

West Coast Transplant ID

12/4/2024

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Emergency Department

ED consult:

■ yo ■■■■■, DDKT ■■■/■■■/2024, BK virus, "on some protocol," sent to ED from echo due to atrial flutter, h/o mitral valve repair, febrile to 38.2, light-headed, tachypneic in ED

HPI

- Unwell for a few months
 - Night sweats
 - Chills
 - Decreased appetite and weight loss
 - Shortness of breath, non-productive cough
 - No hemoptysis
- Echo due to palpitations at home, prior ECGs NSR
- Symptoms started around when he started anti-BKV protocol
- Denied sick contacts

yo

fever, tachycardia,
tachypnea

2-3 months chills, night sweats, weight loss, SOB, non-productive cough

- s/p 2nd DDKT █/█/24 secondary to IgA nephropathy
 - CMV +/+, EBV +/+, toxo D-/R+
 - GFR>60, persistent proteinuria
 - 1st DDKT █/█/15 (██████), failed ~2021 2/2 BK virus
 - HD 2010-2015, 2021-2024
- Recurrent BK viremia, viruria on anti-BKV MEMO study since █/█/24 (3 infusions █/█/24, █/█/24, █/█/24)
 - Mycophenolate stopped █/█/24
- Anemia of CKD (Hgb ~10)
- Mitral valve repair 2004 (██████████), s/p rheumatic fever
- Hepatitis B on entecavir
- Quantiferon negative █/█/2021, █/█/2023 (mitogen>10.0)

Emergency Department

yo

CC:

fever, tachycardia, tachypnea

HPI:

2-3 months chills, night sweats,
weight loss, SOB, non-
productive cough

PMH:

DDKT x 2, last / /24
BK viremia/viruria on MEMO
Hep B on entecavir
Mitral valve repair, s/p RF

Social History/Exposures

- Born in Philippines, returned /2023
- Between 2003 and 2014, bounced between Philippines and Guam
- As a child, had aunt with TB who visited frequently
- No Midwest or Southwest travel
- Gardens, waters plants
- No animal or water exposures
- No ETOH, tobacco, illicit or IDU
- Lives in with multiple family members

Emergency Department
yo

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SH/Exposures
Philippines, Guam, Hawaii, WA
Gardener
Aunt with TB as a child

Physical Exam

T 38.2 BP 115/79 HR 122 RR 25 93% on room air

Thin, dyspneic, appears ill

MMM, no oral lesions

Neck supple, no LAD

Regular but tachycardic

Tachypneic, clear to auscultation – no wheezes, no crackles, no rhonchi

+BS, palpable left abdominal kidney, non-tender

No LE edema

No skin breakdown or rashes

Cognition intact, no focal neuro deficits

129	97	28	147	9.61	10.5	321	21	0.8
4.1	20	1.64			32		39	79

Lactate 2.0

Calcium 10.4 Alb 3.5

Emergency Department

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SH/Exposures

Philippines, Guam, Hawaii, WA
Gardener
Aunt with TB as a child

Physical Exam/Labs

febrile, tachypneic, tachycardic, not
hypoxic, looks sick
Na 129 (133), WNC 9.6 (7.6)

Chest X-Ray (AP Erect)



What's Your Diagnosis?

Diagnosis

- Toxoplasmosis
- Histoplasmosis
- Tuberculosis
- Pneumocystis
- Hypersensitivity pneumonitis

Emergency Department

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Na 129 (133), WNC 9.6 (7.6)

