

Pulmonary Infections: Fungus



Part I: Background Information and
Dimorphic Fungus

Part II: Opportunistic
Yeast and Molds

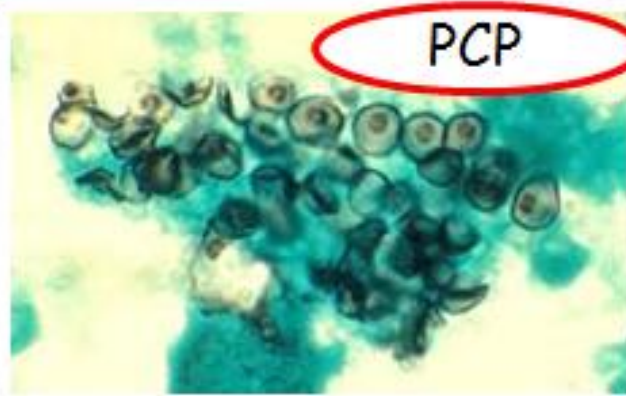
Howard J. Sachs, MD
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Opportunistic, Yeast

Crypto



PCP

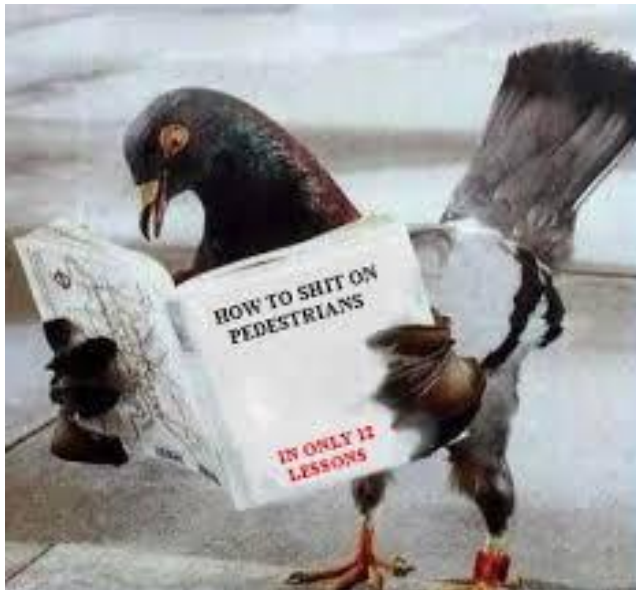


Candida



Classification: Unicellular Budding Yeast, Opportunistic ⇒ **Cryptococcus**

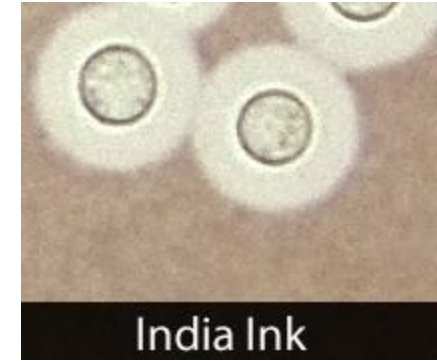
- When to suspect?
 - **Environment**: Soil, bird droppings (**pigeon**, chicken) cause infection when inhaled.
 - **Transmission**: Aerosolized spore → **lung** [primary site of infection (**pneumonitis**)]
 - Subsequent spread to CNS in immunocompromised host (**NEUROTROPIC fungus** → **meningoencephalitis**)



India ink, CSF



Classification: Unicellular Budding Yeast, Opportunistic \Rightarrow Cryptococcus



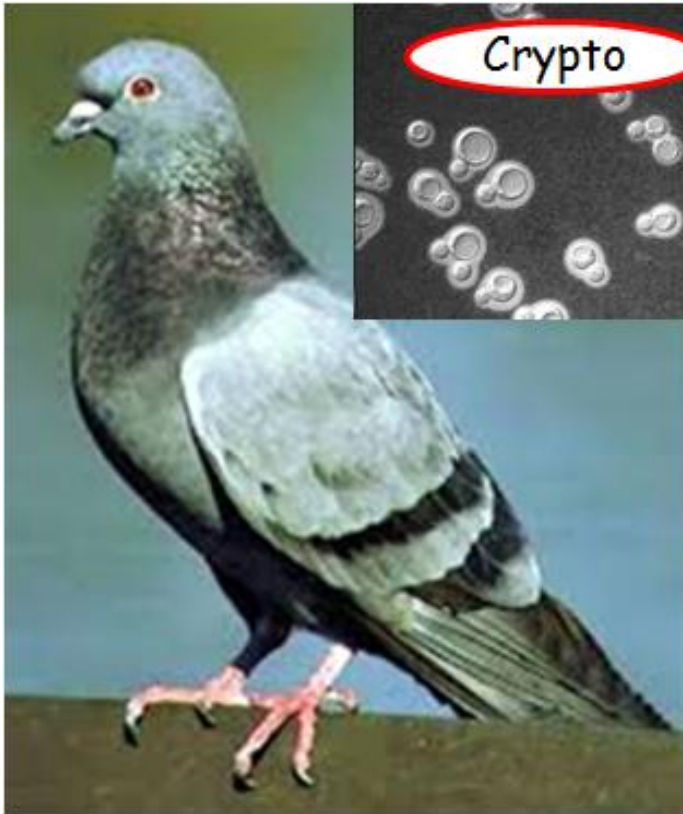
- Relevant Microbiology

- Morphology: **only fungus with polysaccharide capsule**; unequal narrow based buds
- Stains: mucicarmine \rightarrow red; India ink \rightarrow clear zone on black background (halo from capsule)

