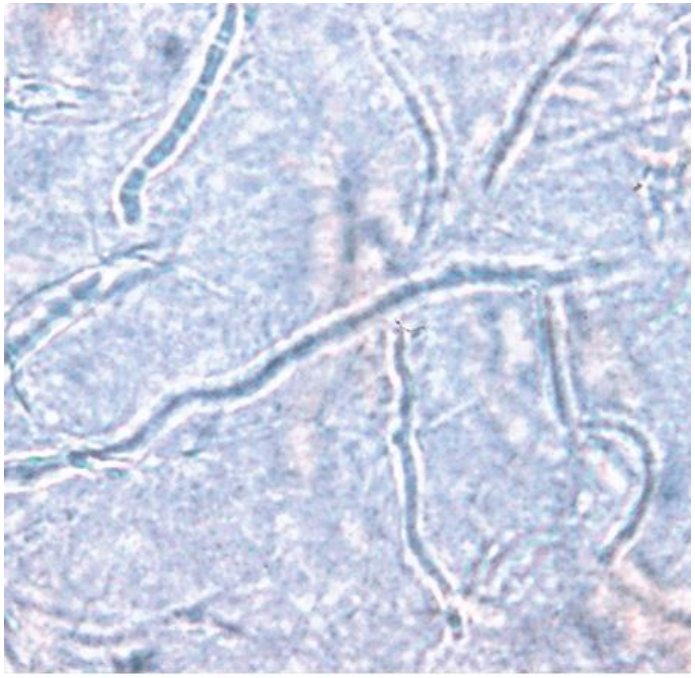
# FUNGI

Kenneth Alonso, MD, FACP

# Cutaneous mycoses

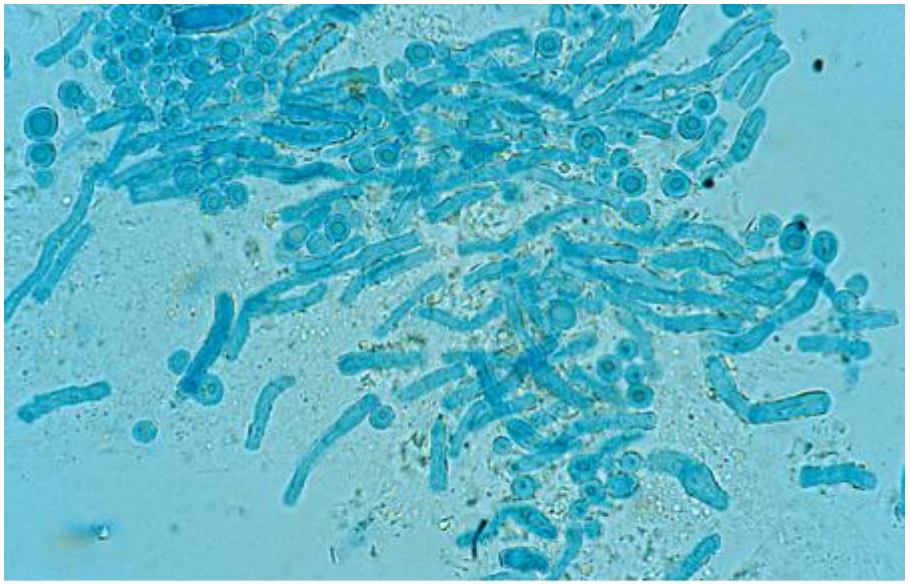
- Dermatophytes are molds that use keratin as a nutritional source.
- Produce keratinase.
- Not dimorphic.
- Live on human skin.
- Mold hyphae seen on KOH prep.
- If the lesion fluoresces with a Wood's lamp (UV), Microsporum species is the cause.
- Topical antifungals effective

# KOH preparations





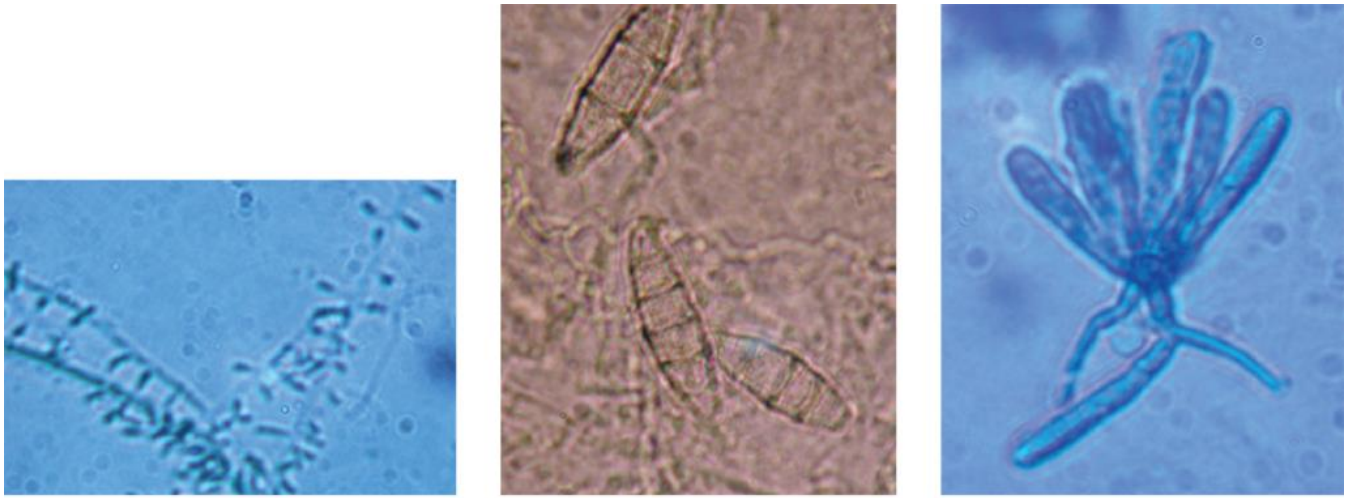
Multiple, septated, tube-like structures (hyphae or mycelia) and spore formation in scales from an individual with epidermal dermatophytosis.





Malassezia furfur. Round yeast and elongated pseudohyphal forms, so-called "spaghetti and meatballs."

Figs. 25-1 and 25-37 Accessed 07/01/2010






Examples of the three genera of dermatophytes. A:T. tonsurans is characterized by the production of elongated microcondia attached to a supporting hypha. B:M. gypseum produces individual thin- and rough-walled macroconidia. C:E. floccosum has club-shaped, thin- and smooth-walled macroconidia that typically arise in small clusters.

# Superficial fungal infections

- Pityriasis versicolor
- Young adults
- Tinea versicolor
- Hypopigmented, sharply marginated, scaling macules
- Sites of sebum production
- Malassezia furfur (yeast)
- Has “spaghetti and meatball” appearance on KOH prep.
- May cause seborrheic dermatitis in the immunocompromised.

# Pityriasis versicolor

- Oval scaly macules, papules on skin where sebaceous glands are found.



Hyperpigmentation – light skin



Hypopigmentation – dark skin

Figs. 25-35 and 25-36 Accessed 07/01/2010

# Dermatophyte infections

- Dermatophytoses of keratinized epidermis (epidermal dermatophytosis, epidermomycosis):
- Tinea facialis, tinea corporis, tinea cruris, tinea manus, tinea pedis.
- Dermatophytoses of nail apparatus (onychomychosis):
- Tinea unguium (toenails, fingernails).
- Dermatophytoses of hair and hair follicle
- (Trichomycosis): Dermatophytic folliculitis, Majocchi
- (Trichophytic) granuloma, tinea capitis, tinea barbae.

# Tinea

- Tinea rubrum is the most common cause of epidermal dermatophytosis and onychomycosis in industrialized nations.
- Classical findings are erythema, scaling, maceration.
- May have vesicles (T. mentagrophytes)
- Moist areas preferred sites.
- Often interdigital (tinea pedis)

# Tinea infection



Tinea infection (scaling) involving the scalp, neck, and upper back of this HIV-infected patient. Three different dermatophytes are the usual source of infection: epidermophyton, trichophyton, and microsporum.

(Photo contributor: Seth W. Wright, MD.)

Fig. 20-33 Accessed 07/01/2010

# Superficial fungal infections

- Tinea unguium
- Distal onycholysis and hyperkeratosis of nails
- T. mentagorophytes
- Tinea barbae
- Men
- Pustular folliculitis
- T. mentagorophytes
- Tinea nigra
- Presents with darkly pigmented macules with irregular edges (commonly found on palms).
- Most common in children, young adults.
- Caused by black fungus, Hortaea werneckii.