CT Chest



CT Abd/pelvis

Mesenteric and
retroperitoneal
adenopathy

No
granulomatous
disease



Emergency Department

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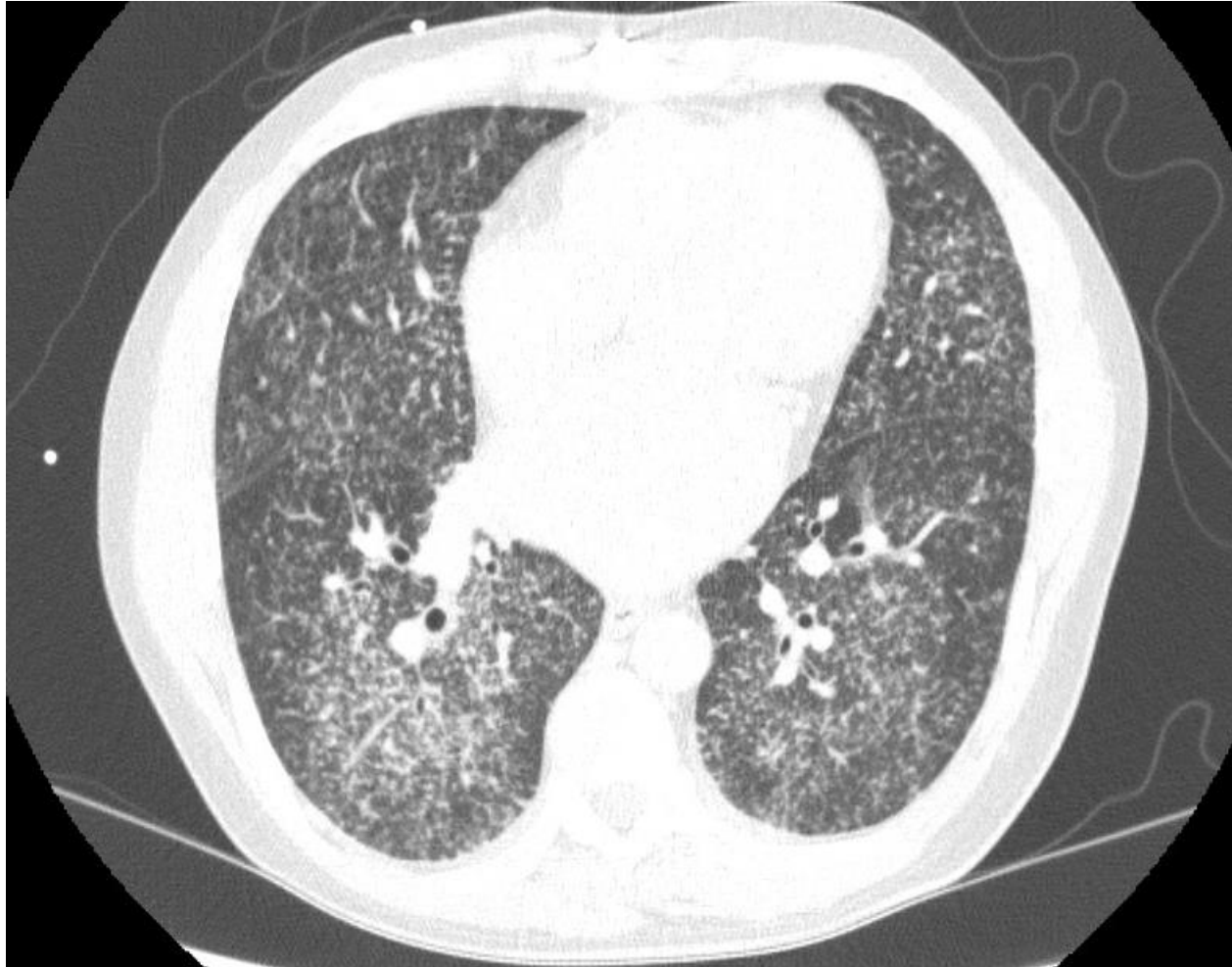
SH/Exposures

Philippines, Guam, Hawaii, WA
Gardener
Aunt with TB as a child

Physical Exam/Labs

febrile, tachypneic, tachycardic, not
hypoxic, looks sick
Na 129 (133), WNC 9.6 (7.6)

Diagnostic testing?



