Fungal Infections

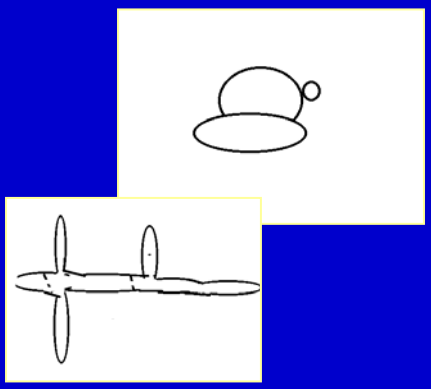
- Once exotic and rare
- Now increasingly common
- Fungi are not "virulent"
- But they are good at taking advantage
- "Opportunistic"

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 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 schenkii
  - 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:

- Gardners 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

Coccioidomycosis

- 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

Blastomycosis

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

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/granulo-matous host response
- Similar to TB
- Infection ~= 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 broncho-pulmonary 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

Mucormycosis

Pathophysiology:

- Alveolar MPH/PML clear organisms

BUT

- 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