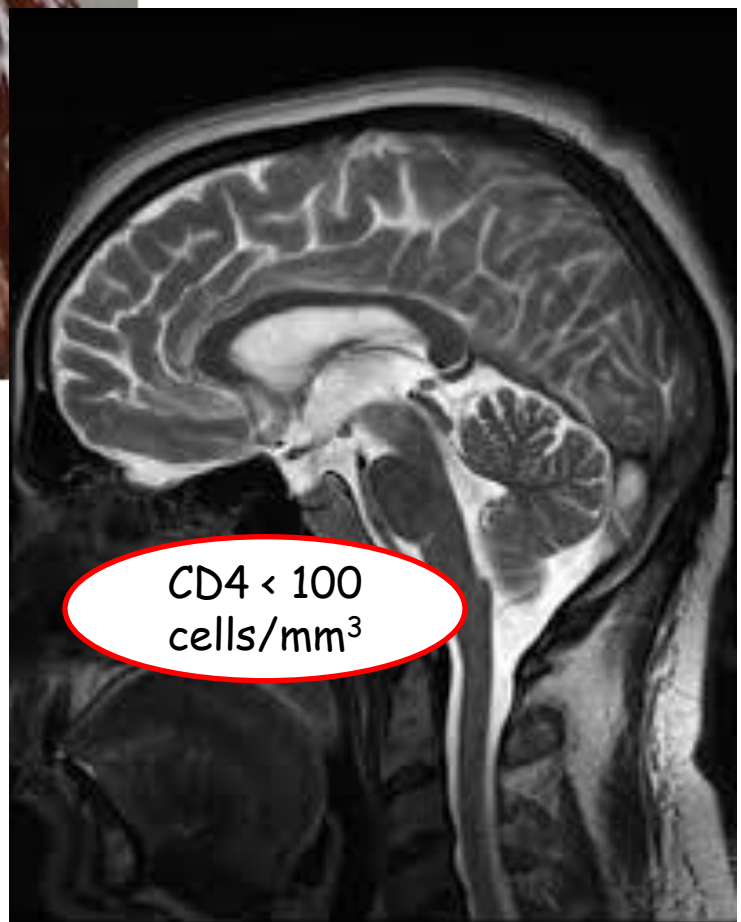


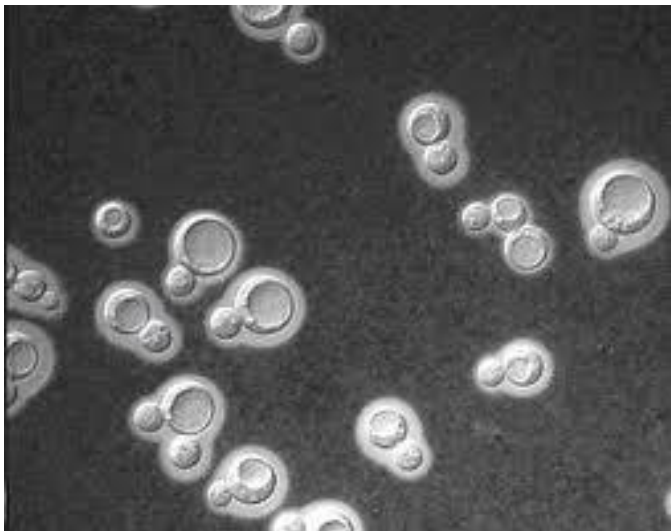
Classification: Unicellular Budding Yeast, Opportunistic \Rightarrow Cryptococcus

- Pathology
 - Pulmonary: Granulomatous response, CNS: minimal inflammatory response (lymphocytosis)
 - Immune: initial PMN and $M\Phi$; once capsule produced, phagocytosis is inhibited. T-cell immunity becomes crucial.
- Notes:
 - Immunocompetent: mild or asymptomatic pulmonary infection; (+) granuloma
 - Uncommon but can develop meningoencephalitis
 - Immunocompromised [HIV ($CD4 < 100$), transplant, CCS]:
 - Mild or asymptomatic pulmonary infection;
 - Subacute-chronic meningoencephalitis (neurotropic)
 - Rx:
 - Induction: amphotericin B and flucytosine (pyrimidine inhibitor converted to 5-FU by fungus, competes with uracil interfering with fungal RNA/DNA and protein synthesis)
 - Maintenance: fluconazole (\downarrow ergosterol synthesis)



