

Pulmonary Infections: Fungus



Howard J. Sachs, MD
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Confession

On this topic, I was quite stubborn



Confession

I thought the details you were being asked to memorize were picayune and ridiculous...

Confession

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...until I saw the light.

Limited
Organisms (8)



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Helpful
Categories (3)



Limited
Organisms (8)

Helpful
Categories (3)

Many Distinguishing Features
and Characteristics



Geography
Ecology
Non-pulmonary
Immune Status
Morphology
Special Stains

So what's the good news...

- This is totally doable.
- Major Obstacle: Inertia
- Once you overcome inertia, you'll wish there were more questions on pulmonary fungal infections.



Pulmonary Infections: Fungus

Part I: Background Information and Dimorphic Fungus

Part II: Opportunistic Yeast and Molds

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Fungal Infections, Definitions

- **Mold**: multicellular, threadlike filaments \Rightarrow **hyphae**
- **Yeast**: unicellular
- **Dimorphic**, Endemic

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 - Buds that fail to detach become **pseudohyphae**
- **Dimorphic**, Endemic (Histo, Blasto, Coccidio):
 - Mold at environmental temps (25°C)
 - Yeast at body temp (37°C)
 - Endemic: can cause disease in healthy hosts.

Fungi, fun facts

- Cell membrane: lipids, glycoproteins and **sterols** (ergosterol; fungal version of cholesterol)
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- Cell wall (chitin, mannan and **glucan**): humans lack cell walls and bacteria/plants have different types
 - Rx: echinocandins (β -(1,3)-D-glucans)

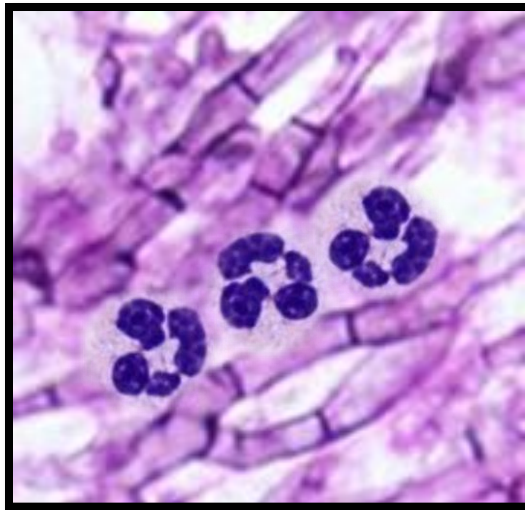
Echinocandins inhibit glucan synthase (and cell wall synthesis)

Fungi, fun facts

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 - Rx: amphotericin (alter permeability), azoles (↓ synthesis)
- Cell wall (chitin, mannan and **glucan**): humans lack cell walls and bacteria/plants have different types
 - Rx: echinocandins (β -(1,3)-D-glucans)
- Derive nutrition from **decaying matter** (reason they love bird/bat crap and live in the soil).

Fungi: Immune Defense

- Neutrophil: phagocytosis and extracellular killing (lysozymes) is primary mechanism
 - Neutrophils line up on the hyphal surface of large filamentous fungi and secrete lysozymes.

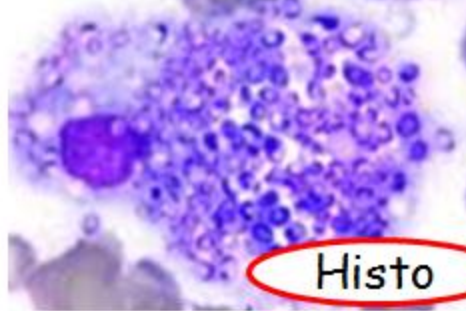


Fungi: Immune Defense

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 - Neutrophils line up on the hyphal surface of large filamentous fungi and secrete lysozymes.
- T-cell mediated immunity is vital: MΦ can contain organism but T-cells required
 - Thus, opportunistic infex with T-cell defects
- Humoral immunity plays minor role.

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

Transmitted as (micro-, conidia, arthro-) conidia...this is what molds do.



Histo



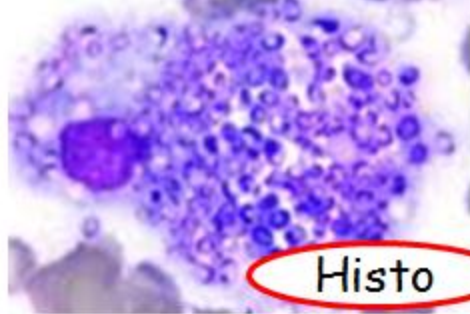
Blasto



Coccidio

Endemic, Dimorphic (environment mold, body yeast)
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Histo



