Infections of the respiratory system
Lecture 17 - Chapter 21

Topics

- Respiratory tract system
- Protection
- Normal flora
- Diseases caused by bacteria & viruses

Anatomy of the respiratory tract system

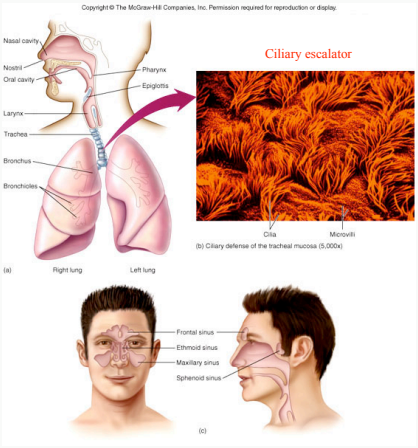


Fig. 21.1

Respiratory tract system

- **Most common** entry point for infections
- Upper tract
  - Mouth, nose, nasal cavity, sinuses, throat, epiglottis, and larynx
- Lower tract
  - Trachea, bronchi, and bronchioles in the lungs

Protection (barriers)

- Nasal hair (URT)
- Cilia (ciliatory escalator) (LRT)
- Bronchi
- Mucus
- Involuntary responses (coughing, etc.)
- Immune cells (leukocytes)

The RT Normal Flora

- Commensal microorganisms
- Limited to the upper tract
- Mostly Gram-positive bacteria
- Microbial antagonists (competition)

Special situation:
- Immuno-compromised individuals are at risk

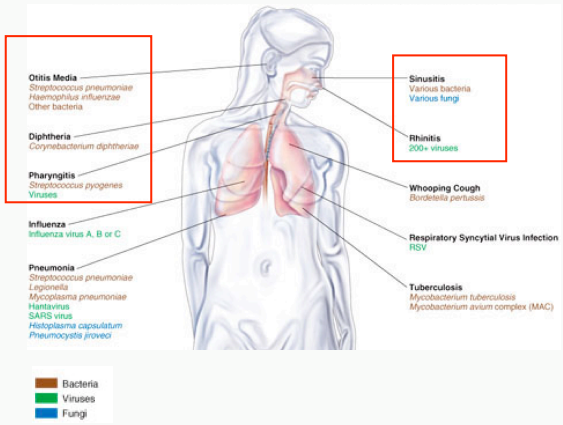
Diseases

- Upper Respiratory Tract
- Both upper and lower Respiratory Tract
- Lower Respiratory Tract

Upper respiratory tract

- Common cold
- Sinusitis
- Ear infections
- Pharyngitis
- Diphtheria

Infectious Diseases Affecting the Respiratory System.



Common cold (Rhinitis)

- Viral infection
  - Over 200 viruses are involved
- Prevalent among human population
- Prone to secondary bacterial infections
- No vaccine
- No chemotherapeutic agents
- Costly

Features of rhinitis.

CHECKPOINT 21.1 Rhinitis

Causative Organism(s)	200-plus viruses
Most Common Modes of Transmission	Indirect contact, droplet contact
Virulence Factors	Adhesins; most symptoms induced by host response
Culture/Diagnosis	Not necessary
Prevention	Hygiene practices
Treatment	For symptoms only

Checkpoint 21.1 Rhinitis

Sinusitis

- Bacterial infection
- Viral infections
- Inflammation of the sinuses
- Rare fungal infection

- Noninfectious allergies are primary cause of most sinus infections

Features of sinusitis.

CHECKPOINT 21.2 Sinusitis

Causative Organism(s)	Various bacteria, often mixed infection	Various fungi
Most Common Modes of Transmission	Endogenous (opportunism)	Introduction by trauma *or* opportunistic overgrowth
Virulence Factors	–	–
Culture/Diagnosis	Culture not usually performed; diagnosis based on clinical presentation, occasionally X rays or other imaging technique used	Same
Prevention	–	–
Treatment	Broad-spectrum antibiotics	Physical removal of fungus; in severe cases antifungals used
Distinctive Features	Much more common than fungal	Suspect in immunocompromised patients

Checkpoint 21.2 Sinusitis

Ear infection (acute otitis media)

- Bacterial infection
- Common sequela of rhinitis
- Effusion
- Biofilm bacteria may be associated with chronic otitis media

Bacteria can migrate along the Eustachian tube from the upper respiratory tract, and a buildup of mucus and fluids can cause inflammation and effusion.