# Tinea unguium

https://media.sciencephoto.com/image/m2700171/800wm/M2700171-Toenails_showing_Tinea_unguium_fungal_infections.jpg Accessed 12/10/2019

# Superficial fungal infections

- Tinea mannum
- Papules and vesicles on hands in dyshydrotic type
- Red annular scaling patches confined to palmar creases in hyperkeratotic form
- May fissure
- “One hand, two feet” characteristic
- Tinea cruris
- Large, scaling well demarcated plaques
- Groin area
- Majority of patients also have Tinea pedis

# Tinea cruris


https://www.dermnetnz.org/topics/tinea-cruris/
Accessed 12/10/2019

# Superficial fungal infections

- Tinea corporis (“ringworm”)
- Well-demarcated, red scaling plaque with raised border of tiny vesicles and central clearing
- May present on face (Tinea facialis)
- Epidermophyton flocculosum, Tinea rubrum most common agents
- M. canis also noted

# Tinea corporis (“ringworm”)

http://3.bp.blogspot.com/-xspofJUHqTU/UMngJeA25DI/AAAAAAAAGp0/R89YCyea_fA/s320/tinea_b3301.jpg
Accessed 12/10/2019

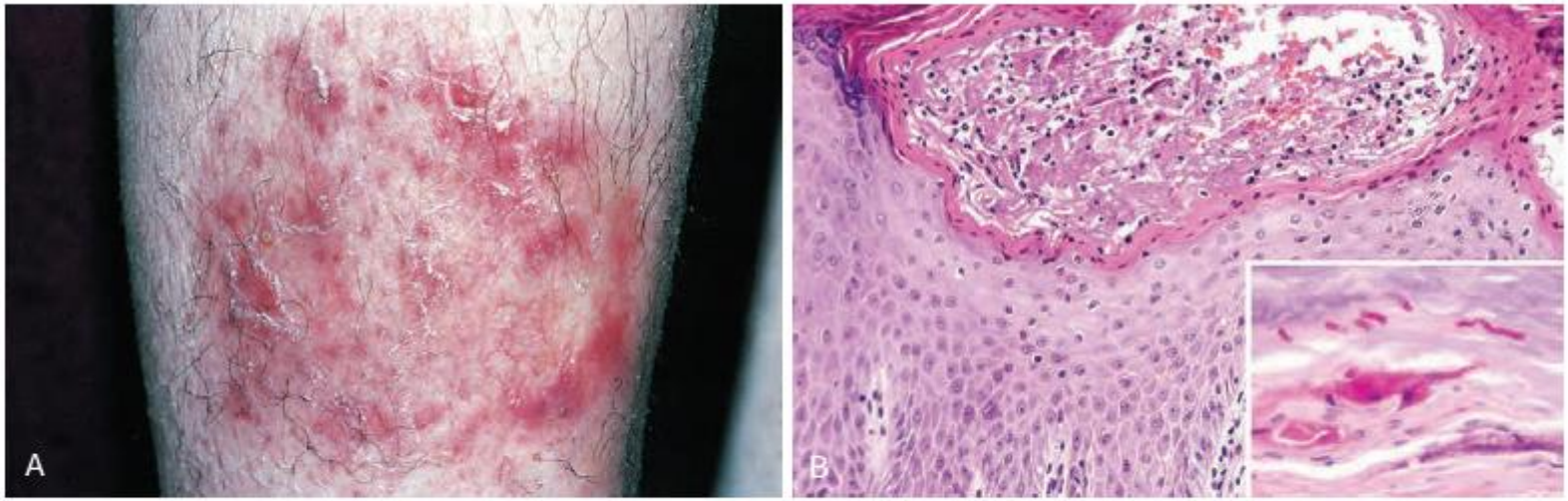



**Figure 25-40** Tinea. **A,** Characteristic plaque of tinea corporis. **B,** Routine histology shows a mild eczematous (spongiotic) dermatitis and focal neutrophilic abscesses. A periodic acid–Schiff stain *(inset)* reveals deep red hyphae within the stratum corneum.

# Superficial fungal infections

- Tinea capitis
- Toddlers and school aged children
- Common in blacks
- Ectothrix infection (outside hairshaft) with cuticle destruction
- “Gray patch”
- Microsporum species
- Endothrix infection (hairshaft) without cuticle destruction
- “Black dot” alopecia
- Kerion type associated with inflammatory plaques
- Tricophyton species

# Tinea capitis

https://diseasespictures.com/wp-content/uploads/2014/04/Tinea-Capitis-5.jpg
Accessed 12/10/2019

# Subcutaneous mycoses

- Sporotrichum schenkii.
- Dimorphic fungus (mold at 25C, yeast at 37C).
- Soil organism, sphagnum moss.
- Initial lesion is a papule, may ulcerate. Secondary chain of nodules along lymphatic drainage follows 2 weeks later.
- Responds to Iodine.

Fig. 25-43 Accessed 07/01/2010

# Other subcutaneous mycoses

- Chromomycosis
- Dematiaceous soil fungi, having melanized cell walls
- Crusty abscesses and warty nodules spread along lymphatics.
- Euycetoma
- Madura foot
- Localized abscess caused by any soil fungus



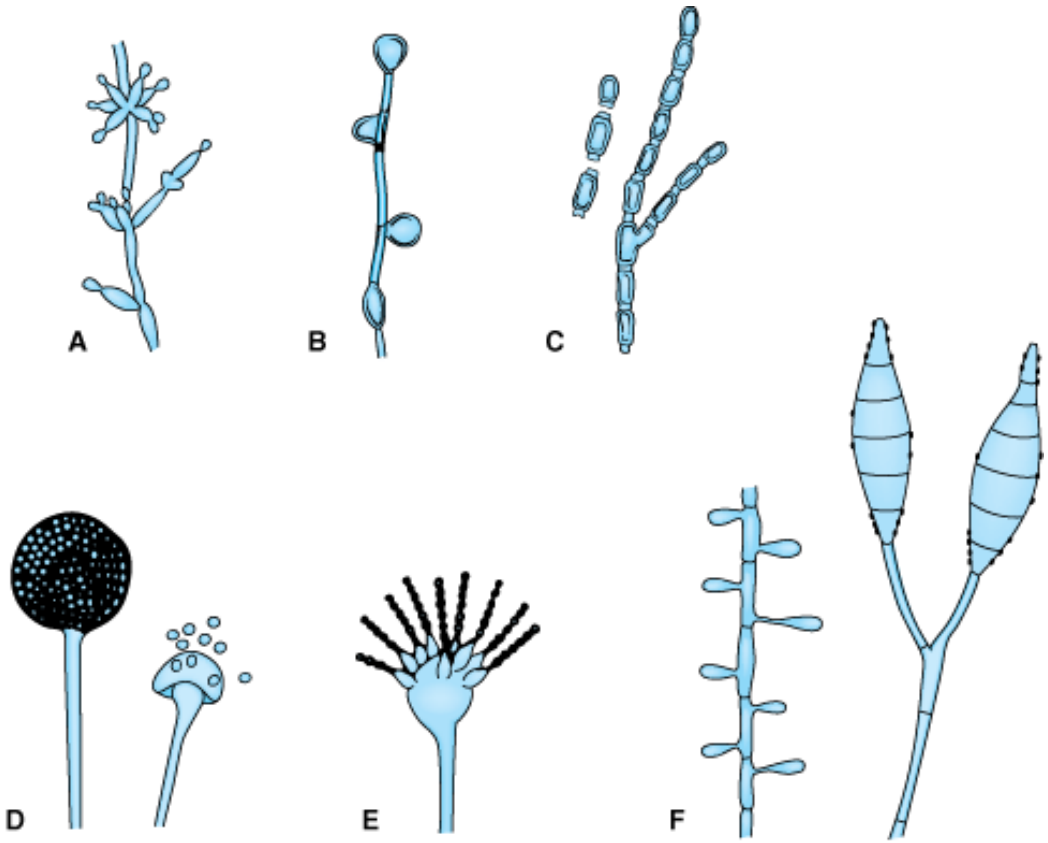


Figs. 25-41 and 25-42 Accessed 07/01/2010

# Reproduction

- Conidia:
- Arthroconidia result from a pre-existing, entire hyphae.
- Break loose and initiate another cycle of reproduction by germination.
- Blastocondia: Elongate into pseudohyphae.
- Macroconidia/ microconidia
- Sporangiospore
- Reproduction by cytoplasmic cleavage within a structure called sporangium.
- Aseptate hyphae.

