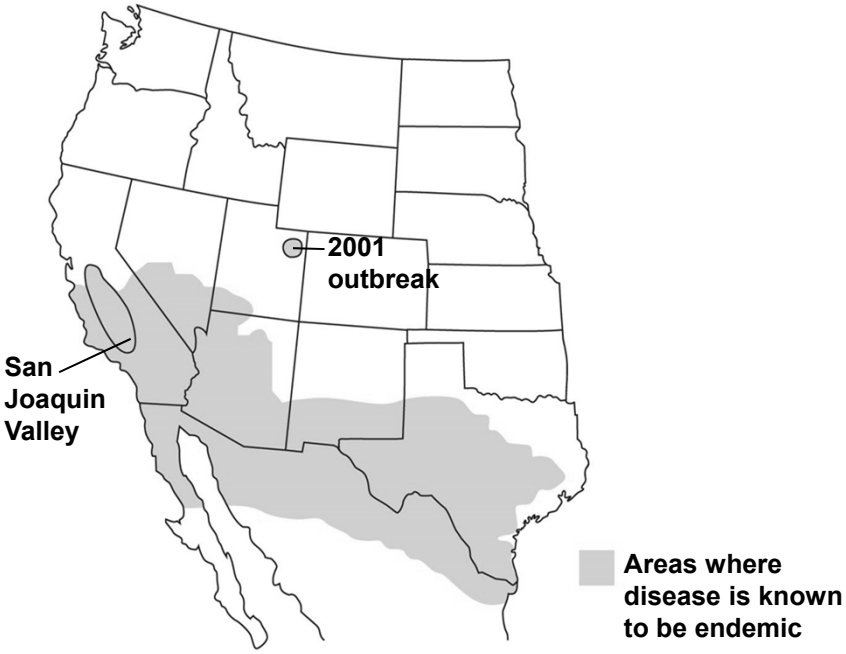





Figure 24.18 The U.S. endemic area for coccidioidomycosis.

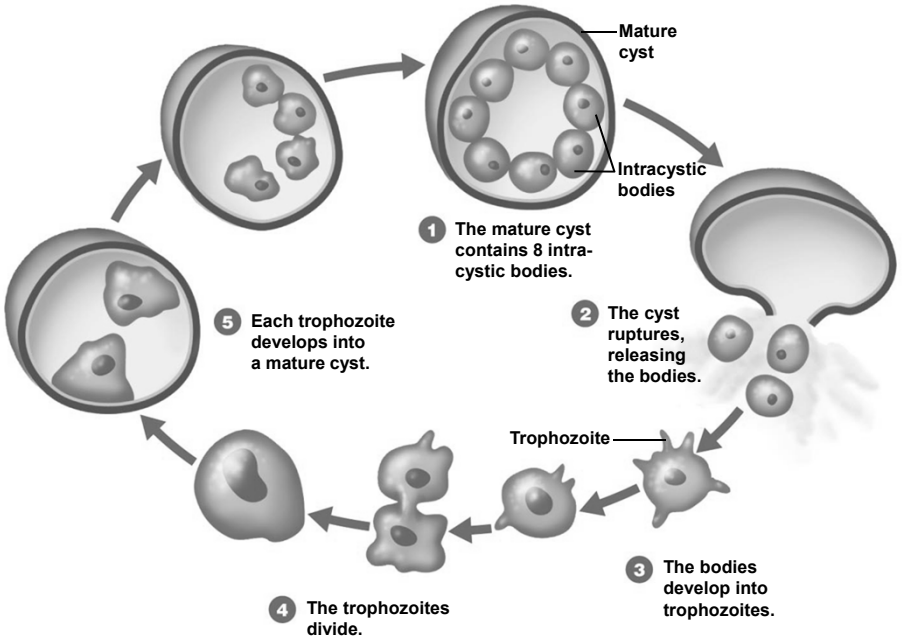


# Pneumocystis Pneumonia

- Caused by *Pneumocystis jirovecii*
  - No universal agreement if it is a protozoan or fungus
- Asymptomatic in the immunocompetent; causes pneumonia in the immunocompromised
  - Primary indicator of AIDS
- Found in the lining of the alveoli
  - Forms a cyst
  - Cysts rupture, releasing eight trophozoites
- Treated with trimethoprim-sulfamethoxazole



**Figure 24.19 The life cycle of *Pneumocystis jirovecii*, the cause of *Pneumocystis* pneumonia.**



## Blastomycosis (North American Blastomycosis)

- Caused by *Blastomyces dermatitidis*
  - Dimorphic fungus
  - Grows in soil
- Symptoms resemble bacterial pneumonia; cutaneous abscesses; extensive tissue damage
- 30 to 60 deaths annually
- Treated with amphotericin B



