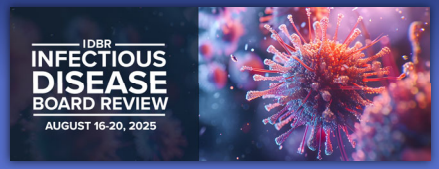


Deep Mycoses in Normal and Abnormal Hosts

John E. Bennett, MD
Bethesda, Maryland

8/4/2025

1

Disclosures of Financial Relationships with Relevant Commercial Interests

- None

2

Mycology Basics

- Most fungi live in nature, form spores, infect by inhalation into lung
  - Histo, blasto,cocci, crypto, paracocci, etc
  - No transmission between humans. Case clusters are common exposure
- Exceptions
  - Candida is human commensal, invades mucosa, skin, vagina
  - Ringworm lives in skin of humans and animals, spread by contact
  - Sporo lives in nature and invades skin by minor trauma

3

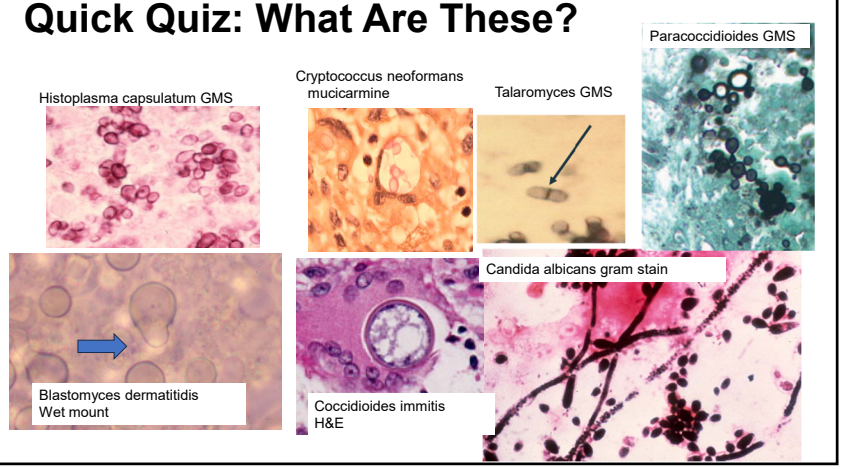
More Basic Mycology

- Yeasts reproduce by budding
  - All Candida have pseudohyphae in tissue except *C.glabrata (Nakaseomyces*)
  - Crypto has capsule, stains burgundy with mucicarmine

- Molds have hyphae in tissue and culture
  - Septate: Aspergillus, Fusarium, Scedosporium, others
  - Rare or no septae (Mucorales): Rhizopus, Mucor, Cunninghamella, others
  - Dark-walled fungi: many cause infection of skin, paranasal sinus, brain
    - Phaeohyphomycosis
- Dimorphic fungi are round cells in tissue, hyphae in culture
  - Histoplasma, Coccidioides, Blastomyces, Sporothrix , Paracoccidioides

4

Quick Quiz: What Are These?



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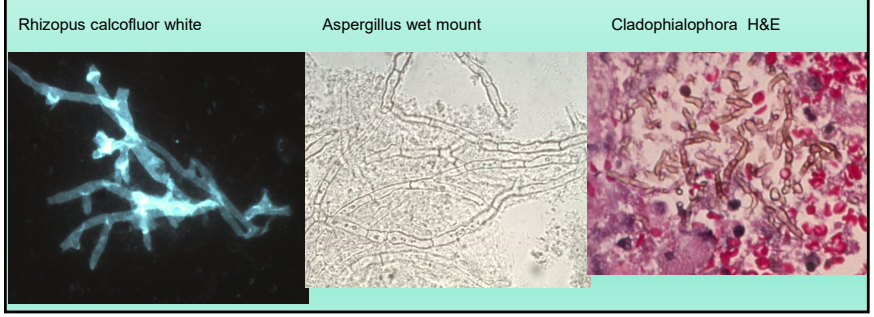
Quick Quiz: What Are These?



