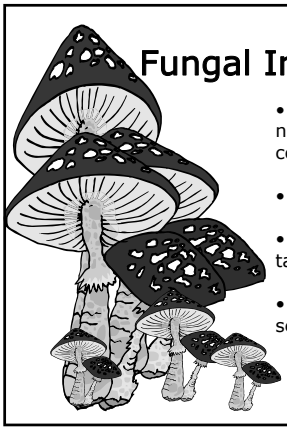


Fungal Infections

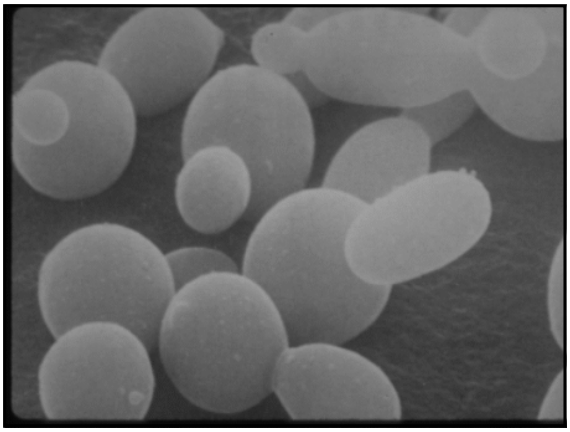
- Once exotic and rare; now increasingly common
- Fungi are not "virulent"
- But they are good at taking advantage
- "Opportunistic" in many senses

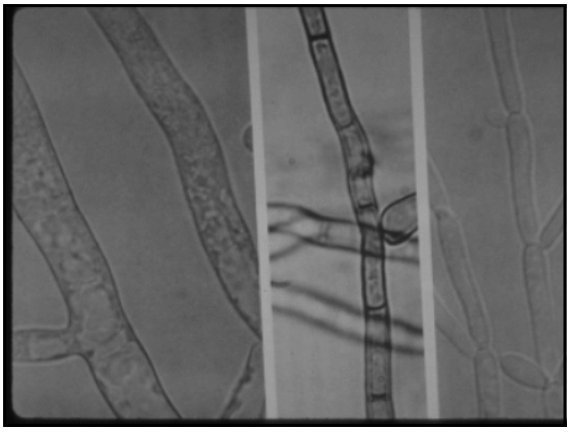
Fungal biology

- Eukaryotic (organized nucleus and cell structure)
- Non-motile
- Aerobic
- Saphrophytic 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 pedis
- Tinea capitis
- Tinea cruris
- Tinea unguum

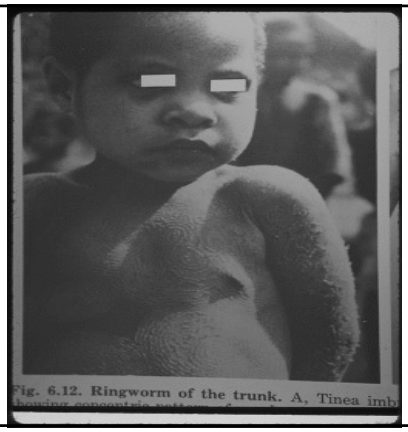
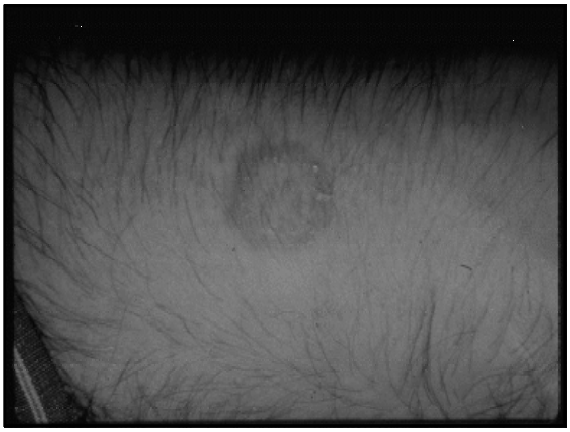
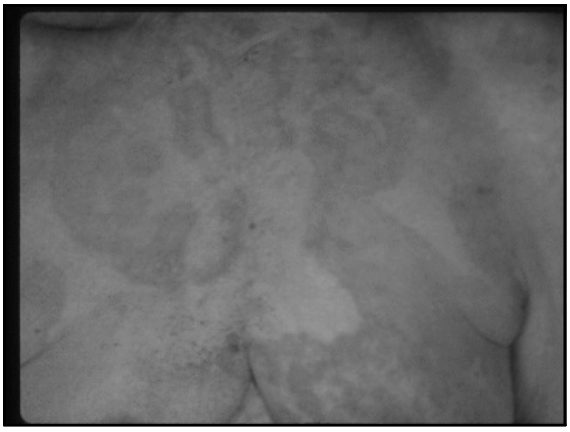
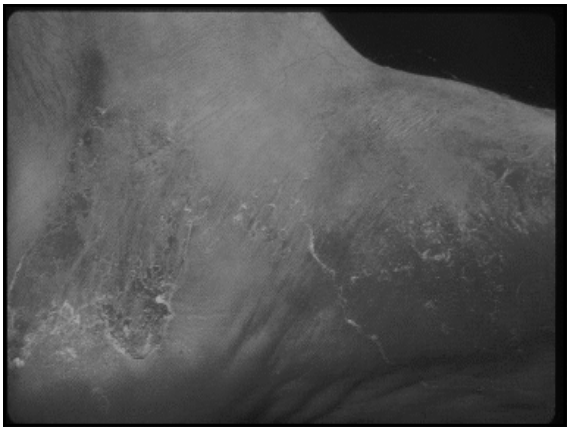
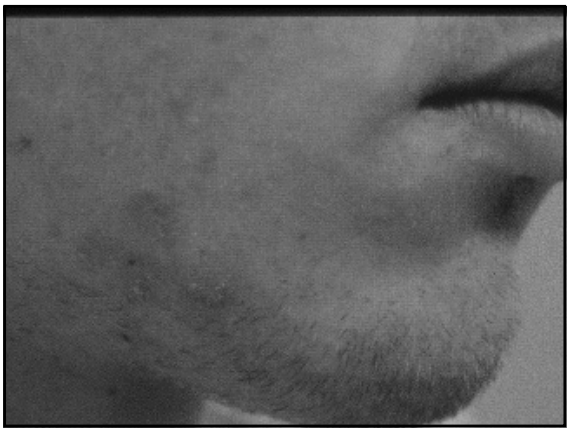


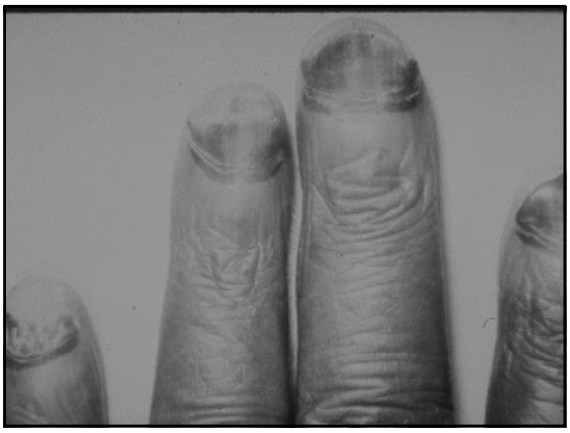
Fig. 6.12. Ringworm of the trunk. A, Tinea imb