Blasto

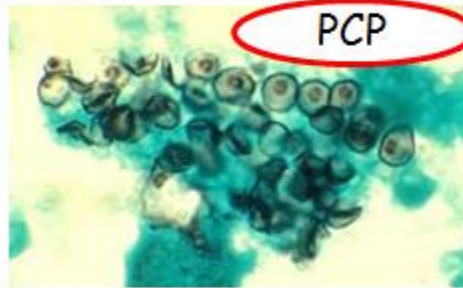


Coccidio

Opportunistic, Yeast



Crypto

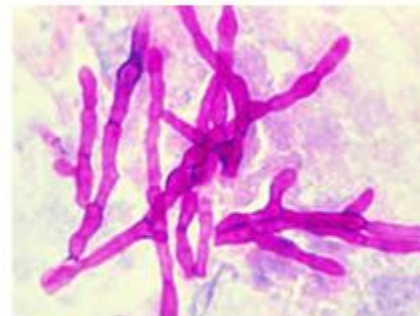


PCP



Candida

Opportunistic, Mold



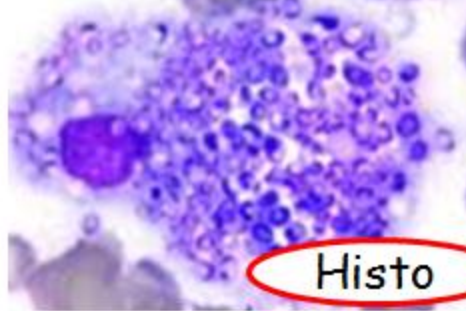
Aspergillus



Mucor

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Histo



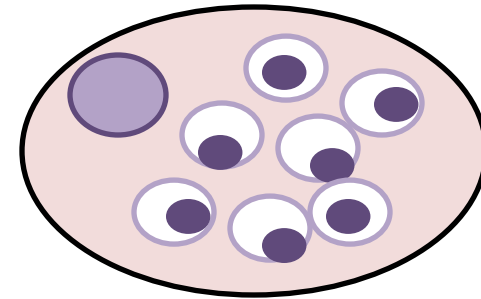
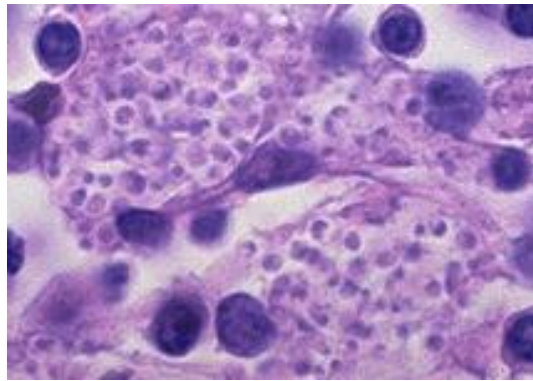
Blasto



Coccidio

Classification: Dimorphic Fungi, Endemic Histoplasmosis

Reticuloendothelial System



Macrophage

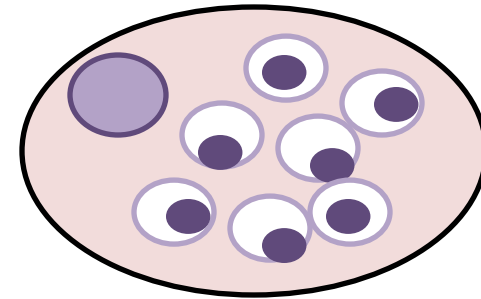
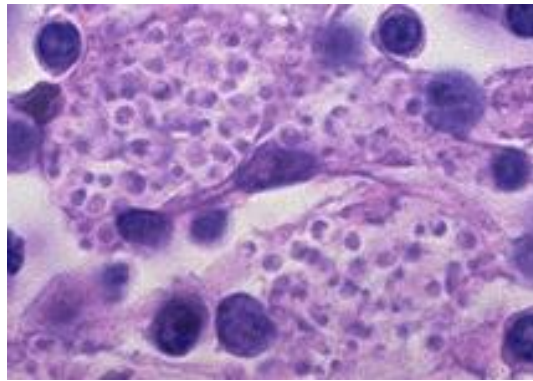
Dissemination = HSM & LAN

HSM: hepatosplenomegaly

LAN: lymphadenopathy

Classification: Dimorphic Fungi, Endemic Histoplasmosis

Reticuloendothelial System



Macrophage

H. capsulatum?



Staining artifact

Classification: Dimorphic Fungi, Endemic

Histoplasmosis: 'infection of the reticuloendothelial system'

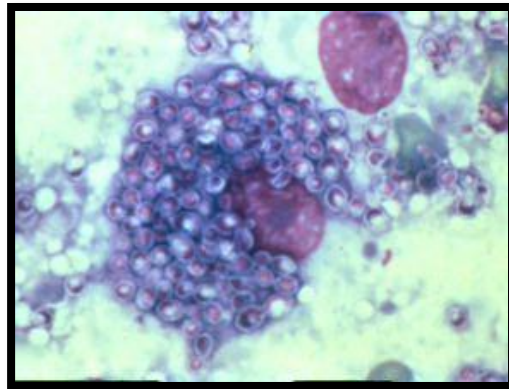
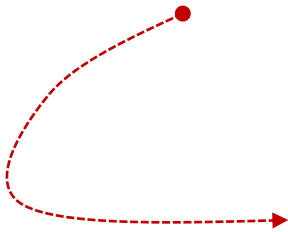
- When to suspect?
 - **Environment**: Mississippi/Ohio River Valley; grows as mold in 'enriched' soil
 - **Ecology**: ↑ Nitrogenous content in bird or bat droppings (**chicken** coops/farms or **caves**; spelunking)
 - **Transmission**: aerosolized spores (microconidia) transform into yeast after inhalation (i.e. lungs are portal of entry)