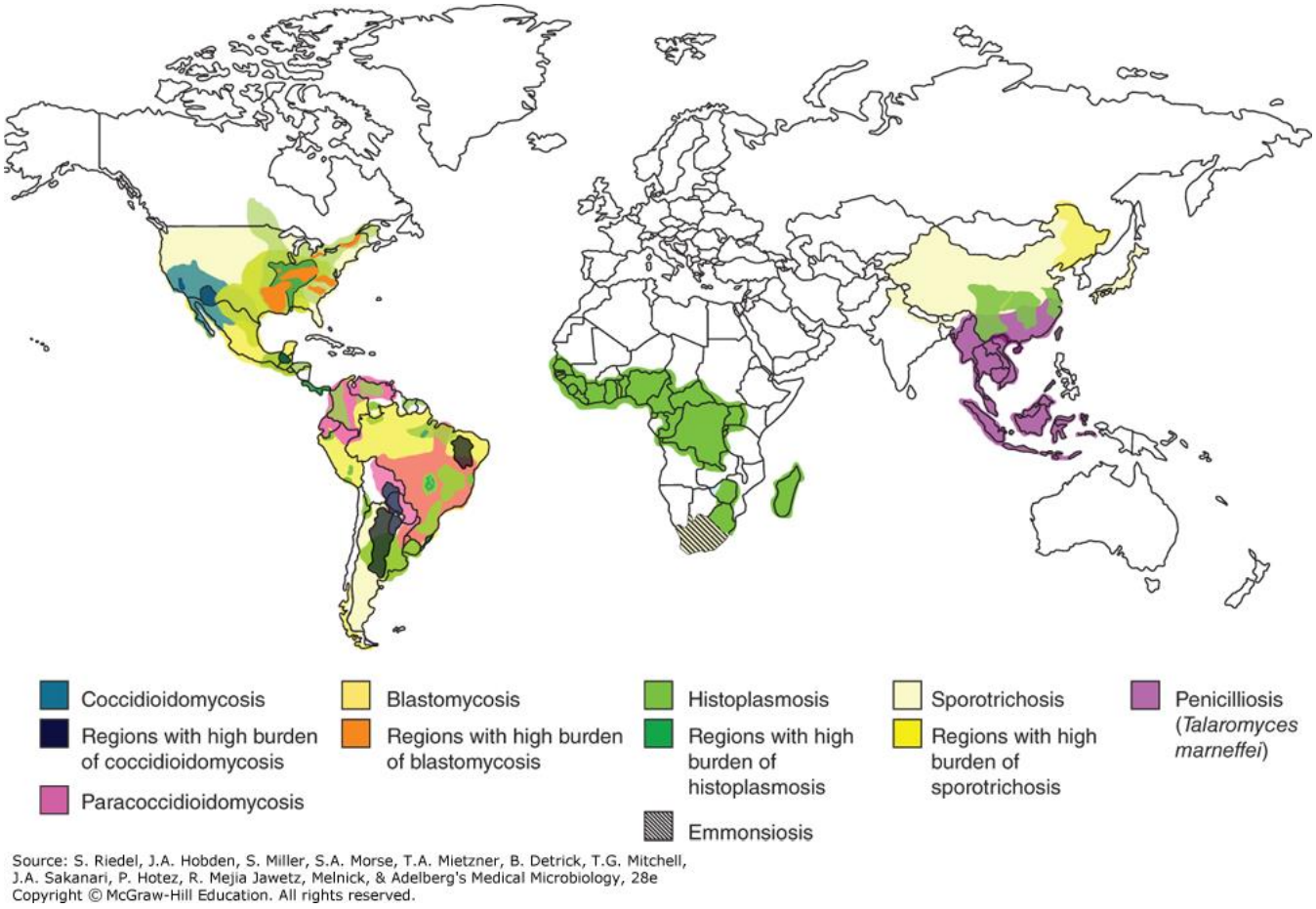
# Asexual fungal spores




Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com



- A: Blastoconidia and pseudohyphae (Candida); B: Chlamydospores (Candida) ; C: Arthrospores (Coccidiodes); D: Sporangia and sporangiospores (Mucor); E: Microconidia (Aspergillus); F: Microconidia and macroconidia (Microsporum).
- (Modified and reproduced, with permission, from Conant NF et al: *Manual of Clinical Mycology,* 3rd ed. Saunders, 1971.)
- Fig. 47-1 Accessed 08/01/2010



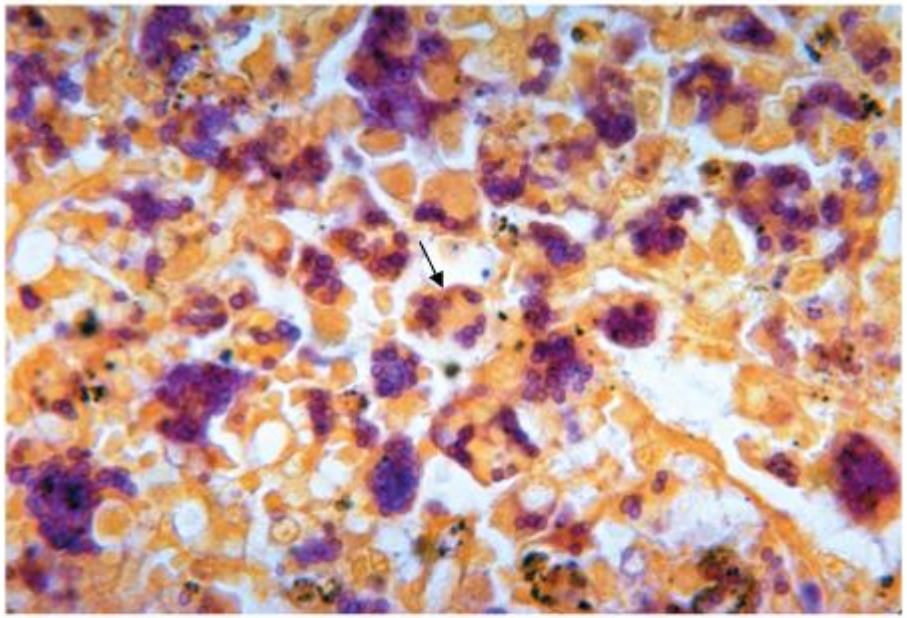

Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e


Global distribution of endemic mycoses. Each is caused by a dimorphic environmental mold and undergoes morphogenesis within the host. (Reproduced with permission from Lee PP, Lau Y-L: Cellular and molecular defects underlying invasive fungal infections—revelations from endemic mycoses. Front Immunol 2017;8:375.)

# Systemic mycoses

- Histoplasma is thermally dimorphic.
- Small.
- Asexual spores inhaled.
- Yeast cells proliferate in unactivated alveolar macrophages.
- If large inoculum inhaled, may present with fever, chills, malaise, non-productive cough
- Clear spontaneously
- If immune compromised, may disseminate throughout reticuloendothelial system
- Men, generally
- Tuberculate chlamydospores in culture are diagnostic.

# Histoplasma capsulatum



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com



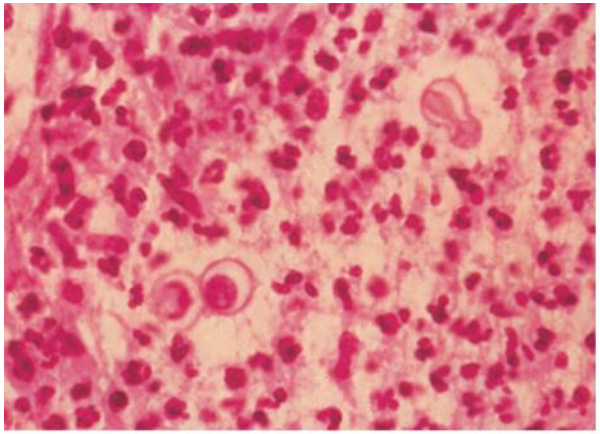
Arrow points to a macrophage containing several purple-stained yeasts in the cytoplasm. Yeasts within macrophages can be seen in many macrophages in this specimen of spleen.

Provider: CDC/Dr. M. Hicklin.

