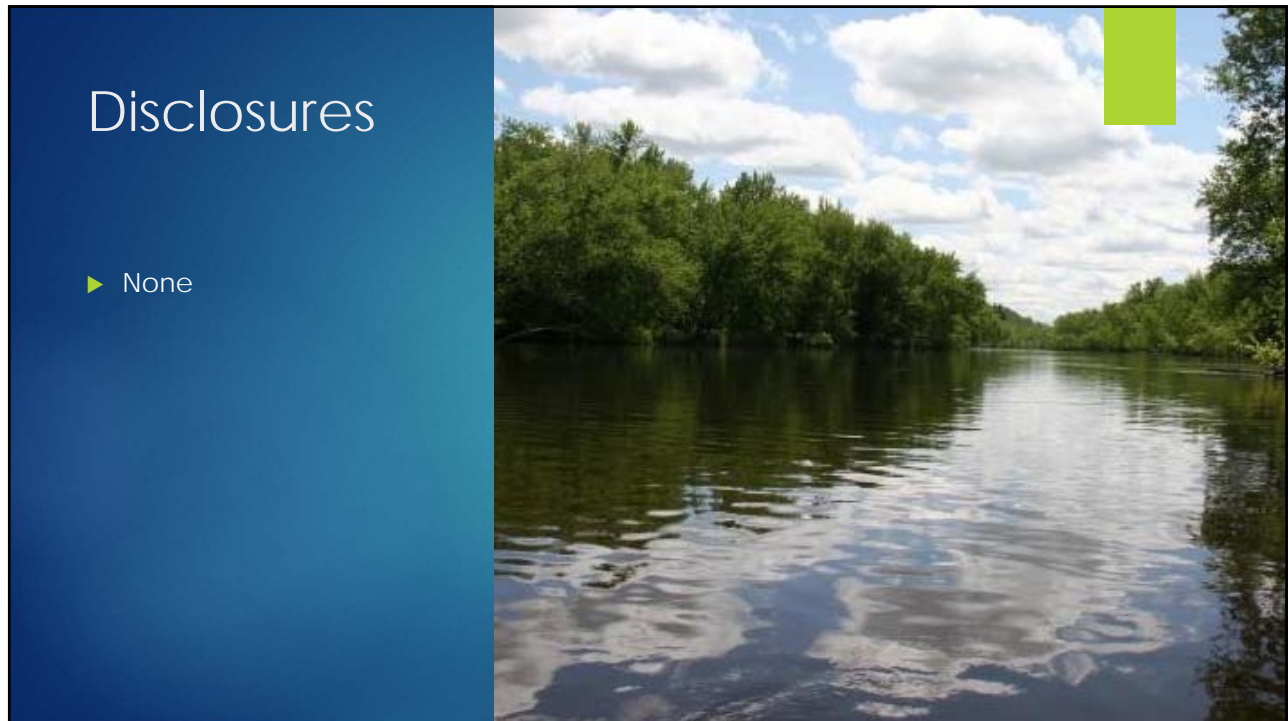




Thermal Dimorphs of Wisconsin

SARAH STONER MS, MB(ASCP)CM
TECHNICAL LEAD-MICROBIOLOGY
GUNDERSEN HEALTH SYSTEM, LA CROSSE WI



Disclosures

▶ None

Goals of this Webinar

- ▶ Become knowledgeable of the epidemiology of endemic dimorphs Blast and Histo
- ▶ Recognize the clinical features of illness caused by endemic dimorphs
- ▶ How to test for them
 - ▶ Culture
 - ▶ Other methods
- ▶ Recognize growth and staining characteristics of endemic thermal dimorphs in WI
 - ▶ Blastomyces
 - ▶ Histoplasma
- ▶ Share some cases!

What are thermal dimorphic fungi?