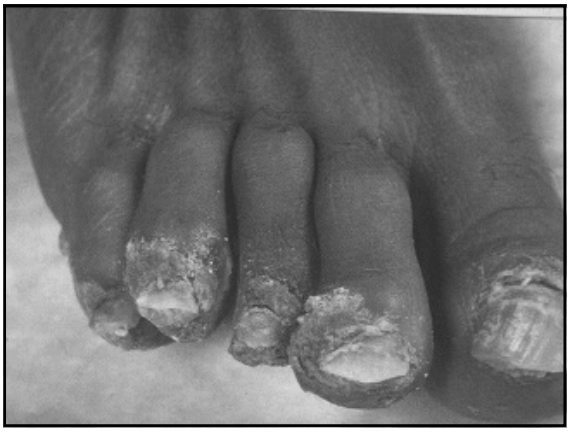


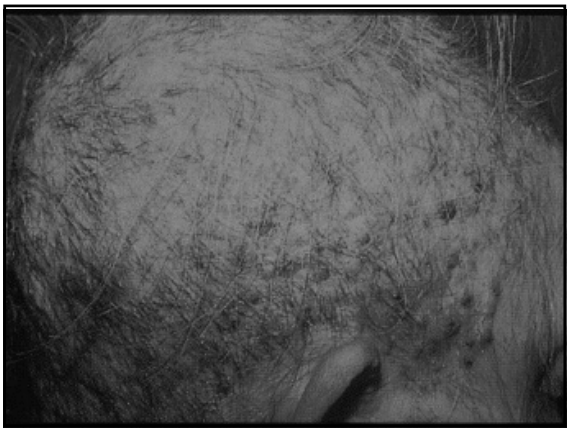


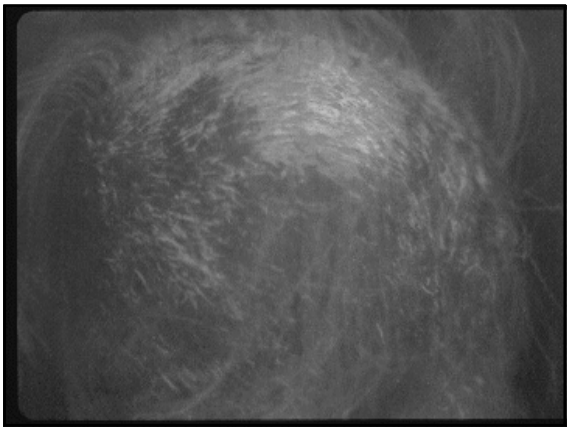












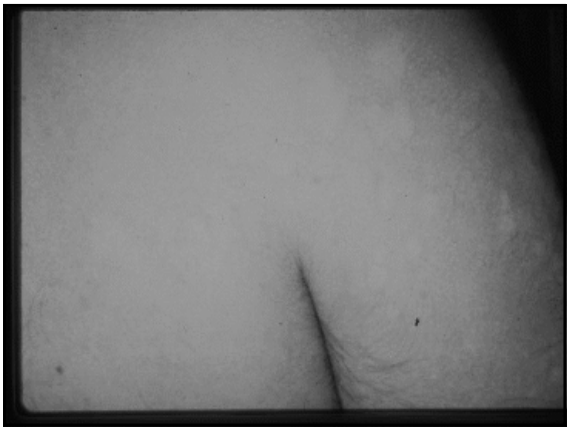
Superficial fungal infections

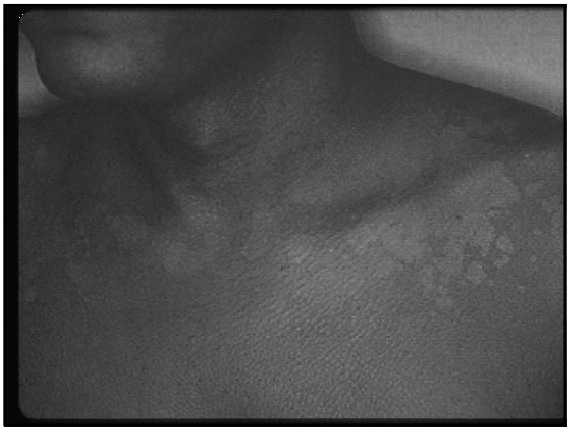
Malassezia furfur: lipophilic yeast (derives nourishment from skin lipids)

Pathogenesis: lives on skin, causes pigment changes and itch underneath

Diseases:

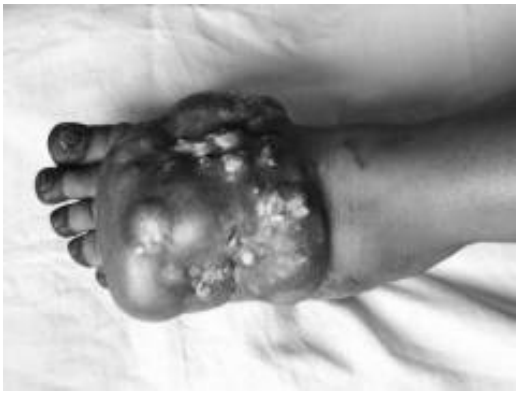
- Tinea versicolor
- Occasionally fungemia with lipid infusion





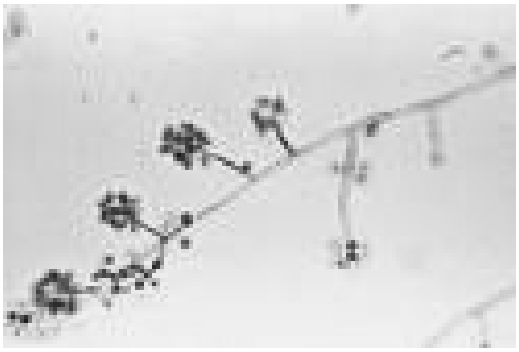
Subcutaneous fungal infections

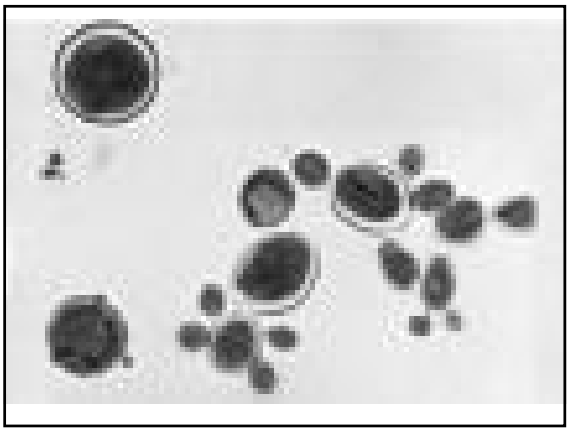
- Pathogenesis: introduced through skin by foreign body, grow in subcutaneous tissues, spread via lymphatics
- Disease; usual local; may disseminate to adjacent bones, joints.
- Most common in nonindustrialized world (mycetoma of feet)



Subcutaneous fungal infection: Sporotrichosis

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





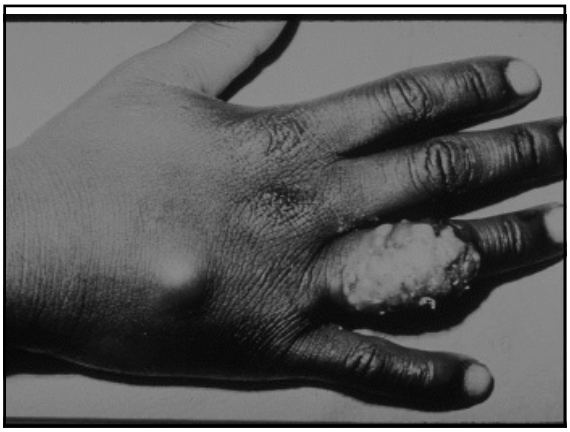
Sporotrichosis

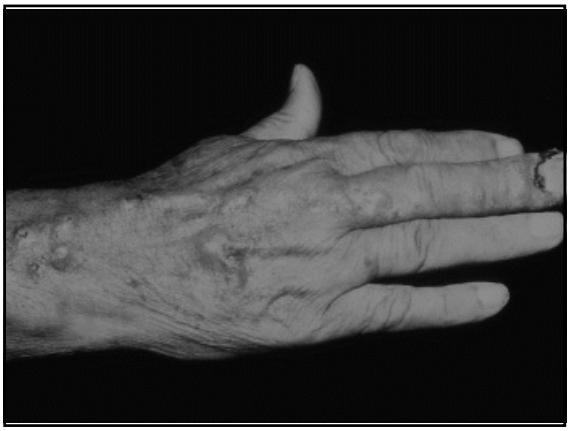
Pathophysiology:

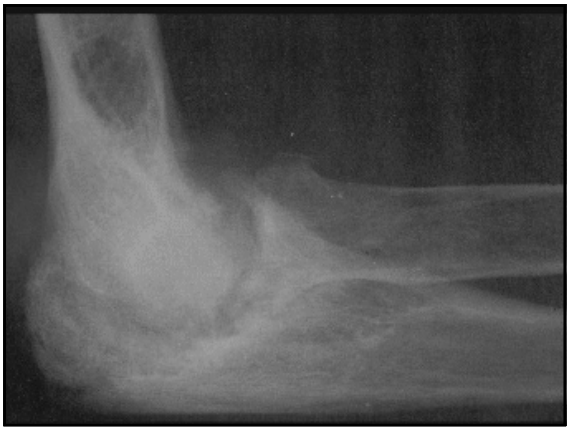
- Spore inoculated by foreign body
- Yeasts travel along lymphatics
- Elicit mixed pyogenic-granulomatous reaction