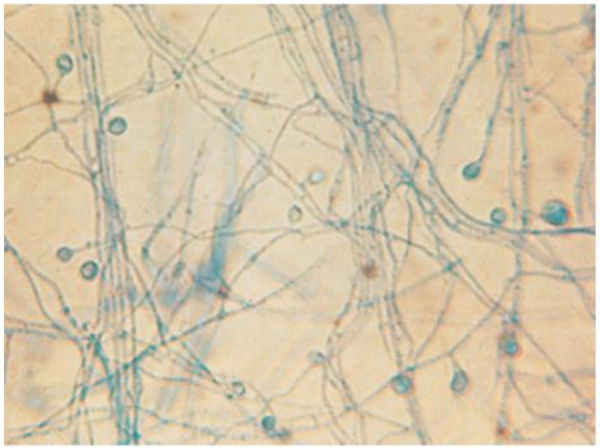
Color plate 34 Accessed 08/02/2010

# Systemic mycoses

- Blastomyces is thermally dimorphic.
- Spores inhaled.
- May cause fever, malaise, night sweats, cough, myalgia
- Big, broad-based, budding yeast.
- Forms granulomatous nodules.
- If disseminated, cutaneous nodules may ulcerate
- Men, generally



A



B

Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

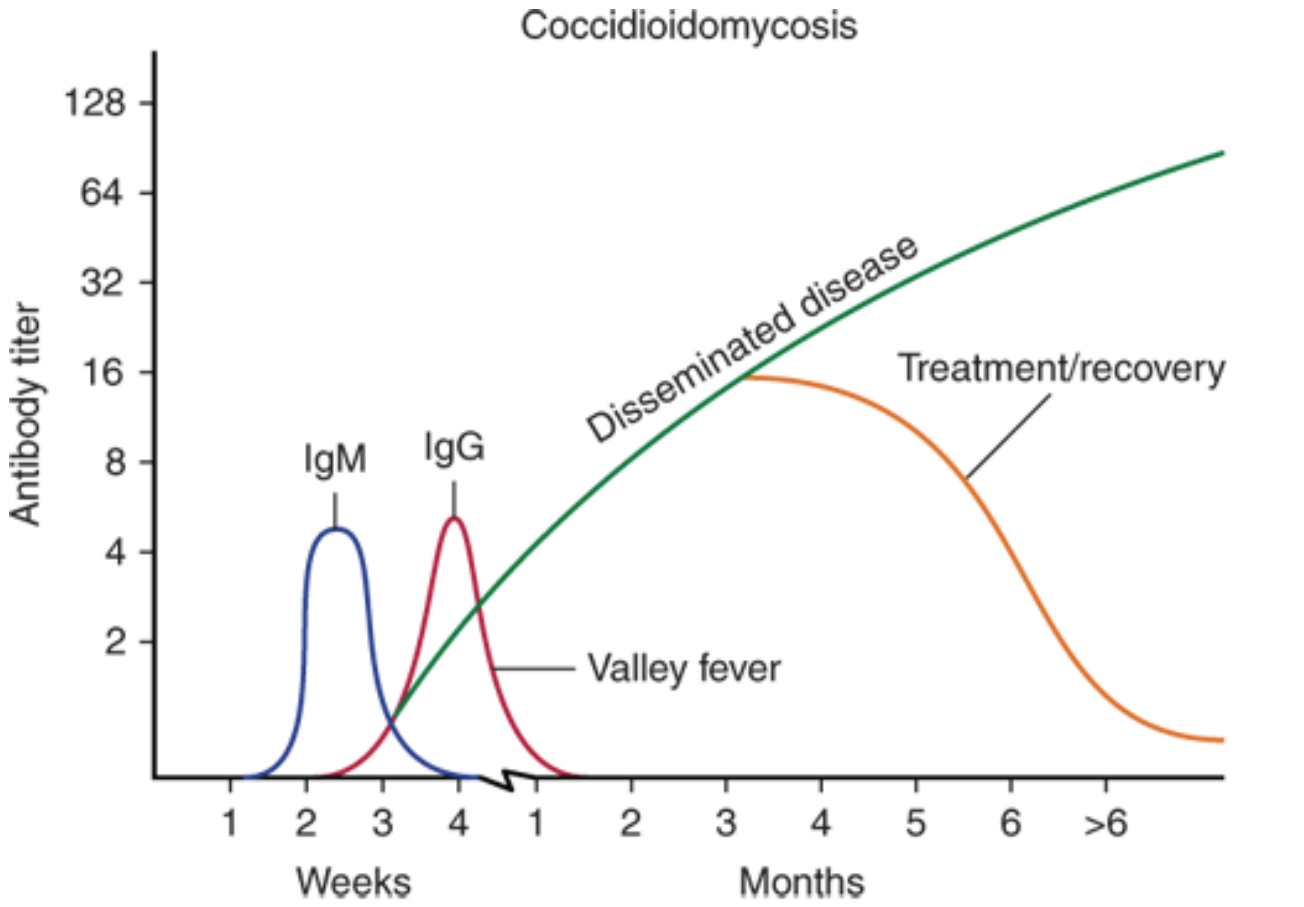

Blastomycosis and B. dermatitidis. A: Note the large, spherical thick-walled yeast cells (8–15 µm in diameter) in this section of a cutaneous abscess. H&E 400×. B: In culture at ambient temperatures, B. dermatitidis produces hyaline, septate hyphae, and single conidia. 400×.

# Systemic mycoses

- Coccidioides is thermally dimorphic.
- Arthrospores inhaled.
- Spherules are very large
- When rupture, release new endospores.
- 40% of patients develop self-limited illness characterized by fever, malaise, headache, and arthralgia (“Valley fever”)
- After 1 week, 15% may have hypersensitivity reaction
- Erythema nodosum
- Rarely disseminates
- Residual pulmonary nodule

# Systemic mycoses

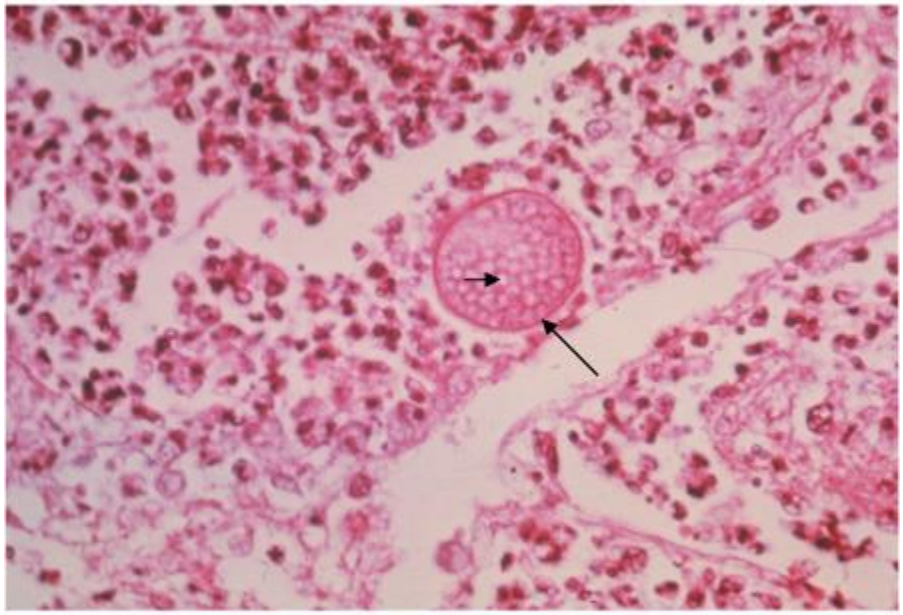
- At risk:
- Filipinos, African ancestry, Native Americans, Hispanics, and Asians (descending order).
- Men are more susceptible than women except in pregnancy
- C. immitis has estrogen-binding proteins, Paracoccidioides is thermally dimorphic.
- Chronic disease presenting decades after infection
- Men
- 30-60 years of age
- Inhaled
- Large budding yeast with appearance of “captain’s wheel”




Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e


In non-AIDS patients, the immunoglobulin G (IgG) antibody titers to coccidioidin are inversely related to the severity of coccidioidomycosis. IgM, immunoglobulin M. (Reproduced with permission from Ryan KJ, Ray CG [editors]: Sherris Medical Microbiology, 5th ed. McGraw-Hill, 2010, p 753. © McGraw-Hill Education.)

# Coccioides imitis



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com



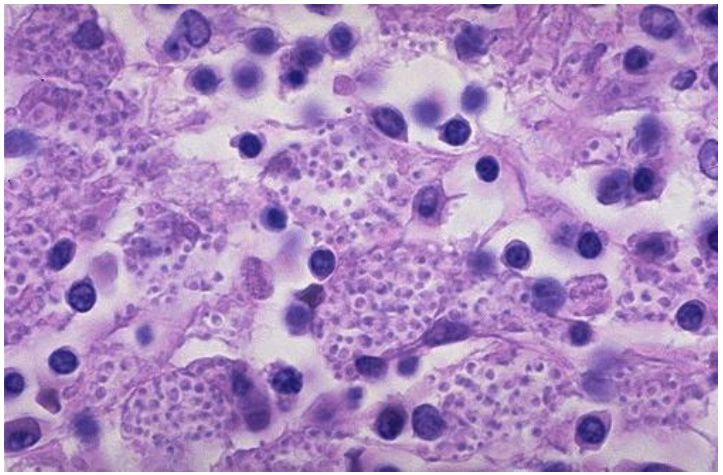
Long arrow points to a spherule in lung tissue. Spherules are large thick-walled structures containing many endospores. Short arrow points to an endospore.