- ▶ Unlike other fungi, these change their morphologic form based on temperature to adapt to the environment (or host)
 - ▶ Filamentous (fuzzy) at ambient room temperature
 - ▶ Yeast phase at body temperature
- ▶ These all have a geographic niche
- ▶ Infection is acquired by breathing in spores while the fungi are in their filamentous form
 - ▶ Usually manifest in pulmonary infections

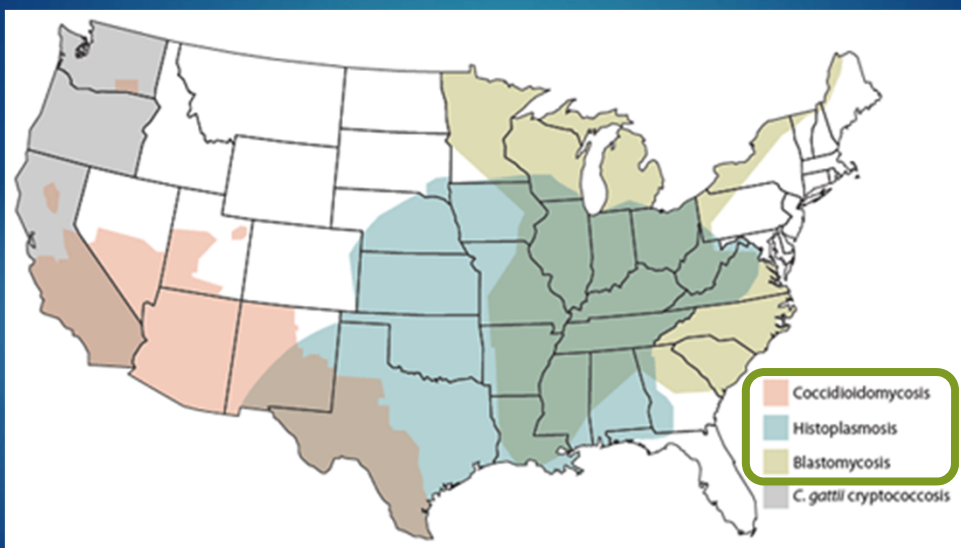
<https://mycology.adelaide.edu.au/descriptions/dimorphic-pathogens/>



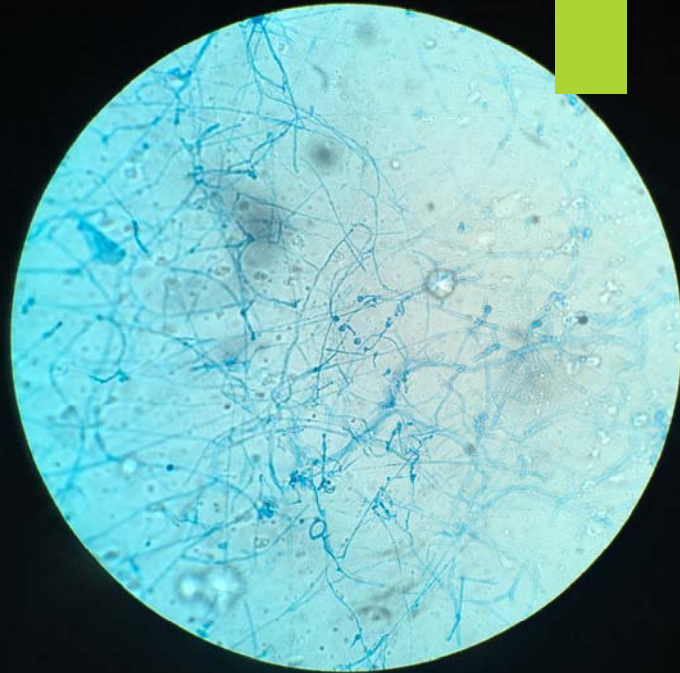
Who are the clinically significant thermal dimorphs?

- ▶ *Blastomyces dermatitidis* a.k.a "Blasto"
- ▶ *Histoplasma capsulatum* a.k.a "Histo"
- ▶ *Coccidioides immitis/posadasii* a.k.a "Cocci"
- ▶ *Sporothrix schenckii*
- ▶ *Paracoccidioides brasiliensis/lutzii* (S. America)
- ▶ *Talaromyces marneffeii* (formerly *Penicillium marneffeii*) (South East Asia)

Geographic ranges



Blastomyces dermatitidis —a.k.a “Blasto”



Blastomycosis Epidemiology

- ▶ A specific niche in nature is still unknown but:
 - ▶ Blasto loves flood prone areas near water
 - ▶ Blasto loves decaying/dead plant matter
- ▶ Geographic range reflects its love of waterways