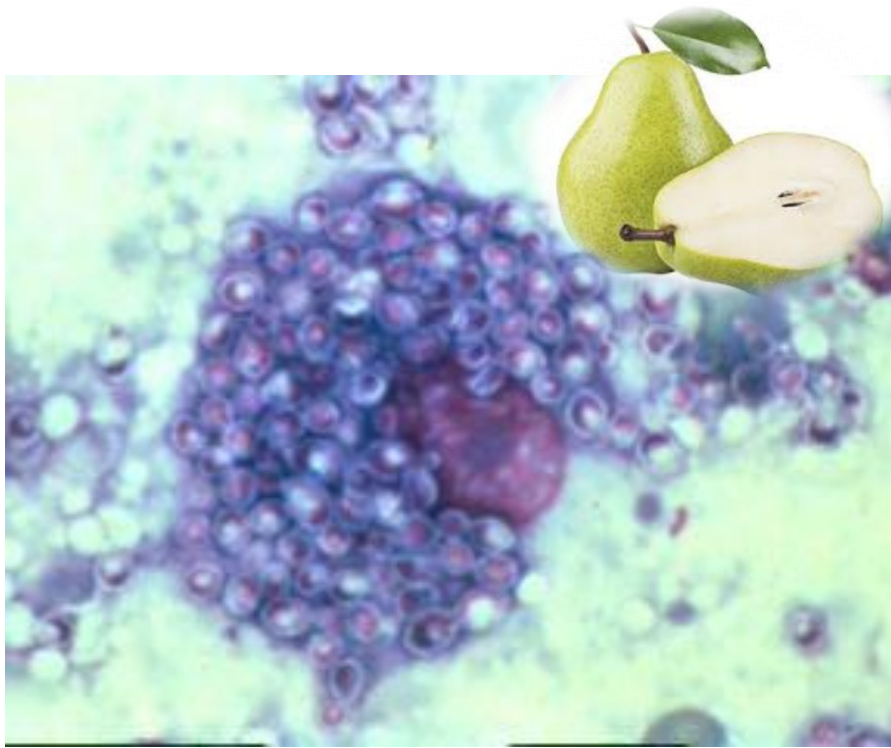


Classification: Dimorphic Fungi, Endemic

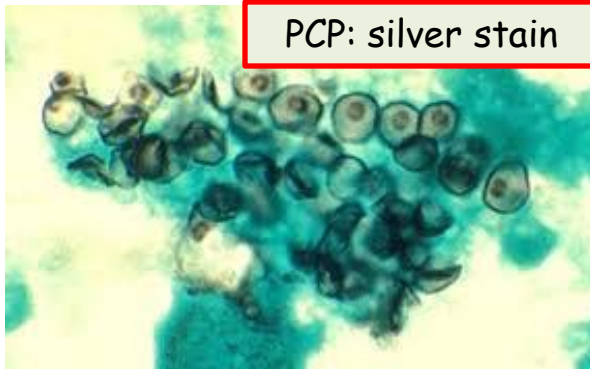
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 - Transmission: aerosolized spores (microconidia) transform into yeast after inhalation (i.e. lungs are portal of entry)
- Relevant Microbiology
 - Morphology: **small-tiny (2-5 μ m)**, ovoid, pear shaped, thin budding yeast, found **within M Φ**

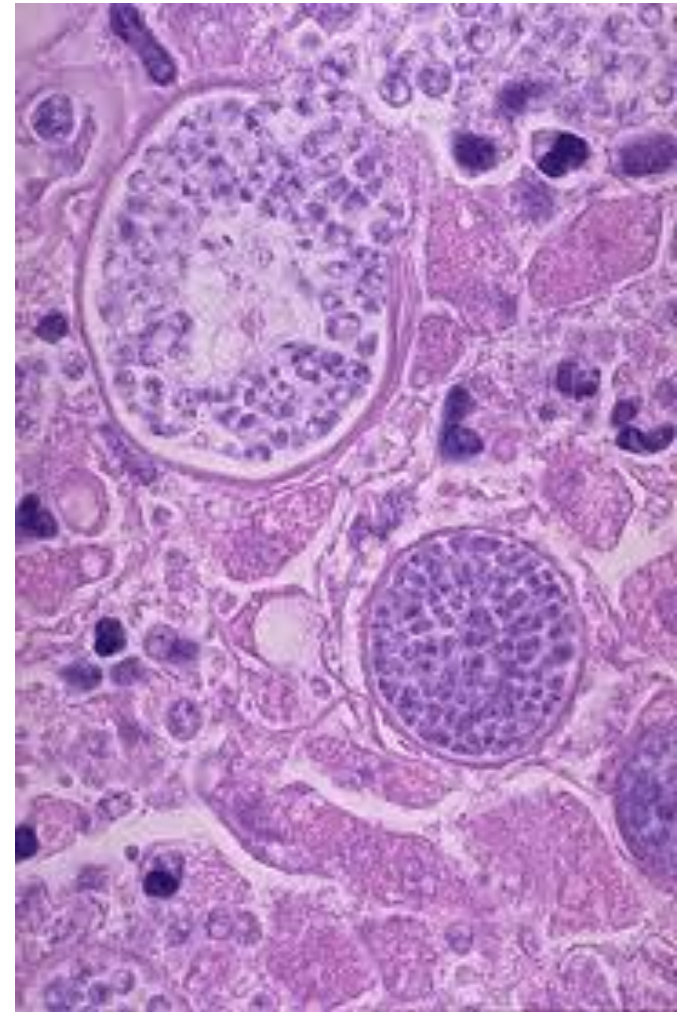




Macrophage ingests but don't kill organism



PCP: silver stain



Compare with spherule containing endospores (Coccidiomycosis)

