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
  – “opportunists” 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 cruris
• Tinea pedis
• Tinea unguum
• Tinea capitis
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

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

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 Sonora 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
**Blastomycosis**

**Pathophysiology:**
- Spores transform into yeast in lung, disseminate
- No good antigen test to define exposed population

**Clinical:**
- Acute or chronic lung disease (nodular/cavitary)
- Disseminated disease:
  - Skin
  - Bone
  - Urinary tract in men
Systemic fungal infections:
B. “the opportunists”

**Histo, 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

Aspergillosis

Pathophysiology
Spores in lung may:
  – Elicit allergy
  – Grow in preexisting cavity
  – Invade vasculature, disseminate with local and distant disease
  – Neutrophils prime defenders

Clinical
• Allergic bronchopulmonary aspergillosis
• Aspergilloma
• Invasive aspergillosis with pneumonia, other end-organ disease
Mucormycosis

- Organism: species of Mucorales, genera Rhizopus and Mucor (Zygomycetes)
  - Molds without a yeast phase
- Habitat: everywhere, worldwide
- Pathogenesis: inhalation of spores
Mucormycosis

Pathophysiology:
Alveolar MPH/PML clear organisms, BUT:
• Metabolic acidosis
• Diabetes
• Neutrophil dysfunction
• Iron overload
May enable relentless growth

Clinical:
The most acute and fulminant fungal infection known
Lower airways: pneumonia progressing to infarction
Upper airways: sinusitis progressing to brain abscess
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)