Hospital Day 2

Day 1

- COVID, flu, RSV neg

Day 2

- AFB sputum stain x2 neg

- Sputum cx OP flora

- RVP CoV 229E pos

- CrAg neg

- BAL GS no organisms

- Bronch bx GS no orgs

Initial Plan:

- Procedures
 - Bronchoscopy with BAL/biopsy
- Laboratory Studies
 - Blood cultures
 - Sputum cx
 - AFB blood and sputum
 - Respiratory TB PCR
 - Respiratory virus panel
 - Serum CrAg
 - Strongyloides
 - For BAL: immunocompromised panel and include bacterial and fungal cultures and PCRs (pan-fungal, aspergillus, etc), Asp GM, AFB smear and cultures, TB & NTM PCRs
 - If AFB smear negative, then urine histo Ag, serum Asp GM, cocci Ab and urine Ag
- Medications
 - Vancomycin + Cefepime
 - Ivermectin
 - If decompensates or no bronchoscopy planned:
 - R (rifabutin) IPE + B6

Hospital Day 3

Day 1 - COVID, flu, RSV neg

Day 2

- AFB sputum stain x2 neg
- Sputum cx OP flora
- RVP CoV 229E pos
- CrAg neg
- BAL GS no organisms
- Bronch bx GS no orgs

Day 3

- AFB sputum stain neg
- Legionella Ag neg
- Step pneumo Ag neg
- EPP neg
- BAL MTB complex neg
- BAL AFB x 2 neg
- Bronchial AFB stain x 2 neg
- Bronchial MTBC PCR neg
- Blood cx NGTD

Clinical course

- Worsened respiratory status
- Lactate 2.4

What would you add next?

- RIPE
- SMX-TMP (PJP dosing)
- Liposomal amphotericin
- Levofloxacin
- Steroids

Hospital Day 3

Day 1 - COVID, flu, RSV neg

Day 2

- AFB sputum stain x2 neg
- Sputum cx OP flora
- RVP CoV 229E pos
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- BAL GS no organisms
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Day 3

- AFB sputum stain neg
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- Step pneumo Ag neg
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- Bronchial AFB stain x 2 neg
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Clinical course

- Worsened respiratory status
- Lactate 2.4

Interventions

- Medications
 - Vancomycin + cefepime
 - levofloxacin
 - Ivermectin
 - R (rifabutin) IPE + B6
- Transferred to MICU
- high flow -> intubation
- Urine histo/blast Ag sent

Hospital Day 4

Day 3

- AFB sputum stain neg
- Legionella Ag neg
- Step pneumo Ag neg
- EPP neg
- BAL MTB complex neg
- BAL AFB x 2 neg
- Bronchial AFB stain x 2 neg
- Bronchial MTBC PCR neg

Day 4

- ADV PCR none detected
- Urine AFB neg
- AFB sputum cx NG
- bronchial AFB cx NG
- Aspergillus GM neg
- BAL fungal cx NG
- BAL bacterial cx NG
- Blood cx NGTD
- AFB blood cx x2 NG
- MRSA swab neg

Clinical course

- ARDS/dexamethasone
- Septic shock
- Lactate 2.1, Cr 2.17, Ca 12.0
- Prone ventilation
- Norepinephrine

What would you add next?

- Pyrimethamine + leucovorin
- SMX-TMP
- Liposomal amphotericin
- Voriconazole

Hospital Day 5

Day 4

- ADV PCR none detected
- urine AFB neg
- AFB sputum cx NG
- bronchial AFB cx NG
- Aspergillus GM neg
- MRSA swab neg

Day 5

- BAL NMTB PCR neg
- BAL PJP PCR none det
- BAL bacterial PCR none det
- BAL bacterial cx NG
- BAL fungal cx NG
- AFB Blood cx NGx2 (4 days)
- bronchial bx cx NG
- Blood cx NGTD
- Strongyloides neg
- Bronch biopsy – no lung tissue, bronchial mucosa/submucosa with no granulomas or neoplasm