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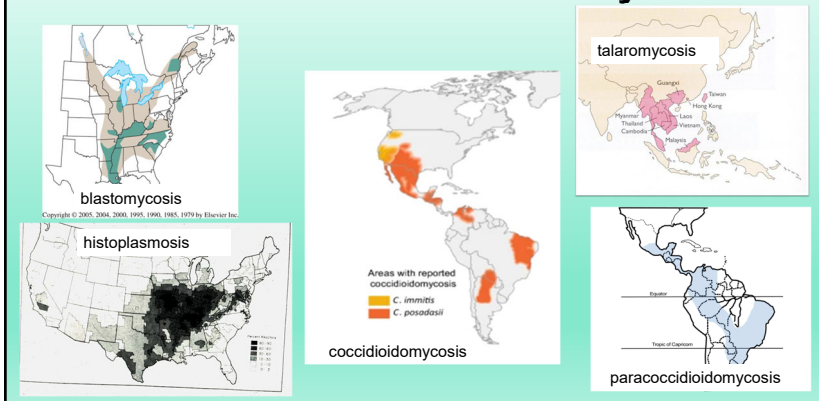
More on Dimorphic Fungi: Most Are Endemic Mycoses

- Geographically restricted
- Infection by inhaling spores in nature
- No person-to-person transmission
- Cluster of cases with fever, cough after soil exposure
  - No secondary cases
  - Desert dust=cocci. Rich earth, bat guano=histo
    - Streams, rivers=blasto

7

What Are These Endemic Mycoses?



8

27 Deep Mycoses in Normal and Abnormal Hosts
Speaker: John Bennett, MD

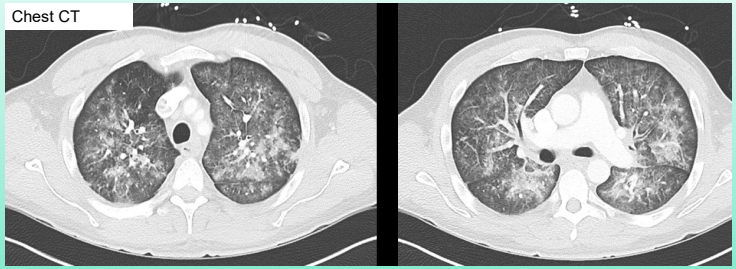
Question #1

Courtesy of Shanan Immel, MD

- Formerly healthy 48-year-old M with 3 months of chronic fevers, cough, 25 lb weight loss, night sweats, presented with acute worsening on dyspnea and was found to have a high fever and diffuse lung infiltrates bilaterally. Office worker in Md. No travel. Wife healthy.
- Vitals: 39.3C, HR 97, RR 29, BP 97/54, O2: 88% on room air
- Crackle all over lung, spleen tip felt.
- WBC: 5,300, HgB 10.1 Plt 119,000, ALP 218, ALT 43, AST54, lactate 2.5, ferritin 2418, triglycerides 250. HIV neg.
- Intubation, pressors, ceftriaxone, voriconazole

9

Question #1



What is the preferred diagnostic procedure?