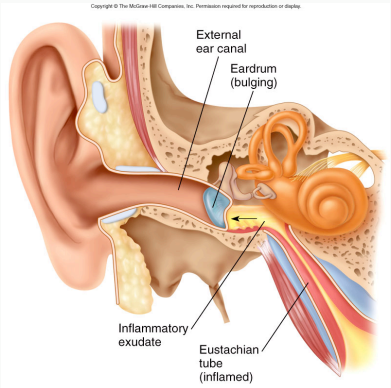


Fig. 21.2 An infected middle ear.

Features of otitis media.

CHECKPOINT 21.3 Otitis Media

Causative Organism(s)	*Streptococcus pneumoniae*	*Haemophilus influenzae*	Other bacteria
Most Common Modes of Transmission	Endogenous (may follow upper respiratory tract infection by *S. pneumoniae* or other microorganisms)	Endogenous (follows upper respiratory tract infection)	Endogenous
Virulence Factors	Capsule, hemolysin	Capsule, fimbriae	–
Culture/Diagnosis	Usually relies on clinical symptoms and failure to resolve within 72 hours	Same	Same
Prevention	Pneumococcal conjugate vaccine (heptavalent)	Hib vaccine	None
Treatment	Wait for resolution; if needed, amoxicillin (are high rates of resistance) or trimethoprim/sulfamethoxazole	Wait for resolution; if needed, ceftriaxone or ampicillin if isolate is sensitive	Wait for resolution; if needed, a broad-spectrum antibiotic (azithromycin) might be used in absence of etiological diagnosis
Distinctive Features	–	–	Suspect if fully vaccinated against other two

Checkpoint 21.3 Otitis media.

Streptococcus pyogenes

- Group A is virulent
- Groups B and C are commensals
- Streptolysins - toxin (hemolysins)
- Erythrogenic - toxin
- Toxins can act as superantigens
  - Overstimulate T cells
    - Tumor necrosis factor

The surface antigens of group A Streptococcus serve as virulence factors.

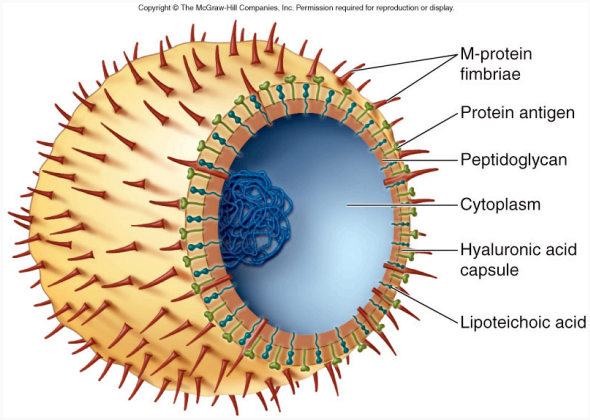


Fig. 21.5 Cutaway view of group A Streptococcus.

Dr. Lancefield developed the Lancefield classification, which distinguishes the different cell wall carbohydrates (A,B,C, etc.)

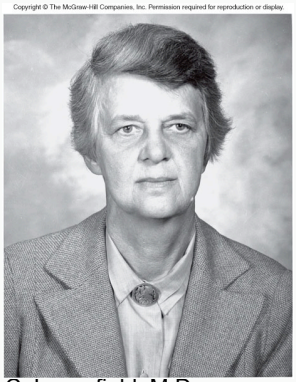


Fig. 21.6 Rebecca C. Lancefield, M.D.

Scarlet fever

- *S. pyogenes* may be infected with a phage
  - Erythrogenic toxin - rash
  - Sandpaper-like rash
    - Neck, chest, elbows, inner thighs
- Children are at risk

Rheumatic fever

- *Streptococcus* M protein
- Immunological cross-reaction (molecular mimicry)
- Can cause damage to heart valves
- Can cause nodules over bony surfaces leading to Arthritis

Group A streptococcal infections can damage the heart valves due a cross-reactions of bacterial-induced antibodies and heart proteins.

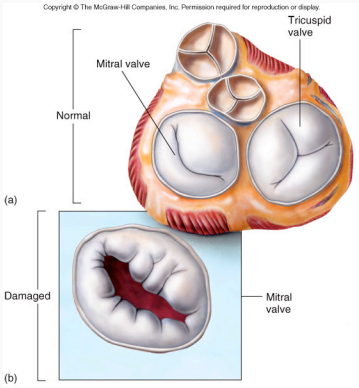


Fig. 21.4 The cardiac complications of rheumatic fever.

Glomerulonephritis

- Bacterial antigen-antibody complexes
- Deposit on the glomerulus of the kidney
- Kidney damage

Pharyngitis

- Bacterial infection
- Viral infection
- *Streptococcus pyogenes* – most serious type
  - Scarlet fever
  - Rheumatic fever
  - Glomerulonephritis

Streptococcus infection: inflammation of the throat & tonsils.