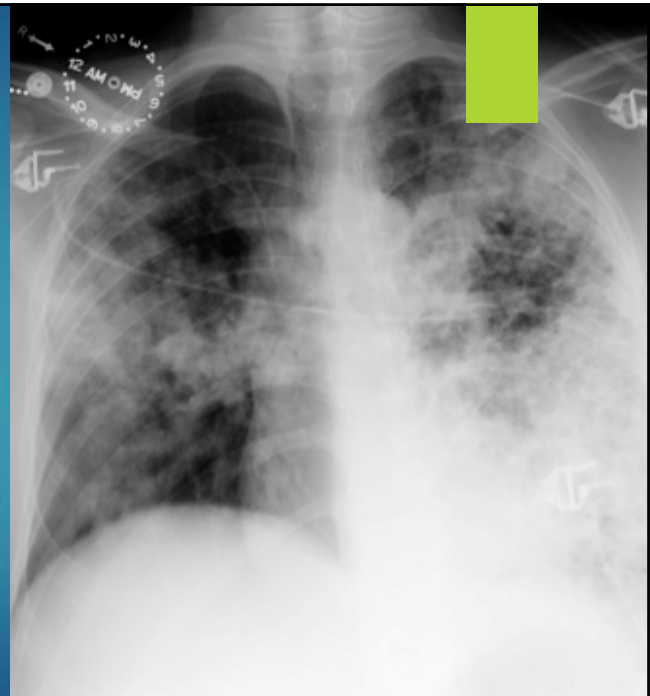


Blasto Epidemiology and Clinical Presentation

- ▶ Risk factors:
 - ▶ Construction
 - ▶ Outdoor activities—hunting, fishing, camping, hiking
 - ▶ Travel history to endemic areas
- ▶ Affects males more than females
 - ▶ Social aspects—
 - ▶ Less likely to seek medical attention
 - ▶ More likely to do outdoor activities such as hunting, fishing, construction, etc...
- ▶ All health backgrounds affected
 - ▶ Young and healthy
 - ▶ Old, medically complex
- ▶ A detailed social history is KEY in diagnosing Blastomycosis
 - ▶ Travel to endemic area
 - ▶ Outdoor exposure
 - ▶ Pets? Blasto is deadly in dogs.

Blasto Clinical Presentation

- ▶ Incubation period: weeks to months
- ▶ Chronic disease can present similar to TB or even certain types of cancers
 - ▶ Unexplained weight loss
 - ▶ Night sweats/intermittent fever
 - ▶ Cough
 - ▶ X-rays are non-distinct
- ▶ Acute disease presents as a severe community acquired pneumonia
 - ▶ Flu like symptoms: fever, chills, body aches, productive cough
 - ▶ Chest X-rays can be quite impressive and are distinct
 - ▶ Extensive infiltrates and confluent nodules



<https://bestpractice.bmj.com/topics/en-us/1095/investigations>

Blasto Clinical Presentation

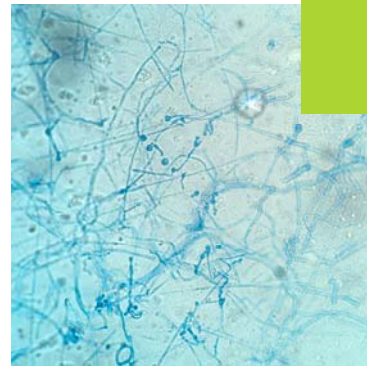
- ▶ Primary disease is pulmonary in nature
 - ▶ Spore inhalation in environment
 - ▶ Can progress to chronic (old calcified granulomas) or acute respiratory illness (acute respiratory distress syndrome)
 - ▶ Host factors that decide this are still unknown
- ▶ From the lungs can disseminate to form abscesses/granulomas:
 - ▶ Bone and joints—has a propensity for this
 - ▶ Skin
 - ▶ CNS—6-10% of cases have involvement
 - ▶ Genitourinary systems
- ▶ Traumatic introduction of spores into skin/soft tissue can also occur
 - ▶ Present as non-healing sores on face or limbs
 - ▶ Very inflammatory looking (because of the body's response to the fungi)
- ▶ **Commonly misdiagnosed!**



<https://cmr.asm.org/content/23/2/367>

Blasto Growth and Morphology

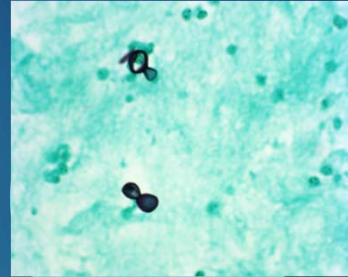
- ▶ Grows as a white to beige fluffy mold on brain heart infusion based medias at room temperature
 - ▶ Dangerous to work with in lab when in this phase
 - ▶ Tape prep with lactophenol analine blue will inactivate it
- ▶ Microscopic exam yields delicate hyphae with "lollipop" fruiting structures
- ▶ "Spikey" textured yeast colonies at body temperature
 - ▶ Broad-based budding yeast