Clinical course

- ARDS
- Lactate 2.7, Cr 3.12, Ca 12.2

Interventions

- HD catheter placed, c/b L PTX
- Left chest tubes (2) placed
- Continued
 - Vanco + cefepime
 - Levofloxacin
 - RIPE
 - Leucovorin + pyrimethamine
 - SMX-TMP

Hospital Day 6

Results

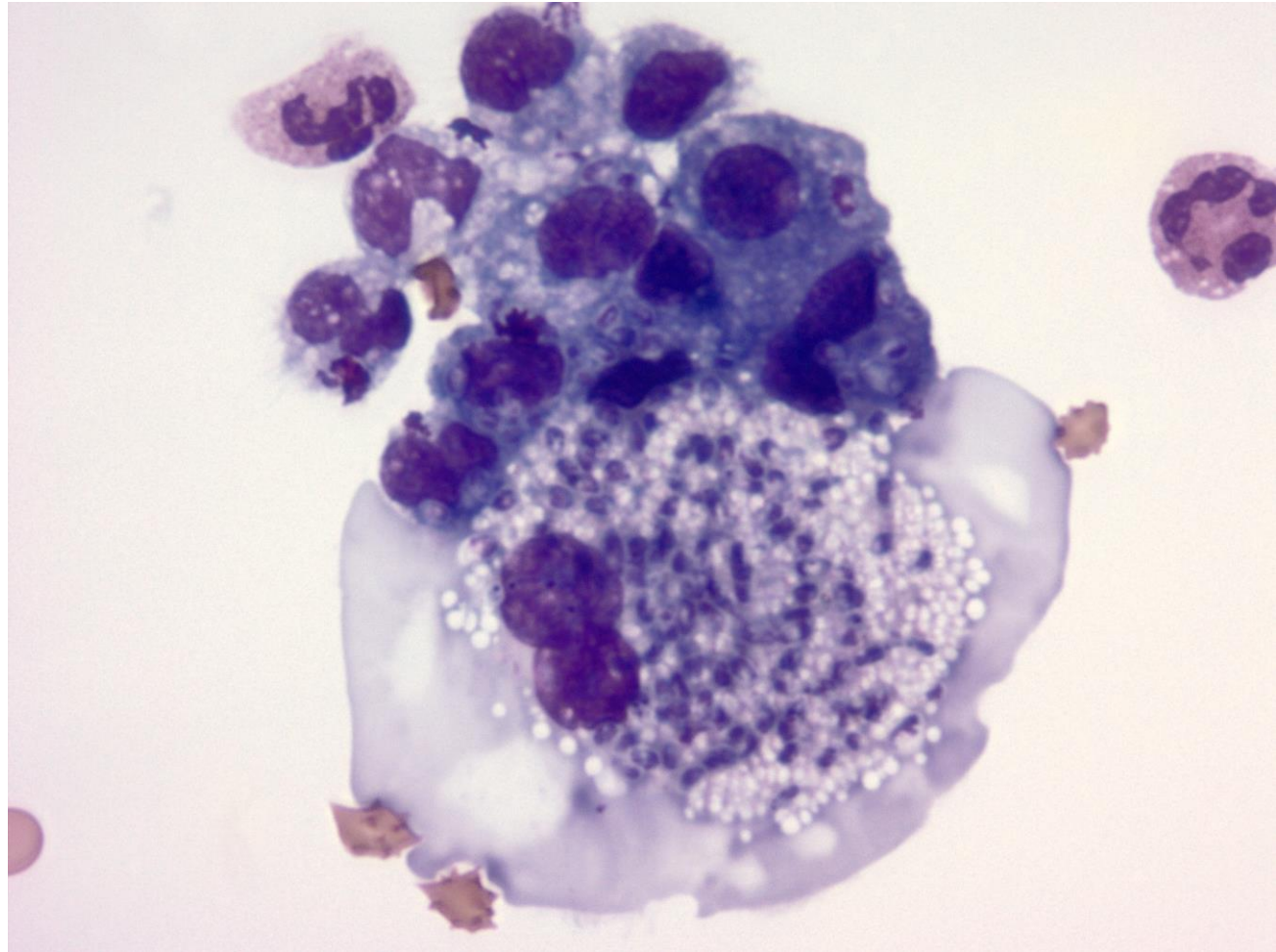
Day 6

- BAL NMTB PCR ND
- BAL PJP PCR ND
- BAL bacterial PCR ND
- BAL bacterial cx NG
- BAL fungal cx NG
- AFB Blood cx NGx2 (4 days)
- bronchial bx cx NG
- Blood cx NGTD
- Strongyloides NR

Day 7

- 1130 slide
- 1349 BAL fungal PCR

What is the diagnosis?



Hospital Day 6

Day 6

histopath suggested of histo
BAL fungal PCR positive for
histoplasmosis

Post-mortem

8/9 urine histo/blasto detected
8/12 BAL Legionella cx 10 colonies
mold
8/13 blood hist/blasto Ag det
8/14 BAL legionella cx >30 colonies
histoplasma capsulatum
8/15 BAL fungal cx NG
8/17 BAL fungal cx NG
8/19 BAL fungal cx >30 colonies
histoplasma capsulatum

Clinical course

- Worsening shock and ARDS
- Worsening lactic acidosis

Interventions

- Started liposomal amphotericin 5mg/kg daily
- Changed dexamethasone to methylprednisolone