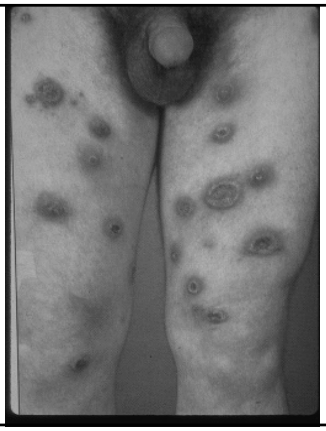
Clinical:

- Gardeners and outdoorspersons
- Ulcerating nodules along hard cord
- Bone and joint destruction
- Dissemination rare









Systemic fungal infections: the “true pathogens”

Histoplasmosis, Coccidioidomycosis, Blastomycosis

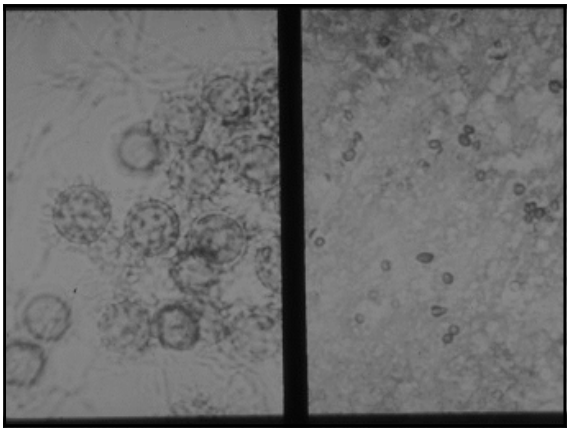
- Dimorphic
- Respiratory acquisition
- Restricted geographic distribution
- Infect normal hosts
- Disease reminiscent of TB

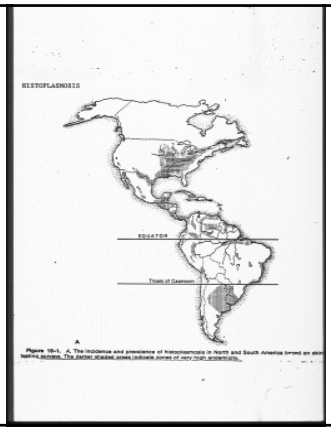
Histoplasmosis

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



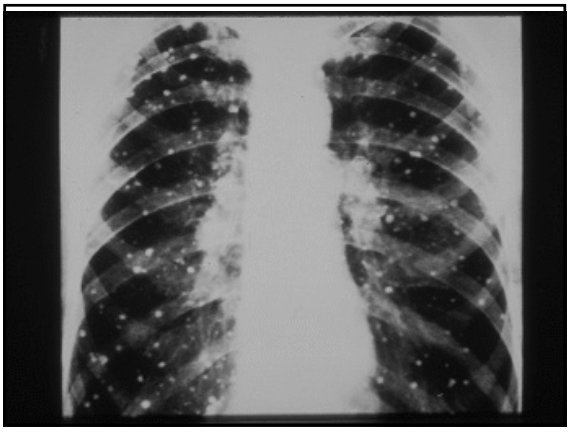


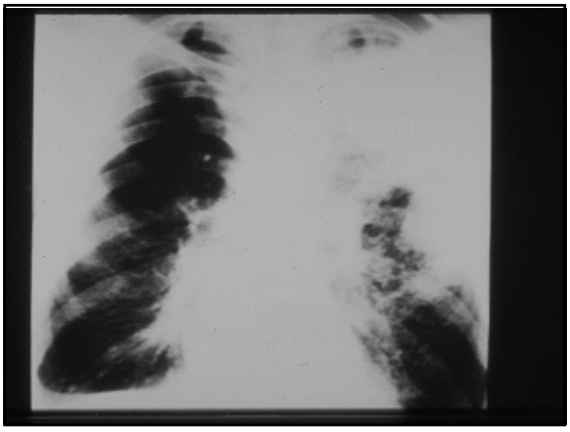
Histoplasmosis

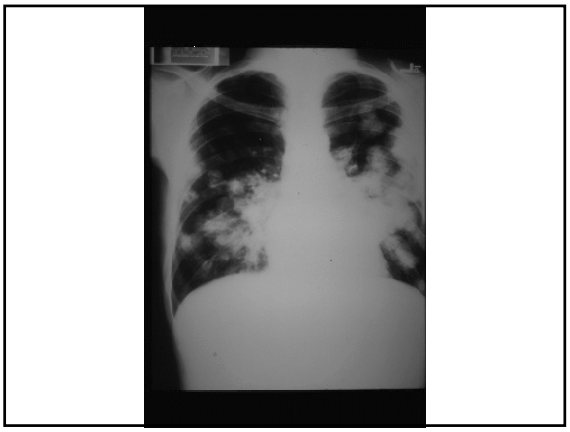
Pathophysiology:
- Mold spores transform into yeast in lung, elicit cellular immunity as per TB
- Hematogenous dissemination
- Skin test reactivity
- Walled off granulomata

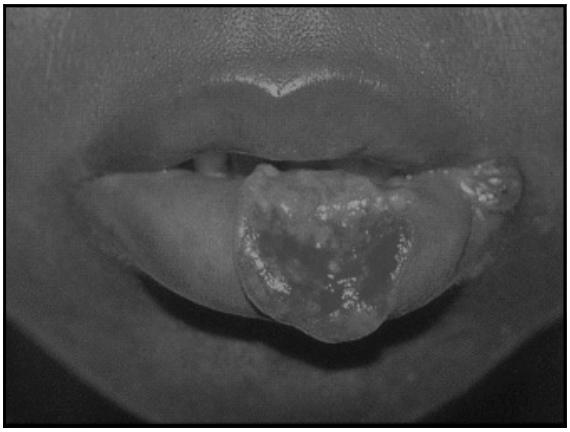
Clinical:

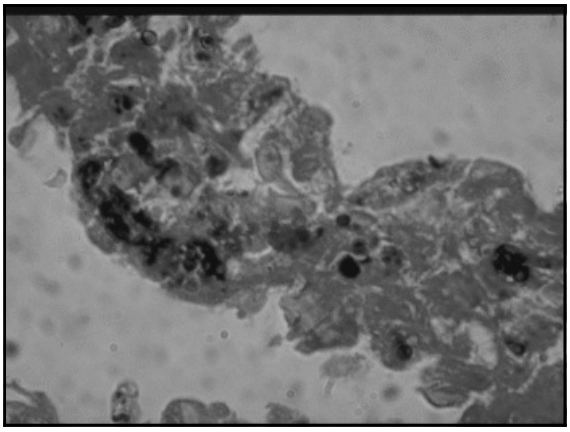
Mimics TB. Usually latent disease, but
- may cause acute/chronic cavitary lung disease
- may disseminate after infection (infancy, immunocompromise)
- may reactivate years later