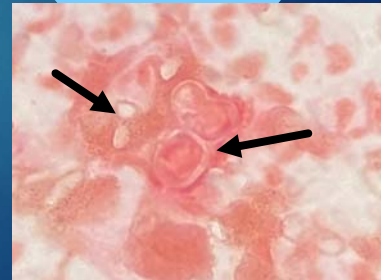
Photos courtesy of S. Stoner GHS Micro

Blasto Growth and Morphology

- ▶ Yeast phase is most often encountered on direct staining
 - ▶ Best seen by GMS or calcofluor staining
 - ▶ KOH and Gram stain also but tricky to the inexperienced
 - ▶ Refractile, crystalline appearance due to thick cell wall
 - ▶ May or may not uptake crystal violet or safranin, the key giveaway is the shape and arrangement
 - ▶ Provider suspicion helps tremendously with interpretation!
- ▶ Mold phase growth can be mistaken for *Chryseosporum*
 - ▶ Definitive ID by 35°C conversion to yeast phase, MALDI-TOF, or PCR
 - ▶ Urine and CSF antigen testing is also helpful but not necessarily definitive due to cross reactivity with *Histoplasma*



GMS Courtesy of Dr. C. Cogbill GHS Pathology



Gram stain courtesy of S. Stoner GHS-La Crosse

Treatment

- ▶ Mild to moderate Blastomycosis can be treated with Itraconazole
- ▶ Severe disease is typically treated with Amphotericin B
- ▶ This takes several months to successfully treat

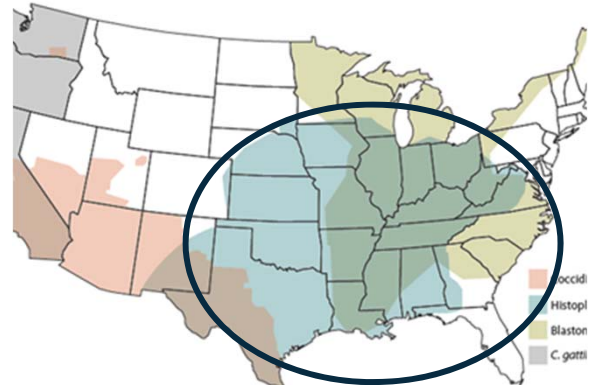


<https://www.nhm.ac.uk/discover/news/2018/december/towns-and-cities-benefit-the-same-animals-and-plants-everywhere.html>

Histoplasma
capsulatum
(a.k.a Histo)

Histoplasma capsulatum Epidemiology

- ▶ In general, more is known about Histoplasma than Blastomyces
 - ▶ Identified as an illness in the 50s and 60s
- ▶ Known niche in nature:
 - ▶ Association with bird/bat feces but details of this unknown
- ▶ Lots of serologic studies



Histoplasma capsulatum Epidemiology:

- ▶ Evidence of exposure via serology is widespread according to studies done in the 1960s/70s
- ▶ Stands to reason that it's widespread in the environment



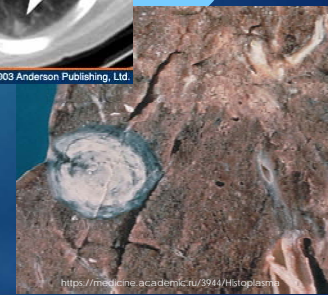
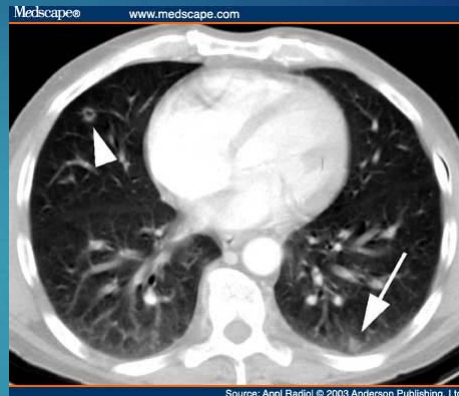
Histo Epidemiology and Clinical Presentation

