Infectious Diseases Affecting the Respiratory System
Student Learning Outcomes

Describe how microorganisms are prevented from entering the respiratory system and the natural defenses present in the respiratory tract.

Characterize the normal microbiota of the upper and lower respiratory systems.

List the possible causative agents, modes of transmission, virulence factors, diagnostic techniques, prevention/treatment, etc. for pharyngitis, Rhinitis, Otitis media, Diphtheria, Pertussis, Influenza, TB, Pneumonias, etc.

Compare and contrast antigenic shift and drift.
19.1/2 Respiratory and Its Defenses

Most common portal of entry

**URS:** Includes larynx. Resident microbiota similar to oral. Also *S. pyogenes*, *H. influenzae*, *S. pneumoniae*, *N. meningitidis*, and *S. aureus*

**LRS:** Trachea to lungs. Limited microbiota because of mucociliary escalator action.

Fu. of normal microbiota?
Fig 19.1

(a) Anatomy of the respiratory system

(b) Ciliary defense of the tracheal mucosa
Pharyngitis

*Fusobacterium necrophorum* children and young adults, *S. pyogenes*

Droplet Transmission

Symptoms: Sore throat, high fever, coughing, swollen LN, *otitis media* may also occur

Both may be part of normal flora

**Rapid Strep Test** detects unique *S.p.* ags.

Penicillin works for both!
Complications of Strep Throat

S. pyogenes causes two major nonsuppurative autoimmune complications (antibodies cross-react)

1. Acute rheumatic fever (see page 648):
   Short period of arthritis and fever followed in ~50% of affected by rheumatic heart disease
   $\implies$ heart valve damage $\implies$ chronic valvular disease (stenosis and/or incompetence) $\implies$
   heart failure and/or subacute bacterial endocarditis

2. Acute poststreptococcal glomerulonephritis
Mitral stenosis and incompetence, due to scarring from rheumatic fever.
About 200 different viruses can cause the common cold:

- ~ 50% of cases caused by rhinoviruses (>100 types)
- ~ 15-20% caused by coronaviruses

Many additional cold viruses (adenoviruses, RSV, and many others)

Symptoms: Sneezing, nasal secretions and congestion

Possible complications: fever, sinus infections, lower respiratory tract infections, laryngitis, otitis media

Why no Vaccine for common cold?

Incidence of colds ↑ during cold weather. Why?

Antibodies are produced against the specific viruses
(Acute) Otitis Media

Complication of nose and throat infections

Pus accumulation causes pressure on the eardrum

Bacterial causes include

- **S. pneumoniae** (35%)
- **H. influenzae** (20-30%)
- **M. catarrhalis** (10-15%)
- **S. pyogenes** (8-10%)
- **S. aureus** (1-2%)

- Treated with broad-spectrum antibiotics
- Incidence of **S. pneumoniae** reduced by vaccine
Diphtheria

- *Corynebacterium diphtheriae*

- **Pseudomembrane** formation (fibrin, dead tissue and bacteria)

- Not very invasive, but **prophage encoded exotoxin** inhibits protein synthesis $\Rightarrow$ absorbed into blood $\Rightarrow$ heart, nerve and kidney damage. Use antitoxin early!

- DTaP

- Boosters: get Tdap once then Td boosters every 10 years
Pseudomembrane on tonsils can lead to respiratory blockage.

