Fungal Infections
• Once exotic and rare
• Now increasingly common
• Fungi are not “virulent”
• But they are good at taking advantage
• “Opportunistic”

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

Fungal cell structure
• Yeasts (unicellular, budding)
• Molds (mycelial, 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 (skin or mucosa)
• Subcutaneous
• Systemic:
  – “True pathogens” – infect healthy hosts, although disease worsens with immunocompromise
  – “Opportunists” – disease almost exclusively in immunocompromise

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

Diseases:
• tinea corporis  tinea capitis
• tinea cruris  tinea pedis
  • tinea unguium
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

---

**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

---

**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

---

**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

---

**Blastomycosis**

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, immunocompromised)
  - Skin
  - Bone
  - CNS

---

**Blastomycosis**

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

Clinical: Acute or chronic lung disease (nodular/cavitary)
- Disseminated disease
  - skin
  - bone
  - urinary tract

---

**Systemic fungal infections: the “opportunists”**

"True pathogens"
- geographic restriction
- Dimorphic
- Infection by inhalation
- Pyogenic/granulomatous host response
  - Similar to TB
- Infection $\approx$ immunity

"Opportunists"
- Omnipresent
- 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

Clinical:
- Meningoencephalitis
  - acute or chronic
  - fever, headache, stiff neck, loss of vision
  - complicated by hydrocephalus
  - cryptococcal antigen for diagnosis

Candidiasis

- Organism: Candida albicans et al
- Habitat: normal human flora
- Pathogenesis:
  - colonized areas: overgrowth
  - noncolonized areas: invasion

Candidiasis

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

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

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
Pathophysiology:
- Alveolar MPH/PML clear organisms
- Acid
- Sugar
- Neutrophil dysfunction
- May enable relentless growth
Clinical:
- The most acute and fulminant fungal infection known
- Pneumonia progressing to infarction
- Sinusitis progressing to brain abscess

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