- ▶ Similar symptoms and disease progression to tuberculosis!
 - ▶ A detailed history social and travel history is KEY
- ▶ Risk factors are very similar to Blasto:
 - ▶ Outdoor activities—construction, hiking, cave diving, rock climbing
- ▶ Like Blasto affects males more than females for the same social factors
- ▶ **Unlike Blasto, the young and healthy will typically clear infection**
 - ▶ Age and immunosuppression are risk factors



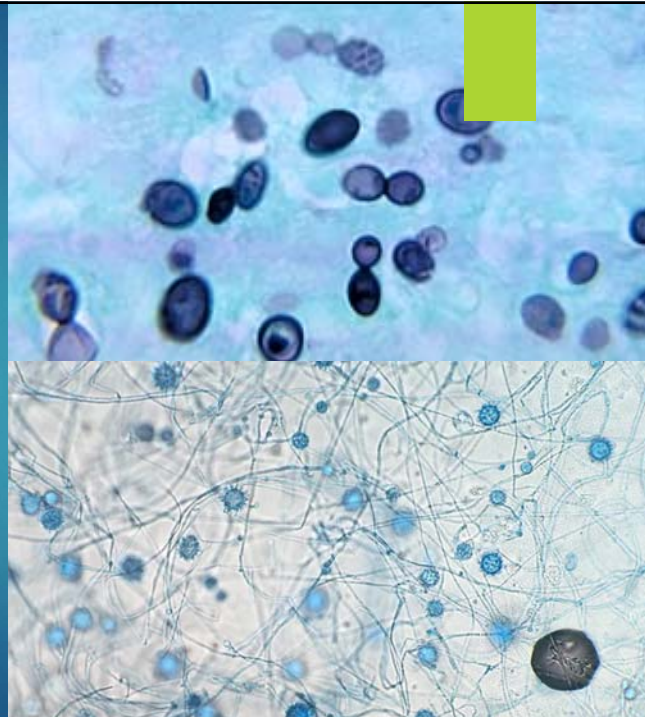
Histo Clinical Presentation

- ▶ Primary disease is pulmonary in nature
 - ▶ Spore inhalation in environment
- ▶ Acute illness presents with flu like symptoms
 - ▶ Incubation of weeks to months
- ▶ Can progress to chronic lung disease
 - ▶ Cavitory lung lesions
 - ▶ Granulomas (can become calcified)
 - ▶ Fibrosis
- ▶ From the lungs can disseminate to from abscesses/granulomas:
 - ▶ CNS
 - ▶ Spleen
 - ▶ Lymph nodes
 - ▶ Blood stream—more apt to see with histo than blasto
 - ▶ Development of adrenal insufficiency is common
- ▶ **Commonly misdiagnosed!**



Histo Growth and Morphology

- ▶ Grows as a white to beige filamentous mold on various media at room temperature
 - ▶ Dangerous to work with in lab when in this phase
 - ▶ Tape prep with lactophenol aniline blue will inactivate it
- ▶ Microscopic exam yields delicate hyphae with "starburst" shaped macroconidia and tear shaped microconidia
- ▶ "Spikey" textured yeast colonies at body temperature
 - ▶ Narrow based, almost "lancet" shaped, budding yeast
 - ▶ Abortive delicate hyphae may be present
 - ▶ May take several passages to convert to yeast phase



Histo Growth and Morphology

- ▶ Yeast phase is most often encountered on direct staining
 - ▶ Best seen by GMS or calcofluor staining
 - ▶ Gram staining: May or may not uptake crystal violet or safranin, the key giveaway is the shape and arrangement
 - ▶ **Provider suspicion helps tremendously with interpretation!**
- ▶ Mold phase growth can be mistaken for *Sepedonium*
 - ▶ Big hint: Histo makes micro conidia
 - ▶ Definitive ID by 35°C conversion to yeast phase, MALDI-TOF, or PCR
 - ▶ Urine and CSF antigen testing is also helpful but not definitive due to cross reactivity with *Blastomyces*