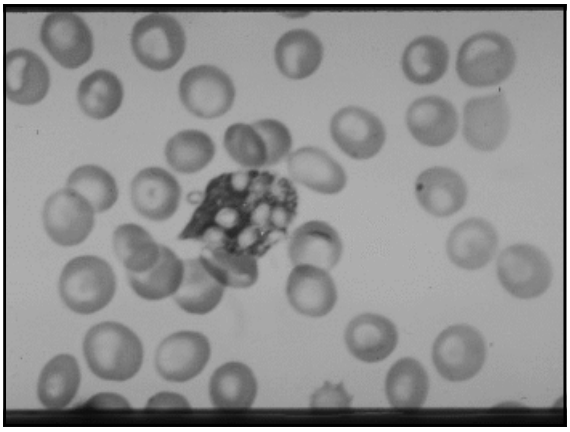










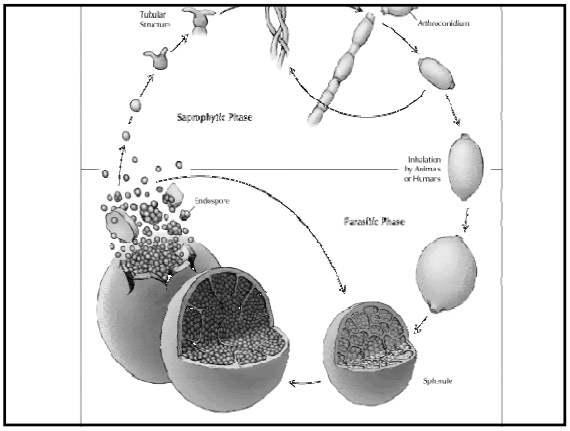


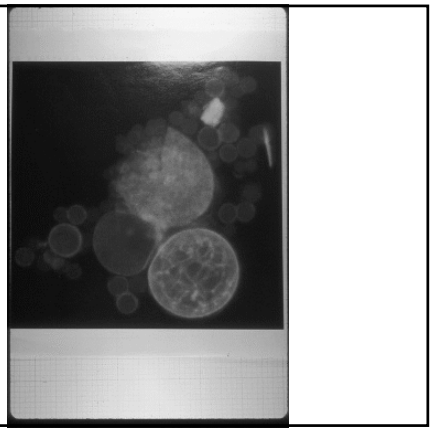
Coccidioidomycosis

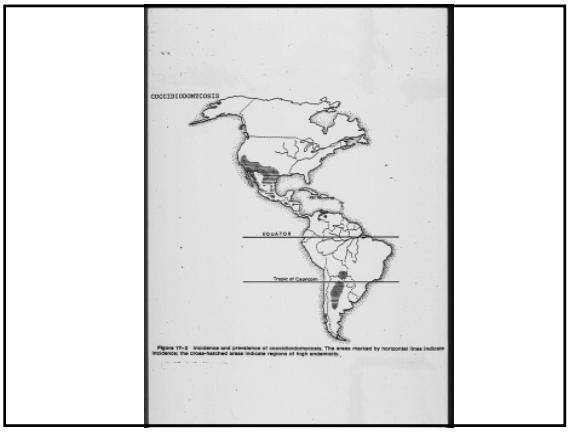
Organism: Coccidioides immitis
- Dimorph: mold in soil, spherules and endospores in host

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

Pathogenesis: inhalation of spores



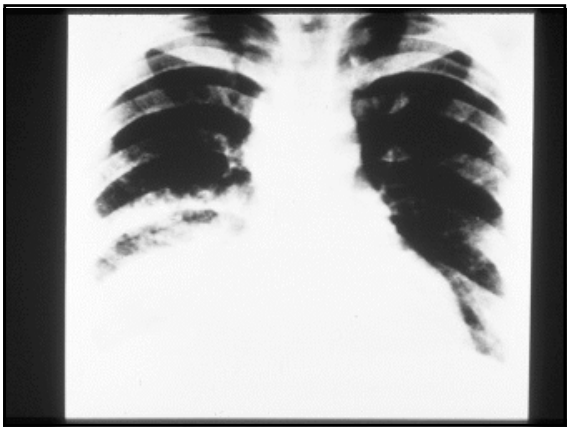


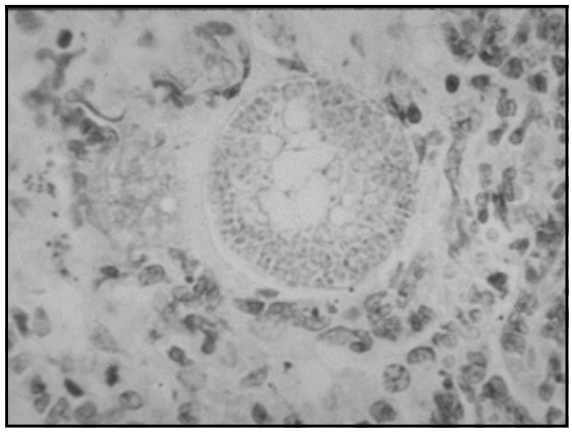


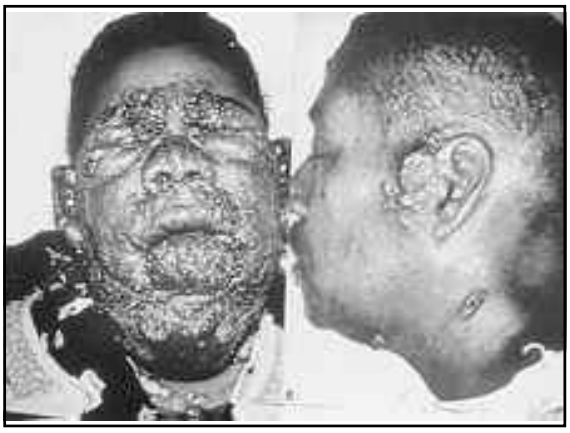
Cocci

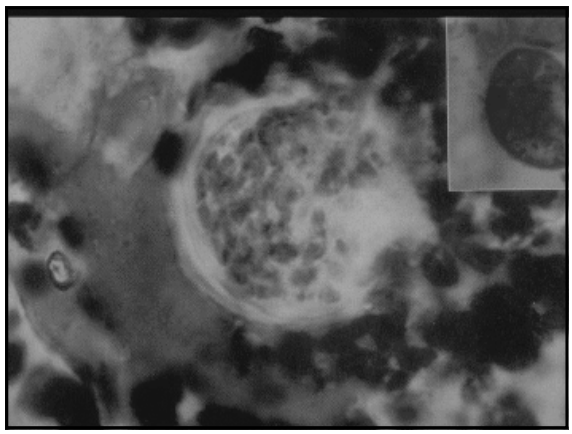
Pathophysiology:
- Spores transform into spherules in lung, elicit cellular immunity as per TB
- Hematogenous dissemination
- Skin test reactivity
- Walled off granulomas

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









Blastomycosis

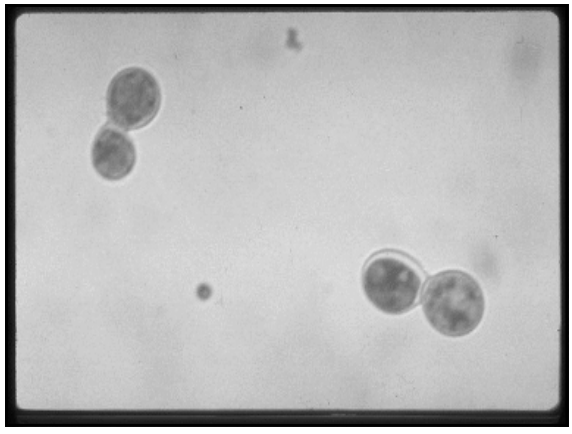
Organism: Blastomyces dermatiditis

dimorph: mold to yeast

Habitat: humid woodlands

- MidAtlantic zone
- Beaver dams, peanut farms
- Organic debris rather than soil

Pathogenesis: inhalation of spores



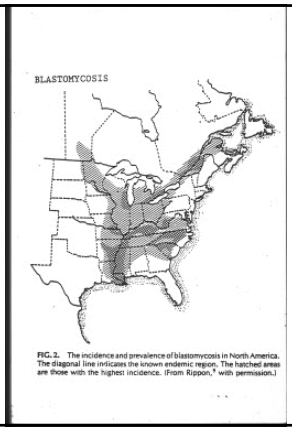


FIG. 2. The incidence and prevalence of blastomycosis in North America. The diagonal line inticates the known endemic region. The hatched areas are those with the highest incidence. (From Rippon,[9] with permission.)