## Other Fungi Involved in Respiratory Disease

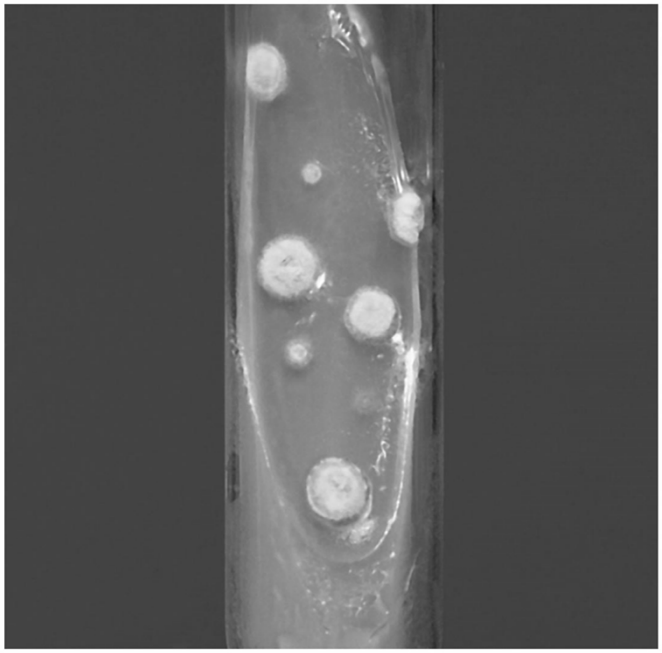
- *Aspergillus fumigatus*
  - Causes **aspergillosis**
  - Airborne conidia; grows in compost piles
- *Rhizopus* and *Mucor*
  - Mold spores
- Predisposing factors:
  - Immunocompromised state
  - Cancer
  - Diabetes

## Diseases in Focus: Microbial Diseases of the Lower Respiratory System

- Three weeks after working on the demolition of an abandoned building in Kentucky, a worker is hospitalized for acute respiratory illness. At the time of demolition, a colony of bats inhabited the building. An X-ray examination reveals a lung mass. A purified protein derivative test is negative; a cytological examination of the mass reveals ovoid yeast cells.
- Can you identify infections that could cause these symptoms?



**Diseases in Focus 24.3 (1 of 2)**



**Diseases in Focus 24.3 (2 of 2)**

| Disease | Pathogen | Symptoms | Reservoir | Diagnosis | Treatment |
|---|---|---|---|---|---|
| **BACTERIAL DISEASES** | | | | | |
| **Bacterial Pneumonia** (see Diseases in Focus 24.2, page 691) | | | | | |
| **Pertussis** (whooping cough) | *Bordetella pertussis* | Spasms of intense coughing to clear mucus | Humans | Bacterial culture | Erythromycin<br>Prevention: DTaP vaccine |
| **Tuberculosis** | *Mycobacterium tuberculosis*<br>*M. bovis*<br>*M. avium-intracellulare* | Cough, blood in mucus | Humans, cows: can be transmitted via unpasteurized milk | X-ray imaging; presence of acid-fast bacilli in sputum; tests for IFN-γ; PCR test for *M. tuberculosis* | Multiple-antimycobacterial drugs<br>Prevention: pasteurizing milk; BCG vaccine |
| **Melioidosis** | *Burkholderia pseudomallei* | Pneumonia, or as tissue abscesses and severe sepsis | Moist soil | Bacterial culture | Ceftazidime |
| **VIRAL DISEASES** | | | | | |
| **Respiratory Syncytial Virus (RSV) Disease** | Respiratory syncytial virus | Pneumonia in infants | Humans | Serological tests | Palivizumab (if life-threatening) |
| **Influenza** | *Influenzavirus;* several serotypes | Chills, fever, headache, and muscular aches | Humans, pigs, birds | Serological EIA tests | Amantadine, oseltamivir phosphate (Tamiflu) |
| **FUNGAL DISEASES** | | | | | |
| **Histoplasmosis** | *Histoplasma capsulatum* | Resembles tuberculosis | Soil; widespread in Ohio and Mississippi river valleys | Serological tests | Amphotericin B |
| **Coccidioidomycosis** | *Coccidioides immitis* | Fever, coughing, weight loss | Desert soils of U.S. Southwest | Serological tests | Amphotericin B |
| ***Pneumocystis* Pneumonia** | *Pneumocystis jirovecii* | Pneumonia | Unknown; possibly humans or soil | Microscopy | Trimethoprim-sulfamethoxazole, pentamidine |
| **Blastomycosis** | *Blastomyces dermatitidis* | Abscesses; extensive tissue damage | Soil in Mississippi Valley area | Isolation of pathogen | Amphotericin B |