Fungal Infections

- Once exotic and rare; now increasingly common
- Fungi are not "virulent"
- But they are good at taking advantage
- "Opportunistic" in many senses

Fungal biology

- Eukaryotic (organized nucleus and cell structure)
- Non-motile
- Aerobic
- Saprophytic or parasitic
- Cell wall contains glucan and chitin
- Cell membrane contains ergosterol

Fungal cell structure

- Yeasts (unicellular, budding)
- Molds (hyphae, mycelia, spores)
- Dimorphs (both)

Pathogenesis

Toxins: produced, but not relevant to human infections

Disease from:
- Bulk of organisms
- Immune response to them or their byproducts

Overview of fungal infections

- Superficial or cutaneous (skin, hair, nails)
- Subcutaneous
- Systemic
  - "true pathogens" may cause disease in normal hosts although worse with immunocompromise
  - "opportunist" cause disease almost exclusively in immunocompromised hosts

Superficial fungal infections

Dermatophytes: molds producing keratinase
Pathogenesis: grow as saprophytes on skin/nails; cause inflammation below

Clinical:
- Tinea corporis
- Tinea pedis
- Tinea capitis
- Tinea cruris
- Tinea unguium
Superficial fungal infections

Malassezia furfur: lipophilic yeast (derives nourishment from skin lipids)
Pathogenesis: lives on skin, causes pigment changes and itch underneath
Diseases:
• Tinea versicolor
• Occasionally fungemia with lipid infusion

Subcutaneous fungal infections

• Pathogenesis: introduced through skin by foreign body, grow in subcutaneous tissues, spread via lymphatics
• Disease: usual local; may disseminate to adjacent bones, joints.
• Most common in nonindustrialized world (mycetoma of feet)

Subcutaneous fungal infection: Sporotrichosis

• Organism: Sporothrix schenckii
  – Dimorphic soil fungus (mold in environment, yeast in body)
• Habitat: soil, worldwide
• Pathogenesis: splinters or thorns inoculate organism into subcutaneous tissues

Sporotrichosis

Pathophysiology:
• Spore inoculated by foreign body
• Yeasts travel along lymphatics
• Elicit mixed pyogenic-granulomatous reaction

Clinical:
• Gardeners and outdoorspersons
• Ulcerating nodules along hard cord
• Bone and joint destruction
• Dissemination rare

Systemic fungal infections: the “true pathogens”

Histoplasmosis, Coccidioidomycosis, Blastomycosis
• Dimorphic
• Respiratory acquisition
• Restricted geographic distribution
• Infect normal hosts
• Disease reminiscent of TB

Histoplasmosis

Organism: Histoplasma capsulatum
• Soil dimorph (yeast in body, mold in environment)
Habitat: soils with high N content
  – Ohio-Mississippi valley; Caribbean; Central and S. America
  – Guano of bats, birds, poultry (chicken coops and caves
Pathogenesis: inhalation of spores
Histoplasmosis

Pathophysiology:
- Mold spores transform into yeast in lung, elicit cellular immunity as per TB
- Hematogenous dissemination
- Skin test reactivity
- Walled off granulomata

Clinical:
- Mimics TB. Usually latent disease, but
  - may cause acute/chronic cavitary lung disease
  - may disseminate after infection (infancy, immunocompromise)
  - may reactivate years later

Coccidioidomycosis

Organism: Coccidioides immitis
- Dimorph: mold in soil, spherules and endospores in host

Habitat: lower Sonoral life zone (arid): Southwest US, Mexico, Central and South America

Pathogenesis: inhalation of spores

Cocci

Pathophysiology:
- Spores transform into spherules in lung, elicit cellular immunity as per TB
- Hematogenous dissemination
- Skin test reactivity
- Walled off granulomas

Clinical:
- Acute self-limited flu-like seroconversion syndrome ("Valley fever")
- Acute or chronic lung disease
- Dissemination (pregnancy, dark skin, immunocompromise)
  - Skin
  - Bone
  - CNS