Mucicarmine
India Ink

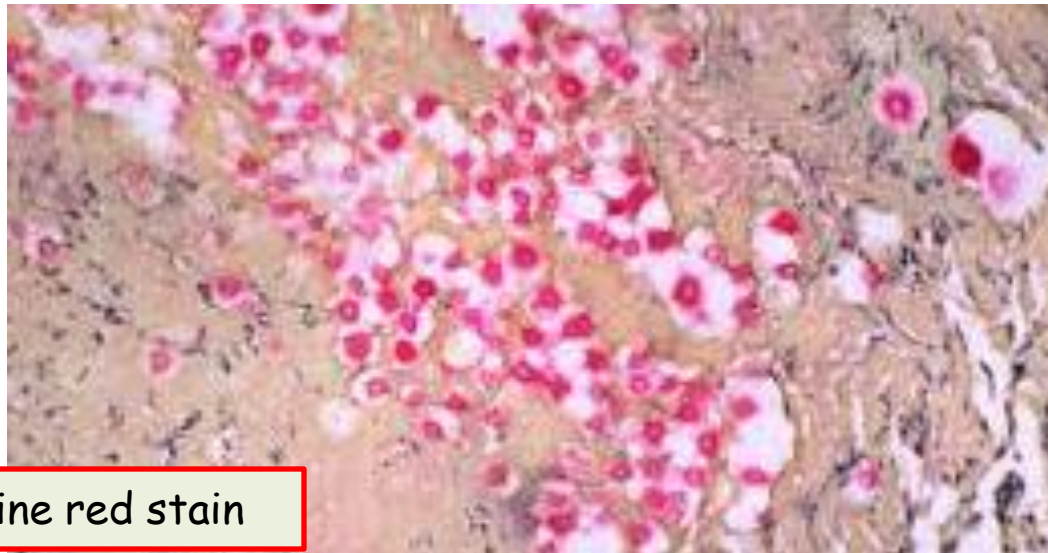




Narrow base budding, uneven



India ink prep

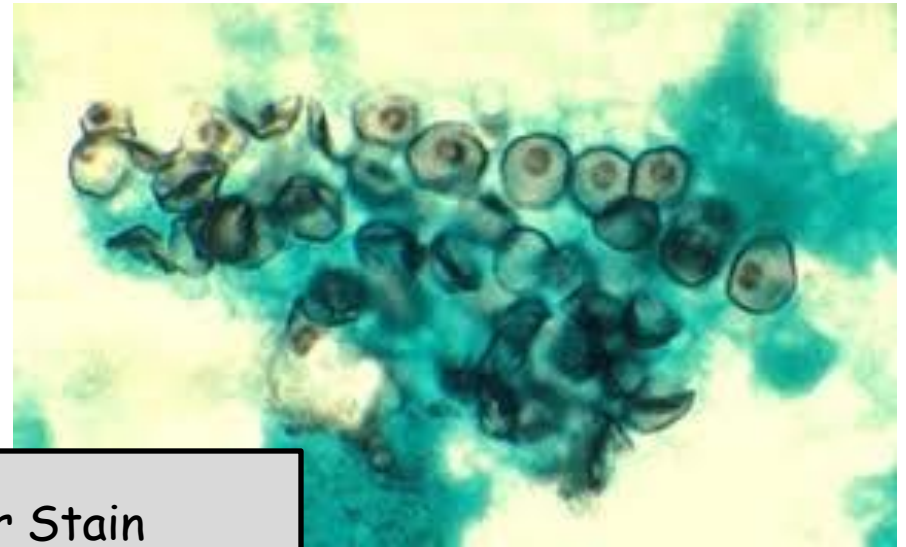
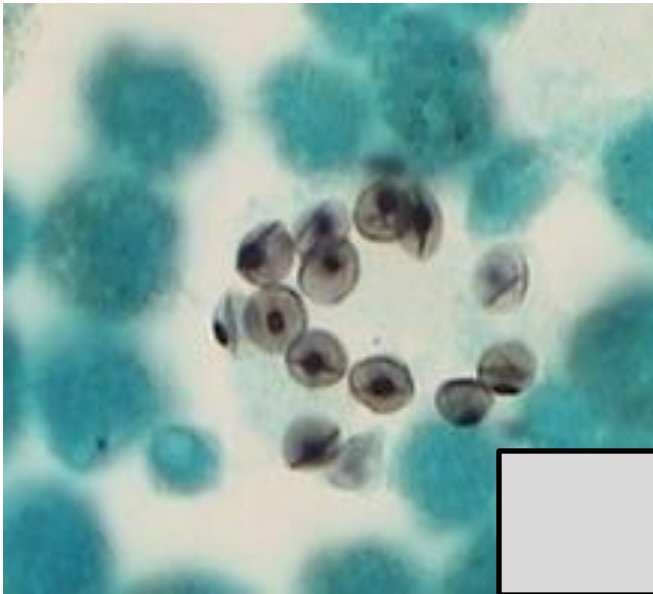


Mucicarmine red stain

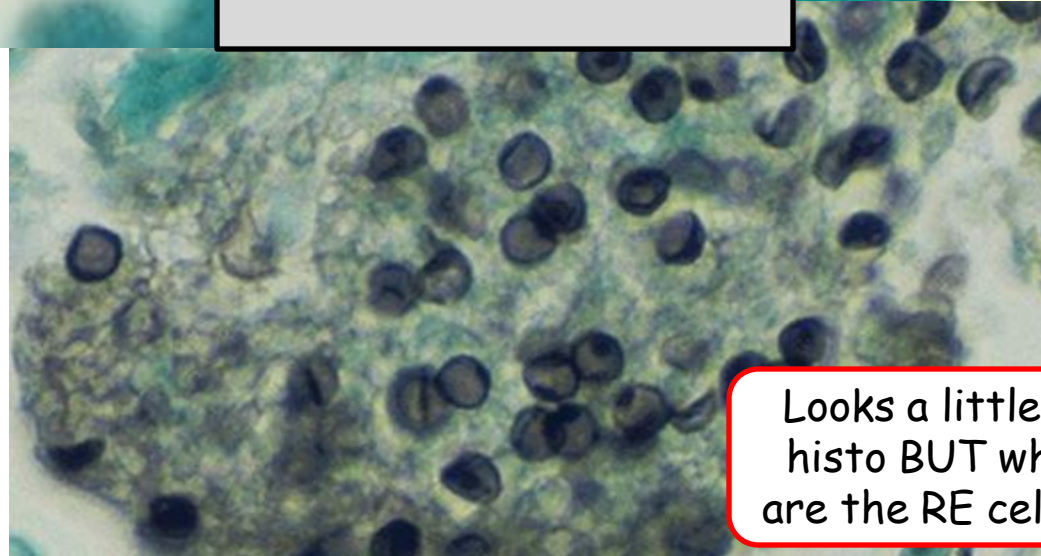
Yeast, Opportunistic: Pneumocystis jirovecii (PCP)

- When to suspect?
 - Environment: Alveoli (PNEUMOCYSTIS sounds like **pneumocyte?**)
 - Transmission: airborne & person to person
- Relevant Microbiology
 - **Disc** shaped yeast on **methenamine** silver stain (on BAL).
- Pathology:
 - Immunocompromised: CD4 T-cells (infection when count **<200 cells/mm³**)
 - Lung/BAL: organisms mixed with protein, edema and desquamated cells
- Notes:
 - Presentation: gradual onset of fever, cough and dyspnea. CXR reveals either nothing or diffuse, bilateral interstitial infiltrates. Wide A-a gradient and elevated LDH (prognosticator)





Silver Stain



Looks a little like
histo BUT where
are the RE cells???

Frothy exudate filling the alveolar spaces
Q. Intracellular or **Extracellular?**

Pleomorphic **Yeast**, Opportunistic: *Candida*

How *Candida* finds its way into this section is uncertain.

It is a rare cause of pulmonary infection that is usually from hematogenous, not oropharyngeal, spread.

Be prepared, therefore, to identify this organism as a **commensal organism seen on BAL specimens.**

The microbiology has some key features that make for good question targets.