Compare to Fig 19.6
19.4 Microbial Diseases of Upper AND Lower Respiratory System

- **Influenza**: *Influenzavirus*; ssRNA, 8 segments

- Symptoms: Chills, fever, headache, muscle aches (no intestinal symptoms)

- Grouped according to antigenic differences in surface proteins:
  - Type A → mammals and birds (most severe and extensive); currently most common antigenic variants of influenza A virus: H1N1 and H3N2
  - Types B and C → humans only

- Viral isolates identified via serological testing
**Hemagglutinin** (H) spikes used for attachment to host cells

**Neuraminidase** (N) spikes used to release virus from cell

H and N are *virulence factors* and *antigens*

*Fig 19.8*
Mutations in H and N lead to

- **antigenic shift** (major changes only for type A) or
- **antigenic drift** (minor changes for all types)

⇒ natural immunity and vaccination obsolete

Compare to Fig 19.9
Antigenic drift:
- Influenza virion from an animal
- Human influenza virion
- Reassortment of genome segments
- Host cell

Possible only for A, B, C

Antigenic shift:
- Genome segments
  - H antigen
  - N antigen
- Mutation #1
- Mutation #2
- Result of
  - Mutation #1
  - Mutation #2
Pandemics, Prevention and Treatment

• Wide spread epidemics due to antigenic shifts → Pandemics

• \(\sim 50,000 - 70,000\) deaths/year in US - also Guillain-Barré and Reye’s syndrome

• Complications often due to bacterial secondary infections (??)

• **Vaccine** produced in chicken embryos
  – flu shot (..... ) and
  – nasal spray (LAIV)

• Effective antiviral drugs must be taken early on
**Bordetella pertussis**, highly contagious

Various toxins:
- **Tracheal cytotoxin** damages ciliated cells
- **Pertussis toxin** enters blood $\rightarrow$ systemic symptoms

*Three stages of disease*

1. **Catarrhal stage** resembles a cold

2. **Paroxysmal stage** due to accumulation of mucus in trachea and bronchi $\Rightarrow$ deep paroxysmal coughs (brain and eye hemorrhage)

3. **Convalescence stage** can last for months

Laboratory diagnosis based on isolation of bacteria on enrichment and selective media, followed by serological tests
19.4 Microbial Diseases of the Lower Respiratory System

Bacteria, viruses, and fungi cause

- Bronchitis
- Bronchiolitis
- Pneumonia

What keeps LRS relatively sparsely colonized?
Tuberculosis - Consumption

- *Mycobacterium tuberculosis*: Aerosol transmission

- *M. bovis*: <1% U.S. cases, usually extrapulmonary, affecting bones or lymphatic system (Pott disease)

- *M. avium-intracellulare* complex in late stage AIDS

- All Mycobacteria resistant to drying and disinfectants

- **BCG vaccine**: live, attenuated *M. bovis*

- Diagnostic gold standard is still **Acid Fast Stain**
**Tuberculin Sensitivity (Mantoux) test:** Inject PPD, wait for delayed hypersensitivity reaction (problem: BCG vaccination!)

Diagnostic tool for presymptomatic tuberculosis

PPD (taken from dead TB bacteria) is injected into the area

Purified protein derivative

induration
TB blood test as an alternative to Mantoux test: Interferon Gamma Release Assay or IGRA

Two types of TB blood tests:

• QuantiFERON®-TB
• T-SPOT®.TB
TB Pathogenesis

- *M. tuberculosis* can reproduce in **MΦ**
- Lesions formed = tubercles (granulomas)
- **Caseous lesions** of Neutrophils, dead tissue cells, dead **MΦ** and bacteria
  - Bacterial growth arrested $\Rightarrow$ tubercle calcifies (Ghon’s complex)
  - Bacteria still grow $\Rightarrow$ caseous lesion becomes **liquid** $\Rightarrow$ tuberculous cavity in which *M. tuberculosis* can grow
- If caseous lesions rupture $\Rightarrow$ bacteria released into blood or lymph vessels $\Rightarrow$ miliary tuberculosis

*Review Fig 24.9*
Miliary tuberculosis due to massive lymphhaematogeneous dissemination. Due to impaired CMI ⇒ potentially lethal. Weight loss, coughing of blood, loss of vigor

3 or 4 drugs taken for at least 6 months
MDR-TB becoming prevalent!
Globally, nearly 9 million new TB cases and approximately 1.5 million TB-related deaths each year.