A. Bronchoscopy
B. Transthoracic needle lung biopsy
C. VATS lung biopsy
D. Serum antigen
E. Bone marrow

10

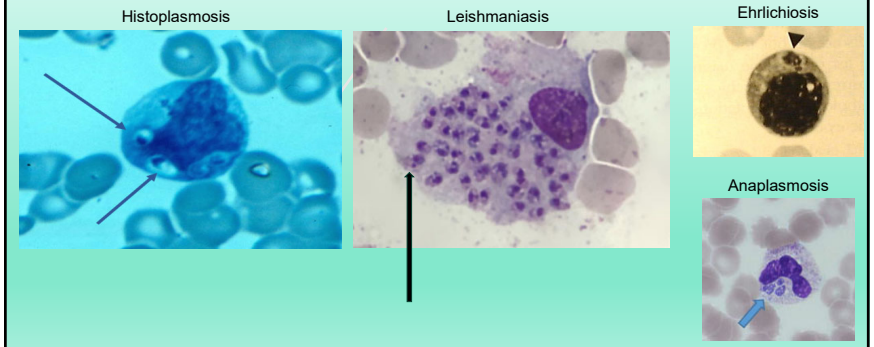
Recognizing Mycoses on the Board Exam

Histoplasma capsulatum complex

- Case clusters of acute pneumonia two weeks after soil exposure (rare: bat caves)
- Immunosuppressed patient with febrile disseminated disease
  - Cytopenias
  - Miliary lung infiltrate can look like PJP, miliary TB
  - Mucosal lesions resemble squamous carcinoma
  - Adrenal insufficiency
  - Can mimic HLH (hemophagocytic lymphohistiocytosis) or miliary TB
  - HIV patients can have IRIS after starting ARV
- Urine or serum antigen good diagnostic test
- Biopsy: small budding yeast, mold on culture
- Rx: ampho then itraconazole for disseminated
- Histoplasma duboisii (African histoplasmosis)
  - Skin and bone lesions

11

Quick Quiz: What Is The Disease Associated With These Intracellular Particles?



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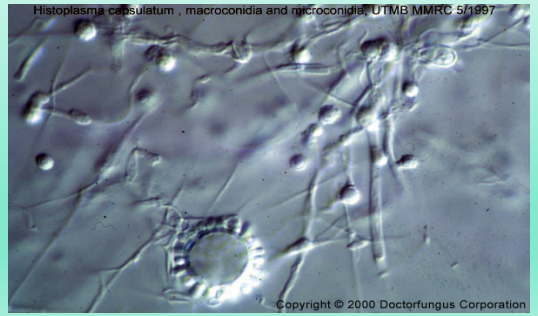
Histoplasma capsulatum Growing at Room Temperature

Histoplasma capsulatum mold form



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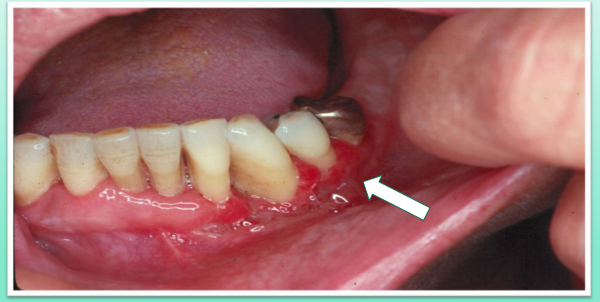
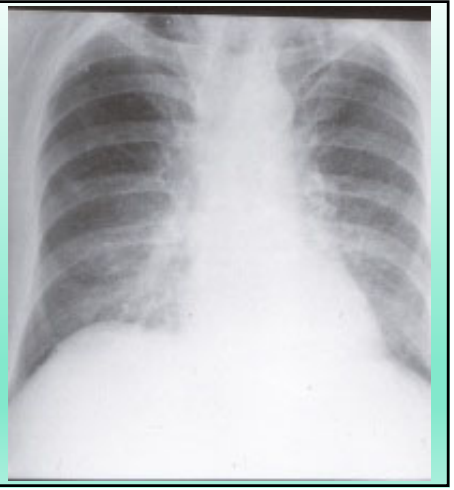
Gingival Ulcer



¼ Cases have oral lesion in disseminated histo

14

Miliary Lung Lesion in Disseminated Histoplasmosis (Looks Like PJP on Imaging)



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Question #2

44-year-old previously healthy male accountant in Washington DC presented with the acute onset of confusion that was preceded by three months of headache. Cranial MRI was normal. Lumbar CSF had an opening pressure of 350mm CSF, WBC 250/cu mm, glucose 22 mg /dl, protein 125 mg/dl and cryptococcal antigen titer 1:512. Liposomal amphotericin B was begun at 5.0 mg/kg IV daily. On the third day of treatment, he complained that the room was too dark and was found to have visual acuity of hand motion only in both eyes.

17

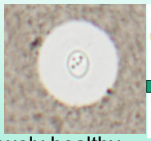
Question #2

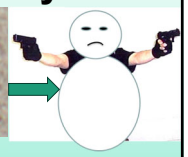
Which is the most important next step in this patient?