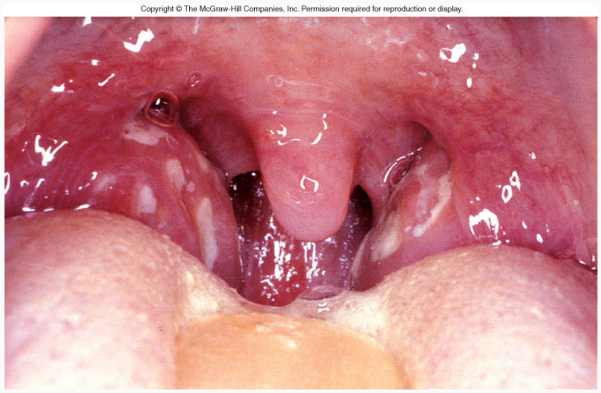


Fig. 21.3 The appearance of the throat in Pharyngitis and Tonsilitis.

The agglutination test and the zone of inhibition test are used to identify *Streptococcus pyogenes,* the causative agent of pharyngitis.

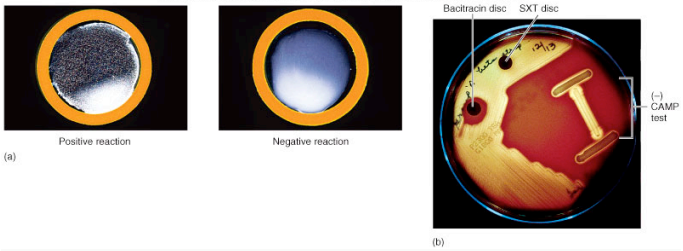


Fig. 21.7 Streptococcal test

Features of pharyngitis.

CHECKPOINT 21.4 Pharyngitis

Causative Organism(s)	*Streptococcus pyogenes*	Viruses
Most Common Modes of Transmission	Droplet or direct contact	All forms of contact
Virulence Factors	LTA, M protein, hyaluronic acid capsule, SLS and SLO, superantigens	–
Culture/Diagnosis	β-hemolytic on blood agar, sensitive to bacitracin, rapid antigen tests	Goal is to rule out *S. pyogenes*, further diagnosis usually not performed
Prevention	Hygiene practices	Hygiene practices
Treatment	Penicillin, cephalexin in penicillin-allergic	Symptom relief only
Distinctive Features	Generally more severe than viral pharyngitis	Hoarseness frequently accompanies viral pharyngitis

Checkpoint 21.4 Pharyngitis

Diphtheria

- Bacterial infection
- Membrane formation on tonsils or pharynx
- A-B toxin

- Vaccine (**DT**P vaccine)

Corynebacterium diphtheriae, the causative agent of diphtheria, has a unique club-shape appearance.

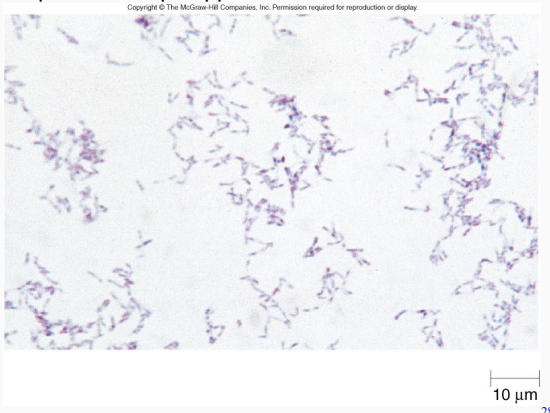


Fig. 21.8 *Corynebacterium diphtheriae*

Inflamed pharynx and tonsils marked by a grayish “pseudo-membrane” formed by the bacteria are characteristic signs of diphtheria.

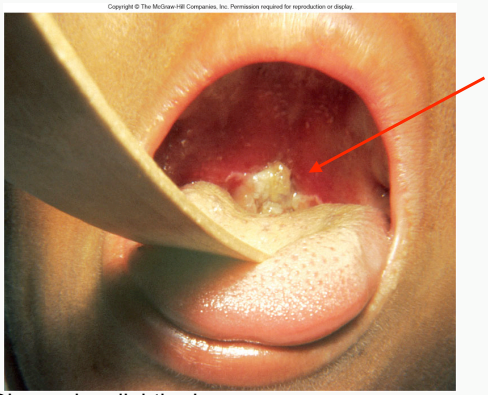
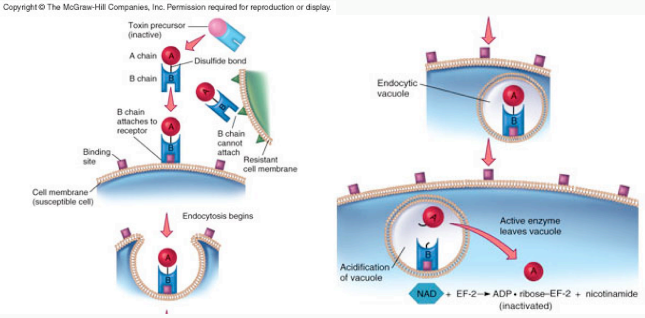


Fig. 21.9 Diagnosing diphtheria



Inhibited protein synthesis -> cell death

Fig. 21.10 A-B toxin of *Corynbacterium diphtheriae*

Features of diphtheria.