Classification: Dimorphic Fungi, Endemic

Histoplasmosis: 'infection of the reticuloendothelial system'

- Pathology
 - Ingested by $M\Phi$ and PMNs but killing is problematic
 - They multiply within the phagosome, lyse the cell and can disseminate.
 - Immunity: CD4 T-cells and activated $M\Phi$ \Rightarrow **Granulomatous** response (caseating)
- Notes (clinical):
 - Presentation: patchy PNA with hilar/mediastinal adenopathy
 - Immunodeficiency (HIV/Anti-TNF) \rightarrow Dissemination
 - HSM and LAN due to living intracellular
 - Do Not Confuse: Clinical presentation similar to TB and sarcoid, including *e. nodusum*
 - Rx: amphotericin B (binds ergosterol; severe); itraconazole (mild-moderate; \downarrow ergosterol synthesis)

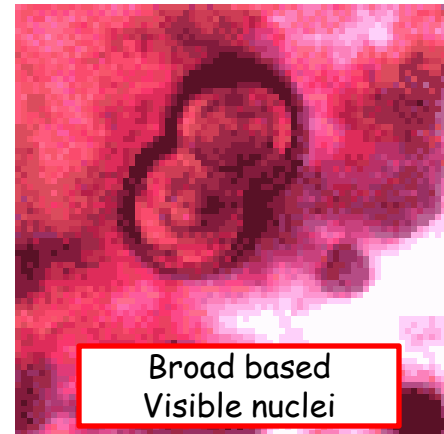
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PNA that fails to improve with antibacterial therapy suggests the possibility of fungal PNA

- Notes (clinical):
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Classification: Dimorphic Fungi, Endemic Blastomyces dermatitides

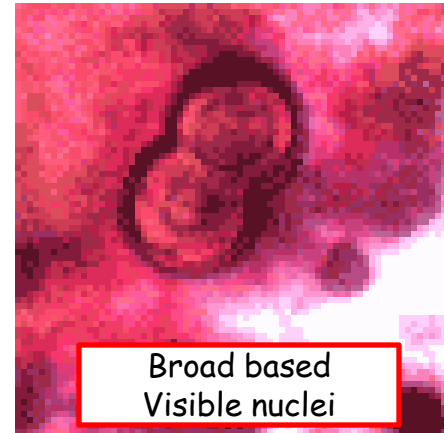
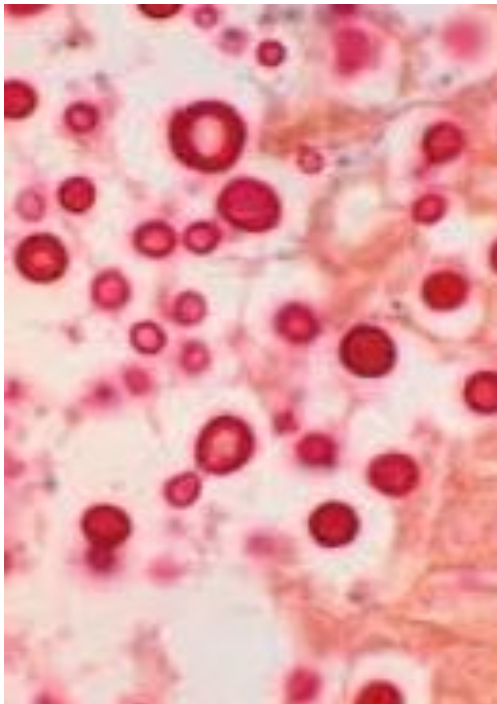
- When to suspect?
 - Mississippi River Valley (like histo) so the distinction is highly dependent on the morphologic description:
 - ~Single Broad Base Budding and Double Contour Sign~



Double contour: Thick, refractory cell wall

Classification: Dimorphic Fungi, Endemic Blastomyces dermatitides

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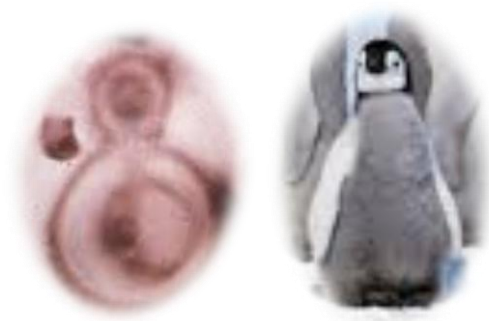


Broad based
Visible nuclei

Looks like crypto?
Crypto: **Uneven**, narrow based budding,
no double contour
(and different stain characteristics)