A. Start flucytosine
B. Start fluconazole
C. Start acetazolamide (Diamox)
D. Begin daily lumbar punctures
E. Start dexamethasone

18

Crypto is a Killer, Not a Currency





- Cryptococcus neoformans species complex:
  - Worldwide, pigeon guano, corticosteroids, transplants, HIV
- Cryptococcus gattii species complex
  - Pacific coast, trees, Australia, tropics, often previously healthy
  - Serum antibody to GM-CSF
- Chronic lymphocytic meningitis
  - Headache, confusion, cranial nerve palsies, +/- fever, vision loss
  - Rx ampho+flucytosine then fluconazole, relieve high opening pressure (LP's, shunt)
  - HIV ARV-naïve: consider delay ARV 2 weeks (IRIS)
  - Skin lesions (10%) like molluscum contagiosum
- Lung only: fluconazole alone (negative LP)
- Cryptococcal antigen in CSF, serum
  - Diagnosis, screening high risk patients

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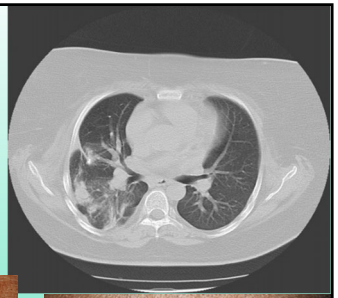
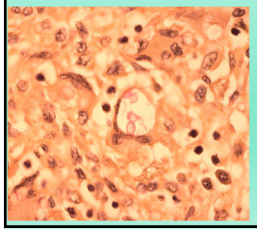
- Cryptococcal lung lesions usually asymptomatic
- Skin lesions can resemble molluscum contagiosum
- Mucicarmine often stains crypto pink





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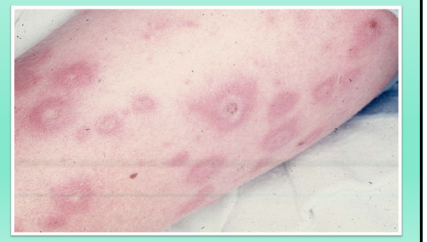
Question #3

PREVIEW QUESTION

35-year-old male 68 days post allogeneic bone marrow transplantation for myelodysplastic syndrome, receiving methylprednisolone 500 mg for Grade III GVHD of the gastrointestinal tract developed fever, several painful, red skin nodules and a blood culture growing a mold.



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Question #3

PREVIEW QUESTION

Which of the following is the most likely fungus?

A. Scedosporium apiospermum (Pseudallescheria boydii)
B. Lomentospora (Scedosporium) prolificans
C. Apophysomyces elegans
D. Fusarium multiforme
E. Alternaria alternata

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Fusariosis

- Severely immunocompromised patients
- Mold, looks like Aspergillus in tissue
- Red, tender skin nodules
- Routine blood culture grows mold in a third to half the patients
- RX: response to amph and vori poor in severe neutropenia. Experimental: PMN transfusion?, fosmanogepix (investigational)??
- Note: fungal meningitis from F. solani, Mexico, epidural anesthesia

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Question #4

- 47-year-old M executive referred from Baltimore because of severe headaches, diplopia, high fever of 1 wk's duration
- 4 wks PTA: Maui resort one week
- 3 wks PTA: ranch outside Tucson, Arizona 1 wk
- 2 wks PTA: back at work in Baltimore
- 1 wk: PTA: Headache began

- Exam: Temp 38.5 C. Looks ill. Photophobia, nuchal rigidity, right CN6 palsy

- CBC, Routine blood chemistries normal. CSF : Glucose 55, Protein 58, WBC 330 (20% eos). Negative cryptococcal antigen on CSF, serum Lyme serology and serum RPR. MRI with contrast normal. Worsens during 2 wks of ceftriaxone. CSF cultures for bacteria, fungi, tbc neg to date.

24

Question #4

What would be the most helpful diagnostic test?