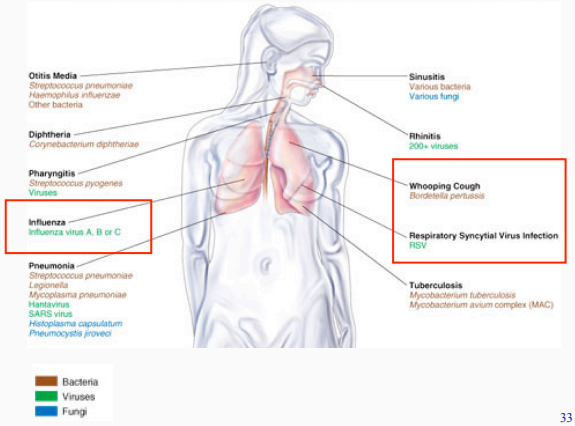
CHECKPOINT 21.5	Diphtheria
Causative Organism(s)	*Corynebacterium diphtheriae*
Most Common Modes of Transmission	Droplet contact, direct contact or indirect contact with contaminated fomites
Virulence Factors	Exotoxin: diphtheria toxin
Culture/Diagnosis	Tellurite medium—gray/black colonies, club-shaped morphology on Gram stain; *treatment begun before definitive identification*
Prevention	Diphtheria toxoid vaccine (part of DTaP)
Treatment	Antitoxin plus penicillin or erythromycin

Checkpoint 21.5 Diphtheria

Upper and lower respiratory tract

- Whooping cough
- Respiratory syncytial virus
- Influenza

Infectious Diseases Affecting the Respiratory System.



Whooping cough - Pertussis

- Bacterial infection (*Bordetella pertussis*)
- Pertussis
  - Catarrhal stage – cold symptoms
  - Paroxysmal stage – severe coughing
  - Convalescent phase - damage of the cilia
- Toxins
  - A-B toxin, tracheal cytotoxin
- Vaccine (DT**P**)

Features of whooping cough.

CHECKPOINT 21.6	Pertussis (Whooping Cough)
Causative Organism(s)	*Bordetella pertussis*
Most Common Modes of Transmission	Droplet contact
Virulence Factors	FHA (adhesion), pertussis toxin and tracheal cytotoxin, endotoxin
Culture/Diagnosis	Grown on B-G, charcoal or potato-glycerol agar; diagnosis can be made on symptoms
Prevention	Acellular vaccine (DTaP), erythromycin or trimethoprim; sulfamethoxazole for contacts
Treatment	Mainly supportive; erythromycin to decrease communicability

Checkpoint 21.6 Whooping cough

RSV- Disease

- Virus infection (Respiratory Syncytial Virus)
- Dyspnea (shortness of breath)
- Syncytia (cell division without cytokinesis)
- Children are at risk
- So far, no vaccine

Features of RSV disease.

CHECKPOINT 21.7	RSV Disease
Causative Organism(s)	Respiratory syncytial virus (RSV)
Most Common Modes of Transmission	Droplet and indirect contact
Virulence Factors	Syncytia formation
Culture/Diagnosis	Direct antigen testing
Prevention	Passive antibody
Treatment	Ribavirin in severe cases

Checkpoint 21.7 RSV Disease

Influenza (Flu)

- Viral infection (Influenza Virus)
- Prevalent during the winter season
- Glycoproteins
  - Hemagglutinin (HA)
  - Neuramindase (N)
- Antigenic drift
- Antigenic shift

The influenza virus is an enveloped virus with two important surface glycoproteins called hemagglutinin and neuraminidase.

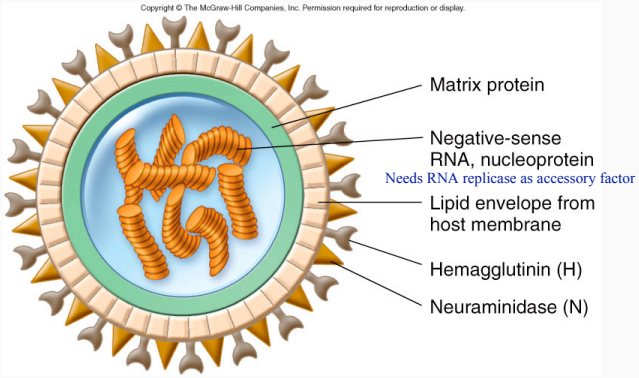


Fig. 21.11 Schematic drawing of influenza virus.

