Medical Mycology

- Field of medicine concerned with the diagnosis, management, and prevention of fungal diseases or 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

Epidemiology of Mycoses

- Fungi and their spores are almost everywhere in the environment
- Because they are widespread, most people will experience a mycosis at some time
- Typically acquired via inhalation, trauma, or ingestion
- Infrequently spread from person-to-person
- Most mycoses are not contagious
  - *Dermatophytes*, fungi found on the skin, are the major exception
**Epidemiology of Mycoses**

- Epidemics result from mass exposure to some environmental source of fungi
- Mycoses are generally not reportable and thus adequate information on their occurrence and spread is often lacking

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**Categories of Fungal Agents**

- Only four fungi are usually considered true pathogens
  - Have the ability to actively attack and invade tissues
  - Exhibit dimorphism
    - Based on differences in temperature
    - In the environment they have mycelium thalli composed of hyphae and within the body they exist as yeast thalli
  - Yeast forms are invasive due to the production of various enzymes and proteins that allow their survival within the body
  - Endemic to certain regions, primarily in the Americas

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**Categories of Fungal Agents**

- Opportunistic fungi account for the remaining diseases in humans
  - Often commensals that take advantage of a weakness in a host’s defenses
  - Distributed throughout the world
  - Dermatophytes are considered in this group because they often occur in individuals susceptible to opportunistic fungi
  - Four factors increase an individual’s risk for acquiring an opportunistic mycoses
Factors that Predispose Individuals to Opportunistic Mycoses

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<tr>
<th>Factors</th>
<th>Examples</th>
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<td>Medical procedures</td>
<td>Surgery; insertion of medical implants (heart valves, artificial joints); catheterization</td>
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<td>Medical therapies</td>
<td>Immunosuppressive therapies; accompanying transplantation; radiation and other cancer therapies; steroid treatments; long-term use of antibacterial agents</td>
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<td>Preexisting conditions</td>
<td>Inherited immune defects; leukemia and lymphomas; AIDS; diabetes and other metabolic disorders; severe burns; preexisting chronic illnesses</td>
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<td>Lifestyle factors</td>
<td>Poor diet; poor hygiene; IV drug abuse</td>
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Clinical Manifestations of Fungal Disease

- Fungal diseases are grouped in three categories of clinical manifestation
  - **Fungal infections**
    - Most common mycoses
    - Caused by the presence in the body of either true pathogens or opportunists
  - **Toxicoses**
    - Acquired through ingestion
    - Occurs when poisonous mushrooms are eaten
  - **Allergies**
    - Most often result from the inhalation of fungal spores

Diagnosis of Fungal Infections

- A patient’s history is critical for diagnosis of most mycoses
- Definitive diagnosis often requires isolation, laboratory culture, and morphological analysis of the fungus involved
  - **Sabouraud dextrose agar** is used to culture fungi collected from patients
    - This medium favors fungal growth over bacterial growth
  - Various techniques are used to detect fungal cells in patient specimens
Diagnosis of Fungal Infections

- Immunological tests are not always useful for fungi
  - Due to the prevalence of fungi in the environment it is often hard to distinguish between an infection and simple exposure
- Opportunistic infections are particularly difficult to diagnose
  - Fungi can display abnormal morphology in tissues where infection wouldn’t normally occur

Antifungal Therapies

- Mycoses are among the most difficult diseases to heal
  - Fungi can often resist the oxidative damage of T cells during cell-mediated immune responses
  - Fungi are biochemically similar to human cells and antifungal drugs can harm human tissues
  - Fungi have ergosterol in their membranes rather than cholesterol and it is often a target for antifungal treatment
    - Side effects can still result, especially with long-term use

- Amphotericin B is the “gold standard” of antifungal agents but also the most toxic
- Other antifungal agents include various azole drugs, fluorocytosine, and griseofulvin
- Opportunistic infections treatment requires two steps
  - High-dose treatment to eliminate or reduce the fungal pathogens
  - Long-term maintenance therapy to control and prevent reinfection
Systemic Mycoses Caused by Pathogenic Fungi

- Infections spread throughout the body
- Caused by one of the four pathogenic, dimorphic fungi of the division **Ascomycota**
  - **Blastomyces**, Coccidioides, Histoplasma, and Paracoccidioides
- Acquired through inhalation
- Begin as a generalized pulmonary infection that disseminates via the blood to the rest of the body
- Individuals working with dimorphic fungi in the laboratory must take multiple precautions to avoid exposure to spores

Blastomycosis

- **Blastomyces dermatitidis** is the causative agent
- Endemic in the southeastern United States north to Canada
- Fungi found in soils rich in organic matter
- Inhalation of dust can carry fungal spores or hyphal pieces into the lungs
- Pulmonary blastomycosis is the most common manifestation in humans
  - Initial pulmonary lesions are mostly asymptomatic and symptoms, when they develop, are often vague
  - The disease resolves in most people but in others it may be chronic
- Treatment is with amphotericin B

Blastomycosis

Figure 22.3
Systemic Mycoses Caused by Opportunistic Fungi

- Opportunistic mycoses don’t typically affect healthy humans
- Infections usually limited to people with poor immunity
- Becoming more important as the number of immunocompromised individuals rises
- Can be difficult to identify because their symptoms are often atypical
- Five genera routinely encountered
  - *Aspergillus*, *Candida*, *Cryptococcus*, *Pneumocystis*, and *Mucor*