A. CSF cytology
B. Stool O&P
C. Dietary history
D. Fungal serology
E. Leptospirosis serology

25

Coccidioidomycosis = Valley Fever

- Two species, one disease:
  - C. immitis and C. posadasii. Both serious lab hazards
  Southwest USA. Washington state
- Acute pneumonia 2 wks after inhalation: arthralgias or erythema nodosum may accompany. Resolves.
- Residual nodule or thin-walled cavity may persist
- Dissemination: African Americans, HIV, SOT, TNF inhibitors
- Bone, skin, chronic meningitis. Eosinophils
- Rx: fluconazole. Nonmeningeal: itraconazole

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Coccidioidomycosis Diagnosis

Serology

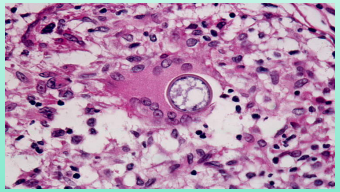
- CSF CF serology useful. Serum CF >16 suggests dissemination, falls with Rx
- Serum IgG by EIA converts to positive late, stays positive .
- Serum antigen in severe disease

Culture

- Routine cultures negative, fungal cultures positive. Lab hazard

Biopsy

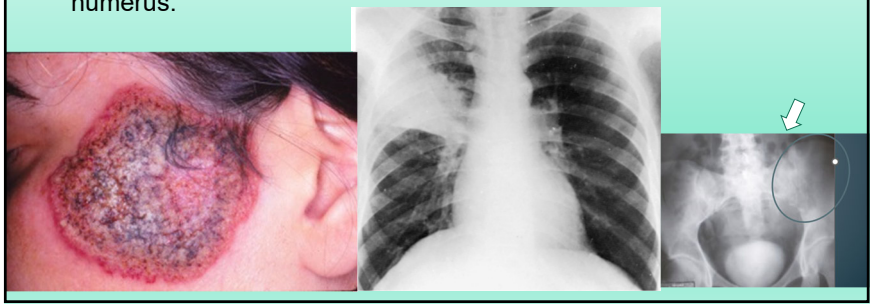
- Distinctive non-budding spherules



27

Question #5

A previously healthy 52-year-old old Wisconsin man presented with a leg lesion, painful elbow swelling and asymptomatic lung lesion on chest x-ray and lytic lesion on condyle of his humerus.



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Question #5

Which of the following is most likely?

A. Candida auris
B. Trichosporon cutaneum
C. Leishmania donovani
D. Blastomyces dermatitidis
E. Histoplasma capsulatum var. duboisii

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Blastomyces dermatitidis , B. gilchristii

- Central USA and Canada, mold in nature
- Large broad-based budding in tissue
- Moist earth near river, beaver dams
- Normal host
- Yeast with broad based bud, thick wall
- Acute pneumonia may self heal
- Indolent, progressive pneumonia
  - Disseminates to skin, bone, male GU tract
- Often presents as skin lesions
- Rx: itraconazole, Ampho B

30

Question #6

What are these lesions in a febrile, recently neutropenic patient?

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Question #6

Which is the most likely?

A. Babesia microti
B. Candida tropicalis
C. Fusarium oxysporum
D. Aspergillus flavus
E. Streptococcus anginosus

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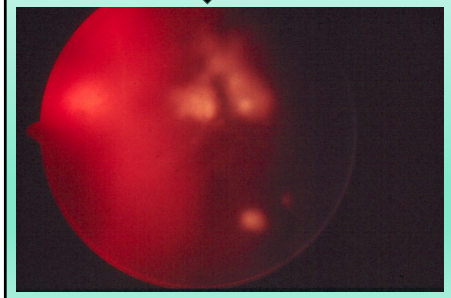
Candidiasis Makes the Sick Get Sicker

- Fundoscopy for retinal lesions in candidemia patients.
  - Intravitreal Rx may be needed
- Remove intravenous catheter with candidemia
- *Candida auris* hospital outbreaks. Spreads on hands, surfaces
- Fluconazole resistance in C. auris, C. krusei (Pichia kudriavzevii)
  - C. glabrata (Nakaseomyces glabratus)
- Fungitell (1-3) beta-D-glucan positive in serum