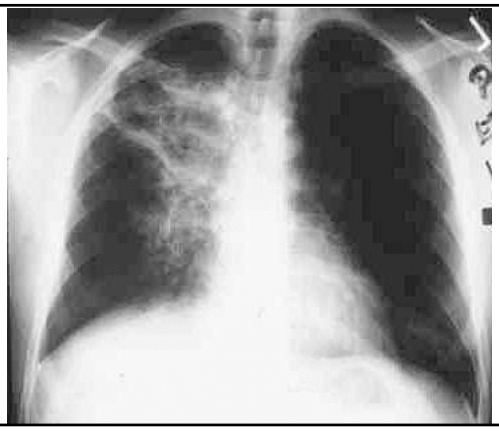
Blastomycosis

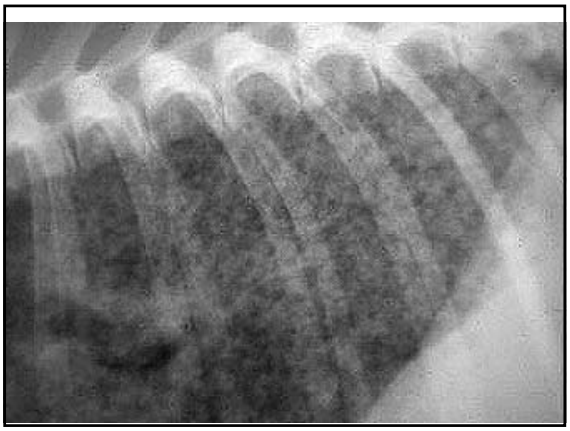
Pathophysiology:

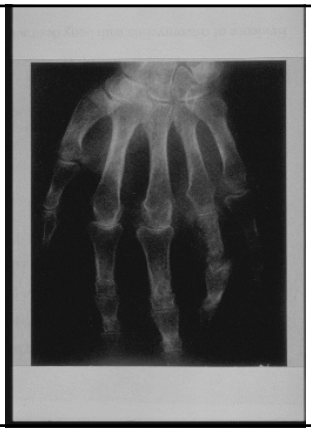
- Spores transform into yeast in lung, disseminate
- No good antigen test to define exposed population

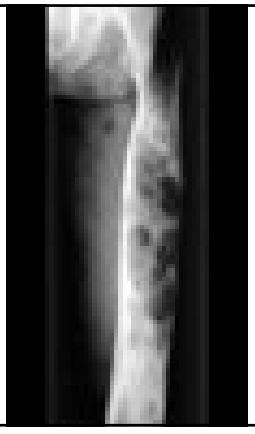
Clinical:

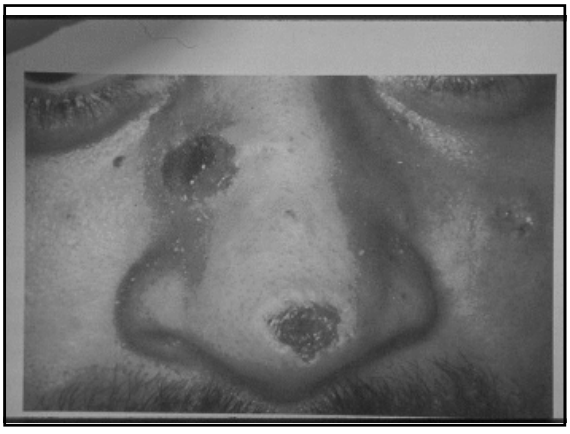
- Acute or chronic lung disease (nodular/cavitary)
- Disseminated disease:
  - Skin
  - Bone
  - Urinary tract in men

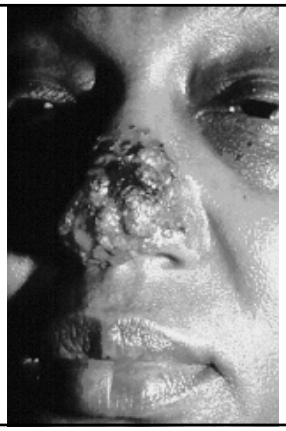


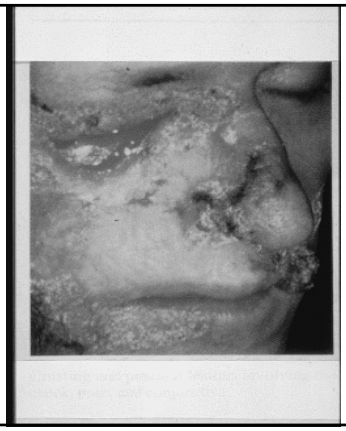


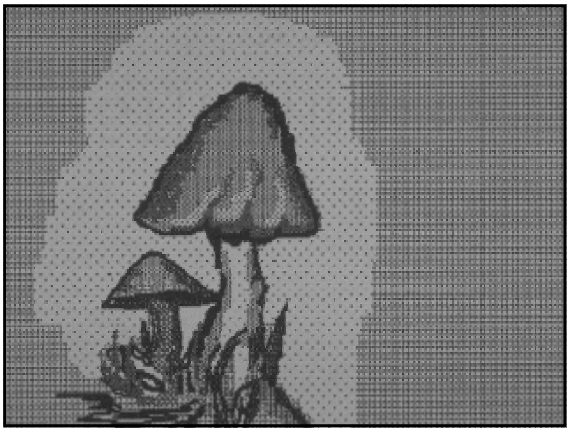












Systemic fungal infections: B. "the opportunists"

Histo, Blasto, Cocci

- Geographic distribution
- Dimorphic
- Infection by inhalation
- Pyogenic/granulomatous host response
- Similar to TB
- Infection =~ immunity

Opportunists

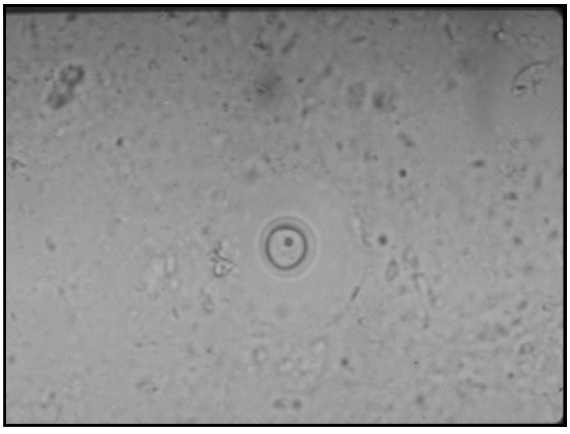
- Omnipresent
- Yeasts or molds
- Various routes of infection
- Host response varies
- Clinical syndromes vary
- No lasting immunity

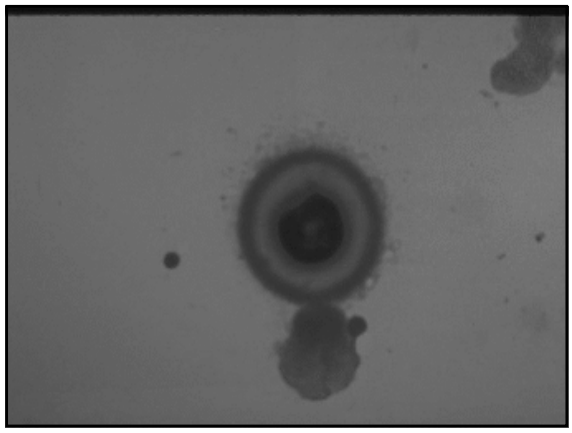
Cryptococcosis

Organism: Cryptococcus neoformans
yeast with a thick polysaccharide capsule

Habitat: bioterrorists (of a sort), worldwide

Pathogenesis: inhalation of yeasts





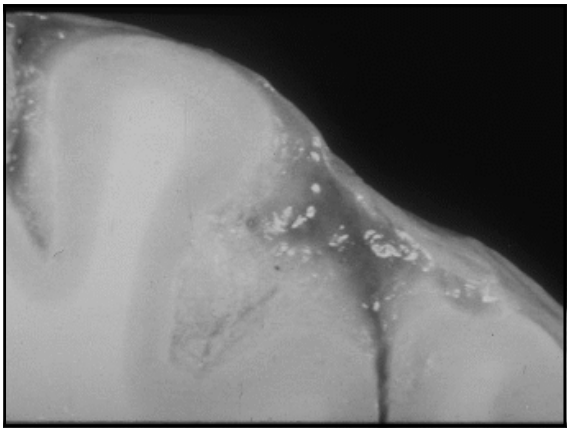
Cryptococcosis

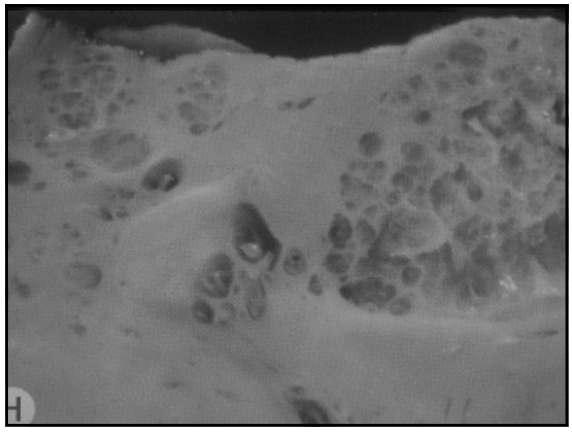
Pathophysiology:

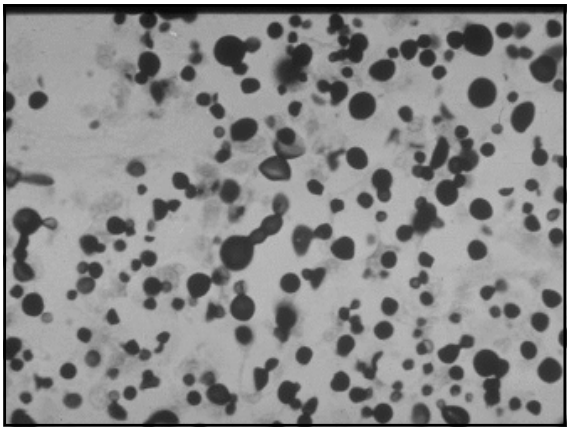
- Inhalation leads to
- Transient colonization OR
- Acute/chronic lung disease OR
- CNS invasion

Clinical

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

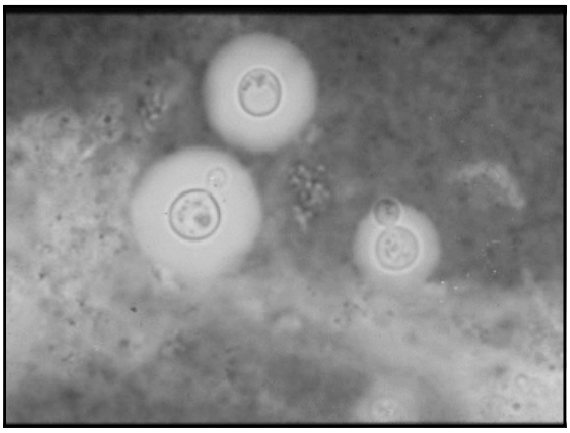






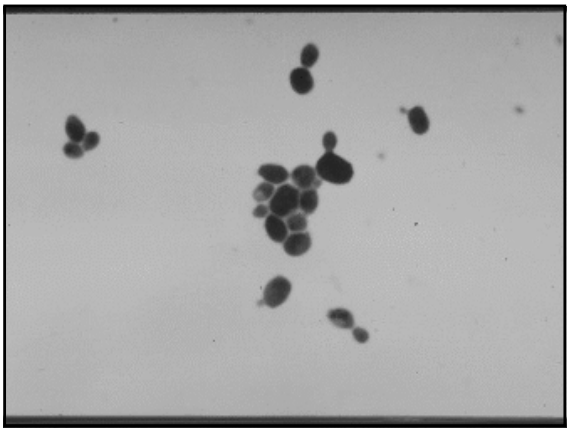
Cryptococcal meningitis

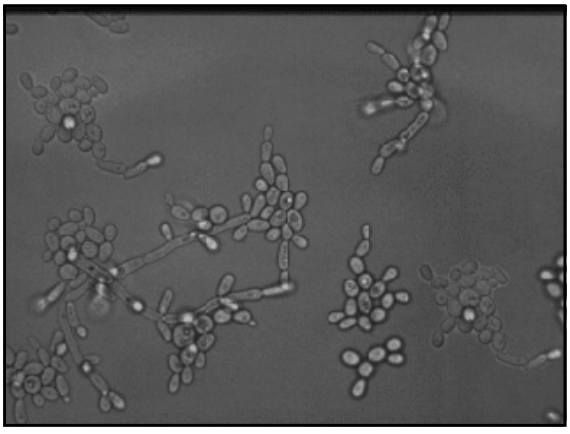
- India ink preparation of CSF may show organisms
- Serum or CSF antigen assay diagnostic in >95% cases of CNS disease

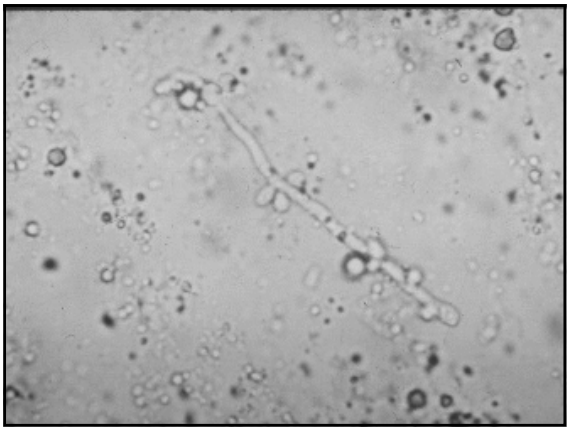


Candidiasis

- 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





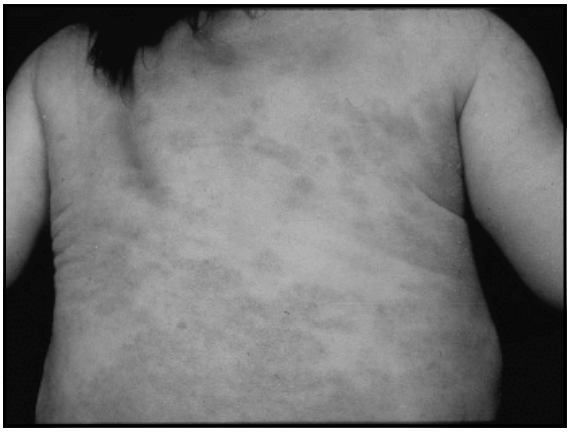


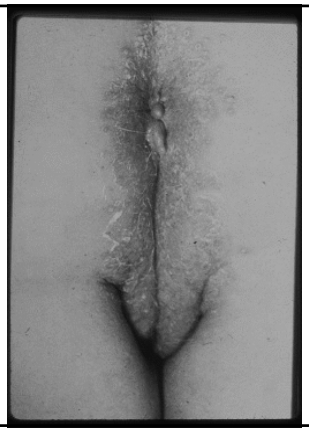
Pathogenesis of Candida infections

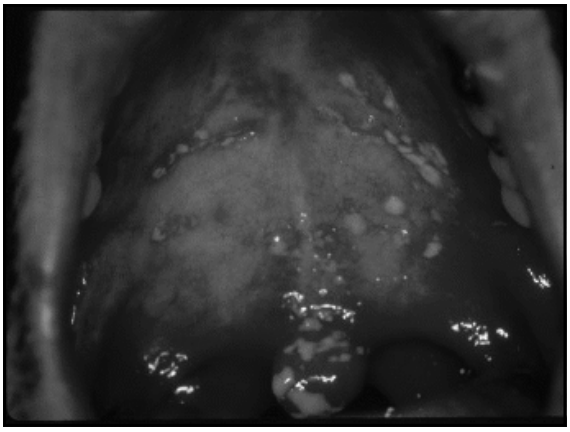
- Primary host defenses:
  - Intact skin
  - Intact mucosa with normal pH and normal flora
  - Functioning lymphocytes
  - Functioning neutrophils

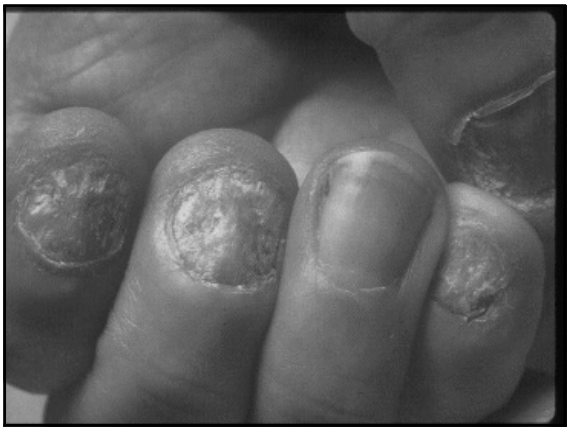
Pathogenesis of local Candida infections

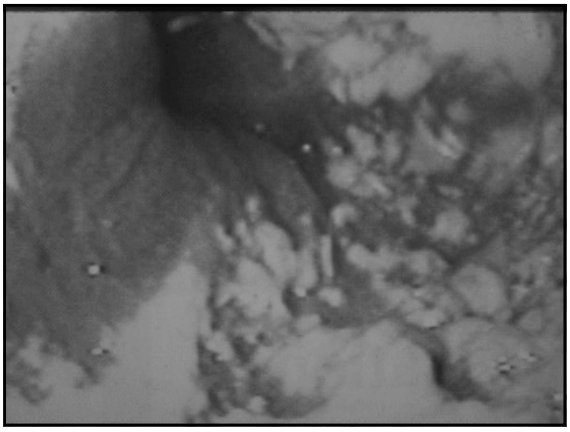
- Environmental changes
  - Wet skin
  - Changes in local flora
  - Hormones, foreign bodies
- Lymphocyte dysfunction
  - Immaturity
  - Destruction (HIV)