Pleomorphic **Yeast**, Opportunistic: *Candida*

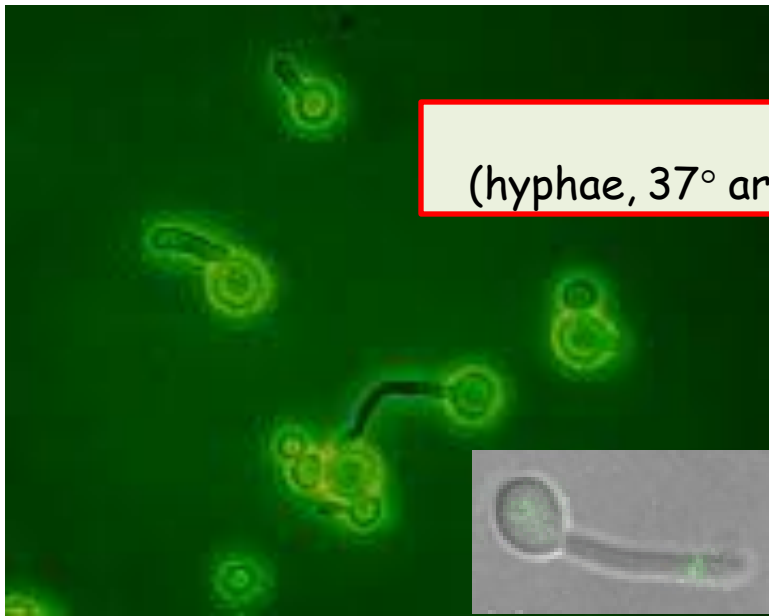
- Background:
 - Environment: Common **commensal** organism seen in GI tract (mouth → rectum), vagina, skin
 - Majority of infections are **mucosal**/superficial
 - Infection: acute/chronic; local/systemic
 - Depends on mucosal breach (i.e. catheters) and/or compromise [including alteration of normal flora (i.e. antibiotics)]
- Relevant Microbiology
 - Classification, **Pleomorphic** Yeast: Unicellular budding yeast with pseudo- and true hyphae
 - **Pseudohyphae** elongated buds attached to one another through repeated cycles of budding (characterized by constriction 'bands')
 - **Hyphae** elongate without budding; represented by '**germ tubes**' (grow at 37°)
 - Immune response: T-cell mediated and **PMN** (defense against invasion)

Pleomorphic *Yeast*, Opportunistic: *Candida*

- Notes:
 - Invasive/Disseminated infection: neutropenia, HIV, CCS, heme malignancy, transplant, catheters.
 - Histopathologic feature is microabscess.
 - *Candida albicans* distinguished from other species by growth of germ tubes.

Pulmonary Infection(?):

Limited inquiry with focus on commensal organism in sputum/BAL culture.
Other questions seem to focus on growth characteristics.



Germ tubes
(hyphae, 37° are distinguishing feature of *Candida albicans*)

