Infectious Diseases Affecting the Respiratory System
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
Anatomy of the respiratory tract.

Fig. 21.1 The respiratory tract.
Structure of the Respiratory System

• Normal Microbiota of the Respiratory System
  – Lower respiratory system
    • Typically microorganisms are not present
  – Upper respiratory system
    • Colonized by many microorganisms
    • Normal microbiota limit growth of pathogens
    • Normal microbiota may be opportunistic pathogens
Protection

- Nasal hair
- Cilia
- Bronchi
- Mucus
- Involuntary responses (coughing, etc.)
- Immune cells
Diseases

- Upper Respiratory tract
- Both Upper and lower tract
- Lower Respiratory tract
Upper respiratory tract

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

• Viral infection
  – Over 200 viruses are involved
• Rhinitis
• Prevalent among human population
• Prone to secondary bacterial infections
• No vaccine
• No chemotherapeutic agents
• Costly
Common cold

• Caused by a Rhinovirus
• Headache, runny nose, muscle pain.
• Transmitted by respiratory droplets.
• Rx – supportive therapy, fluids, rest, chicken soup.
• Wash your hands!!! Zycam, Zinc.
Figure 22.4  Rhinoviruses, the most common cause of colds
Features of rhinitis.

### Checkpoint 21.1 Rhinitis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causative Organism(s)</strong></td>
<td>200-plus viruses</td>
</tr>
<tr>
<td><strong>Most Common Modes of Transmission</strong></td>
<td>Indirect contact, droplet contact</td>
</tr>
<tr>
<td><strong>Virulence Factors</strong></td>
<td>Adhesins; most symptoms induced by host response</td>
</tr>
<tr>
<td><strong>Culture/Diagnosis</strong></td>
<td>Not necessary</td>
</tr>
<tr>
<td><strong>Prevention</strong></td>
<td>Hygiene practices</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>For symptoms only</td>
</tr>
</tbody>
</table>
Sinusitis

- Bacterial infection
- Viral infections
- Rare fungal infection
- Inflammation of the sinuses
- Noninfectious allergies are primary cause of most sinus infections
Features of sinusitis.

<table>
<thead>
<tr>
<th>CHECKPOINT 21.2 Sinusitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative Organism(s)</td>
</tr>
<tr>
<td>Most Common Modes of Transmission</td>
</tr>
<tr>
<td>Virulence Factors</td>
</tr>
<tr>
<td>Culture/Diagnosis</td>
</tr>
<tr>
<td>Prevention</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Distinctive Features</td>
</tr>
</tbody>
</table>

Checkpoint 21.2 Sinusitis
Ear infection

• Bacterial infection
• Acute otitis media
• 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.

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

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

- Group A is virulent
- Streptolysins - toxin (hemolysins)
- Erythrogenic – toxin
- Toxins can act as superantigens
  - Overstimulate T cells
    - Tumor necrosis factor
Scarlet fever

- *S. pyogenes* is infected with a bacteriophage
  - Erythrogenic toxin - rash
- Sandpaper-like rash
  - Neck, chest, elbows, inner thighs
- Children are at risk
Rheumatic fever

- M protein
- Immunological cross-reaction (molecular mimicry)
- Damage heart valves
- Arthritis, nodules over bony surfaces
*Streptococcus* infection causing inflammation of the throat and tonsils.

Fig. 21.3 The appearance of the throat in pharyngitis and Tonsilitis.
Group A streptococcal infections can damage the heart valves due to cross-reactions of bacterial-induced antibodies and heart proteins.

Fig. 21.4 The cardiac complications of rheumatic fever.
The surface antigens of group A streptococcus serve as virulence factors.
## Checkpoint 21.4 Pharyngitis

<table>
<thead>
<tr>
<th>Features of pharyngitis.</th>
</tr>
</thead>
</table>

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

- Bacterial infection
- Vaccine
- Membrane formation on tonsils or pharynx
- A-B toxin
*Corynebacterium diphtheriae*, the causative agent of diphtheriae, has a unique club-shape appearance.

Fig. 21.8 *Corynebacterium diphtheriae*
Inflamed pharynx and tonsils marked by a grayish pseudomembrane formed by the bacteria are characteristic signs of diphtheria.

Fig. 21.9 Diagnosing diphtheria
The mechanism of the A-B toxin of *Corynebacterium diphtheriae*.

- *C. diptheriae* produces diphtheria toxin. Prevents polypeptide synthesis and causes cell death.

Fig. 21.10 A-B toxin of Corynbackterium diphtheriae
Diptheria

- *Corynebacterium diphtheriae* (Lysogenized)

- Respiratory droplets, exotoxin creates a tough, leathery gray pseudo membrane over throat and can cause choking. Swelling of neck.