Influenza virus Glycoproteins:

- **Hemagglutinin**
  - Specific residues bind to host cell receptors of the respiratory mucosa
  - Different residues from above are recognized by the host immune system (antibodies)
    - Residues are subject to changes (antigenic drift)
  - Agglutination of Red Blood Cells

Hemagglutinin is a viral glycoprotein that is involved in binding to host cell receptors on the respiratory mucosa.

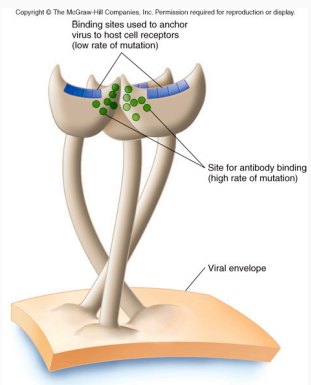


Fig. 21.12 Drawing of hemagglutinin of influenza virus.

Influenza virus Glycoproteins:

- **Neuraminidase (N)**
  - Breaks down protective mucous coating
  - Assist in viral budding
  - Keeps viruses from sticking together
  - Participates in host cell fusion

Antigenic shift involves gene exchange, which encode for viral glycoproteins, between different influenza viruses, thereby the new virus is no longer recognized by the human host.

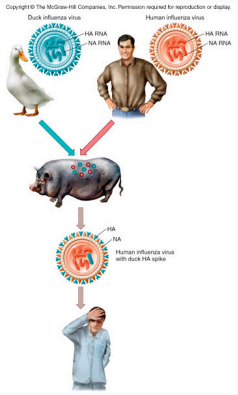


Fig. 21.13 Antigenic shift event. May involve hosts and also alternate hosts.

Features of influenza.

CHECKPOINT 21.8 Influenza

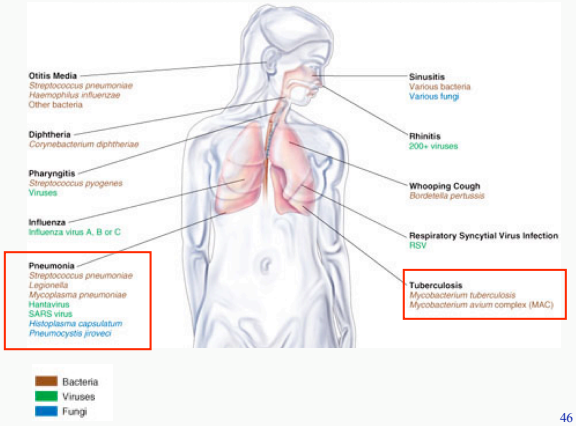
Causative Organism(s)	Influenza A, B, and C viruses
Most Common Modes of Transmission	Droplet contact, direct contact, some indirect contact
Virulence Factors	Glycoprotein spikes, overall ability to change genetically
Culture/Diagnosis	Viral culture (3–10 days) or rapid antigen-based tests
Prevention	Killed injected vaccine or inhaled live attenuated vaccine—taken annually
Treatment	Amantadine, rimantadine, zanamivir, or oseltamivir

Checkpoint 21.8 Influenza

Lower respiratory tract

- Tuberculosis
- Pneumonia

Infectious Diseases Affecting the Respiratory System.



Tuberculosis

- Bacterial infection
  - *Mycobacterium tuberculosis*
  - *Mycobacterium avium* complex (MAC)
    - Disseminated tuberculosis that affects AIDS patients
- Types
  - Primary
  - Secondary
  - Disseminated

M. tuberculosis

- Slow growing (generation time 15-20 hrs)
- Mycolyic acid in cell wall and waxy surface
- Primary (Granuloma formation)
  - Tubercles, caseous lesions, tuberculin reaction
- Secondary (Reactivation)
  - Consumption (wasting disease)
- Extrapulmonary TB
  - Dissemination (lymph nodes, kidneys, bones, genital tract, brain, meninges)

A tubercle in the lung is a granuloma consisting of a central core of TB bacteria inside an enlarged macrophage, and an outer wall of fibroblasts, lymphocytes, and neutrophils.

