Fungal Infections

- Once exotic and rare
- Now increasingly common
- Fungi are not "virulent"
- But they are good at taking advantage
- "Opportunistic"

Pathogenesis

- Toxins: produced but not relevant to human infections
- Disease from:
  - Bulk of organisms
  - Immune response to them or their byproducts

Fungal biology

- Eukaryotes
- Non-motile
- Aerobic
- Saprophytic or parasitic
- Cell wall contains glucan and chitin
- Cell membrane contains ergosterol

Overview of fungal infections

- Superficial (skin or mucosa)
- Subcutaneous
- Systemic:
  - "True pathogens" – infect healthy hosts, although disease worsens with immunocompromise
  - "Opportunists" – disease almost exclusively in immunocompromise

Fungal cell structure

- Yeasts (unicellular, budding)
- Molds (mycelial, spores)
- Dimorphs (both)

Superficial Fungal Infections

Dermatophytes:
Molds producing keratinase
Saprophytes on skin/nails; inflammation below

Diseases:
- tinea corporis
- tinea capitis
- tinea cruris
- tinea pedis
  - tinea unguum
Superficial fungal infections

- Malassezia furfur
  Lipophilic yeast

Disease:
- Tinea versicolor (itch, pigment changes)
- Occasionally, fungemia with lipid infusions

Subcutaneous fungal infections

Pathogenesis: introduced through skin, grow in subcutaneous tissues, spread via lymphatics. May reach distant organs especially bone, joints in path. Most common in nonindustrialized world (“Madura foot”)

Subcutaneous: sporotrichosis

- Organism: Sporothrix schenckii
  - Dimorphic soil organism
  - Worldwide distribution
- Pathogenesis: splinters or thorns inoculate organism into subcutaneous tissues

Sporotrichosis

Pathophysiology:
- Yeast travel along lymphatics
- Elicit mixed pyogenic/granulomatous reaction

Clinical:
- Gardeners and persons of sport
- Ulcerating nodules along hard cord
- Bone and joint destruction
- Occasional dissemination

Systemic fungal infections: the “true pathogens”

Histoplasmosis, Coccidioidomycosis and Blastomycosis

- Dimorphic
- Respiratory acquisition
- Restricted geographic distribution
- Infect normal hosts
- Disease reminiscent of TB

Histoplasmosis

- Organism: Histoplasma capsulatum
  - Dimorphic soil organism
- Habitat: soils with high N content
  - Ohio-Mississippi valley; Puerto Rico, Central and S. America
  - Guano of bats, birds, poultry (chicken coops and caves)
- Pathogenesis: inhalation of spores
Histoplasmosis
Pathophysiology:
- Spores transform to yeast in lung, elicit cellular immunity as per TB
  - Hematogenous dissemination
  - Skin test reactivity (histoplamin)
Clinical: mimics TB
- May disseminate early (infancy, immunodef.)
- May cause acute nodular/cavitary lung disease
- May reactivate years later

Blastomycosis
Organism: Blastomyces dermatitidis
- Dimorphic soil organism
Habitat: humid woodlands
  - MidAtlantic countryside
  - Beaver dams, peanut farms
  - Organic debris
Pathogenesis: inhalation of spores

Coccidioidomycosis
Organism: Coccoides immitis
- Dimorphic soil organism with spherules and endospores in host
Habitat: the lower Sonoran life zone (arid)
  - Southwest US, Mexico, Central and South America
Pathogenesis: inhalation of spores

Cocci
Pathophysiology:
- Spores transform to spherules in lung, elicit cellular immunity as per TB
  - Hematogenous dissemination
  - Skin test reactivity (coccoidin)
Clinical:
- Acute self-limited flu-like seroconversion (Valley fever)
Dissemination
  - Pregnancy, dark skin, immuno-compromised
    - Skin
    - Bone
    - CNS
- No good antigen test to describe exposed population

Systemic fungal infections: the “opportunists”
“True pathogens”
- Geographic restriction
- Dimorphic
- Infection by inhalation
- Pyogenic/granulomatous host response
- Similar to TB
Infection ~ immunity
“Opportunists”
- Omniporesent
- Yeasts or molds
- Varies routes
- Host response varies
- Widely variable
- No lasting immunity
Cryptococcosis
- Organism: Cryptococcus neoformans
  - yeast with thick polysaccharide capsule
- Habitat: Bioterrorism of a sort, worldwide
- Pathogenesis: inhalation of yeast

Cryptococcosis
Pathophysiology:
- transient colonization
  OR
- acute/chronic lung disease
  OR
- CNS invasion

Candidiasis
Pathogenesis:
- Breach in
- Skin or mucosal integrity
- Normal bacteriologic flora
- Neutrophil function or CMI

Candidiasis
Clinical settings:
- Moisture, antibiotics, pregnancy
- HIV infection
- Intravenous catheters
- Chemotherapy or marrow ablation

Candidiasis
Diagnosis:
- Gram stain may help
- Infection and colonization may be difficult to distinguish

Candidiasis
Treatment:
- Remove the breach in defenses, if possible

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 (neutrophils key)

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

Mucormycosis
Organism:
- Species of Mucorales, genera Rhizopus and Mucor
  - Mold without a yeast phase
Habitat:
- Everywhere, worldwide
Pathogenesis:
- Inhalation of spores

Clinical:
- The most acute and fulminant fungal infection known
  - Pneumonia progressing to infarction
  - Sinusitis progressing to brain abscess

Mucormycosis
Pathophysiology:
- Alveolar MPH/PML clear organisms
  - BUT
  - Acid
  - Sugar
  - Neutrophil dysfunction
  - May enable relentless growth

Clinical:
- Alveolar MPH/PML clear organisms
  - BUT
  - Acid
  - Sugar
  - Neutrophil dysfunction
  - May enable relentless growth