33

Candida endophthalmitis:
"fluff balls" floating in the vitreous humor

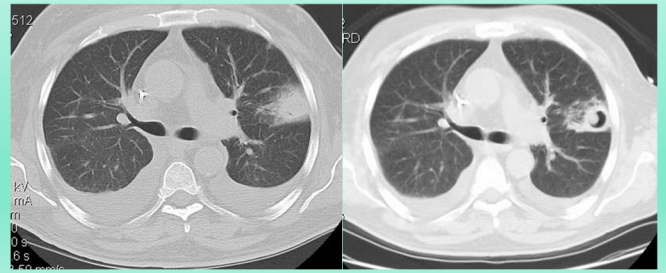


Candida lesions in a neutropenic patient

34

Question #7

32-year-old male with allogeneic hematopoietic stem cell transplant recipient for AML, developed graft versus host disease, given high dose prednisone, discharged and re-admitted for fever not responding to antibacterial antibiotics. These two chest CT 's, were taken at admission and a week later while he was responding to voriconazole.



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Question #7

What is the most likely source of infection?

A. Dirt from his garden
B. His oral flora
C. Contaminated food
D. Intravenous catheter

36

Aspergillus Pneumonia

- Sudden onset of a dense, well circumscribed lesion in a neutropenic patient should suggest a mold pneumonia, most commonly aspergillosis, halo sign early, crescent sign later
- Septated hyphae invade blood vessels, infarct tissue
- Galactomannan useful in CSF, BAL, blood
  - False positives
  - False negatives with azole prophylaxis
- Rx. voriconazole, isavuconazole, posaconazole, ampho B

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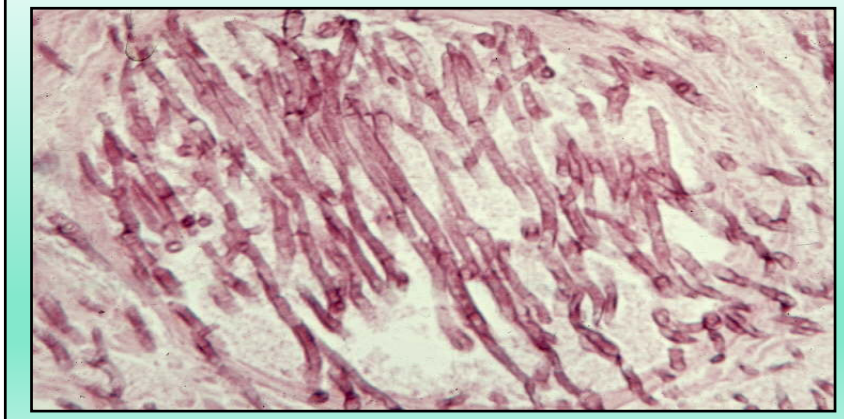
Aspergillus Hyphae in an Arteriole



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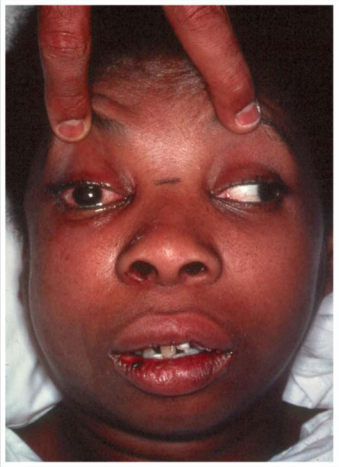
Question #8

25-year-old female admitted with diabetic ketoacidosis and blindness in her right eye. On exam the right eye was fixed in position and proptotic. CT showed dense mass in adjacent ethmoid sinus with extension into the orbit. Surgical exploration of the sinus showed broad, aseptate hyphae.

Which is the most likely fungus?

A. Rhizopus
B. Fusarium
C. Aspergillus
D. Scedosporium
E. Candida



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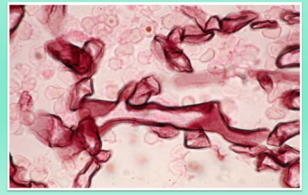
Mucormycosis

- Infection acquired by inhaling spores into lung or paranasal sinus
- Rhizopus, Rhizomucor, Mucor, Cunninghamella, Apophysomyces, Saksenaea
- Broad, flexible nonseptate hyphae, right angle branching
- Rhinoorbital: poorly controlled Diabetes mellitus or immunosuppression
  - India: severe COVID + DM2+steroids
- Pulmonary: neutropenia, immunosuppression