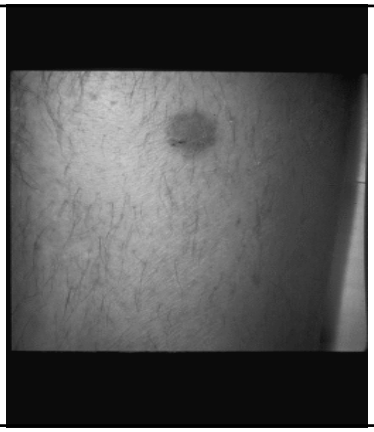


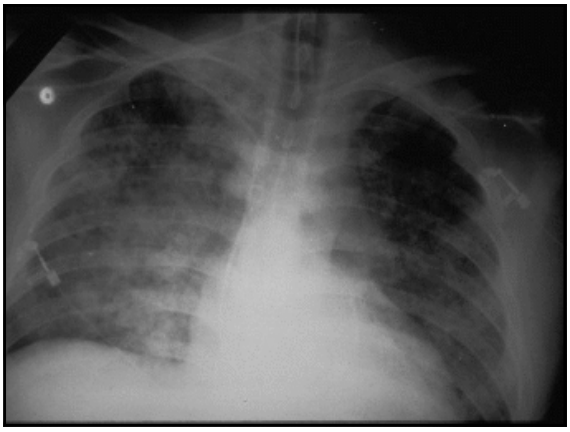
Pathogenesis of invasive Candida infections

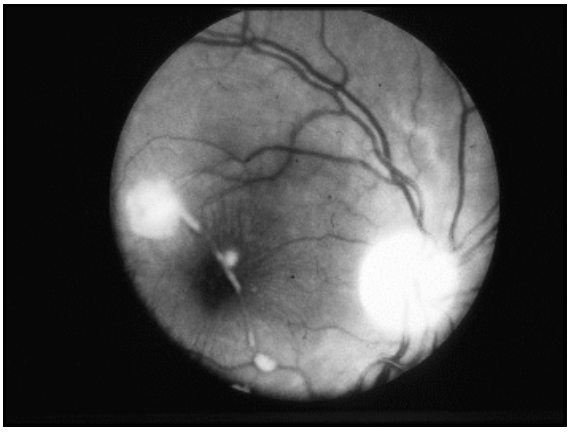
- Breach in anatomic integrity (often biofilm on catheter)
- Defective PML function (first line of defense)
  - Myeloperoxidase, complement necessary but not sufficient defense
  - Cytokines also essential for recruiting phagocytes in disseminated disease
  - Antibody may or may not be present; may or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



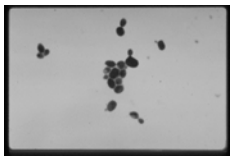




"Virulence" of Candida?

- 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

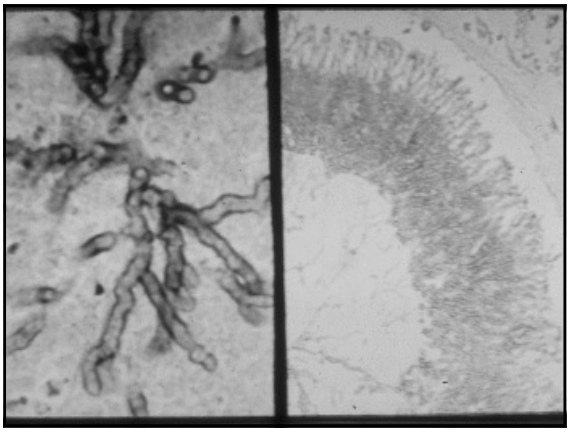
Additional comments on candidiasis



- 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

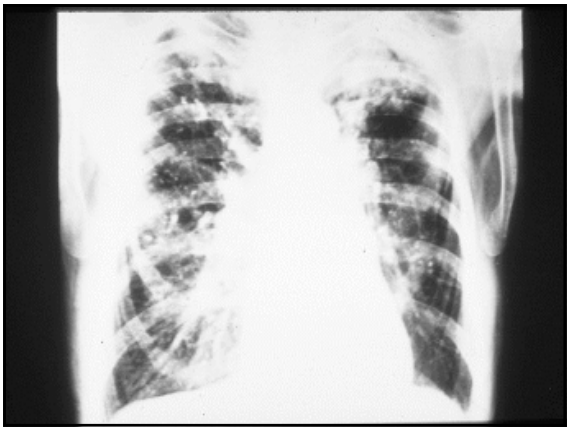
<u>Pathophysiology</u>

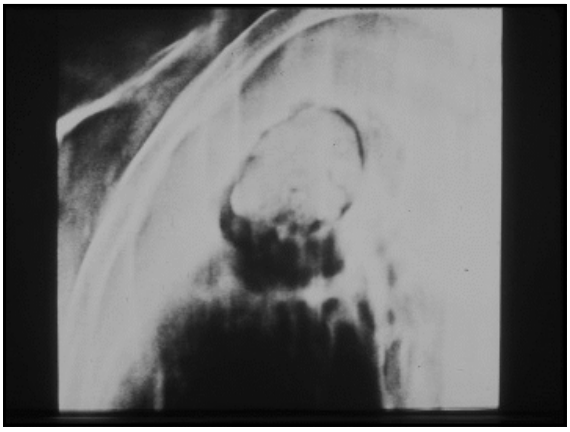
Spores in lung may:

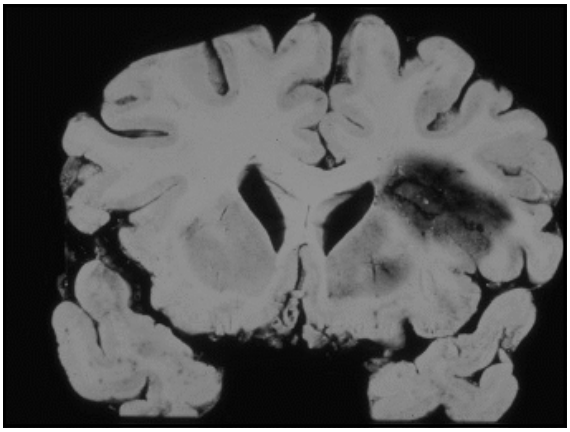
- Elicit allergy
- Grow in preexisting cavity
- Invade vasculature, disseminate with local and distant disease
- Neutrophils prime defenders

