CHAPTER 24 - Microbial Diseases of the Respiratory System

Introduction

- Infections of the upper respiratory system are the most common type of human infection.
- Pathogens that enter the respiratory system may infect other parts of the body by hematogenous spread (Ex: septicemia, meningitis, distant focal infection).

I. Structure and Function of the Respiratory System

A. The upper respiratory system consists of the nose, pharynx, and associated structures, such as the middle ear and auditory tubes.
B. Coarse hairs in the nose filter large particles from air entering the respiratory tract.
C. The ciliated mucous membranes of the nose and upper respiratory system trap airborne particles and remove them from the body.
D. Lymphoid tissue, tonsils, and adenoids provide immunity to certain infections.
E. The ciliary escalator of the lower respiratory system helps prevent microorganisms from reaching the lungs.
F. The lower respiratory system consists of the larynx, trachea, bronchial tubes, and alveoli.
G. Microbes in the lungs can be phagocytized by alveolar macrophages.
H. Respiratory mucus contains IgA antibodies.

II. Normal Microbiota of the Respiratory System

A. The normal microbiota of the nasal cavity and throat can include pathogenic microorganisms in a carrier status.
B. Don’t cause disease because of competition with predominant microorganisms.
C. The lower respiratory system is usually sterile because of the action of the ciliary escalator.

III. Microbial Diseases of the Upper Respiratory System

- Specific areas of the upper respiratory system can become infected to produce pharyngitis, laryngitis, tonsillitis, sinusitis, and epiglottitis.
- Pharyngitis – sore throat
- Laryngitis – infected larynx
- Tonsillitis – inflamed tonsils
- Sinusitis – infected sinus
• *Epiglottitis* – inflammation of the flap like structures of cartilage that prevents swallowed material from entering the larynx – possible life-threatening when inflamed and occludes airway. *H. influenzae* type b can cause epiglottitis.
• These infections may be caused by several bacteria and viruses, often in combination.
• Most respiratory tract infections are self-limiting.

A. **Streptococcal Pharyngitis (Strep Throat)**

1. This infection is caused by group A β-hemolytic streptococci, the group that consists of the species *Streptococcus pyogenes*.
2. Symptoms of this infection are inflammation of the mucous membrane and fever, tonsillitis, and otitis media may also occur. At least half of pharyngitis cases are caused by viruses.
3. Preliminary rapid clinic diagnosis is made by indirect agglutination tests or next day culture in the micro lab. Definitive diagnosis is based on a rise in IgM antibodies.
4. Penicillin is used to treat streptococcal pharyngitis.
5. Immunity to streptococcal infections is type-specific.
6. Strep throat is usually transmitted by droplets but at one time was commonly associated with unpasteurized milk.

B. **Scarlet Fever**

1. Strep throat, caused by an erythrogenic toxin-producing *S. pyogenes*, results in scarlet fever.
2. *S. pyogenes* produces erythrogenic toxin (M protein) when lysogenized by a phage.
3. *Means Strep A has to have a bacterial phage carrying the toxin gene.*
4. Symptoms include a red rash, high fever, and a red, enlarged tongue, peeled skin. Death is a possible outcome.

C. **Diphtheria - Corynebacterium diphtheriae**

1. Diphtheria is caused by exotoxin-producing *Corynebacterium diphtheriae*.
2. *Gram positive non-spore forming pleomorphic rod. Dividing cells often fold into V and Y shapes.*
3. Exotoxin is produced when the bacteria are lysogenized by a phage.
4. *Many well people are symptomless carriers.*
5. A membrane, containing fibrin and dead human and bacterial cells, forms in the throat and can block the passage of air. *“diphtheria” means leather*
6. The exotoxin inhibits protein synthesis, and heart, kidney, or nerve damage may result.
7. Laboratory diagnosis is based on isolation of the bacteria and the appearance of
growth on differential media.
8. Antitoxin must be administered to neutralize the toxin, and antibiotics can stop
growth of the bacteria.
9. Routine immunization in the U.S. includes diphtheria toxoid in the DTaP vaccine.
Prior to this diphtheria was the leading killer of children.
10. Slow-healing skin ulcerations are characteristic of cutaneous diphtheria.
    a) Cutaneous diphtheria characterized by skin lesions is fairly common in
tropical countries. In US affects mainly lower socio economic groups.
    b) There is minimal dissemination of the exotoxin in the bloodstream.

D. Otitis Media: an uncomfortable infections of the middle ear.

1. Earache, or otitis media, can occur as a complication of nose and throat
   infections.
2. Pus accumulation causes pressure on the eardrum. 8 million cases/yr.
3. Bacterial causes include Streptococcus pneumoniae, Hemophilus influenzae,
   Moraxella (Branhamella) catarrhalis, Streptococcus pyogenes, and
   Staphylococcus aureus.