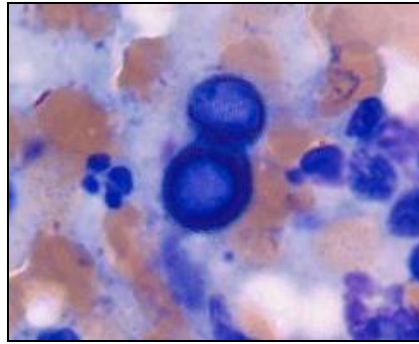
Classification Dimorphic Fungi, Endemic: *Blastomyces dermatitides*

- When to suspect?
 - **Environment**: Mississippi River Valley, lives in the soil/organic matter as mold.
 - Transmission: aerosolized **conidia** that transforms into yeast after inhaled
- Relevant Microbiology
 - Morphology: Round yeast with **SINGLE broad-based budding, thick double contoured cell wall (that looks like a capsule) and visible nuclei.**

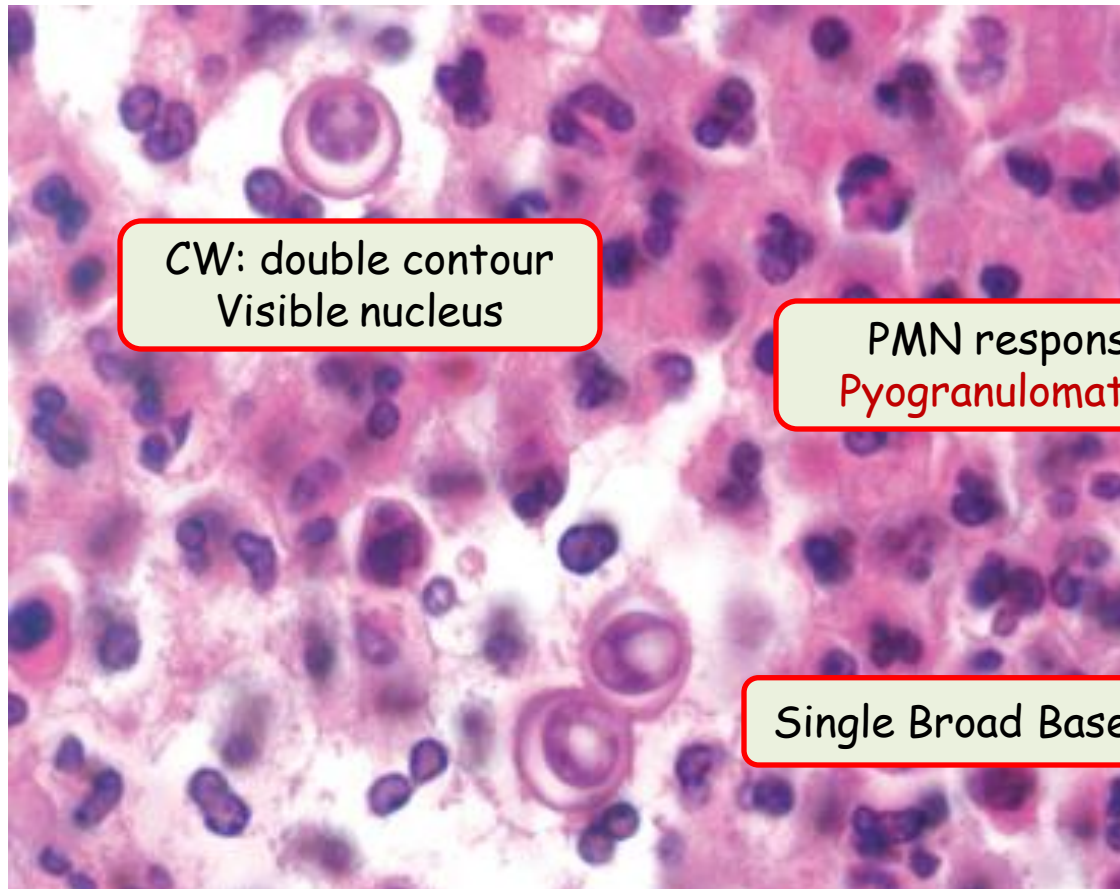


Classification Dimorphic Fungi, Endemic: Blastomycosis

- Pathology
 - Immunity: PMN, T-cell and MΦ
 - Pyogranulomatous infection (i.e. suppurative)
 - Phagocytized by MΦ and PMN (more significant role due to size and thick cell wall)



- Notes:
 - Presentation: acute PNA, lobar consolidation, nodules involving the upper lobes
 - Dissemination is common including skin (raised border, central microabscess), bones and GU tract
 - Expect this infection to be distinguished by suppurative skin lesions.