- Stopped vanco, cefepime, levofloxacin, RIPE, leucovorin, pyrimethamine
- Changed SMX-TMP to prophylactic dosing

Clinical course

- Progressive decompensation resulting in death early am day 8

Differential Diagnoses

Miliary Nodules

- Bacterial infections
 - Tuberculosis, NTM
 - Frequently AFB sputum negative (hematogenous)
- Fungal infections
 - Pneumocystis
 - Aspergillus
 - Coccidioides
 - Cryptococcus
 - Blastomycosis
 - Histoplasmosis
 - Talaromyces
- Metastatic disease
 - Often vascular tumors
 - melanoma, renal cell carcinoma
 - Thyroid (especially papillary thyroid)
 - Primary adenocarcinoma lung
 - Associated with EGFR exon 19 mutation
- Other
 - Hypersensitivity pneumonitis
 - Silicosis
 - Sarcoidosis

Mechanism of Disease

- Primary infection
- Reactivation with immune suppression
 - Occurs but controversial
 - Attempts to culture latent yeast from granulomas have been unsuccessful
 - Series of 449 Indiana SOT patients followed for 3 years, 28% with serologic or radiographic evidence of old histoplasma, no clinical histoplasmosis developed, no fungal prophylaxis
 - Presence of antibodies does not predict subsequent histoplasmosis
- Donor-derived