IV. Viral Disease of the Upper Respiratory System

A. The Common Cold - rhinoviruses (50%), corona viruses (15-20%)

Any one of approximately 200 different viruses can cause the common cold; rhinoviruses cause about 50% of all colds.
1. Symptoms include sneezing, nasal secretions, and congestion.
2. Sinus infections, lower respiratory tract infections, laryngitis, and otitis media
can occur as complications of a cold. Usually no fever in uncomplicated cases.
3. Colds are most often transmitted by indirect contact.
4. Rhinoviruses prefer temperatures slightly lower than body temperature.

5. The incidence of colds increases during cold weather, possibly because of
   increased interpersonal indoor contact or physiological changes.
6. Antibodies are produced against the specific viruses.

Microbial Diseases of the Lower Respiratory System

V. Anatomy & Collection of Specimen from Lower Respiratory System
VI. Bacterial Diseases of the Lower Respiratory System

- Many of the same microorganisms that infect the upper respiratory system also infect the lower respiratory system.
- Diseases of the lower respiratory system include bronchitis and pneumonia.
- *Pneumonia is a term applied to severe complications of bronchitis with the alveoli involved.*

A. Pertussis (Whooping Cough) - *Bordetella pertussis*
1. Pertussis is caused by *Bordetella pertussis*, a Gram –itive coccal bacillus
2. The initial stage of pertussis resembles a cold and is called the catarrhal stage.
3. The accumulation of mucus in the trachea and bronchi causes deep coughs characteristic of the paroxysmal (second) stage.
4. Trying to clear mucous leads to violent coughing with gasping (whooping) for breaths. Ciliary action is blocked by accumulation of dense masses of these bacteria in the trachea and bronchi.
5. The convalescence (third) stage can last for months.
6. Laboratory diagnosis is based on isolation of the bacteria on enrichment and selective media (or PCR), followed by serological tests.
7. Have to collect specimen with thin wire with a special swab. See slide below.
8. Regular immunization for children has decreased the incidence of pertussis. The acellular vaccine has minimal side effects vs. the whole cell.

B. Tuberculosis - *Mycobacterium tuberculosis*.
1. Tuberculosis is caused by *Mycobacterium tuberculosis*, a slow growing acid-fast bacillus
2. Large amounts of lipids in the cell wall account for the bacterium’s acid-fast characteristic as well as its resistance to drying and disinfectants.
3. *M. tuberculosis* may be ingested by alveolar macrophages. If not killed, the bacteria reproduce in the macrophages. Resistant to phagocytosis.
4. Lesions formed by *M. tuberculosis* are called tubercles; dead macrophages and bacteria form the caseous lesion that might calcify and appear in an X ray as a Ghon complex. Ghon complex means calcified caseous lesions. *Caused by hypersensitivity reaction.*
5. Liquefaction of the caseous lesion results in a tuberculous cavity in which *M. tuberculosis* can grow.
6. New foci of infection can develop when a caseous lesion ruptures and releases bacteria into blood or lymph vessels; this is called miliary tuberculosis.
7. Miliary (characterized by lesions resembling millet seeds) tuberculosis is characterized by weight loss, coughing, and loss of vigor.
8. Chemotherapy usually involves two drugs taken for 1-2 years; multidrug-resistant *M. tuberculosis* is becoming prevalent. DOT therapy.

9. Drugs are Streptomycin, rifampin, isoniazid (INH) and ethanbutol.

10. *Intracellular growth shields TB from antibiotics.*

11. Stress and genetic differences contribute to susceptibility.

12. A positive tuberculin skin test can indicate either an active case of TB, or prior infection, or vaccination and immunity to the disease.

13. Sensitized T-cells are present at site of infection or skin test.

14. Laboratory diagnosis is based on the presence of acid-fast bacilli and isolation of the bacteria, which requires incubation of up to 8 weeks.

15. *Mycobacterium bovis* causes bovine tuberculosis and can be transmitted to humans by unpasteurized milk.
   a) *M. bovis infections usually affect the bones or lymphatic system.*
   b) BCG vaccine for tuberculosis consists of a live, avirulent culture of *M. bovis.*
      *Useful if given early in childhood. Mainly outside of US>*

16. *M. avium-intracellulare* complex infects patients in the late stages of HIV infection.

C. Bacterial Pneumonias-

1. *Streptococcus pneumoniae*
   a) *Pneumococcal pneumonia is caused by encapsulated Streptococcus pneumoniae.*
   b) *Symptoms are fever, breathing difficulty, chest pain, and rust-colored sputum.*
   c) *The bacteria can be identified by the production of alpha-hemolysins, inhibition by optochin, bile solubility, and through serological tests.*
   d) *A vaccine consists of purified capsular material from 23 serotypes of S. pneumoniae.*

2. *Hemophilus influenzae*
   a) Alcoholism, poor nutrition, cancer, and diabetes are predisposing factors for *H. influenzae pneumonia.*
   b) *H. influenzae is a small gram-negative coccobacillus.*

3. *Mycoplasmal Pneumonia - Mycoplasma pneumoniae*
   a) *Mycoplasmal pneumonia is common in children and young adults; as many as 20% of cases. Lowgrade fever, cough of long 2-3 weeks duration.*
   b) *Organism has no cell wall so is difficult to grow so presents like a viral infection.*
   c) Described as “atypical” or “walking pneumonia”.
   d) *M. pneumoniae produces small fried-egg colonies after 2 weeks’ incubation on enriched media containing horse serum and yeast extract.*
e) A complement-fixation test, used to diagnose the disease, is based on the rising of antibody titer.

f) Treated with tetracyclines.