Blastomycosis

Organism: Blastomyces dermatiditis
- Dimorph: mold to yeast

Habitat: humid woodlands
- MidAtlantic zone
- Beaver dams, peanut farms
- Organic debris rather than soil

Pathogenesis: inhalation of spores

Systemic fungal infections: B. "the opportunists"

Hist. Blasto, Cocci
- Geographic distribution
- Dimorphic
- Infection by inhalation
- Pyogenic/granulomatous host response
- Similar to TB
- Infection =~ immunity

Opportunists
- Omnipresent
- Yeasts or molds
- Various routes of infection
- Host response varies
- Clinical syndromes vary
- No lasting immunity
**Cryptococcosis**

**Organism:** Cryptococcus neoformans

- Yeast with a thick polysaccharide capsule

**Habitat:** Bioterrorists (of a sort), worldwide

**Pathogenesis:** Inhalation of yeasts

**Cryptococcosis**

**Pathophysiology:**
- Inhalation leads to
- Transient colonization OR
- Acute/chronic lung disease OR
- CNS invasion

**Clinical**
- Pneumonia OR
- Meningoencephalitis
- Acute or chronic
- Fever, headache, stiff neck, fever, delirium
- Hydrocephalus

**Cryptococcal meningitis**

- India ink preparation of CSF may show organisms
- Serum or CSF antigen assay diagnostic in >95% cases of CNS disease

**Candidiasis**

**Organism:** Candida albicans et al (yeasts with hyphal forms)

**Habitat:** Normal human flora

**Pathogenesis:**
- Colonized areas: change in environment leads to overgrowth
- Noncolonized areas: change in immunity leads to invasion

**Pathogenesis of Candida infections**

- Primary host defenses:
  - Intact skin
  - Intact mucosa with normal pH and normal flora
  - Functioning lymphocytes
  - Functioning neutrophils

**Pathogenesis of local Candida infections**

- Environmental changes
  - Wet skin
  - Changes in local flora
  - Hormones, foreign bodies
- Lymphocyte dysfunction
  - Immaturity
  - Destruction (HIV)
Pathogenesis of invasive Candida infections

- Breach in anatomic integrity (often biofilm on catheter)
- Defective PML function (first line of defense)
  - Myeloperoxidase, complement necessary but not sufficient defense
  - Cytokines also essential for recruiting phagocytes in disseminated disease
  - Antibody may or may not be present; may or may not be protective

Invasive candidiasis

- Usually in critically ill patients with multiple risks (hospitalized, neutropenic, on antibiotics, many catheters)
- Fever, leukocytosis, organ dysfunction
- Microabscesses in kidney, liver, skin, eye, lung, heart
- Candida endocarditis

“Virulence” of Candida?

- Inherent “virulence”
  - Environmental tolerance
  - Secrete hydrolases, beta proteases, phospholipases
  - Can adhere to plastic
  - Can invade GI, renal epithelium
- Additional hyphal virulence
  - Protects against phagocytosis
  - Knockout strains

Additional comments on candidiasis

- Gram stain may help identify
- Infection and colonization are difficult to distinguish
- Best treatment restores missing defense

Aspergillosis

- Organism: Aspergillus fumigatus and others
  - Mold without a yeast phase
- Habitat: everywhere, worldwide
- Pathogenesis: inhalation of spores

Summary: Fungal “opportunism”

- Metabolic (dermatophytes, M. furfur, mucor)
- Dimorphism (sporo, histo, blasto, cocci)
- Capsule (cryptococcus)
- Adherence (candida)
Summary: antifungal defenses

• Intact skin (dermatophytes, Candida)
• Lymphocyte function (dimorphs, cryptococcus, candida)
• Neutrophil function (candida, aspergillus, mucor)
• Body milieu (candida, mucor)