Epidemiology

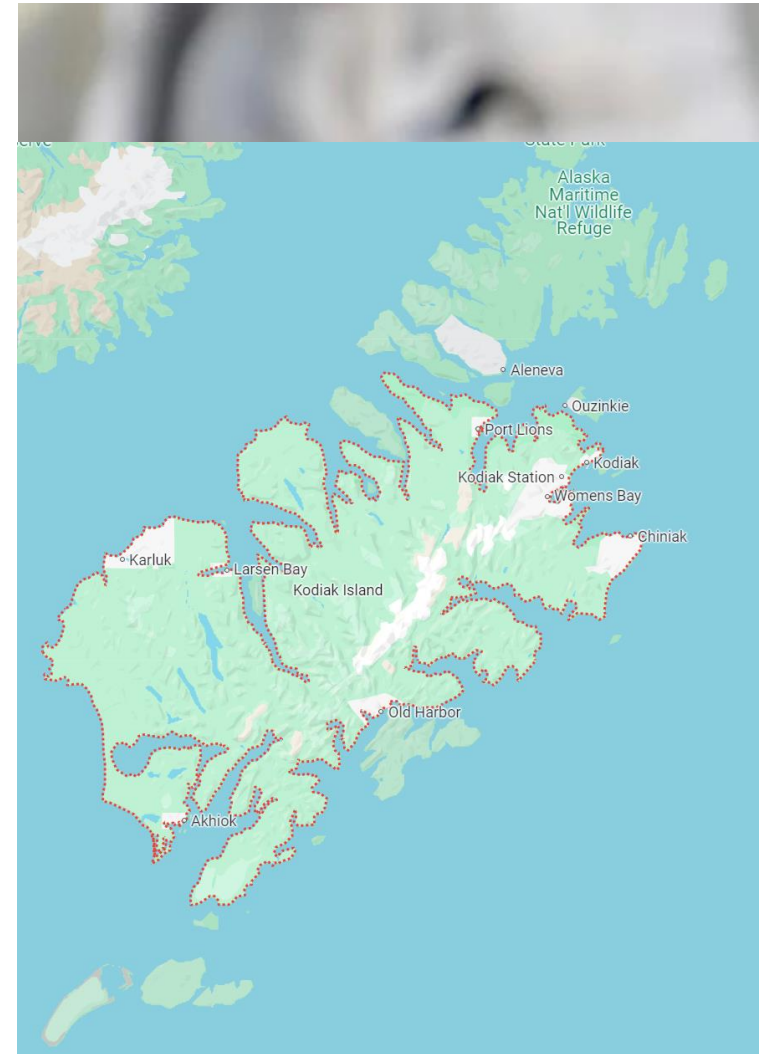
Fun Facts!

On which continent has histoplasma *not* been found?

1. Africa
2. Europe
3. Asia
4. Antarctica

Epidemiology

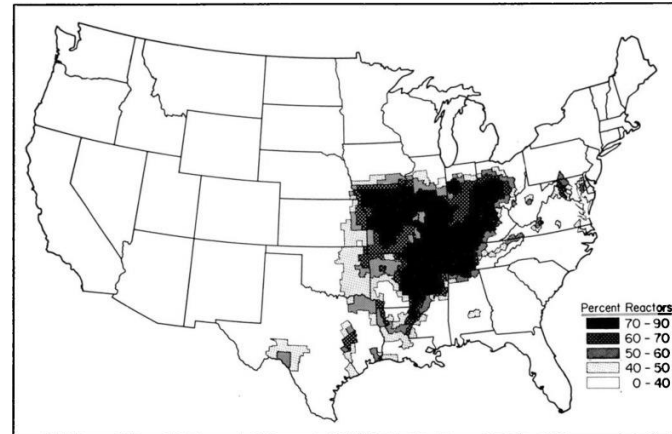
Trick Question!



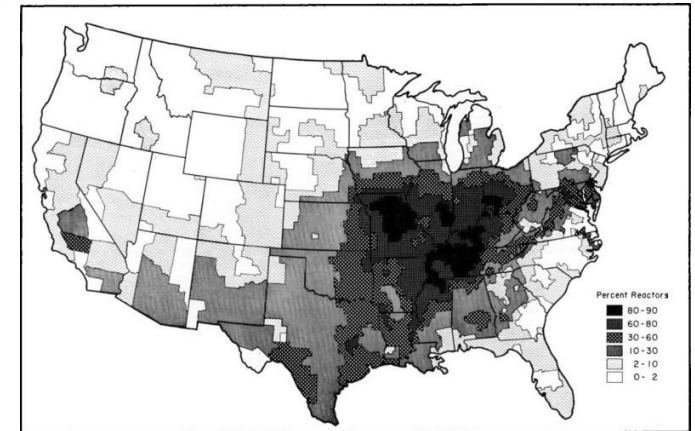
Black Blunt-nose Leech and Death of the Spotted Seal in the Bering Sea, Alaska, USA. J Wildl Dis. 2014 Apr;50(2):389-92.