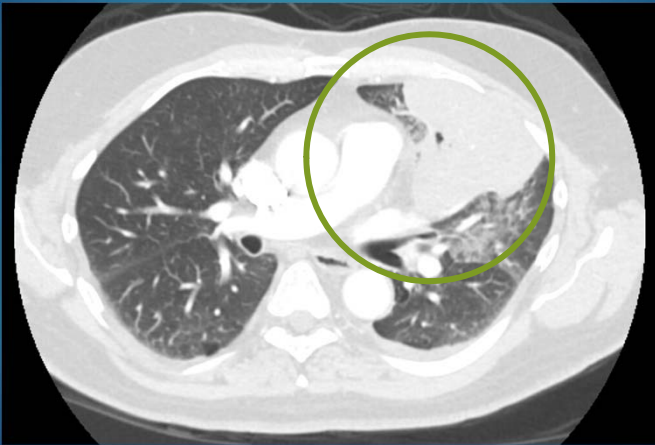
Treatment

- ▶ Same as Blasto!
- ▶ Mild to moderate disease can be treated with Itraconazole
- ▶ Severe disease is typically treated with Amphotericin B
- ▶ Also takes several months to successfully treat

Case #1: the cabin by the lake

- ▶ 57 yr old male presents to out of system ER with influenza like-illness Jan 19th
 - ▶ Felt poorly for 2-3 weeks
 - ▶ General malaise, productive cough, body aches, fevers
- ▶ Past medical hx
 - ▶ Well controlled type 2 diabetic
- ▶ Chest X-ray remarkable for what was interpreted as community acquired pneumonia
 - ▶ Given abx and sent home with instructions to return if symptoms worsened
- ▶ Returned 2 days later with blood tinged sputum and worsening symptoms (1-21)
 - ▶ Chest CT showed impressive lower lobe infiltration
 - ▶ Admitted to outside hospital where pt went into acute respiratory failure
 - ▶ Sent to LaX for more advanced support

Case #1: the cabin by the lake




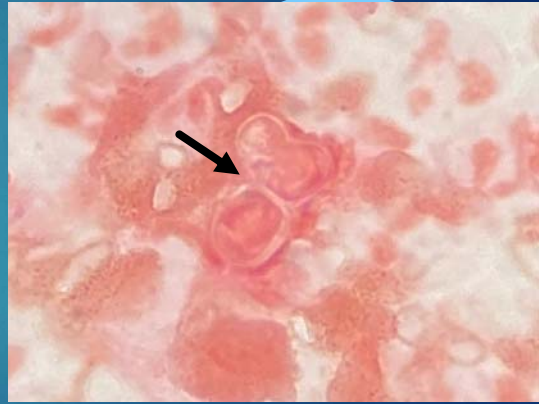


Image courtesy of Dr. A. Saban GHS Infectious Disease

Case #1: the cabin by the lake

- ▶ Upon admission to GHS (1-23), cultures ordered
 - ▶ Sputum culture
 - ▶ Blood cultures
 - ▶ Legionella and S. pneumo urinary antigen screens
- ▶ A gram stain was done on the sputum and yielded something unusual...
 - ▶ Non-staining, refractile, broad based budding yeast
 - ▶ Morph confirmed by calcofluor fluorescent staining
- ▶ ID notified...