Provider: CDC/Dr. L. Georg.

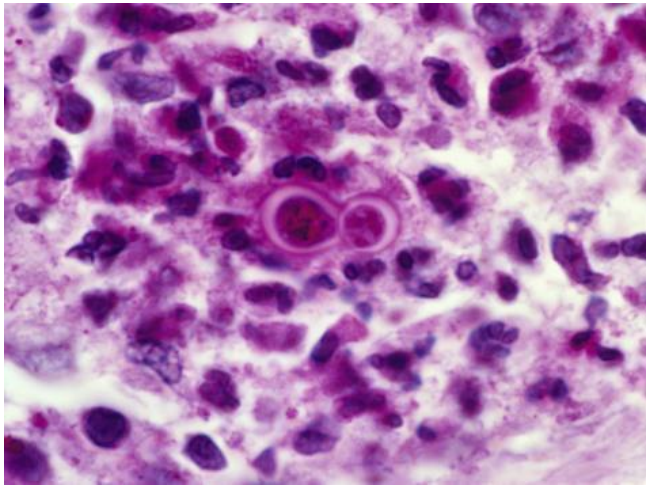
Color plate 33 Accessed 08/01/2010

# Dimorphic fungi

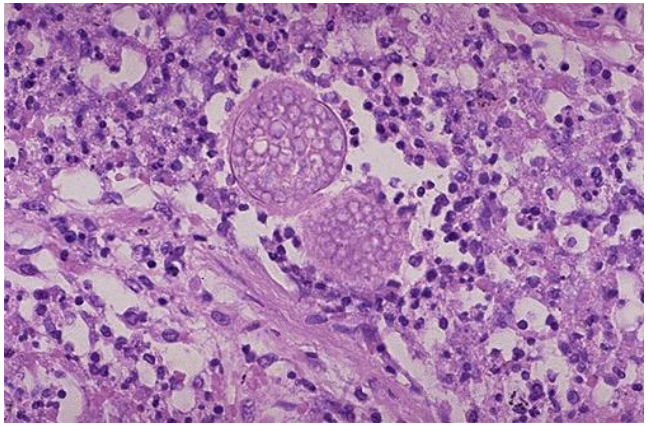
H. capsulatum



B. dermatiditis



C. immitis



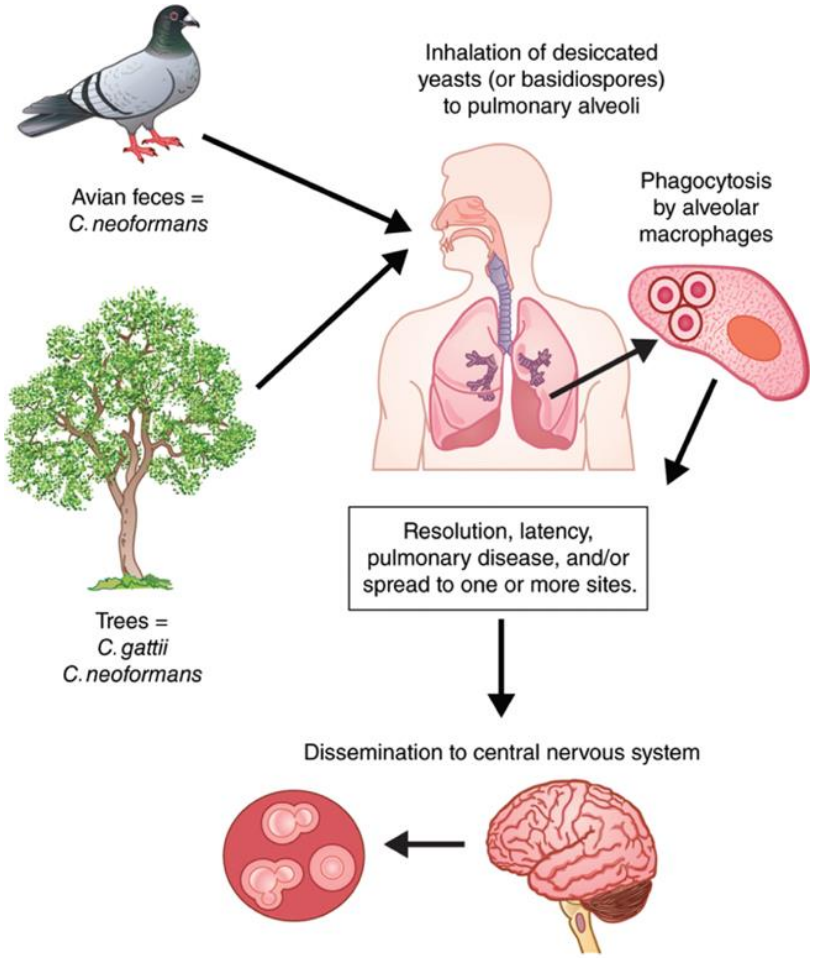
https://classconnection.s3.amazonaws.com/665/flashcards/523665/jpg/ Histoplasma
http://imgc.allpostersimages.com/images/P-473-488-90/64/6471/T7RH100Z/posters/gladden-willis-budding-yeast-of-blastomyces-dermatitidis-fungus.jpg Blastomyces
https://webpath.med.utah.edu/jpeg2/AIDS050.jpg Coccidioides
Accessed 01/20/2020aids0641333549206304.jpg

# Crytpococcus neoformans

- Opportunistic
- Inhaled
- Not thermally dimorphic (37C
- Basidiomyectous yeast
- Heavily encapsulated.
- Cell wall contains chitin (N-acetyl glucosamine polymer).
- Layered on the chitin are glucans (D-glucose polymers), peptides, and complex polysaccharides, but no murein.
- Bilayered sterol ester membrane.

# Crytpococcus neoformans

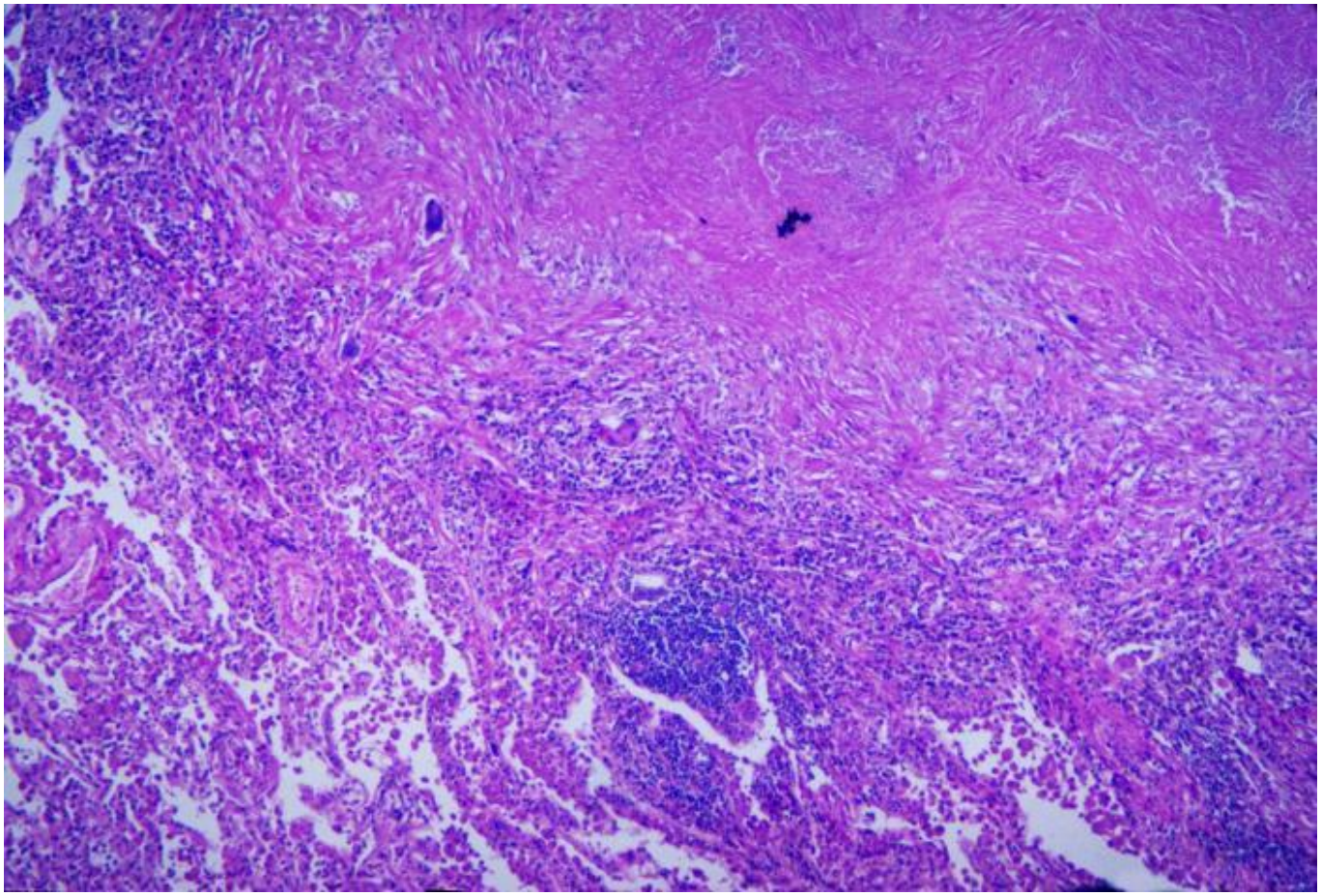
- Produce urease
- Produces laccase (phenol oxidase) which catalyzes the formation of a melanin-like pigment (antioxidant)
- Serine protease cleaves fibronectin, permitting invasion
- Neurotropic
- Chronic meningitis
- C. gatti differs in serotype