Pseudohyphae, elongation with constrictions at site of budding

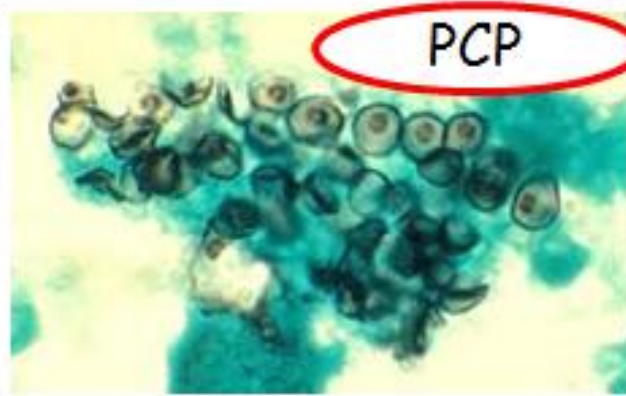


Opportunistic, Yeast

Crypto



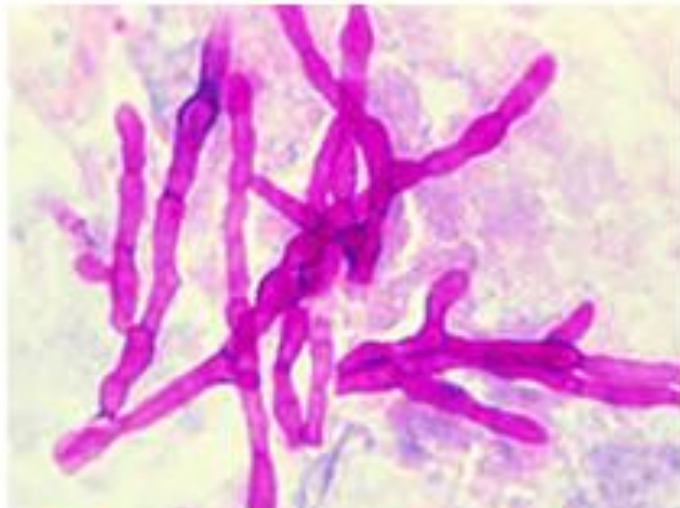
PCP



Candida

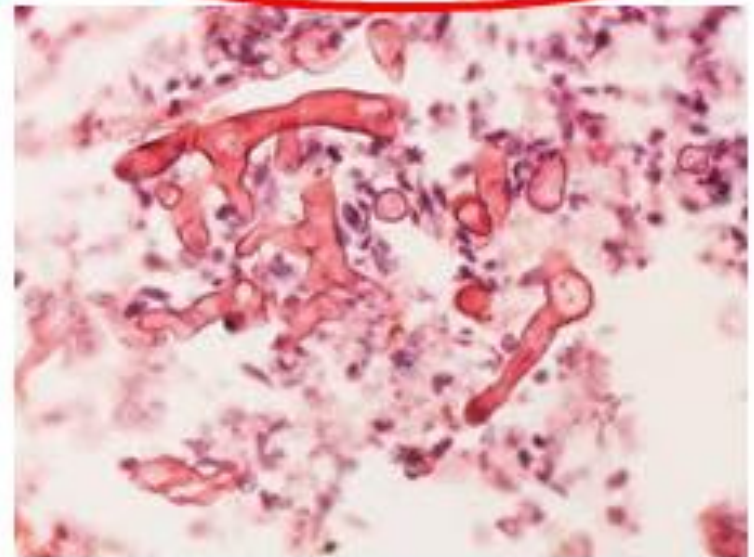


Opportunistic, Mold



Aspergillus

Mucor



The Spectrum of Aspergillosis

Aspergilloma



ABPA

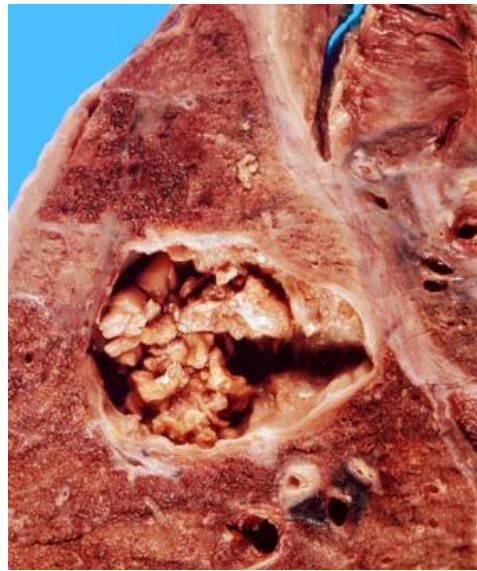
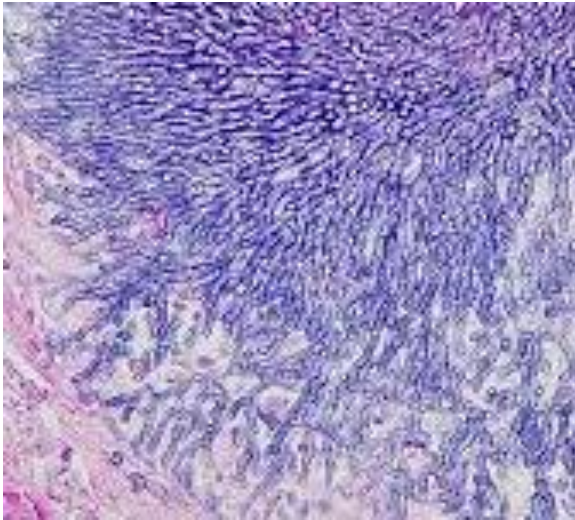


Invasive Aspergillosis



Aspergillosis

Colonizer: Aspergilloma

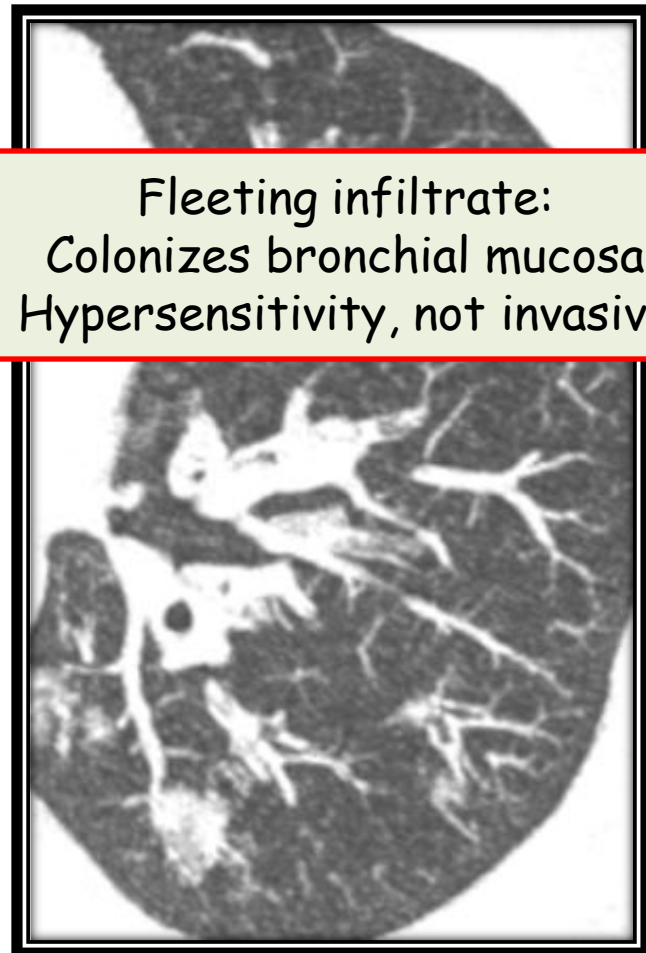
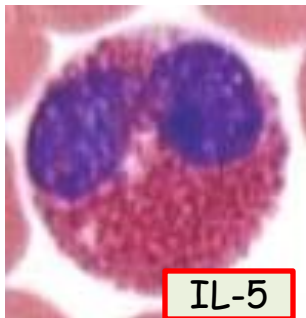
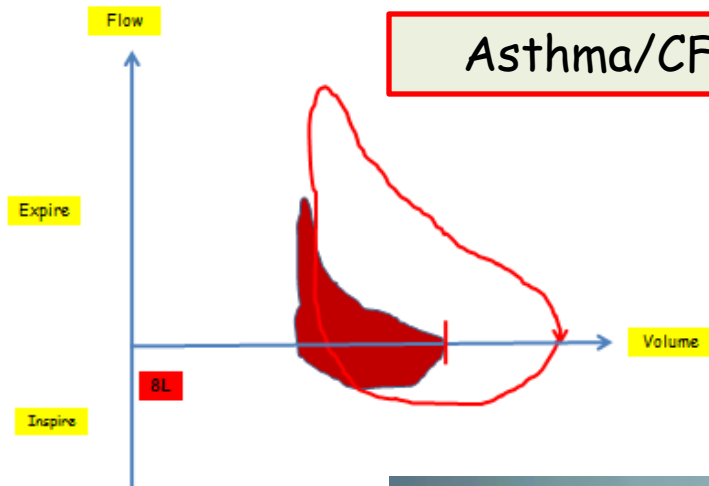


Mycetoma or Fungus Ball
Occupy cavity (old TB)
Noninflammatory
Can be associated with hemoptysis