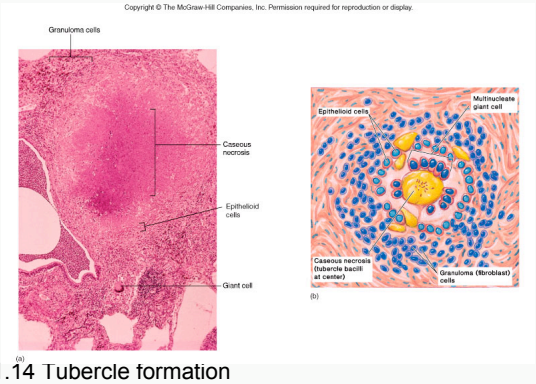


Fig. 21.14 Tubercle formation

The tuberculin reaction enables skin testing for tuberculosis.

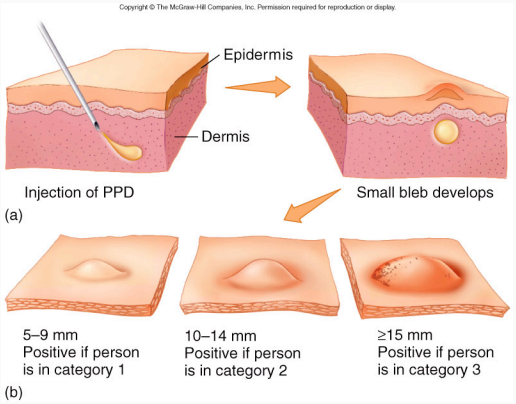


Fig. 21.15 Skin testing for tuberculosis.

Acid-fast staining is a means of identifying *Mycobacterium tuberculosis.*

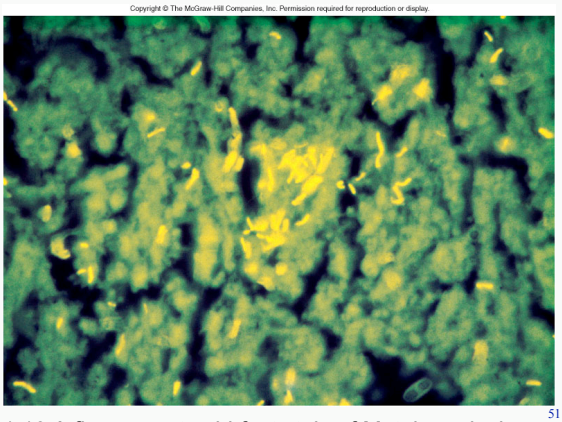


Fig. 21.16 A fluorescent acid-fast stain of M. tuberculosis.

Colonies of *M. tuberculosis* have a characteristic granular and waxy appearance, which enables the bacterium to survive inside macrophages.

Fig. 21.17 Cultural appearance of M. tuberculosis.

An example of a secondary tubercular infection.

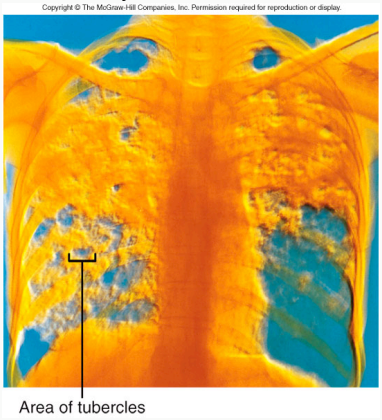


Fig. 21.18 Colorized X-ray showing a secondary tubercular infection.

The Ziehl-Neelson staining is a an acid-fast staining technique used to identify *Mycobacterium tuberculosis.*

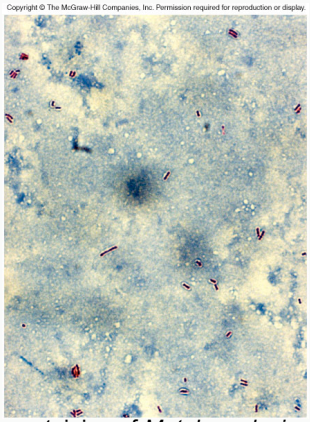


Fig. 21.19 Ziehl-Neelson staining of *M. tuberculosis.*

Features of tuberculosis.

CHECKPOINT 21.9 Tuberculosis

Causative Organism(s)	*Mycobacterium tuberculosis*	*Mycobacterium avium* complex
Most Common Modes of Transmission	Vehicle (airborne)	Vehicle (airborne)
Virulence Factors	Lipids in wall, ability to stimulate strong cell-mediated immunity (CMI)	–
Culture/Diagnosis	Rapid methods plus culture; initial tests are skin testing and chest X ray	Positive blood culture
Prevention	Avoiding airborne *M. tuberculosis*, BCG vaccine in other countries	Rifabutin or azithromycin given to AIDS patients at risk
Treatment	Isoniazid, rifampin, and pyrazinamide for varying lengths of time (always lengthy); if resistant, two other drugs added to regimen	Azithromycin or clarithromycin plus one additional antibiotic
Distinctive Features	Responsible for nearly all TB except for HIV-positive patients	Suspect this in HIV-positive patients