Natural history of cryptococcosis. (Reproduced with permission from Heitman J, Kozel TR, Kwon-Chung KJ, Perfect JR, et al [editors]: Cryptococcus. From Human Pathogen to Model Yeast. Washington, DC, ASM Press, 2011, Figure 1, p. 238. ©2011 American Society for Microbiology. No further reproduction or distribution is permitted without the prior written permission of American Society for Microbiology.)

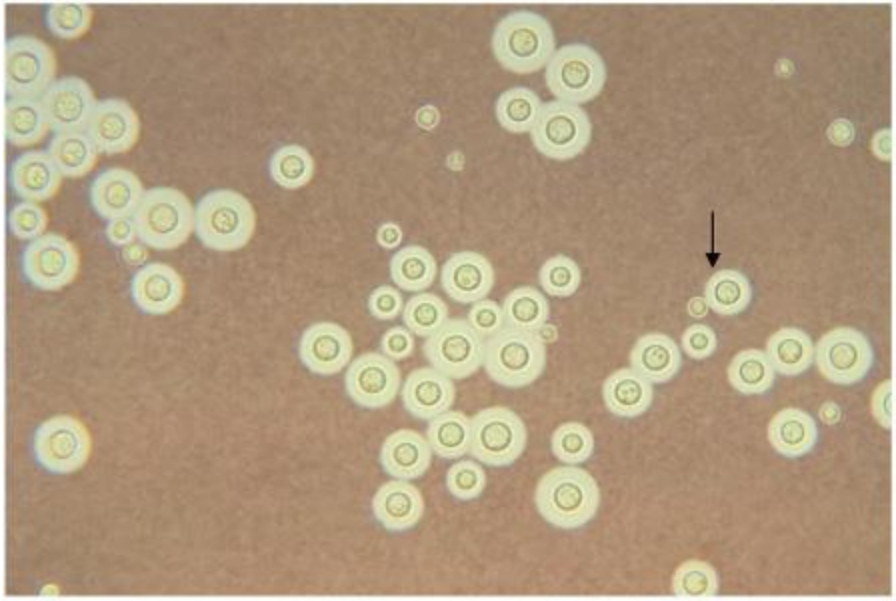
# Cryptococcus neoformans



Present in fibrocaseous nodule is C. neoformans. Below is organizing pneumonia.

Centers for Disease Control and Prevention's Public Health Image Library **#3139 Accessed 01/24/2020**

# Cryptococcus neoformans





India ink preparation. Arrow points to a budding yeast of Cryptococcus neoformans. Note the thick, translucent polysaccharide capsule outlined by the dark India ink particles.

Provider: CDC/Dr. L. Haley.

Color plate 38
Accessed 08/01/2010

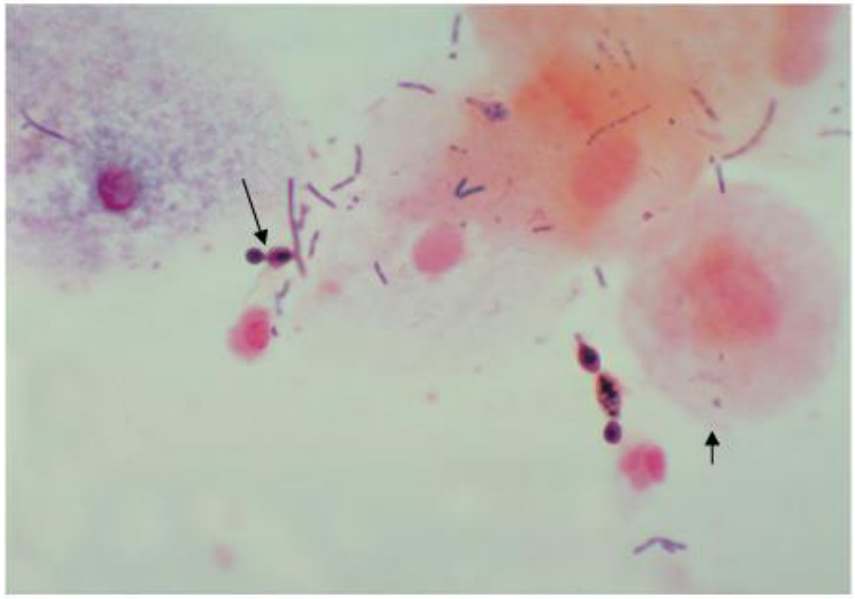
# Candida albicans

- Yeast when part of the normal flora
- Forms pseudohyphae when it invades tissue.
- Not thermally dimorphic.
- Produces germ tubes when incubated in serum at 37C (diagnostic).
- Phenotypic switching common
- Adhesins as virulence factors:
- Integrin-like protein that binds to arginine-glycine-aspartic groups on fibrinogen, fibronectin, and laminin
- Transglutaminase substrates that bind to epithelial cells
- Agglutinins that bind to endothelial cells or fibronectin

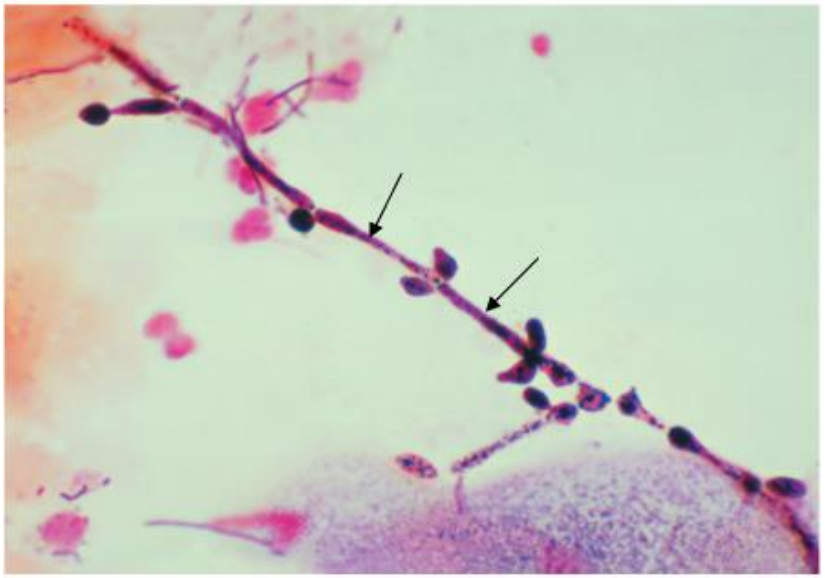
# Candida albicans

- Oxidatively killed by neutrophils and phagocytes
- Yeast forms lead to IL-12 production by dendritic cells
- Produce protective anti-fungal $T_{H1}$ response
- Filamentous forms produce non-protective $T_{H2}$ response
- Host cell dectin-1 binds to the β-1,3-glucan of C. albicans
- Elicit $T_{H17}$ responses

# Candida









Left: Long arrow points to a budding yeast. Short arrow points to the outer membrane of a vaginal epithelial cell. Right: Two arrows point to pseudohyphae of Candida albicans.

Provider: CDC/Dr. S. Brown. Color plates 36 and 37 Accessed 08/01/2010

# Candidiasis

- Thrush can occur on tongue or lips or oral mucosa
- Confluent, whitish pseudomembranous lesion composed of epithelial cells, yeasts, and pseudohyphae
- Usually in immune compromised
- Vulvovaginitis
- White creamy or “cottage cheese” vaginal discharge
- Balanitis
- Reddening of glans penis, usually uncircumcised men.