Aspergillosis

Allergic Bronchopulmonary Aspergillosis

Asthma/CF



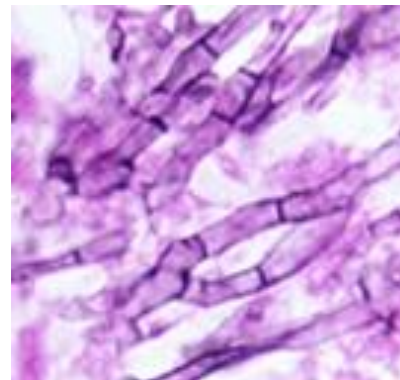
Fleeting infiltrate:
Colonizes bronchial mucosa
Hypersensitivity, not invasive

Eosinophilia, IgE [(+) and v. Af]

Classification: Mold

Opportunistic, Invasive Aspergillosis

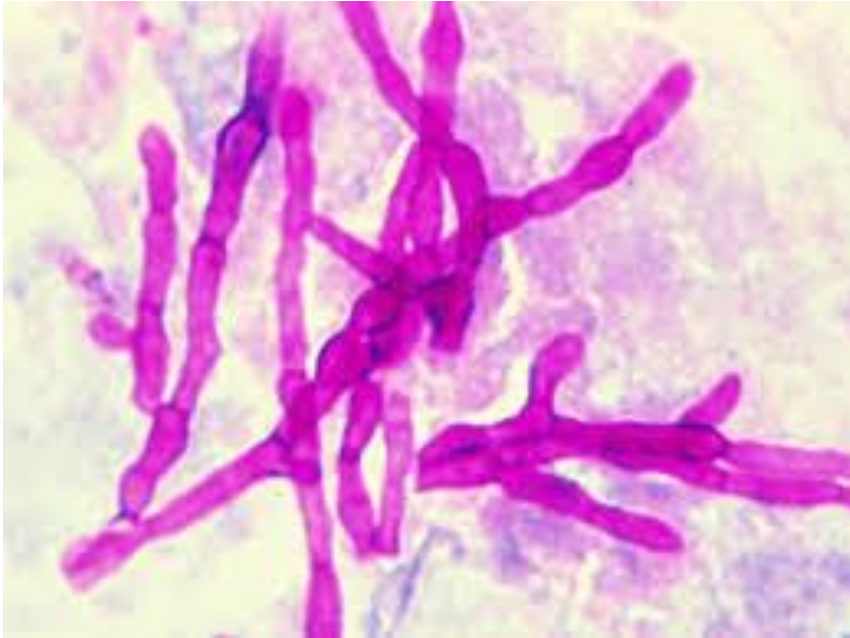
- When to suspect?
 - Environment: **ubiquitous**
 - Transmission: airborne, conidia are inhaled; **if profound immunosuppression (PMNs), they germinate into invasive hyphae**
- Relevant Microbiology/Pathology
 - Morphology: Fruiting bodies and **septate hyphae** (filaments) **branching at acute angles (45°)**



Classification: Mold

Opportunistic, Aspergillus

- Relevant Microbiology/Pathology
 - Morphology: Fruiting bodies and **septate hyphae** (filaments) **branching at acute angles (45°)**
 - Immunity: MΦ (kill conidia but not hyphae); **PMN cannot phagocytize hyphae; instead line up on hyphae surface and secrete oxygen radicals (no T-cell or humoral response)**
 - **Angioinvasive** fungus → invade through blood vessel walls causing ischemia, hemorrhage and necrosis
 - Chronic **Necrotizing** PNA with nodules, cavities and associated hemorrhage. Sinus invasion may occur w/ spread to CNS
 - Immunocompromised: CCS, prolonged **neutropenia**, transplant