- Rx – antibiotics and anti toxin. Vaccine DPT
Features of diphtheria.

### CHECKPOINT 21.5 Diphtheria

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

- Narrows the airway at and below the vocal cords. Parainfluenza virus.
- Toddler develops loud barking cough, with mucus accumulation. Usually in the fall.
- Transmitted by respiratory droplets
- No effective antivirals, or vaccines. Rx is supportive care, humidifier to ease congestion
- Can be a recurring infection
Upper and lower respiratory tract

- Whooping cough
- Influenza
Pertussis—whooping cough

- *Bordetella pertussis*, adheres to cilia and kills it. Characteristic whooping sound at end of cough.

- Catarrhal stage – common cold like

- Paroxysmal stage – severe bouts of extreme coughing. Lasts 1-6 weeks. Broken ribs, convalescence, highly infectious.

- Rx – antibiotics, DPT vaccine.

- Most common in unvaccinated babies under 1 year
Whooping cough

- Bacterial infection
- Pertussis
- Vaccine
- Catarrhal stage – cold symptoms
- Paroxysmal stage – severe coughing
- Convalescent phase - damage cilia
- Toxins
  - A-B toxin, tracheal cytotoxin
Features of whooping cough.

<table>
<thead>
<tr>
<th><strong>CHECKPOINT 21.6</strong></th>
<th>Pertussis (Whooping Cough)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative Organism(s)</td>
<td><em>Bordetella pertussis</em></td>
</tr>
<tr>
<td>Most Common Modes</td>
<td>Droplet contact</td>
</tr>
<tr>
<td>of Transmission</td>
<td></td>
</tr>
<tr>
<td>Virulence Factors</td>
<td>FHA (adhesion), pertussis toxin and tracheal cytotoxin, endotoxin</td>
</tr>
<tr>
<td>Culture/Diagnosis</td>
<td>Grown on B-G, charcoal or potato-glycerol agar; diagnosis can be made on symptoms</td>
</tr>
<tr>
<td>Prevention</td>
<td>Acellular vaccine (DTaP), erythromycin or trimethoprim; sulfamethoxazole for contacts</td>
</tr>
<tr>
<td>Treatment</td>
<td>Mainly supportive; erythromycin to decrease communicability</td>
</tr>
</tbody>
</table>
Figure 22.11 A scene from the flu pandemic of 1918-19
Influenza

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

Fig. 21.12 Schematic drawing of hemagglutinin of 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.
Figure 22.13 The development of new strains of flu viruses—overview

(a) Antigenic Drift

1. Influenza-virus 1 enters host cell.
2. Mutations in antigen genes occur during replication within host cell.
3. Influenza-virus 1', differing slightly from virus 1, exits cell.

(b) Antigenic Shift

1. Influenza-viruses 1 and 2 enter host cell.
2. Genes and antigens from both viral types are incorporated into new virions.
3. Influenza-virus 3, which is very different from viruses 1 and 2, exits cell.

Graphs:

- Biennial outbreaks of mild influenza
- Occasional outbreaks of very severe influenza
### Features of influenza.

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

**Checkpoint 21.8 Influenza**
Lower respiratory tract

- Tuberculosis
- Pneumonia
Tuberculosis

• Bacterial infection
  – *Mycobacterium tuberculosis*
  – *Mycobacterium avian*
    • Disseminated tuberculosis that affects AIDS patients

• Types
  – Primary
  – Secondary
  – Disseminated
**M. tuberculosis**

- Slow growing (generation time 15-20 hrs)
- Mycolytic acid and waxy surface
- Primary
  - Tubercles, caseous, tuberculin reaction
- Secondary (reactivation)
  - Consumption
- Dissemination
  - Extrapulmonary TB (lymph nodes, kidneys, bones, genital tract, brain, meninges)
Figure 22.9  The processes involved in the development of tuberculosis in the lungs—overview
Tuberculosis

- Mycobacterium tuberculosis very resistant, and hardy.

Respiratory droplets

- Bacteria inhaled and are phagocytized by macrophages, survive and multiply.
- Calcify into “Gohn complexes”
- Fever night sweats, fatigue, cough up blood, weight loss.
- Rx – long term treatment 1+ years of antibiotics
• Tuberculosis
  – Epidemiology
    • Immunocompromised individuals are most at risk
    • Tuberculosis is leading killer of HIV+ individuals
  – Diagnosis, treatment, and prevention
    • Tuberculin skin test identifies exposure to tuberculosis
    • Chest X-rays can identify tubercles in the lungs
    • Treatment requires combination of drugs
    • Drug-resistant strains of *M. tuberculosis* have emerged
    • BCG vaccine available where tuberculosis is common
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.
The tuberculin reaction enables skin testing for tuberculosis.

