

Fungal Infections



Fungal Biology and Classification

Fungi: *Eukaryotic, heterotrophic microorganisms* that digest food externally using hydrolytic enzymes. This explains their ability to invade blood vessels, often causing hemorrhage in lesions. They are primarily aerobic and synthesize lysine via the L- α -adipic acid biosynthetic pathway. Key characteristics include chitinous cell walls, ergosterol-containing plasma membranes, 80S rRNA, and tubulin-composed microtubules.

Conidia: *Asexual propagules (reproductive units)* formed in various ways.

Spores: Can be asexual or sexual in origin.

Yeasts: Single-celled fungi reproducing by budding.

Molds: Multicellular fungi forming hyphae (filaments). Hyphae can be sparsely to regularly septate and have a variable number of nuclei.

Dimorphic Fungi: Exhibit both yeast and mold forms depending on environmental conditions (temperature, CO₂, pH, cysteine levels). *Grow as yeasts or spherules in vivo and at 37°C in vitro, but as molds at 25°C.*

Classification based on morphology: This is crucial for identification and understanding the potential severity of infection. Knowing the difference between yeast and mold is fundamental. Understanding dimorphism is important for understanding how fungi adapt to different environments (inside the body vs. outside).



Classification of Fungal Infections

Fungal infections are classified based on several factors:

1. Site of Infection: Superficial, cutaneous, subcutaneous, or systemic (deep). *Systemic infections can spread beyond the initial site of infection.*

2. Route of Acquisition: Exogenous (airborne, cutaneous, percutaneous) or endogenous (from normal flora, e.g., *Candida* in the GI tract). *Endogenous infections are particularly relevant in immunocompromised individuals.*

3. Virulence: Primary pathogens infect healthy individuals, while opportunistic pathogens infect immunocompromised hosts. *Understanding the host's*

immune status is critical in determining the likelihood and severity of fungal infection.

Examples:

- *Candida*: Normal flora in the GI tract, mouth, and vagina. Candidemia (Candida in the bloodstream) is a serious complication.
- *Aspergillus*: Common environmental fungus; can cause invasive aspergillosis, particularly in immunocompromised individuals.
- *Histoplasma capsulatum*: Found in soil contaminated with bird or bat droppings; causes histoplasmosis.



Diagnosis of Fungal Infections

1. Clinical Presentation: Symptoms vary widely depending on the fungus and site of infection. *A thorough history, including travel history and underlying medical conditions, is crucial.*

2. Microscopic Examination: Direct examination of clinical specimens (e.g., skin scrapings, tissue biopsies) to identify fungal elements (hyphae, yeasts). *Gram staining can be useful for initial assessment, but specific stains (e.g., PAS, GMS) are often needed for definitive identification.*

3. Culture: Growth of the fungus on selective media (e.g., Sabouraud dextrose agar) for identification. *Culture is the gold standard for definitive diagnosis, but can be time-consuming.*

4. Serological Tests: Detection of fungal antigens (e.g., galactomannan for *Aspergillus*, 1,3- β -D-glucan for many fungi) or antibodies in serum. *These tests can be helpful for rapid diagnosis, but may have limitations in sensitivity and specificity.*

5. Molecular Diagnostics: PCR-based methods for rapid and sensitive detection of fungal DNA. *Molecular diagnostics are increasingly important for identifying difficult-to-culture fungi or for detecting resistance mutations.*

Important Note: Contamination vs. infection: Finding *Candida* in urine or sputum may indicate contamination, not infection. *Candida* in blood culture is always considered an infection.



Antifungal Treatment

Antifungal drugs target various aspects of fungal cell biology. *Treatment choices depend on the infecting fungus, site of infection, and host factors.*

Major Classes:

- **Azoles:** Inhibit ergosterol synthesis (e.g., fluconazole, itraconazole, voriconazole).
- **Echinocandins:** Inhibit cell wall synthesis (e.g., caspofungin, micafungin, anidulafungin).
- **Polyenes:** Bind to ergosterol, disrupting membrane integrity (e.g., amphotericin B).
- **Allylamines:** Inhibit squalene epoxidase (e.g., terbinafine).

Drug Resistance: *Candida auris*, azole-resistant *Aspergillus fumigatus*, and *Trichophyton indotineae* are significant concerns due to their resistance to commonly used antifungal agents.

Specific Fungal Infections: A Pareto Approach

This section focuses on high-yield fungal infections for your exam.

1. *Candida* Infections:

- **Candidemia:** *Candida* in the bloodstream; requires prompt treatment with echinocandins (caspofungin, anidulafungin) or amphotericin B. Source control (e.g., removal of intravenous catheters) is crucial.
- **Invasive Candidiasis:** Can affect multiple organs (kidneys, liver, lungs, CNS). Risk factors include neutropenia, broad-spectrum antibiotic use, and indwelling devices.
- **Mucocutaneous Candidiasis:** Oral thrush, esophagitis, vulvovaginitis. Treatment typically involves topical or oral azoles.

2. *Aspergillus* Infections:

- **Invasive Aspergillosis:** Severe infection, particularly in immunocompromised individuals. Risk factors include neutropenia, corticosteroids, and hematopoietic stem cell transplantation. Treatment involves voriconazole or other azoles, often combined with echinocandins.
- **Allergic Bronchopulmonary Aspergillosis (ABPA):** Hypersensitivity reaction in patients with asthma. Characterized by elevated IgE levels, eosinophilia, and recurrent exacerbations.

3. Mucormycosis (Zygomycosis):

- Caused by Mucorales (e.g., *Rhizopus*, *Mucor*). Characterized by broad, ribbon-like hyphae with rare septations.
- Risk factors include diabetes mellitus (ketoacidosis), glucocorticoid use, and hematologic malignancies.
- Often presents with rhino-orbital-cerebral involvement, requiring aggressive surgical debridement and antifungal therapy (e.g., amphotericin B, posaconazole).

4. Histoplasmosis:

- Caused by *Histoplasma capsulatum*, found in soil contaminated with bird or bat droppings.
- Most infections are asymptomatic or mild. Severe disease can involve the lungs or disseminate to other organs.
- Treatment depends on the severity of the infection and may involve itraconazole or amphotericin B.