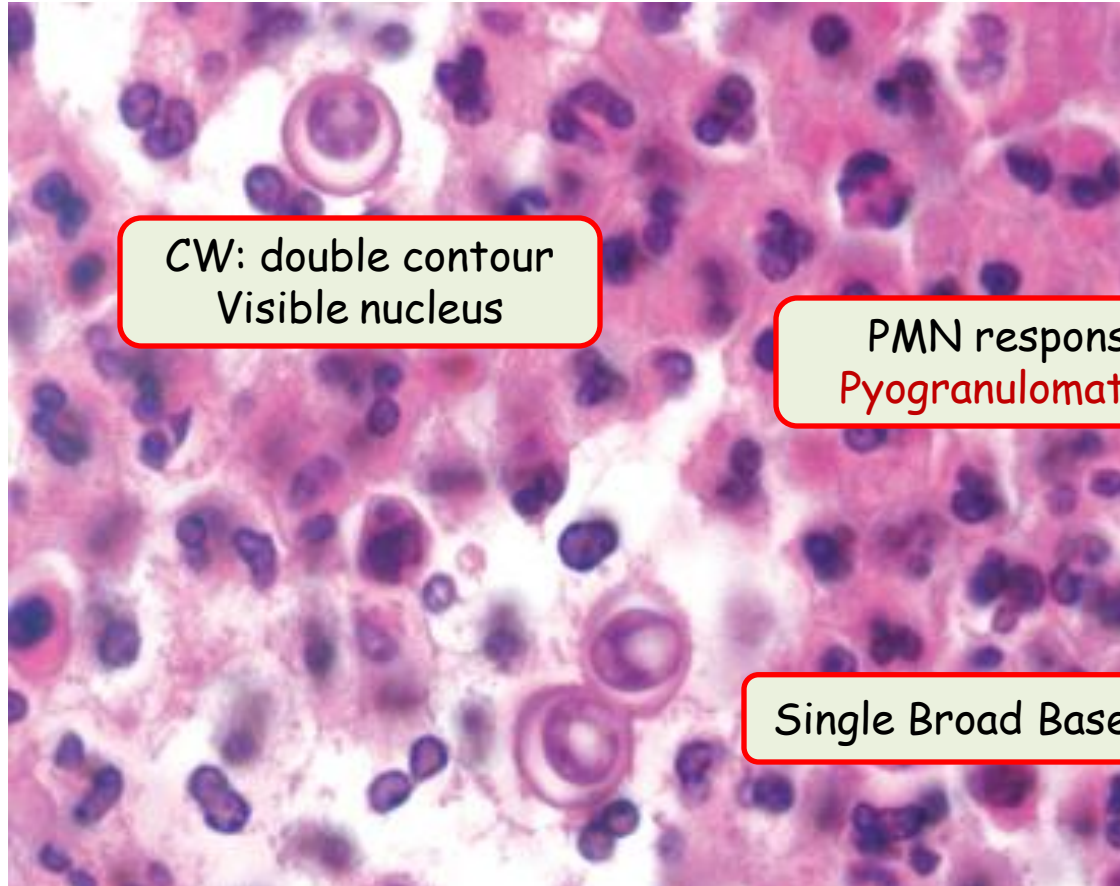
CW: double contour
Visible nucleus

PMN response:
Pyogranulomatous

Single Broad Based Budding

The appearance will be interpreted against
background of vignette.

Dimorphic: pay attention to questions that include temperatures at which organism is grown. If 25°, expect mold form.



CW: double contour
Visible nucleus

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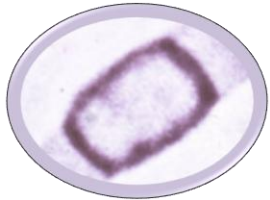
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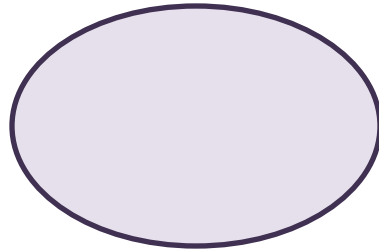
Classification: Dimorphic Fungi, Endemic Coccidiomycosis (*Spherules with endospores*)

- When to suspect?
 - **Environment**: Southwest, esp Arizona & Southern California; grows as a mold (**arthroconidia**) in the **desert** soil
 - Transmission: inhalation of arthro**conidia**, extremely infectious.

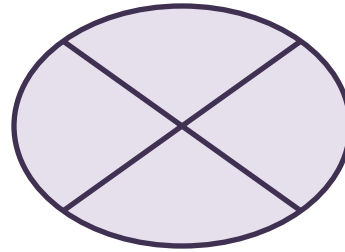
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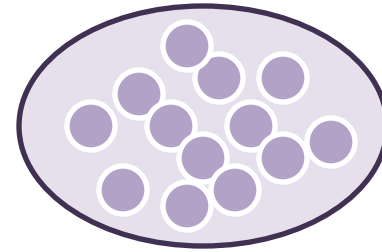
Arthroconidia