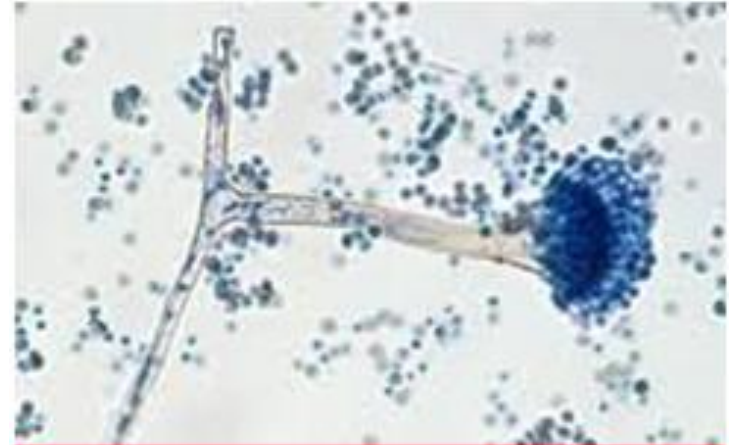


Aspergillus

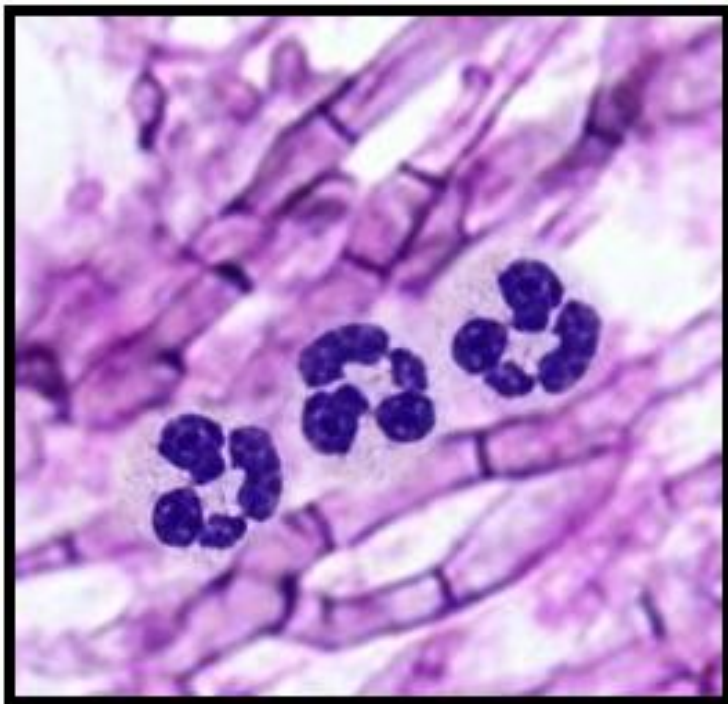
Acute 45° branching, septate, hyphae

Neutropenia

Angioinvasive → Necrotizing PNA



Conidia on Conidiophore

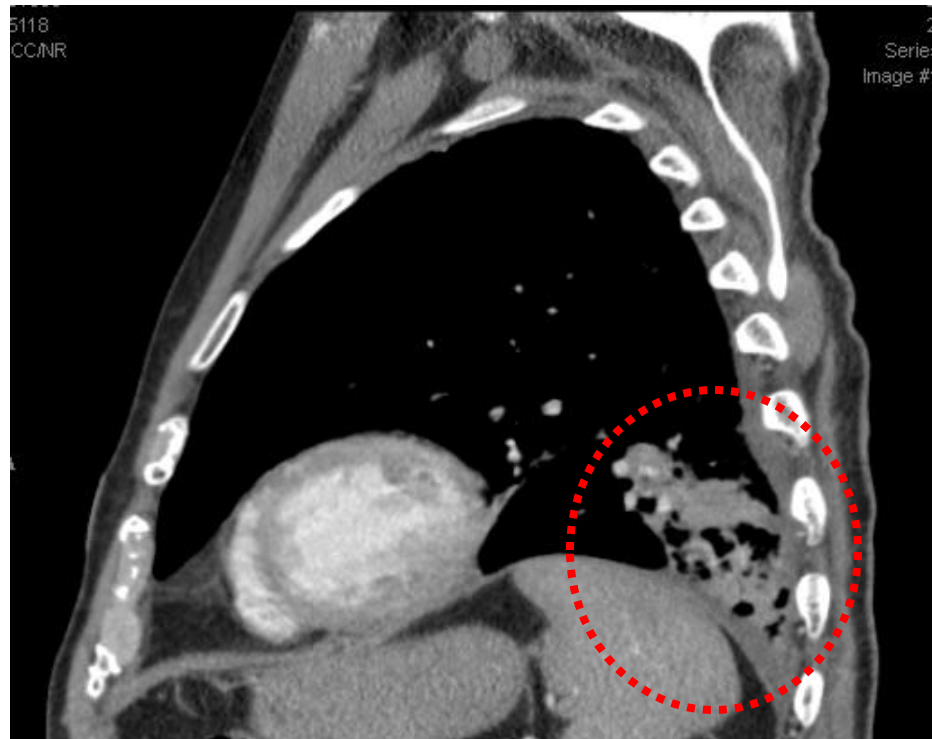


Aspergillus

Acute 45° branching, septate, hyphae

Neutropenia

Angioinvasive → Necrotizing PNA

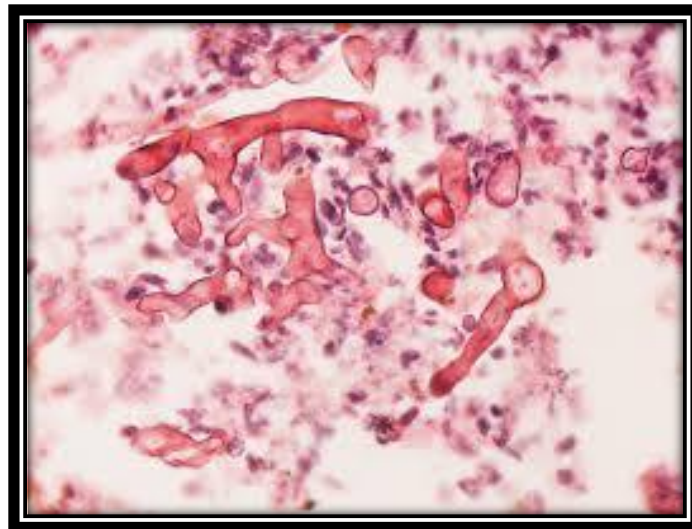


Sagittal view: necrotizing PNA

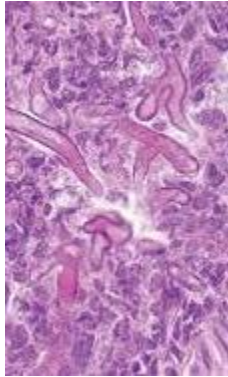
Classification: Mold

Opportunistic, Mucormycosis

- When to suspect?
 - Environment: ubiquitous, soil (include *Mucor* and *Rhizor* species)
 - Transmission: airborne spores, leading to **rhino-orbital-cerebral** and pulmonary infection.
 - **Ecology**: **DKA** (2° ketone reductase) and **deferoxamine** are main risk factors.
- Relevant Microbiology
 - Morphology: **broad** hyphae **without septae**, irregular branches at **wide angles**



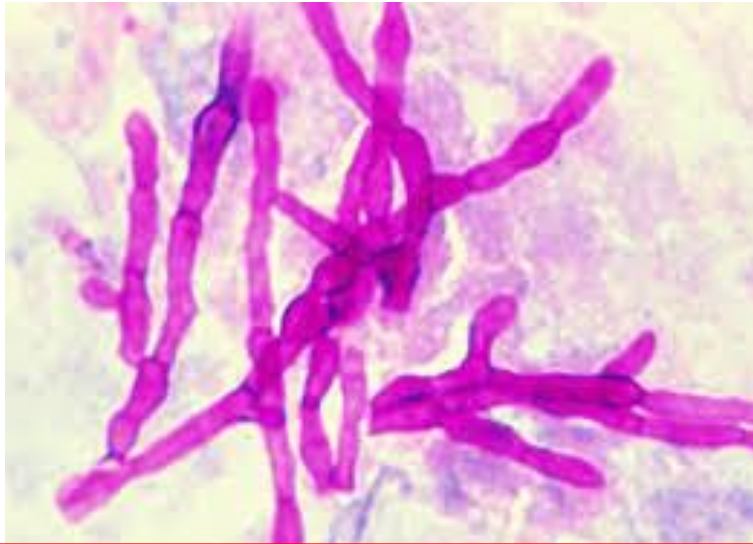
Classification: Mold Opportunistic, Mucormycosis