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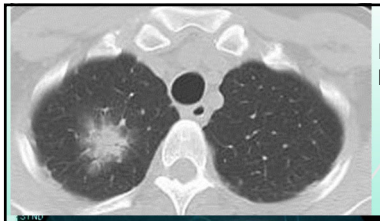
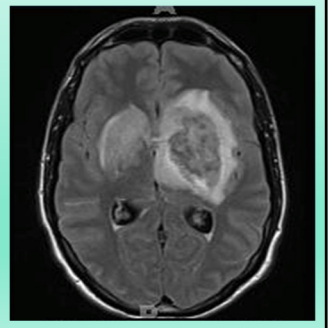


Halo sign in a leukemic

Cavity after PMN Return

Mucormycosis

Brain abscess in a heroin user



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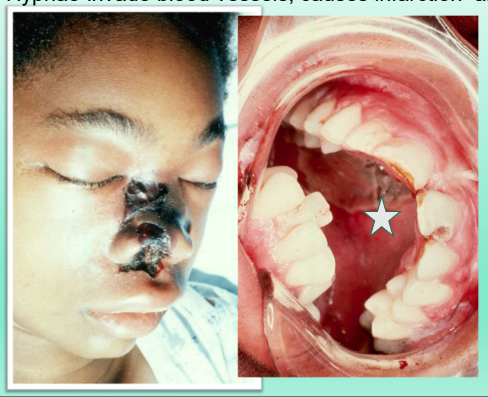
Poorly controlled diabetes mellitus, Prolonged neutropenia, corticosteroids

India: COVID-19+ corticosteroids+ poorly controlled diabetes mellitus

Hyphae invade blood vessels, causes infarction and necrosis.



- Rx. Ampho
- Followup: Posaconazole or Isavuconazole?
- Surgical debridement
- Control diabetes
- Decrease immunosuppression

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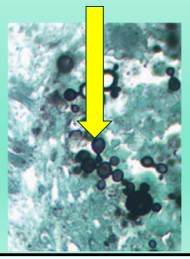
Paracoccidioidomycosis

- Rural Central and South America
- Several species
- Starts in lung, disseminates
- May appear decades after leaving endemic area

Multiple buds



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Sporotrichosis

- Sporothrix schenckii, (brasiliensis, globosa, pallida, mexicana)
- Lives on plants, inoculated by minor trauma
- Brazil and surrounding countries: >10,000 cases from infected cats
- Lymphangitic spread
- Rare: lung, disseminated

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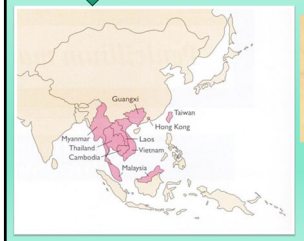
Talaromycosis (Formerly Penicillium Marneffei)

Southeast Asia
Mostly AIDS



Yeast In Biopsy, Mold In Culture
Divides By Fission

Disseminated Infection
With Skin Lesions

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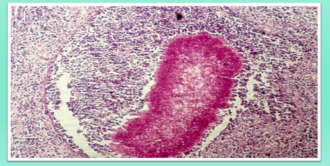
Mycetoma (Madura foot)

Minor trauma to foot or hand
Firm swelling progresses over years
Draining sinuses

Grains in pus
Fungi or higher bacteria



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Mycoses Worth Mentioning

- Scedosporium apiospermum: immunosuppressed host clinically resembling aspergillosis. Brain abscess after near **drowning** in polluted water. ***Amphotericin b resistant***
- Trichosporonosis: like candidiasis but ***echinocandin resistant***

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Key Points

- Endemics: inhaled, case clusters, dimorphic
- Histoplasmosis: antigen test, Addison's
- Blastomycosis: skin + lung, broad based bud
- Coccidioidomycosis: SW USA, meningitis, eosinophils
- Molds: inhaled, most immunocompromised
- Aspergillus: septate, neutropenia
- Mucor: rare septae diabetics,
- Fusarium: blood cult pos, skin lesions
- Cryptococcus: capsule, antigen, LP opening pressure
- Candida: remove IV catheter, fundoscopy

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THAT'S IT!

It's all perfectly clear, isn't it?

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