Checkpoint 21.9 Tuberculosis

Pneumonia

- Inflammation of the lung with fluid filled alveoli
- Bacterial infection
- Viral infection
- Fungal infection
- Community-acquired
- Nosocomial

Bacterial pneumonia

- *Streptococcus pneumoniae*
- *Legionella pneumophila*
- *Mycoplasma pneumoniae*

Streptococcus pneumoniae

- Pneumococcus
- 2/3 of all pneumonia are community-acquired pneumonia
- Cannot survive outside its habitat
- High risk - old age, season, underlying viral infection, diabetes, alcohol and narcotic use
- Variable capsular antigen
- Consolidation

Gram stain reveals unique pairing, and blood agar cultures shows alpha-hemolysis, which are characteristic of *S. pneumoniae.*

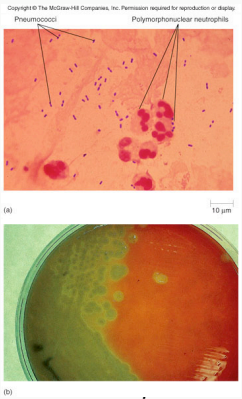


Fig. 21.20 *Streptococcus pneumoniae*

Consolidation is when the bronchioles and alveoli are blocked by inflammatory cells and exudate formation.

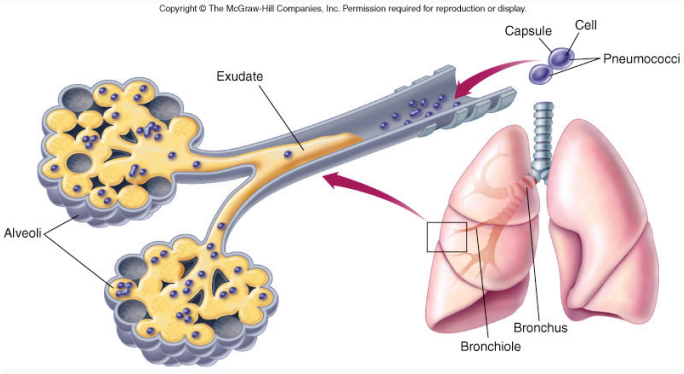


Fig. 21.21 The course of bacterial pneumonia.

Legionella pneumophila

- Less common but still a serious infection
- Survives in natural habitat (tap water, cooling towers, spas, etc.)
- Opportunistic disease

- Common habitat: dental wastewater lines

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Legionella is an intracellular organism that can live in amoebas and in human phagocytes.

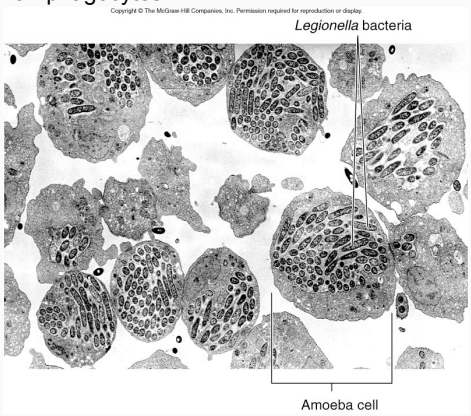

Fig. 21.22 *Legionella* living intracellular

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Mycoplasma pneumoniae

- Smallest known bacterium
- Walking pneumonia – atypical pneumonia
- No cell wall (-> penicillin doesn't work!)

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Viral pneumonia

- Hantavirus
- Severe Acute Respiratory Syndrome (SARS)-associated coronavirus

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Hantavirus

- Emerging disease
- Acute respiratory distress syndrome
  - Hantavirus antigen become disseminated throughout the blood stream
  - Loss of fluid from blood vessels

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Incident of hantavirus cases is high in the western part of the U.S.

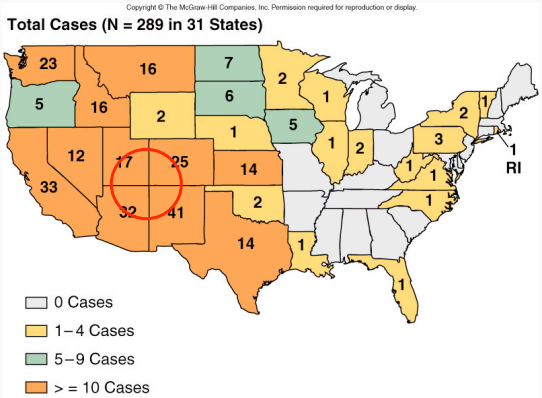

Fig. 21.23 Hantavirus pulmonary syndrome cases.

