Chapter 22 Pathogenic Fungi
An Overview of Medical Mycology

• Medical mycology
  • Diagnosis, management, and prevention of fungal diseases (mycoses)
  • Mycoses are among the most difficult diseases to diagnose and treat
    • Signs of mycoses are often missed or misinterpreted
    • Fungi are often resistant to antifungal agents
An Overview of Medical Mycology

- **Clinical Manifestations of Fungal Diseases**
  - Three categories of clinical manifestation:
    - *Fungal infections*
      - Most common mycoses
      - Caused by presence of true pathogens or opportunists
      - Difficult to diagnose
    - *Fungal toxicoses*
      - Acquired through ingestion
      - Occur when poisonous mushrooms are eaten
    - *Allergies*
      - Most often result from the inhalation of fungal spores
An Overview of Medical Mycology

• **Antifungal Therapies**

  • Mycoses are among the most difficult diseases to heal
    • Fungi often resist T cell–mediated immune responses
    • Fungi biochemically similar to human cells
      • Antifungal drugs can harm human tissues
      • Ergosterol is often a target of antifungal drugs
  
  • Amphotericin B is gold standard of antifungals
    • One of the more toxic antifungal agents
    • Less toxic alternatives include ketoconazole, itraconazole, and fluconazole

  • Some antifungal drugs do not target *ergosterol*
    • *Griseofulvin* - Interferes with microtubule formation and mitosis
    • *Echinocandins* inhibits sugar synthesis in fungal wall
Systemic Mycoses Caused by Pathogenic Fungi

- **Systemic mycoses**
  - Infections spread throughout the body
  - Caused by four pathogenic fungi of the division Ascomycota:
    - *Histoplasma*
    - *Blastomyces*
    - *Coccidioides*
    - *Paracoccidioides*
  - Acquired through inhalation
    - Begins as generalized pulmonary infection
    - Disseminates via the blood to the rest of the body
  - All four pathogenic fungi are *dimorphic*
Figure 22.2 The dimorphic nature of true fungal pathogens.
Systemic Mycoses Caused by Pathogenic Fungi

- **Histoplasmosis**
  - *Histoplasma capsulatum* is the causative agent
    - Most common fungal pathogen affecting humans
  - Found in the eastern United States, Africa, and South America
  - Fungi found in moist soils containing high nitrogen levels
  - Most infections occur through inhalation of spores
  - Cutaneous inoculations are extremely rare
  - *H. capsulatum* is phagocytized by macrophages in the lungs
    - Disperse the fungi beyond the lungs via the blood and lymph
Figure 22.3 Endemic areas for histoplasmosis.
Systemic Mycoses Caused by Pathogenic Fungi

- **Histoplasmosis**
  - Usually asymptomatic and resolves without damage
  - Clinical histoplasmosis results in one of four diseases:
    - *Chronic pulmonary histoplasmosis*
    - *Chronic cutaneous histoplasmosis*
    - *Systemic histoplasmosis*
    - *Ocular histoplasmosis*
  - Diagnosis based on identification of yeast in patient sample
  - Infections in healthy individuals resolve on their own
  - Treated with amphotericin B or ketoconazole when needed
Blastomycosis

- *Blastomyces dermatitidis* is the causative agent
- Endemic in the southeastern United States north to Canada
- Fungi found in soils rich in organic matter
- *Pulmonary blastomycosis*
  - Most common manifestation
  - Initial pulmonary lesions are mostly asymptomatic
    - When symptoms occur they are nonspecific
  - The disease resolves in most people but may become chronic
Figure 22.5 Geographic distribution of *Blastomyces*.
Figure 22.6 Cutaneous blastomycosis in an American woman.
Systemic Mycoses Caused by Pathogenic Fungi

• **Blastomycosis**
  - Cutaneous blastomycosis
    - Painless lesions on the face and upper body
  - Osteoarticular blastomycosis
    - Spread of the fungus to the spine, pelvis, cranium, ribs, long bones, or subcutaneous tissues surrounding joints
• **Meningitis**
  - Dissemination of the fungus to the central nervous system
  - Can occur in AIDS patients
• Diagnosis based on identification of fungi in culture or samples
• Treat with amphotericin B or oral itraconazole
• Relapse is common in AIDS patients
Systemic Mycoses Caused by Pathogenic Fungi

• **Coccidioidomycosis**
  - *Coccidioides immitis* is the causative agent
  - Almost exclusively in the southwestern United States and northern Mexico
  - Fungi in desert soil, rodent burrows, archeological remains, mines
  - Infection rates have risen in endemic areas
    - Population expansion and increased recreational activities
    - Inhaled arthroconidia germinate into spherules in the lung
      - Spherules release large number of spores as they mature
Figure 22.7 Endemic areas of *Coccidioides.*
Figure 22.8 Spherules of *Coccidioides immitis.*
Figure 22.9 Coccidioidomycosis lesions in subcutaneous tissue.
Systemic Mycoses Caused by Opportunistic Fungi

• Opportunistic mycoses don't typically affect healthy humans
• Infections limited to people with poor immunity
• More important as the number of AIDS patients rises
• Difficult to identify because their symptoms are often atypical
Systemic Mycoses Caused by Opportunistic Fungi

- **Candidiasis**
  - Includes various opportunistic infections and diseases
  - *Candida albicans* is the most common causative agent
    - Common microbiota of the skin and mucous membranes
  - *Candida* is one of the few fungi transmitted between individuals
  - All cases of disease result from an opportunistic infection
  - Can produce a wide range of diseases
  - Systemic disease seen mostly in immunocompromised individuals
Systemic Mycoses Caused by Opportunistic Fungi