**MDR-TB** (as high as 20%) resistance to rifampin and isoniazid

**XDR-TB** resistant to two additional drugs
Typical Pneumonia: Pneumococcal Pneumonia

- Encapsulated *S. pneumoniae*
- Can be identified by production of $\alpha$-hemolysis and through serological tests
- Droplet transmission. Asymptomatic carriers $\rightarrow$ illness in case of immune suppression, smoking, viral infection *etc.*
- Symptoms: fever, breathing difficulty, chest pain, rust-colored sputum
- Predominant in elderly
- Penicillin, but MDROs increasing
- **Vaccine** for 23 most common strains (> 90 strains)
Chest x-ray of Pneumococcal Pneumonia
Legionellosis or Legionnaires’ disease

- *Legionella pneumophila*, Gram−rod
- Discovered among a group of elderly men attending an American Legion Convention in Philadelphia (1976)
- Grow in water (pools, lakes, water systems of buildings, air conditioning units, etc.), then disseminated in air

- Transmission by inhaling aerosols; **no person to person transmission**
- Diagnosis: Bacterial culture (selective charcoal-yeast extract medium, FA tests, DNA probes)
- Pneumonia and pleurisy (15−20% mortality rate when hospitalized)
Mycoplasmal Pneumonia – also known as Primary Atypical Pneumonia or Walking Pneumonia

- *Mycoplasma pneumoniae*, pleomorphic, wall-less
- Produce small “fried-egg” colonies after two weeks’ incubation on enriched media containing horse serum and yeast extract
- Common in children and young adults – often mild enough to go undiagnosed for long periods of time
- Diagnosis: PCR or serological tests (IgM antibodies)
Hantavirus Pulmonary Syndrome (HPS)

Korean hemorrhagic fever caused by Hantaan virus of *Bunyaviridae*

HPS first reported in US in spring of 1993.

Transmission through urine, droppings, or saliva of infected rodents → humans inhale aerosolized virus. No person to person transmission in US

Sudden respiratory failure

Mortality rate > 35%

2012 Yosemite
Hantavirus Pulmonary Syndrome (HPS) Cases, by State of Residence
Cumulative Case Count Per State Valid as of January 8, 2016
Fungal Diseases of the Lower Respiratory System (LRS)

- Fungal spores are easily inhaled; they may germinate in the lower respiratory tract
- The incidence of fungal diseases has been increasing in recent years
- Mycoses in the sections below can be treated with amphotericin B
  - *Coccidioidomycosis* (see meningitis p.475)
  - *Pneumocystis Pneumonia*
Coccidioidomycosis = Valley Fever

- *Coccidioides immitis*, dimorphic
- Airborne transmission in endemic areas
- Most cases subclinical, some respiratory infection with flu-like symptoms
- In < 1% of cases (due to predisposing factors, such as fatigue, poor nutrition, *etc.*): progressive, disseminated disease resembling TB; also meningitis (p. 475)
- Diagnosis: serological tests
- 97% of reported cases are from California and Arizona
Pneumocystis Pneumonia (PCP)

*Pneumocystis jiroveci* (previously *P. carinii*)

tiny fungus

Commonly found in nature, in healthy human lungs and animals → Aerosol transmission

Illness and death in newly infected infants and immuno-suppressed individuals

Used to be leading cause of death in AIDS patients – now preventive special antifungal therapy

Diagnosis: detection of cysts in sputum samples
Healthcare-Associated Pneumonia (HAP)

In up to 1% of hospitalized or institutionalized people due to abnormal breathing and aspiration:

– Common in stroke victims
– Mortality rate: 30 – 50%
– Most frequent causes:
  • *Pseudomonas aeruginosa*
  • *Streptococcus pneumoniae*
  • *Klebsiella pneumoniae*
  • *S. aureus*: HAP caused by MRSA
  • Many are polymicrobial