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SARS (coronavirus)

- Concentrated in China and Southeast Asia
- Few cases in Australia, Canada, and the United States.
- Symptoms can resemble influenza and RSV viruses
- Viral genome has been fully sequenced

Fungal pneumonia

- *Histoplasma capsulatum*
- *Pneumocystis jiroveci*

Histoplasma capsulatum

- Associated with many names – Darling's disease, **Ohio Valley fever**, spelunker's disease
  =>Endemic
- Array of manifestations
  - Benign or severe (systemic)
  - Acute or chronic
- Intracellular
- AIDS patients are at risk

Evidence of the prevalent nature of the disease.

Fig. 21.24 Sign in wooded area in Kentucky.

Pneumocystis jiroveci

- Formerly called *Pneumocystis carinii*
- Opportunistic infection in AIDS patients
- Healthy individuals ward off the infection
- Intracellular and extracellular
- Cyanosis

Nosocomial pneumonia

- Multiple bacterial species
- Pneumonia acquired by patients in hospitals and other health care residential facilities
- Second most common nosocomial infection (after UTI)

Features of pneumonia caused by bacteria, virus, and fungi.

CHECKPOINT 21.10 Pneumonia

Causative Organism(s)	*Streptococcus pneumoniae*	*Legionella* species	*Mycoplasma pneumoniae*
Most Common Modes of Transmission	Droplet contact or endogenous transfer	Vehicle (water droplets)	Droplet contact
Virulence Factors	Capsule	–	Adhesins
Culture/Diagnosis	Gram stain often diagnostic, α-hemolytic on blood agar	Requires selective charcoal yeast extract agar; serology unreliable	Rule out other etiological agents
Prevention	Pneumococcal polysaccharide vaccine (23-valent)	–	–
Treatment	Trimethoprim-sulfamethoxazole; ketek; much resistance	Doxycycline, azithromycin, ofloxacin, ciprofloxacin, or levofloxacin	Recommended not to treat in most cases, tetracycline or macrolides may be used if necessary
Distinctive Features	Patient usually severely ill	Mild pneumonias in healthy people; can be severe in elderly or immunocompromised	Usually mild; "walking pneumonia"

Hantavirus	SARS-associated coronavirus	*Histoplasma capsulatum*	*Pneumocystis jirovecі*
Vehicle—airborne virus emitted from rodents	Droplet, direct contact	Vehicle—inhalation of contaminated soil	Droplet contact
Ability to induce inflammatory response	?	Survival in phagocytes	–
Serology (IgM), PCR identification of antigen in tissue	Rule out other agents, serology, PCR	Usually serological (rising Ab titers)	Immunofluorescence
Avoid mouse habitats and droppings	–	Avoid contaminated soil/bat, bird droppings	Antibiotics given to AIDS patients to prevent this
Supportive	Supportive	Amphotericin B and/or itraconazole	Trimethoprim-sulfamethoxazole
Rapid onset; high mortality rate	Rapid onset	Many infections a symptomatic	Vast majority occur in AIDS patients

Checkpoint 21.10 Pneumonia

Summary of the diseases associated with the respiratory tract.

Taxonomic Organization of Microorganisms Causing Disease in the Respiratory Tract

Microorganism	Disease	Chapter Location
Gram-Positive Bacteria		
Streptococcus pneumoniae	Otitis media, pneumonia	Otitis media, p. 657 Pneumonia, p. 675
S. pyogenes	Pharyngitis	Pharyngitis, p. 658
Corynebacterium diphtheriae	Diphtheria	Diphtheria, p. 662
Gram-Negative Bacteria		
Haemophilus influenzae	Otitis media	Otitis media, p. 657
Bordetella pertussis	Whooping cough	Whooping cough, p. 664
Mycobacterium tuberculosis, M. avium* complex	Tuberculosis	Tuberculosis, p. 668
Legionella spp.	Pneumonia	Pneumonia, p. 676
Other Bacteria		
Mycoplasma pneumoniae	Pneumonia	Pneumonia, p. 677
RNA Viruses		
Respiratory syncytial virus	RSV disease	RSV disease, p. 665
Influenza virus A, B, and C	Influenza	Influenza, p. 666
Hantavirus	Hantavirus pulmonary syndrome	Pneumonia, p. 677
SARS-associated coronavirus	SARS	Pneumonia, p. 678
Fungi		
Pneumocystis jirovecі	*Pneumocystis* pneumonia	Pneumonia, p. 681
Histoplasma capsulatum	Histoplasmosis	Pneumonia, p. 679

*There is some debate about the gram status of the genus *Mycobacterium*; it is generally not considered gram positive or gram negative.

Taxonomic organization of microorganisms causing RT disease