Spherule



Septations

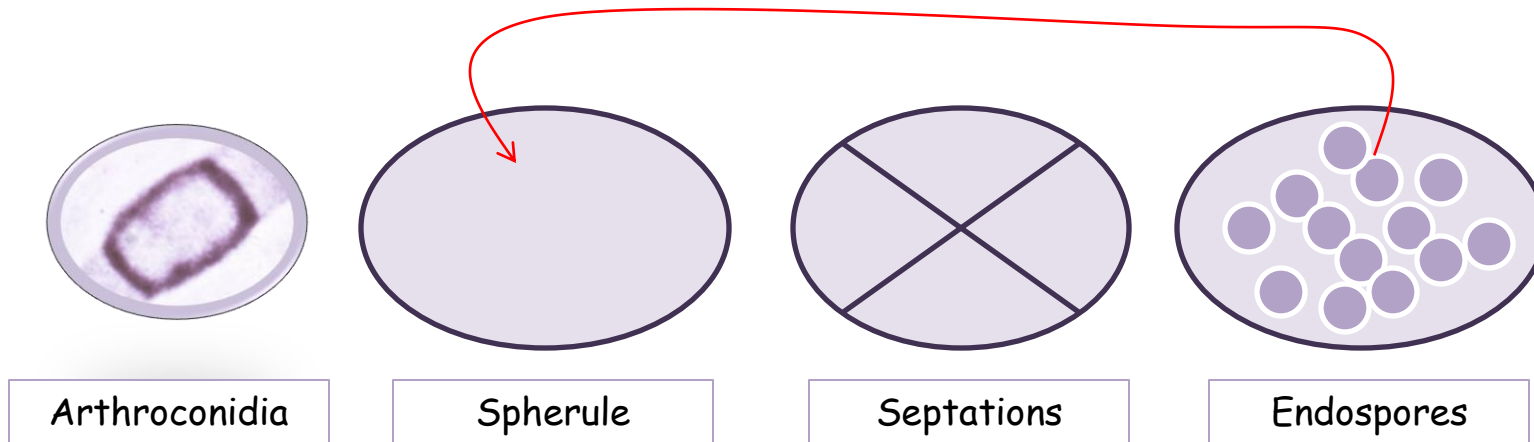


Endospores

• Relevant Microbiology

- Morphology/Pathogenesis: a **single** arthroconidium grows and changes into a spherical structure (spherule) with internal septations (→ endospores)
- Reproduce: Mature spherule ruptures releasing endospores, each of which can create a spherule → destructive process which can lead to cavitory lesions.

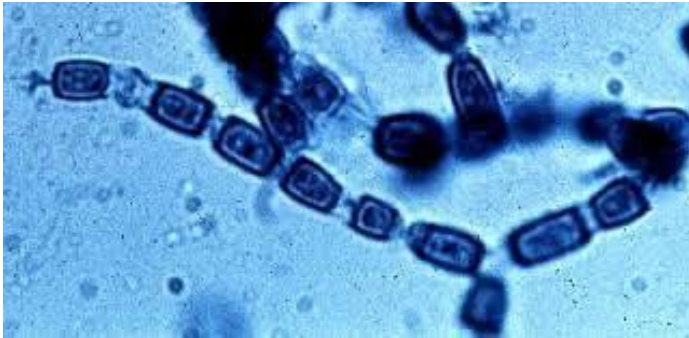
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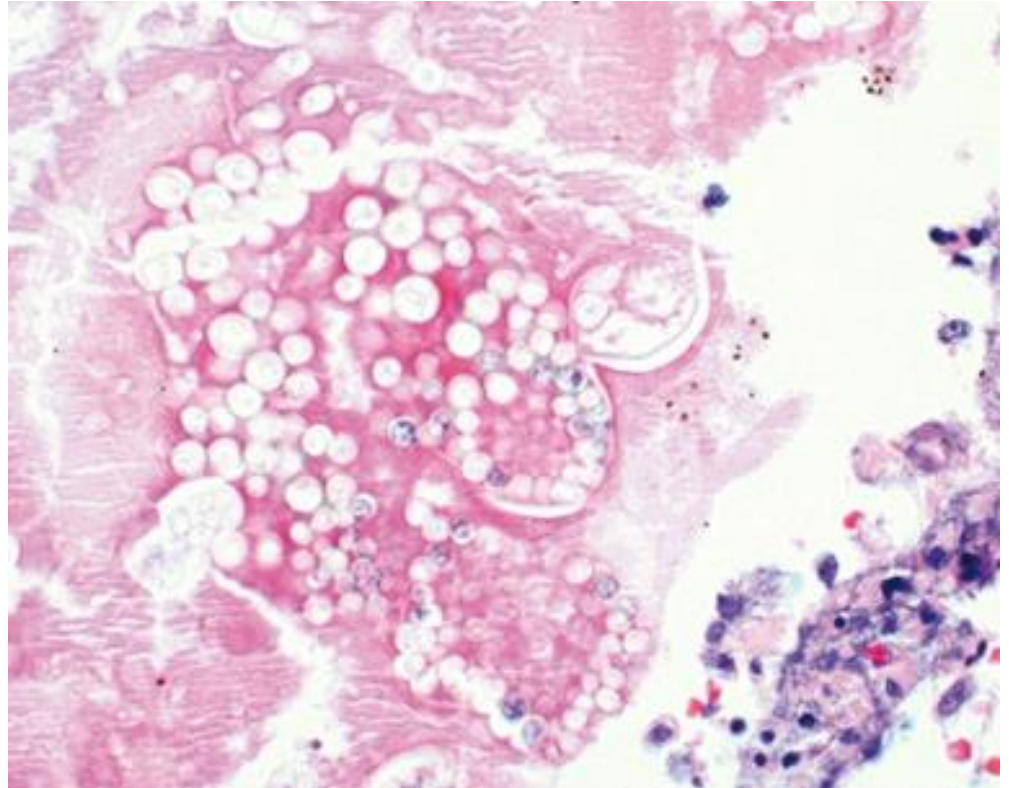
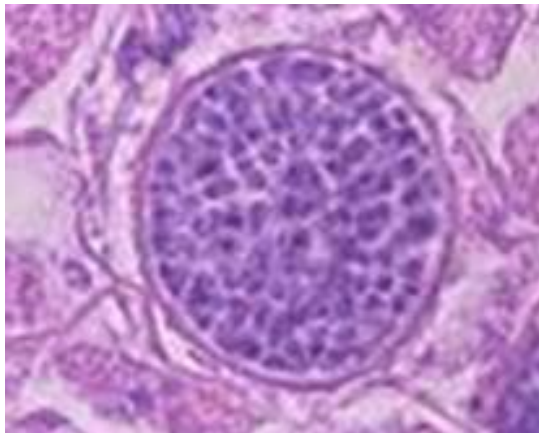
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Barrel-shaped arthroconidia