D. Legionellosis - *Legionella pneumophila*

1. The disease is caused by the aerobic gram-negative rod *Legionella pneumophila*.
2. Legionnaires Disease due to 1976 outbreak of the American Legion meeting.
3. The bacterium can grow in water, such as air-conditioning cooling towers, slow plumbing, and then be disseminated in the air.
4. This pneumonia does not appear to be transmitted from person to person. High fever, cough, general symptoms of pneumonia.
5. Bacterial culture, FA tests, and DNA probes are used for laboratory diagnosis.
6. Treated with Erythromycin and Rifampin

E. Psittacosis (Ornithosis) *Chlamydia psittaci*

1. Chlamydia psittaci is transmitted by contact with contaminated droppings and exudates of fowl.
2. Psittacine birds such as parakeets and parrots but other birds are infected too.
3. Are obligate intracellular parasites but have an elementary body stage that allows the bacteria to survive outside a host.
4. Commercial bird handlers are most susceptible to this disease.
5. The bacteria are isolated in embryonated eggs, mice, or cell culture; identification is based on FA staining. Treated with tetracycline.

F. Other Bacterial Pneumonias

1. Gram-positive bacteria that cause pneumonia include *Staph aureus* and *Strep pyogenes*.
2. Gram-negative bacteria that cause pneumonia include *Moraxella (B.) catarrhalis*, *Klebsiella pneumoniae*, and *Pseudomonas species*.

VII. Viral Diseases of the Lower Respiratory System

A. Viral Pneumonia

1. A number of viruses can cause pneumonia as a complication of infections such as influenza.
2. The etiologies are not usually identified in a clinical laboratory because of the difficulty in isolating and identifying viruses.
B. Respiratory Syncytial Virus (RSV)

1. RSV is the most common cause of pneumonia in infants with 110K hospitalizations and 4500 deaths in US. Epidemics in winter/early spring. Fever and wheezing.
2. Rapid testing using serology.
3. Ribavirin may be given in aerosol to diminish symptoms.

C. Influenza (Flu) Influenza virus

1. Influenza is caused by influenza virus and is characterized by chills, fever, headache, and general muscular aches.
2. Hemagglutinin (H) and neuraminidase (N) spikes project from the outer lipid bilayer of the virus.
3. Viral strains are identified by antigenic differences in the H and N spikes; they are also divided by antigenic differences in their protein coats (A, B, and C).
4. Viral isolates are identified by hemagglutination-inhibition tests and immunofluorescence testing with monoclonal antibodies.
5. Antigenic shifts that alter the antigenic nature of the H and N spikes make natural immunity and vaccination of questionable value and may lead to pandemics. Minor antigenic changes are caused by antigenic drift and are covered by vaccines.
6. Deaths during an influenza epidemic are usually from secondary bacterial infections.
7. Multivalent vaccines are available for the elderly and other high-risk groups that are 70-90% effective for no more than 3 years for that strain.
8. Amantadine and rimantadine given early, reduce symptoms against A-type Influenzavirus. Also zanamivir Relenza and oseltamivir (Tamiflu).

VIII. Fungal Diseases of the Lower Respiratory System

1. Fungal spores are easily inhaled; they may germinate in the lower respiratory tract.
2. The incidence of fungal diseases has been increasing in recent years.
3. The mycoses below can be treated with amphotericin B.

A. Coccidioidomycosis: San Joaquin Valley Fever

1. Inhalation of the airborne arthrospores of Coccidioides immitis can result in coccidioidomycosis, typically limited minor a lung infection. Found dry soils of SW US.
2. Most cases are subclinical with about 1% of cases progressing to a TB like course of illness. Predisposing factors such as fatigue and poor nutrition, older age, HIV may lead to disseminated disease.
3. See dimorphic forms in tissue: spherules with endospores.
4. Same treatment as Histo using fluconazole (dilucan), ketoconazole, and itraconazole. Sometimes use Amphotericin B to treat serious cases but it is very toxic.

B. Pneumocystis Pneumonia - Pneumocystis jiroveci (carinii)

1. *Pneumocystis jiroveci*, currently classified as a fungus, is found in healthy human lungs. Taxonomy in question but probably related to yeasts.
2. *Pneumocytis carinii* causes disease in immunosuppressed patients. Transmitted by direct contact. Causes alveoli to become filled with a frothy exudate.
3. Common in AIDS patients or other immunosuppressed conditions (cancer, transplant pts). Untreated infections maybe lethal in these cases.
4. *Pneumocytis* pneumonia is currently being treated with trimethoprim or pentamidine.