Aspergillosis

- Includes several diseases caused by fungi in the genus *Aspergillus*
- Can be found throughout the environment
- Disease occurs from the inhalation of the fungal spores
- Most commonly causes three pulmonary diseases
  - Hypersensitivity aspergillosis
    - Manifests as asthma or other allergic symptoms
  - Noninvasive aspergillomas
    - Masses of fungal hyphae form in the cavities after a case of pulmonary tuberculosis
- Acute invasive pulmonary aspergillosis
  - May present as mild pneumonia
  - Necrosis of lung tissue can lead to significant respiratory impairment
- Nonpulmonary diseases can also result
  - Includes cutaneous and systemic aspergillosis
- Treatment can include allergy medications for hypersensitivity reactions and amphotericin B for other diseases
Candidiasis

- Includes various opportunistic infections and diseases
- *Candida albicans* is the most common causative agent
- Common members of the microbiota of the skin and mucous membranes
- *Candida* is one of the few fungi that can be transmitted between individuals
- All cases of disease result from an opportunist infection
- Can produce a wide range of diseases
  - Thrush
  - Diaper Rash
  - Onychomycosis
  - Ocular Candidiasis

Thrush

Figure 22.10a

Systemic Mycoses

Valley Fever or Coccidioidomycosis

- Caused by coccidoides immitis, a dimorphic fungus
- Found in soil in southwest, spores carried by wind
- In soil it is a mold, in human tissue it is a yeast
- Causes a respiratory infection with fever, chills, and cough
- Most cases mild, no treatment needed
- If severe, lung lesions, can result in death
- If skin test is positive, must isolate organisms
- Treatment is Amphotericin B (toxic)
Emergence of Fungal Opportunists in Immunosuppressed Individuals

- AIDS patients have permanent immune dysfunction making a full cure of opportunistic infections unlikely
- Mycoses account for most deaths associated with AIDS
- *Candida albicans*, *Aspergillus fumigatus*, and *Cryptococcus neoformans* are so common in HIV-positive individuals their mycoses partly define end-stage AIDS

Superficial, Cutaneous, and Subcutaneous Mycoses

- Are the most commonly reported fungal disease
- Mycoses are localized at the sites at or near the surface of the body
- Can be acquired by healthy individuals via person-to-person contact or through environmental exposure
- Diseases are usually not life threatening but can be chronic or recurring infections

Superficial Mycoses

- Are the most common fungal infections
- Usually acquired by direct contact with the fungus
- Confined to the outer, dead layers of the skin, nails or hair
Black Piedra and White Piedra

- Superficial infection that forms nodules on the hair shaft
- Transmission is often mediated by shared hair brushes or combs
- Several members of a family are usually infected at the same time
- Infected areas must often be shaved to remove the fungi

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Black Piedra

![Image of Black Piedra](image1.png)

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White Piedra

![Image of White Piedra](image2.png)
## Cutaneous and Subcutaneous Mycoses

- Fungi are commonly found in the soil
- Infections are rare
- Requires traumatic introduction of the fungal elements beneath the outer, dead layers of skin
- Most lesions remain localized to the subepidermal tissues in the skin

## Dermatophytoses

- Fungal infections of the skin or nails caused by dermatophytes
- Infections were previously called ringworms because they resemble a worm lying below the surface of the skin
- Result from fungi that use keratin as a nutrient source and thus colonize only dead tissues
- Can provoke cell-mediated immune response that damages living tissues

### Dermatophytes

- Three genera of **ascomycetes** cause most dermatophytoses
  - *Trichophyton*, *Microsporum*, and *Epidermophyton flaccum*
- Dermatophytoses show a variety of clinical manifestations
- Treatment is with topical antifungal agents
  - *Tinea pedis* (“athlete’s foot”)
  - *Tinea cruris* (“jock itch”)
  - *Tinea unguium*
  - *Tinea corporis*
  - *Tinea capitis*
**Malassezia furfur**

- Normal inhabitant of the skin
- Causes various superficial infections that tend to be chronic
  - Pityriasis
    - Fungi interfere with melanin production
    - Characterized by depigmented or hyperpigmented patches of scaly skin
  - Folliculitis
  - Seborrheic dermatitis and dandruff

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**Malassezia furfur**

![Figure 22.13]

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**Mycetomas**

- Tumorlike infections of the skin, fascia, and bones of the hands or feet
- Caused by mycelial fungi in the division Ascomycota
- Fungi are found in the soil
- Humans are infected when the fungi are introduced via pricks or scrapes from contaminated twigs, thorns, or leaves
- Small, hard, subsurface nodules form at the site of infection that slowly worsen and spread
Fungal Intoxications and Allergies

- Some fungi cause allergies or produce toxins that cause toxicosis
- Two types of toxicosis
  - Mycotoxicosis
    - Caused by eating foods contaminated with fungal toxins
  - Mycetismus
    - Mushroom poisoning from eating a fungus
- Fungal allergens can elicit a hypersensitivity response in sensitive individuals
  - Result from inhalation, ingestion, or other contact

Mycotoxicoses

- Mycotoxins are produced by fungi during normal metabolic activities but are poisonous to animals and humans
- Mycotoxins are often consumed in contaminated food crops
- Long-term ingestion of mycotoxins can cause liver and kidney damage, gastrointestinal or gynecological disturbances, or cancers
Mycetismus

- Most mushrooms are not toxic
- Mushrooms that produce poisons can cause neurological dysfunction or hallucinations organ damage, or even death
- Poisoning typically occurs when untrained individuals pick and eat wild mushrooms
- The deadliest mushroom toxin is produced by the “death cap” mushroom

Allergies to Fungi

- **Fungal allergens** are common both indoors and out
- Determining the specific cause can be difficult because of their presence in the environment
- Fungal allergens usually cause type I hypersensitivity reactions that can result in asthma, eczema, and hay fever
- Type II and III hypersensitivity reactions can occur but much less frequently