Spherule with endospores

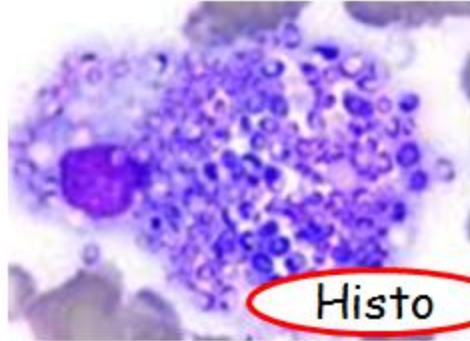


Ruptured Spherule releasing endospores
(each creating a new spherule)

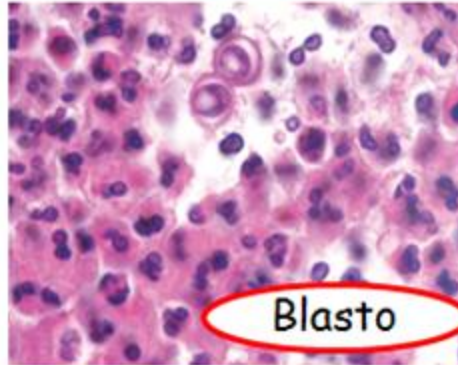
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- Pathology
 - Immunity: PMN (easily kill arthroconidia and endospores but not so much with spherules);
 - T-cell and $M\Phi$ → Granulomatous response (resists intracellular killing; block fusion of phagosome and lysosome)
- Notes (clinical):
 - Valley Fever: respiratory (CAP) plus constitutional symptoms that can last weeks - months. Can be a/w skin symptoms (erythema nodosum/multiforme) and joint complaints ('desert rheumatism'). Hemoptysis implies **cavitation**.
 - Risk factors for disseminated infection: HIV, transplant, anti-TNF, CCS, DM, pregnancy
 - Dissemination: skin, bone (**destructive**) and **meningeal** infection
 - Disrupt desert soil: earthquake and/or archeological digs in SW.

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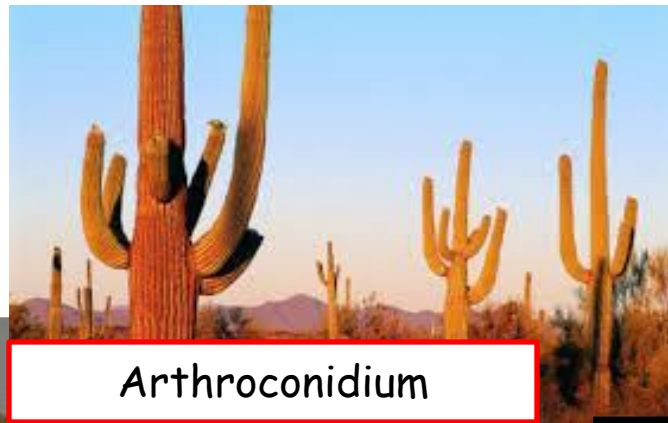
Histo



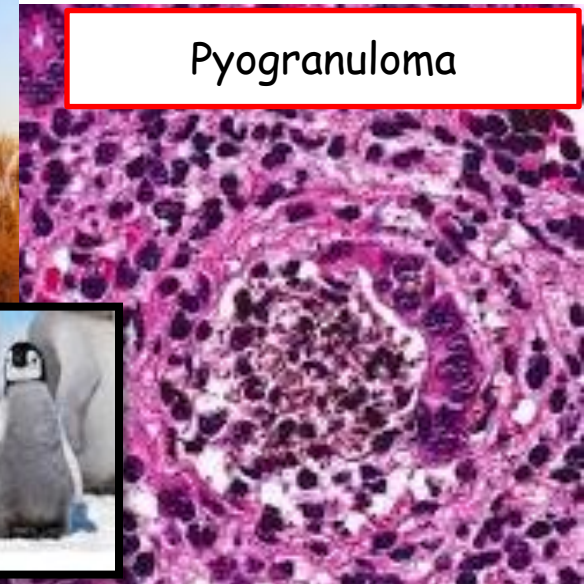
Blasto



Coccidio



Arthroconidium



Pyogranuloma



Histo



Pulmonary Infections: Fungus



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