Fig. 21.15 Skin testing for tuberculosis.
Figure 22.10 Diagnosis of tuberculosis-overview
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.
Features of tuberculosis.

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

Checkpoint 21.9 Tuberculosis
Bacterial Diseases of the Lower Respiratory System

• Inhalational Anthrax
  – Signs and symptoms
    • Initially resembles a cold or flu
    • Progresses to severe coughing, lethargy, shock, and death
  – Pathogen and virulence factors
    • *Bacillus anthracis* is the causative agent
    • Virulence factors include a capsule and anthrax toxin
  – Pathogenesis and epidemiology
    • Anthrax not spread from person to person
    • Acquired by contact or inhalation of endospores
Pneumonia

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

http://www.msnbc.msn.com/id/34045311/ns/health-infectious_diseases
Bacterial Diseases of the Lower Respiratory System

• Bacterial Pneumonias
  – Lung inflammation accompanied by fluid-filled alveoli and bronchioles
  – Described by affected region or organism causing the disease
  – Bacterial pneumonias are the most serious and the most frequent in adults
Bacterial pneumonia

- *Streptococcus pneumoniae*
- *Legionella*
- *Mycoplasma pneumoniae*
Streptococcus pneumonia

- 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
Pneumococcal pneumonia

- Streptococcus pneumoniae
- Spread by respiratory droplets
- Fever, painful breathing, rusty colored sputum, chills
- Rx – pneumovax, penicillin, other antibiotics.
Pneumonia
Gram staining reveals unique pairing, and blood agar cultures shows alpha-hemolysis, which are characteristic of *S. pneumoniae*.

Fig. 21.20 *Streptococcus pneumoniae*
Figure 22.5 *Streptococcus pneumoniae*, the most common cause of bacterial pneumonia.
Consolidation is when the bronchioles and alveoli are blocked by inflammatory cells and exudate formation.

Fig. 21.21 The course of bacterial pneumonia.
Legionella

- Less common but still a serious infection
- Survives in natural habitat (tap water, cooling towers, spas, etc.)
- Opportunistic disease
*Legionella* is an intracellular organism that can live in amoebas and in human phagocytes.

Fig. 21.22 Legionella living intracellular
Legionellosis

- *Legionella pneumophilia*

- Inhaling contaminated water droplets.

- Weakness, headache, cough, fever, chills. Life threatening in weakened, or elderly patients, smokers, drinkers.

- Detection – can be cultured on buffered charcoal yeast extract agar.

- Rx- erythromycin (resistant to penicillin and cephalosporin)

- Outbreak at Foreign Legion convention (July 1976, 182 people 29 dead.) 6 months. Stains poorly, fastidious.
Mycoplasma pneumoniae

- Smallest known bacteria
- No cell wall
- Walking pneumonia – atypical pneumonia
Primary Atypical (Mycoplasmal) Pneumonia

- Signs and symptoms
  - Include fever, malaise, sore throat, excessive sweating
- Pathogen and virulence factors
  - Caused by Mycoplasma pneumoniae
  - Virulence factors include an adhesion protein
- Epidemiology
  - Bacteria spread by nasal secretions
- Diagnosis, treatment, and prevention
  - Treated with tetracycline and erythromycin
  - Prevention difficult since infected individuals may be asymptomatic
Figure 22.6  Pleomorphic forms of *Mycoplasma*
Viral infection

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

- Emerging disease
- Acute respiratory distress syndrome
  - Hantavirus antigen become disseminated throughout the blood stream
  - Loss of fluid from blood vessels
The number of hantavirus cases is increasing in the western part of the U.S.

Fig. 21.23 Hantavirus pulmonary syndrome cases.
SARS

• 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
Histoplasmosis

- Fungal disease: *Histoplasma capsulatum*
- Transmission by inhalation associated with bird or bat droppings (mold grows here)
- Weak, mild fever, chest pain cough.
- Mimics tuberculosis, but test shows negative.
Features of pneumonia caused by bacteria, virus, and fungi.

<table>
<thead>
<tr>
<th>CHECKPOINT 21.10 Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causative Organism(s)</strong></td>
</tr>
<tr>
<td><strong>Most Common Modes of Transmission</strong></td>
</tr>
<tr>
<td><strong>Virulence Factors</strong></td>
</tr>
<tr>
<td><strong>Culture/Diagnosis</strong></td>
</tr>
<tr>
<td><strong>Prevention</strong></td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td><strong>Distinctive Features</strong></td>
</tr>
</tbody>
</table>

Checkpoint 21.10 Pneumonia
Nosocomial pneumonia

- Multiple bacterial species
- Pneumonia acquired by patients in hospitals and other health care residential facilities
- Second most common nosocomial infection
Infectious Diseases Affecting the Respiratory System.