Gram stain courtesy of S. Stoner GHS-La Crosse

Case #1: the cabin by the lake

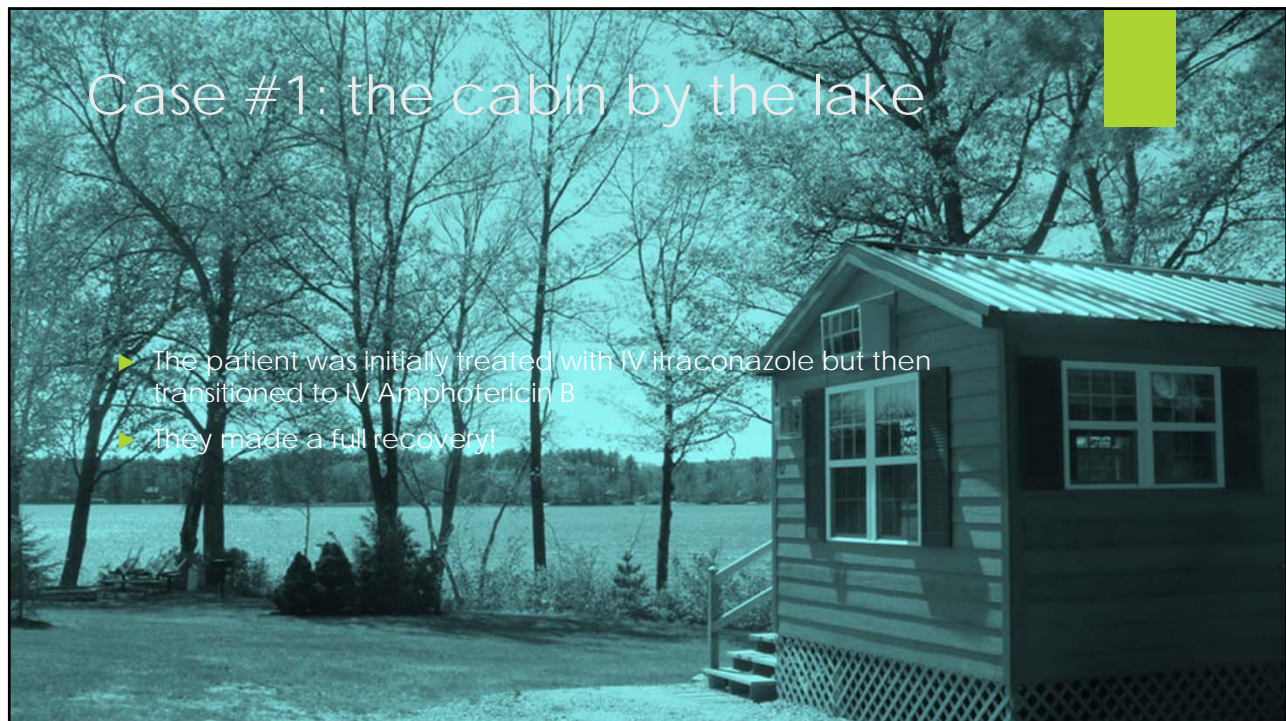
- ▶ A detailed medical and social hx was taken
- ▶ Patient had been remodeling their cabin and boat house in the Hayward area every weekend since early August 2019
 - ▶ Lots of exposure to dust and debris
 - ▶ Lots of dead and decaying plant matter surrounding the boat house





Case #1: the cabin by the lake

- ▶ A Blastomyces urinary antigen was done
 - ▶ Very positive
- ▶ Several respiratory specimens were submitted for fungal culturing
 - ▶ BAL: positive for broad based budding yeast by calcofluor
 - ▶ Expecterated sputum: positive for broad based budding yeast by calcofluor
- ▶ Other specimens were also submitted:
 - ▶ Blood cultures (Wampole Isolators): negative
 - ▶ CSF: negative by culture but antigen positive by referral testing



Case #1: the cabin by the lake

- ▶ The patient was initially treated with IV itraconazole but then transitioned to IV Amphotericin B
- ▶ They made a full recovery!

Case #2: the mechanic

- ▶ 1-16: 58 yr old male presents to CAH ER with community acquired pneumonia
 - ▶ Productive cough, fever, shortness of breath
- ▶ Past medical hx:
 - ▶ Malignant neoplasm of chest wall (melanoma stage 2), no chemo or radiation
 - ▶ ANA positive, autoimmune disorder?
 - ▶ Hx of asthma
- ▶ 1-29: Patient still not feeling well. Visits PCP. A chest CT is ordered and is read as abnormal.
 - ▶ Numerous pulmonary nodules
- ▶ Patient is referred to GHS Pulmonology for further studies to rule out metastatic cancer



Case #2: the mechanic

The differential on this CT:

- Metastatic cancer
- Histo
- Blasto
- TB

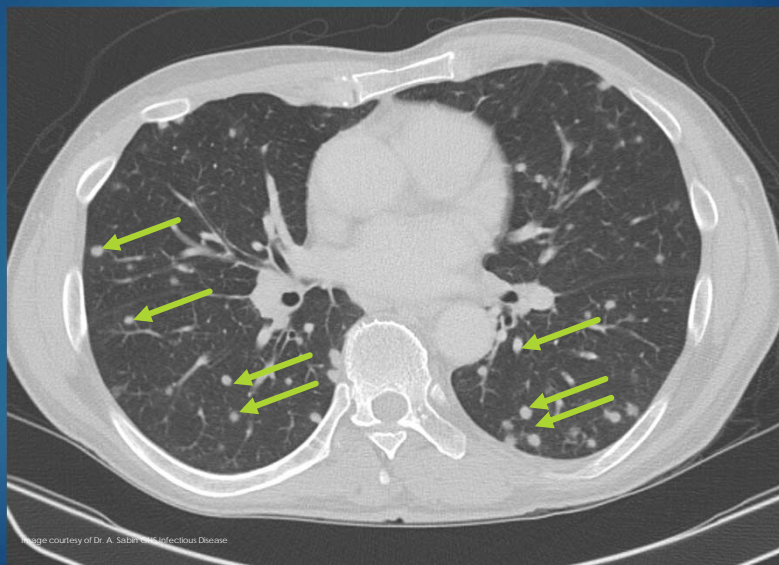


Image courtesy of Dr. A. Sabharwal, Infectious Disease

Case #2: the mechanic

- ▶ 2-3: A BAL and biopsies of hilar lymph nodes are done.
 - ▶ Routine, fungal, and AFB cultures performed.
 - ▶ Smears were all negative
 - ▶ Other referrals are done including Fungitell assay, Histo/Blasto antigens, and PCP PCR
- ▶ 2-7: Urine Blasto antigen comes back positive, Histo detectable but below threshold
- ▶ 2-10: Patient is seen by Infectious Disease.



Case #2: the mechanic

- ▶ A detailed social history is taken by ID at initial consult.
 - ▶ Patient had recently been doing some excavating in an open field
 - ▶ Patient owns chickens
 - ▶ Patient lives near a river
 - ▶ Doesn't hunt or fish
 - ▶ Hasn't had any recent travel out of the Northern IA area
- ▶ Some factors for *Blastomyces*
- ▶ But also so some for *Histoplasma* too

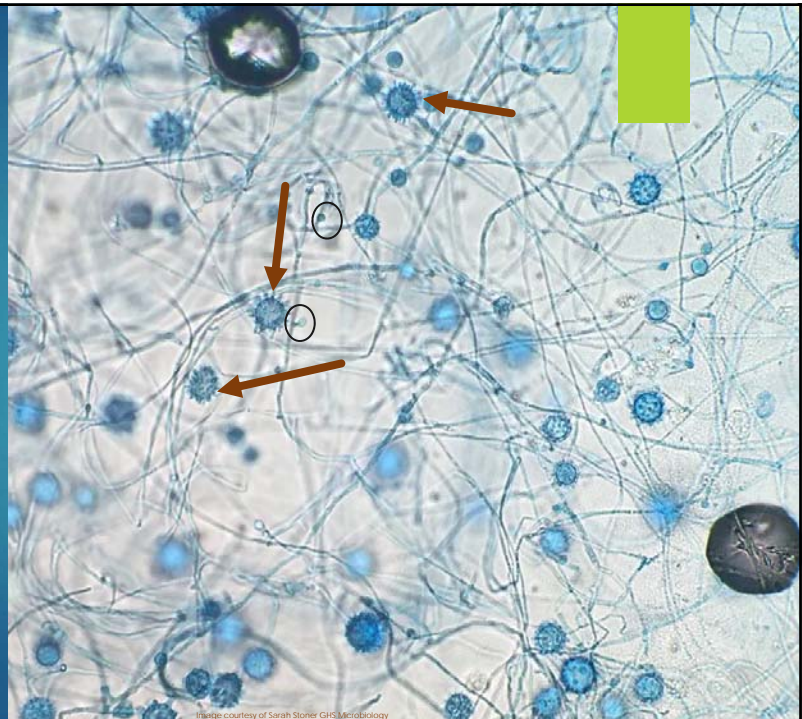
Case #2: the mechanic

- ▶ 2-19: one colony of beige fluffy mold growing on IMA and BHI
- ▶ Tape prep shows....



Case #2: the mechanic

- Numerous tuberculate macroconidia and tear shaped microconidia are noted
- Presumptively ID'd as *Histoplasma!*
- Mold subbed to BHI for conversion to yeast phase 2-19-20
- Conversion 3-2-20



In Sum...

	Blasto	Histo
Range	Upper Midwest/Great Lakes, Canada	Mississippi, Missouri, and Ohio river valleys
Niches	unknown, associated with fluctuant bodies of water	Bird and bat feces
Clinical presentation	Acute and chronic pulmonary disease, likes bone, CNS	Acute and chronic pulmonary disease, likes blood, lymph nodes, adrenals
Patient populations	Young, healthy to old, immunosuppressed	Old, immunosuppressed
Morph at 35C	Broad based budding yeast	Narrow, more <i>Candida</i> like yeast
Morph at 25C	Lollipop fruiting structures	Tuberculate macroconidia
Rapid Testing	Antigen tests exist for both but there are cross-reactivity issues!	

Questions? Thank
you!

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