Chapter 17: Pnuemonia in the Immunocompromised Patient
Objectives

- Define opportunistic infections
- Describe the structure and function of the immune system
- List the common causes of immunosuppression
- List the typical signs and symptoms of opportunistic pulmonary infections
- Describe the treatment of pneumonia in the immunosuppressed patient
- Describe the prophylactic treatment of patients with immunodeficiencies
**Introduction**

- Large pulmonary surface area is exposed to inhaled gases that contain microorganisms
- Less aggressive microorganisms can cause serious pulmonary infection if immune system is damaged
- Infections caused by organisms that don’t usually affect people with healthy immune system are called **opportunistic infections**
- Immune defects
  - Congenital (primary)
    - Not common and can be difficult to diagnose and treat
  - Acquired (secondary)
    - Chemotherapy, AIDS, radiation, malnutrition
Etiology

Basic Function of the Immune System

- Complex group of defense mechanisms
- Immunity has three principles characteristics
  1. Ability to differentiate self from non-self
     - Recognition and targeting of antigens
  2. Specificity
  3. Memory
     - Basis of vaccinations
The Immune System

- Immune cells scattered throughout the body
- Circulate to areas as needed
- Types of cells
  - Lymphocytes
    - T – helper cells and suppressor cells
    - B – cells; antibody-secreting cells (plasma cells)
  - Monocytes
The Immune System

- Immunoglobulins (Ig: G, M, E, A, D)
  - IgM usually the first at onset of infection
  - IgG primary antibody fighting infection
  - IgA produced at tissues adjacent to mucus membranes
  - IgE mediate allergic reactions
The Immune System

- Lymphocytes T
  - Killer: direct cytotoxic effect on target
  - Helper: promotes development of antibodies by lymphocytes B
    - Have the CD4+ antigen on their surface
    - Significant in cell-mediated immunity
    - Responsible for defense against M. tuberculosis
    - The reaction of the cell-mediated immunity to an antigen is called delayed hypersensitivity
  - Suppressor: inhibit immune response
    - Have the CD8+ antigen on their surface
Monocytes circulate in the blood migrate into the tissue to become macrophages
- Play a critical role in the immune system
- Macrophages use phagocytosis to destroy foreign material
The Immune System

- **Granulocytes** (polymorphonuclears PMNs)
  - Formed in the bone marrow
  - Neutrophils
    - Most common PMN
    - Detect and kill invading microorganisms
    - Major constituent of pus
  - Eosinophils
  - Basophils
**Cell Type**

- **B Lymphocyte**
- **T Lymphocyte**

**Function**

- **Plasma Cell**
  - IgG, IgM, IgD: Attach to foreign antigens
  - IgA: Protects mucous membranes
  - IgE: Mediate allergic responses

- **Helper Lymphocyte**
  - Promote most immune functions, critical for cell-mediated immunity

- **Suppressor Lymphocyte**
  - Modulates the immune response by inhibiting immune reactions

- **Natural Killer Cell**
  - Has a direct cytotoxic on cells

- **Granulocyte**
  - Phagocytose invading organisms

- **Monocyte**
  - Phagocytose foreign material, then activate other immune systems
Antibody Deficiency

- Inadequate level of antibodies increase a pt’s suitability to infection
- Infections are more frequent and severe than in normal subjects
- S. Pneumoniae, H. Influenzae
Pathophysiology

- **X-linked agammaglobulinemia**
  - Most severe
  - Starts 6–9 months after birth

- **IgA deficiency**
  - Most common Ig deficiency
  - Recurrent pulmonary infections
Defects in Cellular Immunity

- **T lymphocytes**
- Body’s defense against intracellular pathogens e.g. *M. tuberculosis*
- Another cell-mediated response is cytotoxicity
  - Activated when antigens are recognized
- AIDS is by far the most common acquired defect of cell-mediated immunity
Pathophysiology

Defects in Phagocyte Function

- A significant decrease in phagocytic cells = overwhelming bacterial infections
- Neutropenia (< 500/dL)
  - Congenital
  - Acquired
    - Chemotherapy
    - Overwhelming infection (infection develop during granulocytopenia)
Clinical Features

History

- Suspect opportunistic pneumonia if
  - Recurrent sessions of pneumonia
  - Pneumonia that does not resolve with tx
- Identify risk factors
Clinical Features

Physical Exam
- Similar to common pneumonias
  - Cough, dyspnea, fever
- Pyogenic pneumonias
- Pleuritic chest pain, purulent sputum, hemoptysis, malaise, recent weight loss
- Localized or diffuse crackles
Clinical Features

Chest Radiograph

- Diffuse densities
- Pneumocystis pneumonia
  - Ground-glass appearance
  - If normal = gallium scan or DLCO
- Tuberculosis
  - Upper lobe cavitating densities
Clinical Features

Microbiology

- Gram stain and acid-fast stain
- Culture and microscopic evaluation of sputum
  - Bacteria, acid-fast bacilli, fungi
  - Stain for pneumocystis jivoreci if defect in cell-mediated immunity
- Bronchoscopy with BAL or transbronchial biopsy if induction of sputum fails
Specific Immune Syndromes

Acquired Immunodeficiency S.

- HIV
  - Slowly progressive loss of cell-mediated immunity
  - Infects cells with CD4+ antigen
  - Compromise when helper cells are < 600/µL (normal: 800–1200/µL)
  - Most common opportunistic infections include P. jivoreci, M. avium, Candida albicans
Acquired Immunodeficiency S.

- AIDS
  - Fever, chills, malaise, weight loss
  - Lymphadenopathy
  - Productive cough, pleuritic chest pain
  - Oral thrush
  - Mortality for all cases with pneumocystis pneumonia in AIDS: 10%
    - If respiratory failure: 80%–90%
Specific Immune Syndromes

Transplantation
- Common treatment for end-stage organ failure
- Risk of pulmonary infection increases after bone marrow transplant
- Post-transplantation infection
  - Nonproductive cough
  - Dyspnea
  - Fever
Specific Immune Syndromes

Neutropenia

- Chemotherapy kills WBCs
- Neutropenia may begin 7 days post chemotherapy
- During neutropenia patient prone to infection
  - Pyogenic bacteria
  - Fungus (aspergillus)
Specific Immune Syndromes

Immunosuppressive Drugs

- Agents for
  - Rheumatoid arthritis
  - Systemic lupus erythematosus
  - Scleroderma
  - Asthma

- Such as
  - Corticosteroids
  - Cyclophosphamide
  - azathioprine

- Can suppress the immune system
Empiric Therapy

- Therapy without waiting for the results
- Patient with neutropenia needs coverage for
  - Pyogenic bacteria (*pseudomonas aeruginosa*)
  - Fungi (*aspergillus*)
- Patient with AIDS usually treated with a combination of trimethoprim and sulfamethoxazole
  - *P. Jivoreci*
Specific Therapy

- *P. jivoreci*
  - Sulfa antibiotics
  - Pentamidine if intolerance to sulfas
  - High-dose corticosteroid in moderate to severe pneumonia

- Fungal pneumonia
  - Amphotericin B
  - Oral imidazoles in mild infections
Specific Therapy

- TB
  - Isoniazid, rifampin, pyrazinamide, ethambutol (first 2 months)
  - Isoniazid and rifampin (7 months)
Prophylactic Therapy

- In AIDS patients
  - To prevent pneumocystis pneumonia
    - When CD4+ < 200/µL
    - Trimethoprin-sulfamethoxazole
  - To prevent M. avium complex
    - When CD4+ < 50/µL
    - Rifampin and clarithromycin