- **Cryptococcosis**
  - *Cryptococcus neoformans* is the main causative agent
    - Two varieties:
      - *Cryptococcus neoformans gattii*
        - Infects immunocompetent individuals
      - *Cryptococcus neoformans*
        - Infects AIDS patients
    - Results from inhalation of spores or dried yeast in bird droppings
    - Characteristics enhance the pathogenicity of the fungus
      - Ability to resist phagocytosis
      - Predilection for the central nervous system
  - Occurs in individuals with little immune system function
Figure 22.13 GMS stain of Cryptococcus.
Systemic Mycoses Caused by Opportunistic Fungi

- **Cryptococcosis**
  - Diagnosis based on identification of fungus in appropriate patient sample
  - Treatment is with amphotericin B and 5-fluorocytosine for several weeks
  - Fluconazole is used as maintenance therapy for AIDS patients
Superficial, Cutaneous, and Subcutaneous Mycoses

- Are the most commonly reported fungal diseases
- All are opportunistic infections
- Localized at sites at or near the surface of the body
- Acquired by person-to-person contact or environmental exposure
- Diseases are usually not life threatening
  - Can cause chronic or recurring infections
Superficial, Cutaneous, and Subcutaneous Mycoses

• **Superficial Mycoses**
  • Are the most common fungal infections
  • Confined to the outer, dead layers of the skin, nails, or hair
    • All composed of dead cells that contain *keratin*
    • Primary food of these fungi
Superficial, Cutaneous, and Subcutaneous Mycoses

• **Superficial Mycoses**
  • **Dermatophytoses**
    • Infections of the skin, nails, or hair caused by dermatophytes
    • Previously called ringworms
    • Fungi use keratin as nutrient source and colonize dead tissues
    • May trigger cell-mediated immune response that damages living tissues
    • Can be spread from person to person
    • Genera of ascomycetes cause most dermatophytoses
    • Dermatophytoses show a variety of clinical manifestations
Figure 22.14 Athlete's foot.
### Table 22.3 Common Dermatophytoses

<table>
<thead>
<tr>
<th>Disease</th>
<th>Agents</th>
<th>Common Signs</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinea pedis (&quot;athlete's foot&quot;)</td>
<td><em>Trichophyton rubrum</em>; <em>T. mentagrophytes var. interdigitale</em>; <em>Epidermophyton floccosum</em></td>
<td>Red, raised lesions on and around the toes and soles of the feet; webbing between the toes is heavily infected</td>
<td>Human reservoirs in toe webbing; carpeting holding infected skin cells</td>
</tr>
<tr>
<td>Tinea cruris (&quot;jock itch&quot;)</td>
<td><em>T. rubrum</em>; <em>T. mentagrophytes var. interdigitale</em>; <em>E. floccosum</em></td>
<td>Red, raised lesions on and around the groin and buttocks</td>
<td>Usually spreads from the feet</td>
</tr>
<tr>
<td>Tinea unguium (onychomycosis)</td>
<td><em>T. rubrum</em>; <em>T. mentagrophytes var. interdigitale</em></td>
<td><em>Superficial white onychomycosis</em>: patches or pits on the nail surface <em>Invasive onychomycosis</em>: yellowing and thickening of the distal nail plate, often leading to loss of the nail</td>
<td>Humans</td>
</tr>
<tr>
<td>Tinea corporis</td>
<td><em>T. rubrum</em>; <em>Microsporum gypseum</em>; <em>M. canis</em></td>
<td>Red, raised, ringlike lesions occurring on various skin surfaces (tinea corporis on the trunk, tinea capitis on the scalp, tinea barbae of the beard)</td>
<td>Can spread from other body sites; can be acquired following contact with contaminated soil or animals</td>
</tr>
<tr>
<td>Tinea capitis</td>
<td><em>M. canis</em>; <em>M. gypseum</em>; <em>T. equinum</em>; <em>T. verrucosum</em>; <em>T. tonsurans</em>; <em>T. violaceum</em>; <em>T. schoenleinii</em></td>
<td><em>Ectothrix invasion</em>: fungus develops arthroconidia on the outside of the hair shafts, destroying the cuticle <em>Endothrix invasion</em>: fungus develops arthroconidia inside the hair shaft without destruction <em>Favus</em>: crusts form on the scalp, with associated hair loss</td>
<td>Humans; can be acquired following contact with contaminated soil or animals</td>
</tr>
</tbody>
</table>
Superficial, Cutaneous, and Subcutaneous Mycoses

- **Superficial Mycoses**
  - Dermatophytoses
    - Most dermatophytoses are clinically distinctive
      - Confirm by identification of hyphae or arthroconidia in patient samples
    - Treat limited infections with topical antifungal agents
    - Treat widespread infections with oral antifungal agents
    - Terbinafine is usually effective
    - Griseofulvin is used for chronic or difficult cases
Superficial, Cutaneous, and Subcutaneous Mycoses

• **Cutaneous and Subcutaneous Mycoses**
  
  • **Sporotrichosis**
    
    • *Sporothrix schenckii* is the causative agent
    
    • Subcutaneous infection usually limited to the arms and legs
    
    • Fungi found in the soil
    
    • Those who work with plant material at highest risk for infection
    
    • Most infections occur in Latin America, Mexico, and Africa
Figure 22.19 Sporotrichosis on the arm.