# Candidiasis

- Cutaneous candidiasis
- Intertriginal infection, usually in diabetics
- “Diaper rash”
- Buds or hyphae on wet mount
- Fluconazole once orally should eradicate infection; Vaginal suppository may relieve immediate symptoms.
- may be treated with topical steroid and antifungal.
- Should treat sexual partner as well.

# Candida albicans

Oral thrush





Diaper Rash

.

Figs. 25-23, 25-26, 25-27
Accessed 07/01/2010



Intertriginous areas

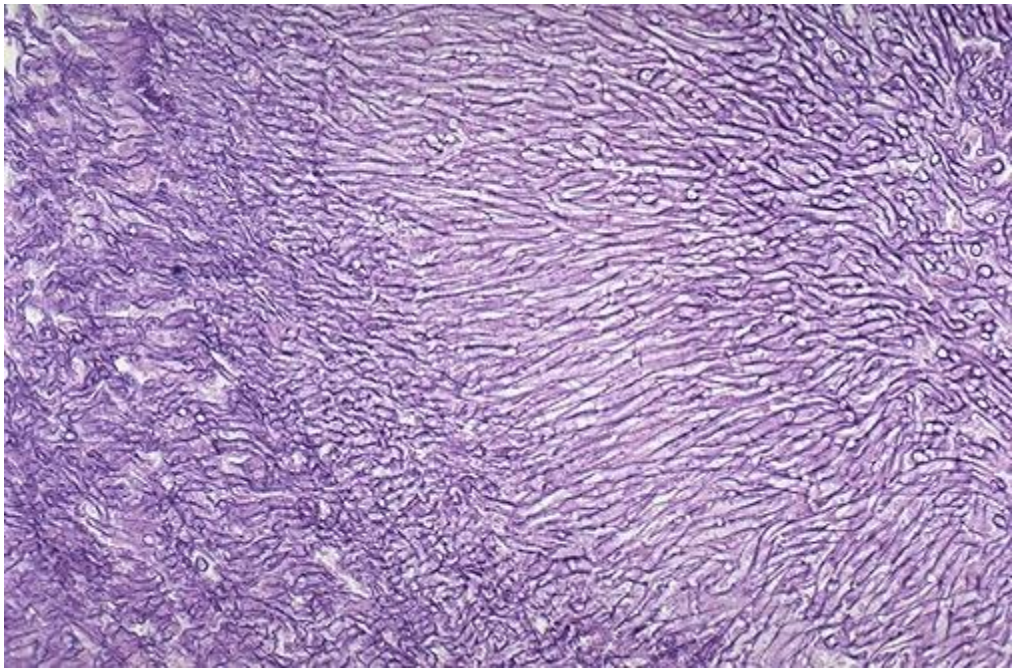
# Aspergillus fumigatus

- Soil mold with septate hyphae that branch at a V-shaped angle (low-angle branching).
- Not thermally dimorphic.
- Spores inhaled.
- Virulence factors:
- Adhesins on conidia
- Antioxidants (melanin, superoxide dimutase, catase, mannitol)
- Ribotoxins inhibit host cell protein synthesis
- Phospholipases and proteases

# Aspergillus fumigatus

- Atopic individuals
- Immediate wheezing precipitated by IgE antibodies to superficial fungal antigens
- In others, the conidia germinate, and hyphae colonize the bronchial tree without invading the lung parenchyma.
- Allergic bronchopulmonary aspergillosis
- Wheezing, recurrent chest infiltrates, eosinophilia, and both type I and type III reactions
- May lead to alveolitis
- Immune compromised
- May develop invasive pneumonia

# Aspergillus fumigatus

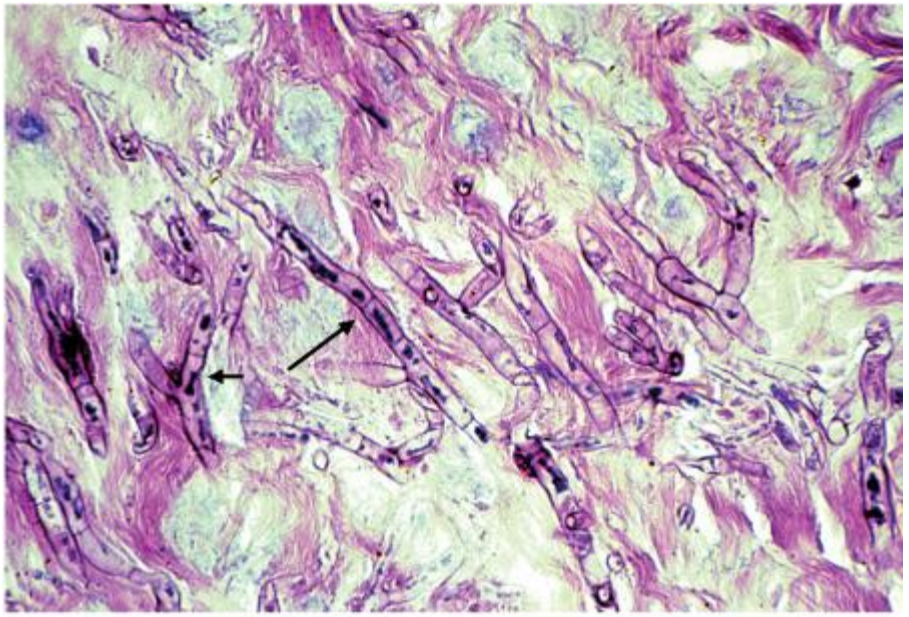


Left:  Lesion has crossed the fissure
Right: Branching, septate hyphae are close-packed here and radiating outward

https://webpath.med.utah.edu/LUNGHTML/LUNG045.html

https://webpath.med.utah.edu/LUNGHTML/LUNG041.html

# Aspergillus fumigatus



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com



Long arrow points to the septate hyphae of Aspergillus. Note the straight parallel cell walls of this mold. Short arrow points to the typical low-angle, Y-shaped branching.

Provider: Professor Henry Sanchez, University of California, San Francisco School of Medicine. With permission.

Color plate 39 Accessed 08/01/2010

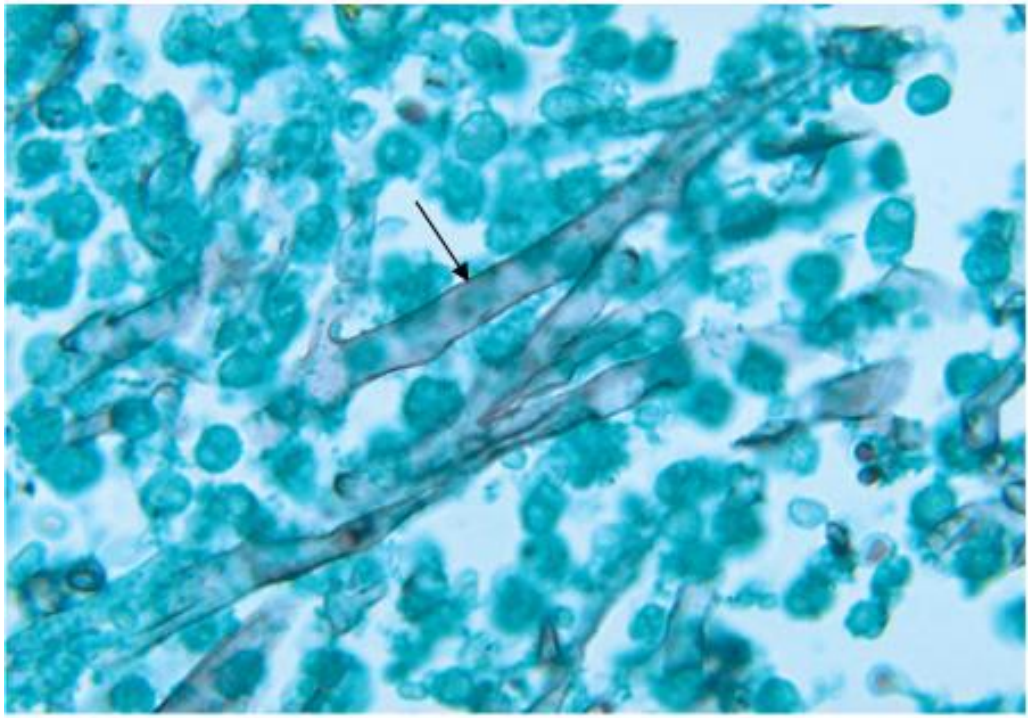
# Mucor and rhizopus

- “Bread mold fungi”  with non-septate hyphae that branch at 90º (wide-angle branching).
- Not thermally dimorphic.
- Spores inhaled.
- Yeasts reproduce by budding.
- Molds grow via tubal (hyphal) extension and branching, reproducing by asexual sporulation.
- Thermotolerant

