Cell wall: chitin, glucan, mannan

Cell membrane: phospholipid bilayer, \( \beta-(1,3) \)-glucan, \( \beta-(1,3) \)-glucan synthase, ergosterol

Drug targets

Yeast: unicellular, divide by budding or fission, daughter cells form pseudohyphae

Mold: multicellular filaments/hyphae together as mycelium, septate or non, vegetative or aerial

Dimorphism: exist in both forms (yeast at higher temps, molds in environment)

**MYCOSES (fungal infections)**

- **Superficial**
  - Mild, little/no inflammatory response, mainly cosmetic, not painful, easy to treat
  - *Malassezia furfur*
    - Normal skin flora
    - Causes tinea versicolor, hypo/hyperpigmentation, especially during puberty and in summer
    - Can also cause dermatitis (dandruff), folliculitis, blepharitis
  - Dx: through clinical appearance, under microscope looks like spaghetti & meatballs (KOH)
  - Tx: topical fluconazole, selenium sulfide shampoo

- **Cutaneous**
  - Epidermis: skin, hair, nails, keratinized layers
  - Caused by dermatophytes (not normal skin flora)
  - Acute or chronic, mostly in tropical climates, gardeners/florists
  - Manifested as ringworm/tinea (on head, feet, body, groin, bearded area, nails)
  - Dx: clinical presentation, KOH prep
  - Tx: topical azoles, terbinafine, ciclopirox nail laquer

- **Subcutaneous**
  - Associated with skin trauma, caused by environmental fungi, mimic bacterial infections
  - Tx: does not respond well to antifungals, may need surgery to excise lesion
  - Lymphocutaneous sporotrichosis: “rose handler’s disease” (*Sporotricha schenckii*)
    - Dx: culture, skin biopsy
    - Tx: SSKI, azoles, terbinafine, amphotericin B, surgical excision

- **Systemic**
  - Dx: culture, tissue biopsy, germ-tube test (differentiates between *C. albicans* and other *Candida* species)
  - Tx: fluconazole (drug of choice) or echinocandin (mod to severely ill, recent azole exposure, *C. glabrata*)
  - Molds that divide at acute angles are more severe than right angles
**SYSTEMIC MYCOSES**

**Yeasts**
- **Candida species**
  - **C. albicans**
    - Normal flora of GI tract, vagina, oral cavity
    - >500 Candida species; ~10 medically significant
  - **C. glabrata**
    - Most commonly isolated, increased AF susceptibility
  - **C. parapsilosis**
    - Associated with central venous catheters, common bloodstream isolates
  - **C. tropicalis**
    - AF susceptible
  - **C. krusei**
    - Fluconazole-resistant
  - **C. lusitaniae**
    - Increased amphophilic activity

**Cryptococcosis**
- **Cryptococcus neoformans**
  - Ubiquitous; yeast found in soil, pigeon droppings
  - Candidates: patients with AIDS, cancer, or transplants
  - Clinical presentation: usually meningitis (although many other organ involvements)
  - Dx: culture, antigen detection
  - Tx: amphotericin B + flucytosine, fluconazole as step-down therapy

**Molds**
- **Aspergillosis** (septate)
  - Everyone’s been exposed from inhalation
  - Ubiquitous: soil, food, water, decaying vegetation
  - Angioinvasive: gets into blood vessels, invades tissues
  - Onset of disease: bimodal → initial neutropenia + graft-vs-host disease
  - Typical host: stem cell transplant recipients (chemo kills cells)
    - Allogeneic>autologous
    - Chemo >2 weeks, high dose steroids, graft-vs-host disease, immunosuppression
  - Sx: pulmonary (most common), sinusitis, cerebral, cutaneous, osteomyelitis, dissemination
  - Dx: difficult to obtain (risky for pt), tissue/sputum culture, look for septate hyphae w/acute branching
  - Tx: amphotericin B (historic drug of choice), voriconazole (current drug of choice)
  - Fluconazole does not work

**Classification of IFI Pathogens**

**Yeasts**
- Candida spp.
- Cryptococcus spp.

**Molds**
- Non-septate
  - Zygomycetes
  - Rhizopus, Mucor, Rhizomucor

**Dimorphic**
- Histoplasma
- Blastomycetes
- Coccioidoides

**Phaeohyphomycetes** (non-dematiaceous)
- Aspergillus spp.
- Fusarium, Paecilomyces

**Scedosporium**
- Wangeria spp., Alternaria

**Invasive Candida Infections**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Candida species</th>
<th>Flu</th>
<th>Itra</th>
<th>Vor</th>
<th>Posa</th>
<th>Amphot</th>
<th>Candies</th>
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<tbody>
<tr>
<td>Acute renal failure</td>
<td>C. albicans</td>
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<td>Central venous catheter</td>
<td>C. albicans</td>
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<td>Surgery/GI Surgery</td>
<td>C. albicans</td>
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<td>Burns</td>
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<td>Antibiotics &gt; 6 days</td>
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<td>≥ 3 antibiotics</td>
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<td>Neutropenia/mucositis (malignancy)</td>
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<td>Diabetes</td>
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<td>TPN (parenteral nutrition)</td>
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<td>Steroids/Transplant</td>
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<td>Multiple trauma</td>
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<td>Colonization</td>
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<td>Prolonged LOS (length of stay)</td>
<td>C. albicans</td>
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<td>AIDS</td>
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**Aspergillus species**

- *A. fumigatus*:
  - Most common species, thermotolerant (grows 20-50°C), may be very angioinvasive
- *A. flavus*:
  - 2nd most common species, angiogvasive
- *A. niger*:
  - 3rd most common species, secondary infection after bacterial otitis
- *A. terreus*:
  - Decreased susceptibility to amphot
- **Zygomycosis** (non-septate)
  - Ubiquitous: decaying matter
  - Non-septate, right angle branching
  - *Rhizopus, Rhizomucor, Absidia, Cunninghamella*
  - Risk factors: uncontrolled diabetes, corticosteroid use, trauma/burns, malignant hematological disorders
  - Clinical presentation: all of a sudden, tissue necrosis, rhinocerebral (most common)
  - Sx: face pain, unilateral headache, drainage, soft tissue swelling
  - Dx: tissue biopsy, doesn’t grow as well as *Aspergillus* in culture
  - Tx: reverse predisposing factors, surgical debridement, antifungal therapy (amphotericin B)

**DIMORPHIC MOLDS** (Endemic: regions of the US)

Dx: culture, tissue biopsy
Tx: [severe] amphotericin B, [mild/mod] itraconazole, fluconazole

- **Histoplasmosis**
  - *Histoplasma capsulatum*
  - Ohio/Mississippi river valleys (common at UIC)
  - Sx: chronic pulmonary infection, disseminated infection, mostly mild/asymptomatic

- **Blastomycosis**
  - Blastomyces dermatitidis
  - Midwest, Canadian provinces bordering the Great Lakes
  - “Chicago Disease”
  - Not that common: histo > blasto
  - Sx: acute/chronic pulmonary infection, disseminated infection (like histo)

- **Coccidiodomycosis**
  - *Coccidioides immitis*: California’s San Joaquin valley (“valley fever”)
  - *Coccidioides posadasii*: Southwest, Mexico, South America
  - Sx: most are mild/asymptomatic, some get respiratory infection → pulmonary nodules/cavities