Fe^{+2}



- Pathology
 - Immunity: $M\Phi$; **PMN** kill hyphae after germination
 - **Angioinvasive** organism causes **tissue necrosis** (nasal **eschars**)
 - **Rapidly progressive infection** with pansinusitis and spread to contiguous structures
- Notes:
 - Immunocompromised: Neutropenia, **CCS**, poorly controlled diabetes/DKA, heme malignancy
 - Enzyme, **ketone reductase**, allows organism to **thrive in high glucose, acidic** conditions
→ easily destroyed in absence of these conditions
 - Likes iron, especially in presence of **deferoxamine** (used in iron overload; **siderophore**)



Aspergillus

Acute 45° branching, septate, hyphae
Neutropenia
Angioinvasive → Necrotizing PNA

Mucormycosis

Hyphae are broad with irregular branching at wide angles

Not septated

~Poorly controlled DM~

Sinusitis

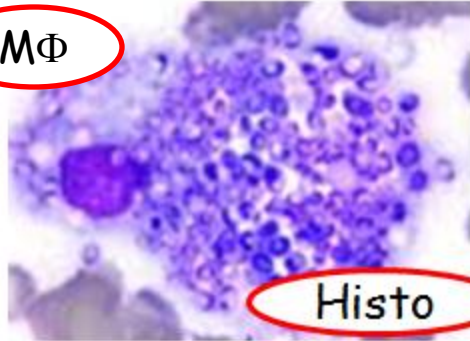
Rhinocerebral



Both organisms are **angioinvasive**, causing tissue necrosis

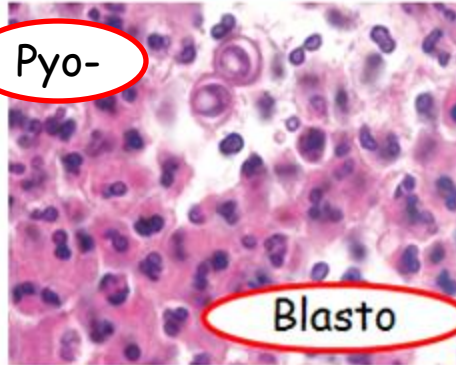
Endemic, Dimorphic (environment mold, body yeast)
Although NOT opportunistic, host response is dependent on CMI
so dissemination occurs with immunodeficiency

MΦ



Histo

Pyo-



Blasto

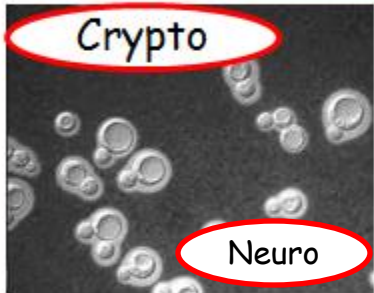
Desert



Coccidio

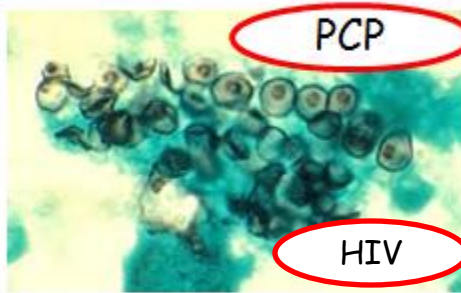
Opportunistic, Yeast

Crypto



Neuro

PCP



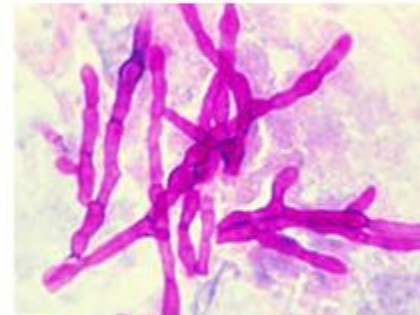
HIV

Germtubes

Candida



Opportunistic, Mold



Aspergillus

Mucor



Thin-Angioinvasive-Fat

Pulmonary Infections: Fungus



A few extra bonus slides (summary) attached

So what's the good news...

Finite number of organisms
(Aspergillus, Blastomyces, Candida,
Coccidiomycosis, Cryptococcus, Histoplasma,
Mucormycosis and Pneumocystis)

Helpful Categories:

Dimorphic: Histoplasma, Blastomyces, Coccidiomycosis

Yeast: Cryptococcus, Pneumocystis (atypical), Candida

Mold: Aspergillus,, Mucormycosis

So what's the good news...
Many Distinguishing Features

Geography

Southwest: Coccidiomycosis

Ohio River Valley: Histoplasma, Blastomycosis

Ecology

Pigeon crap: Cryptococcus

Chicken crap: Histoplasma, Cryptococcus

Bat crap (caves; spelunking): Histoplasma

Desert: Coccidiomycosis

Non-Pulmonary Manifestations

CNS: Cryptococcus, Mucormycosis

RES: Histoplasma

Skin: Blastomyces

Nose/Sinus: Mucormycosis

Arthropathy: Coccidiomycosis

So what's the good news...
Many Distinguishing Features

Immune Status/Predisposing Conditions
HIV: Pneumocystis, Cryptococcus
DKA: Mucormycosis
Neutropenia: Aspergillus
Anti-TNF Rx: Histoplasma, Cryptococcus

And then there is the microbiology...

Growth/Reproduction/Morphology

Intracellular (MΦ): Histoplasma

Alveolar fluid: Pneumocystis

Budding: Uniform/Broad - Blastomyces

Capsule: Cryptococcus

Temperature: Germ tubes (Candida), Dimorphic

Hyphae, thick: Mucormycosis

Hyphae, branching: Aspergilla

Staining Characteristics

Mucicarmine/India Ink: Cryptococcus

Methenamine Silver: Pneumocystis, Cryptococcus



Thank you for coming and drive home safely!