# Mucor and rhizopus

- Major clinical presentation is rhinocerebral mucormycosis
- Results from germination of the sporangiospores in the nasal passages and invasion of the hyphae into the blood vessels, causing thrombosis, infarction, and necrosis.
- The disease can progress rapidly with invasion of the sinuses, eyes, cranial bones, and brain.
- Blood vessels and nerves are damaged, and patients develop edema of the involved facial area, a bloody nasal exudate, and orbital cellulitis.
- Poorly controlled diabetics as well as the immune compromised

# Mucor



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

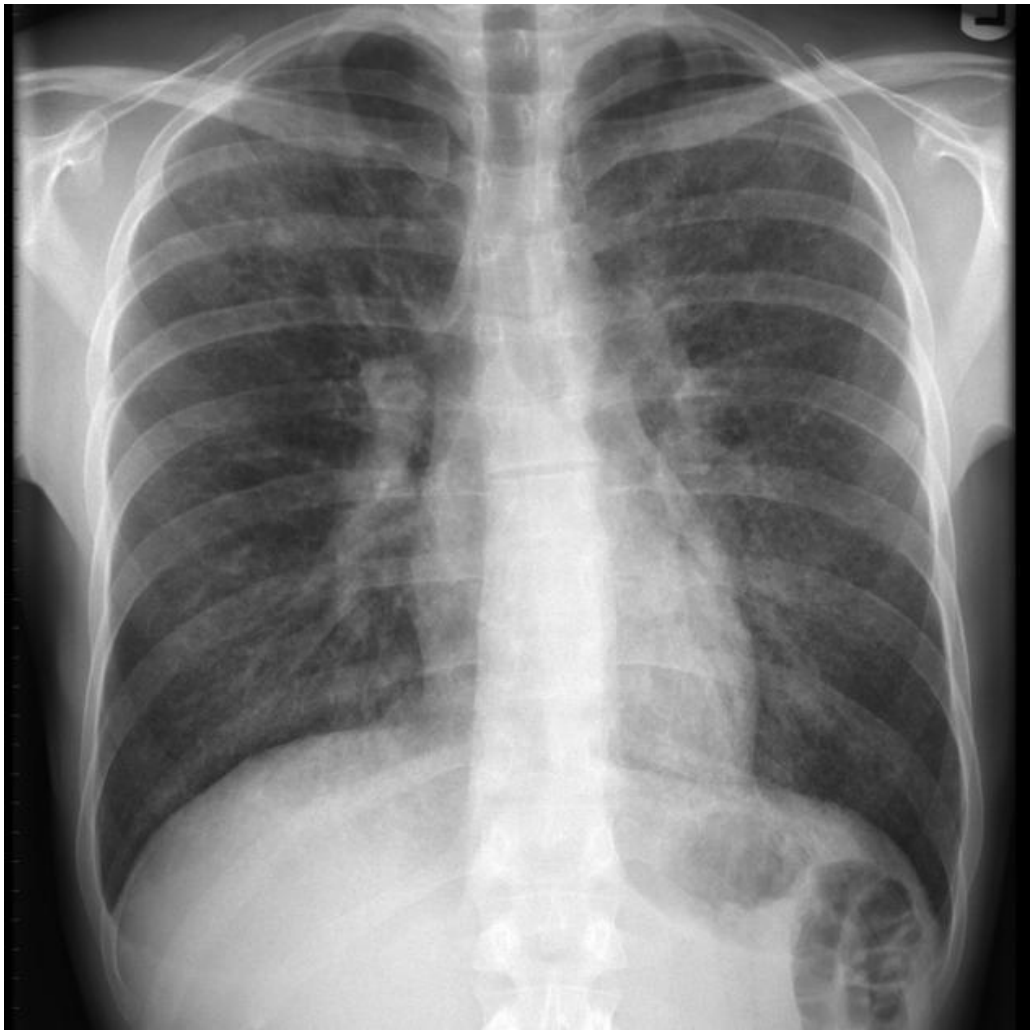


Arrow points to irregular-shaped, non-septate hyphae of Mucor.

Provider: CDC/Dr. L. Ajello.

Color plate 40 Accessed 08/01/2010

# Pneumocystis jiroveci pneumonia



Bilateral, diffuse, often perihilar, fine, reticular interstitial opacification, which may appear somewhat granular (ground glass).

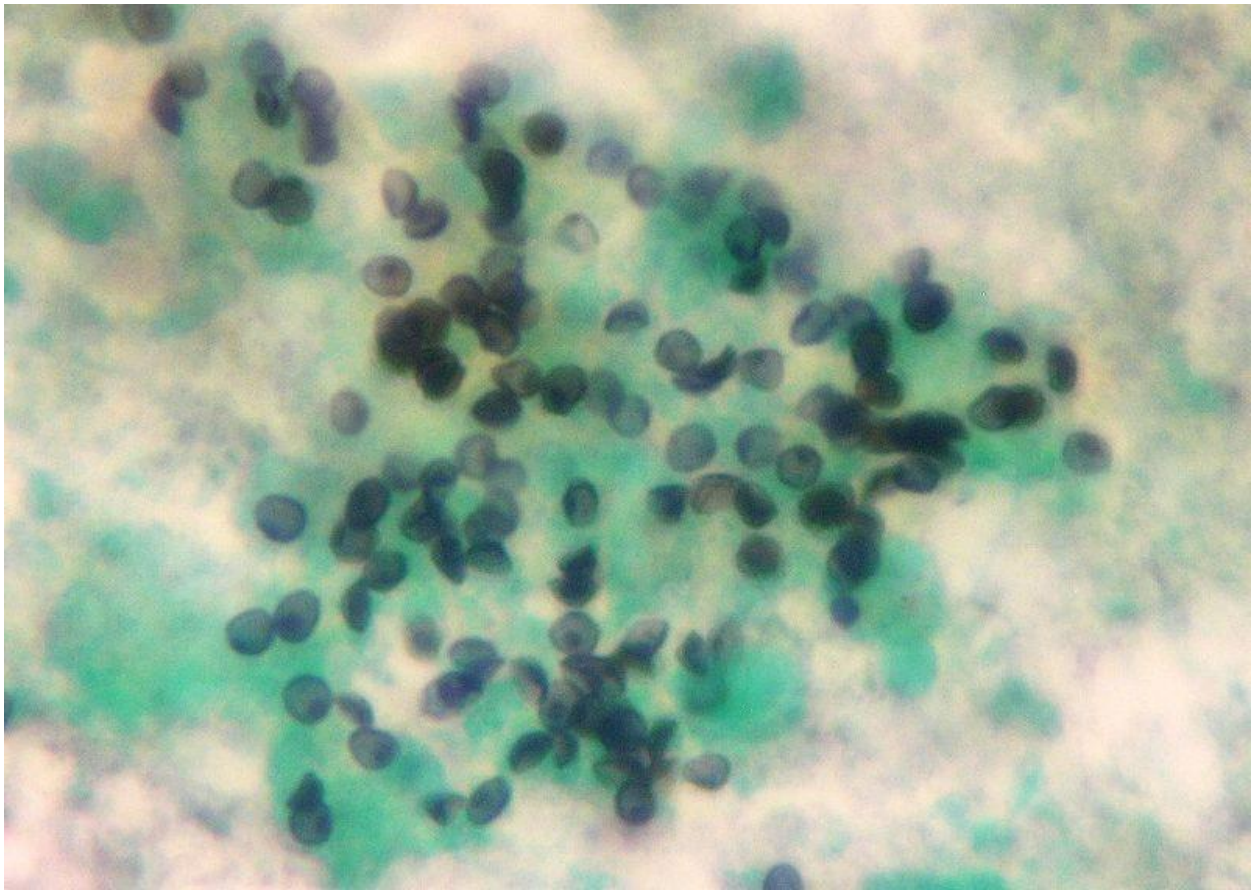
May see pneumatoceles in 30%.

Insidious presentation. Dyspnea out of proportion to clinical findings.

Isolated elevated LDH in serum.

https://radiopaedia.org/articles/pulmonary-pneumocystis-jiroveci-infection?lang=us Accessed 12/10/2019

# Pneumocystis jiroveci pneumonia



Gomori Methenamine Silver stain demonstrating the sporozoites in sputum. This is a yeast.

https://en.wikipedia.org/wiki/File:Pneumocystisjiroveci.jpg

Accessed 12/10/2019