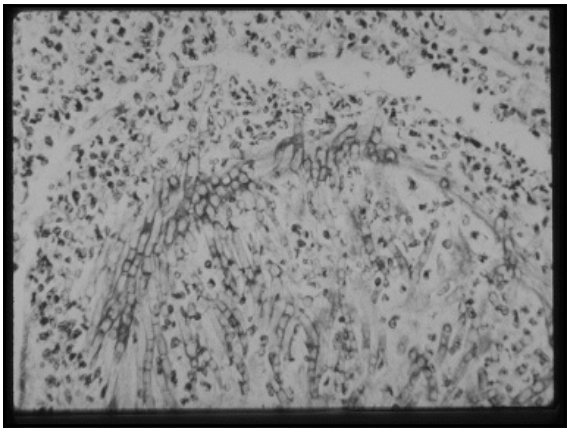
<u>Clinical</u>

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



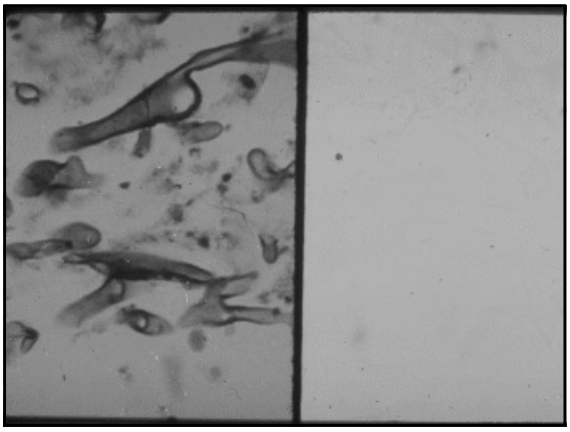


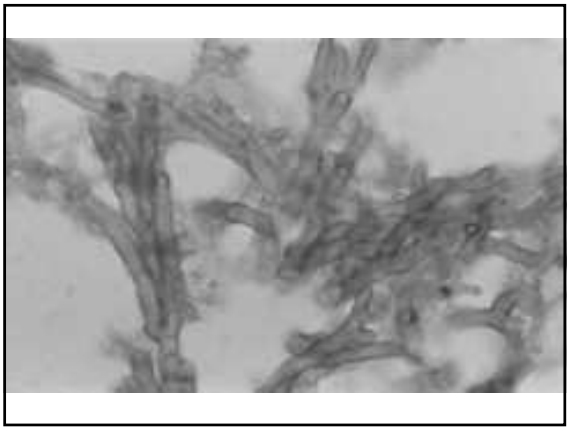


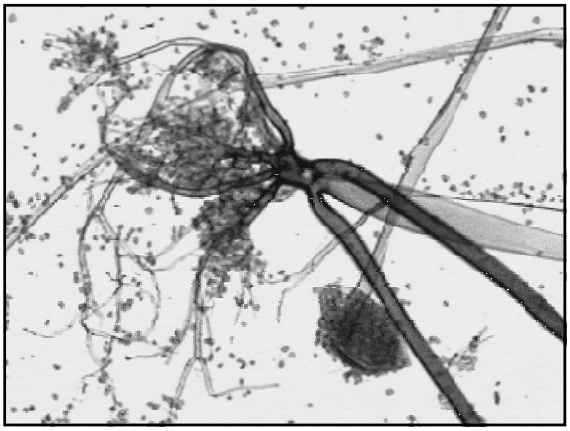


Mucormycosis

- 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

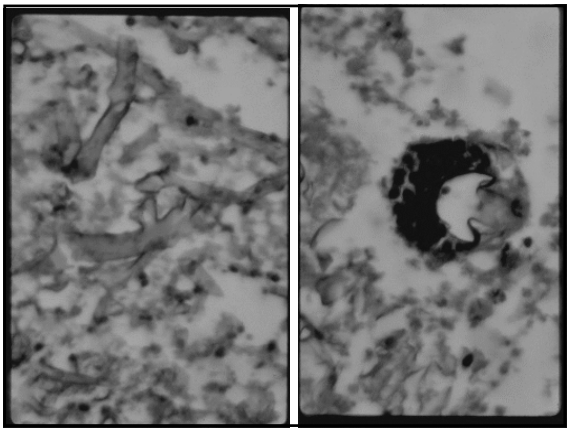
May enable relentless growth

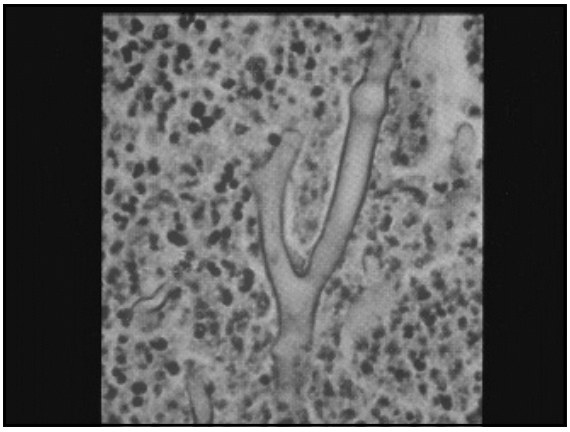
Clinical:

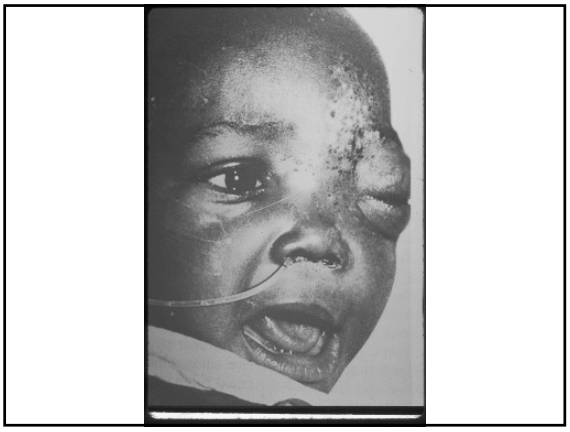
The most acute and fulminant fungal infection known

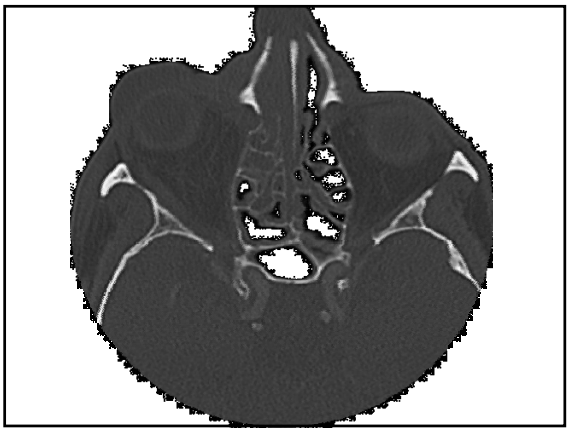
Lower airways: pneumonia progressing to infarction

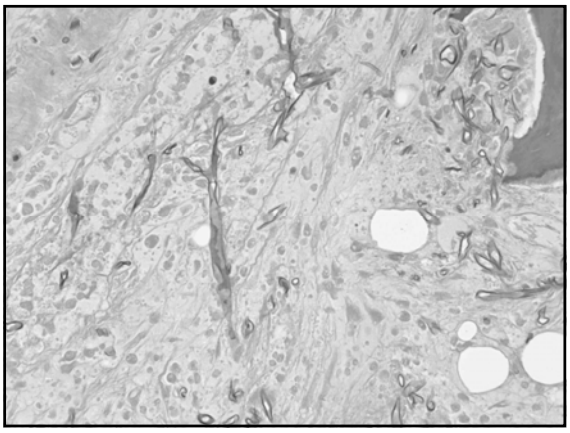
Upper airways: sinusitis progressing to brain abscess

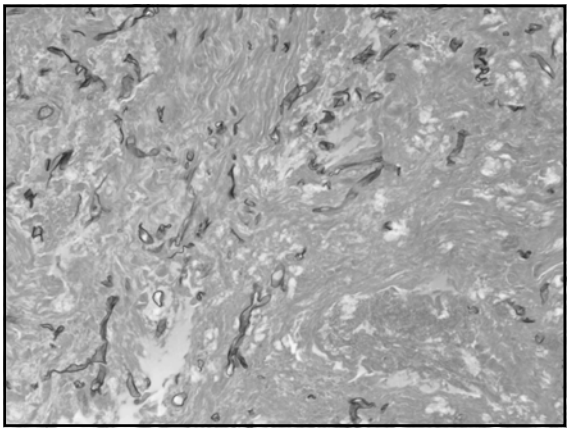


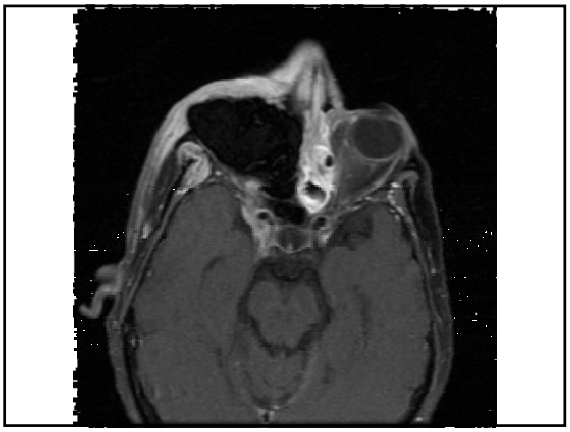


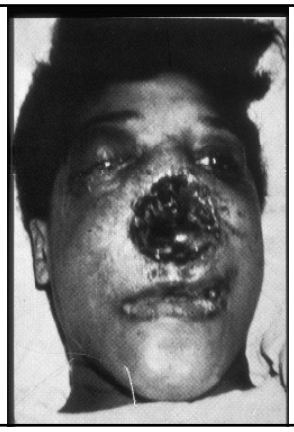












Summary: Fungal “opportunism”

- 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)