Epidemiology - US

- Understanding hampered by under-reporting
 - Reportable only in 13 states
- Skin antigen testing no longer done in US
- Initial mapping:



40-90% positive

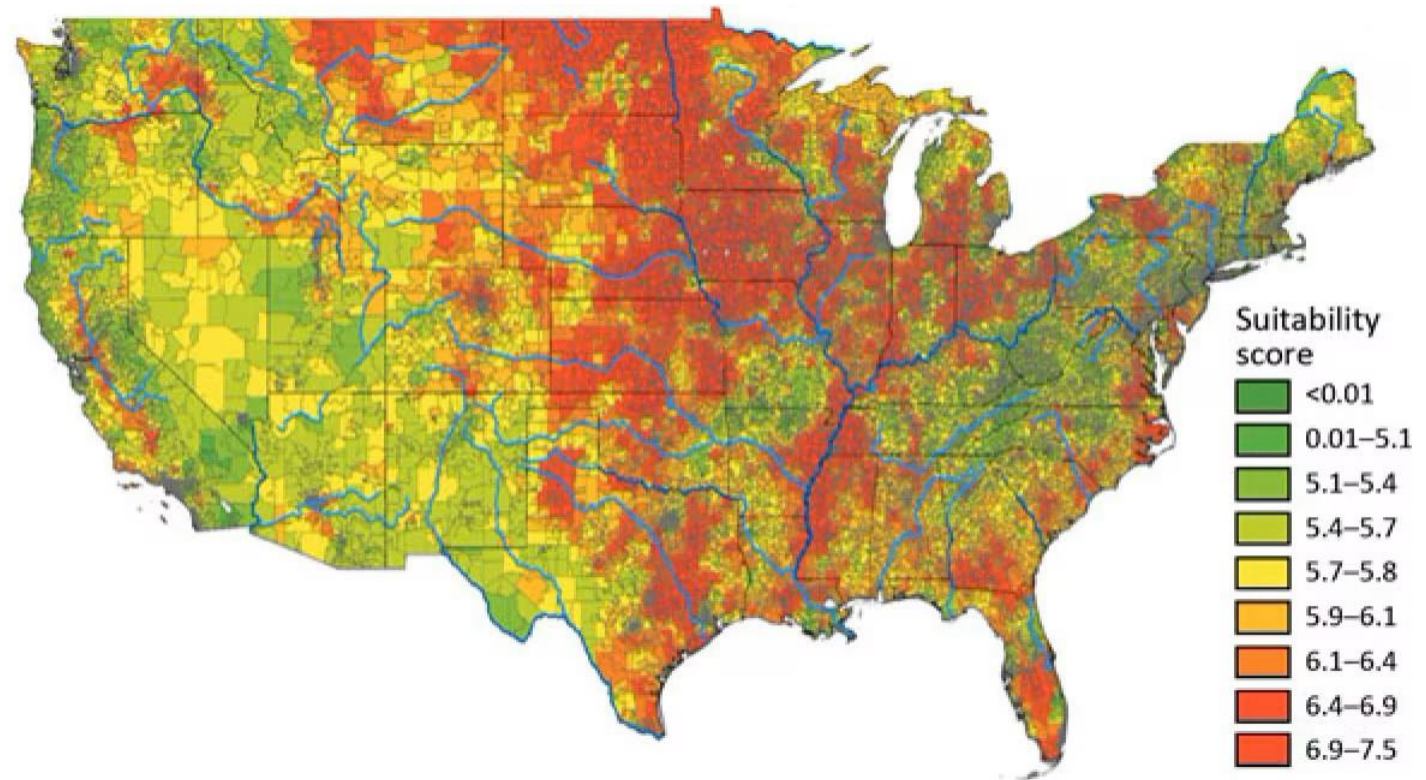


2-90% positive

Epidemiology - US

CDC Suitability Modeling

- Considers:
 - Land cover
 - Soil acidity
 - Distance from water



Epidemiology - US

Medicare Claims-Based Mapping

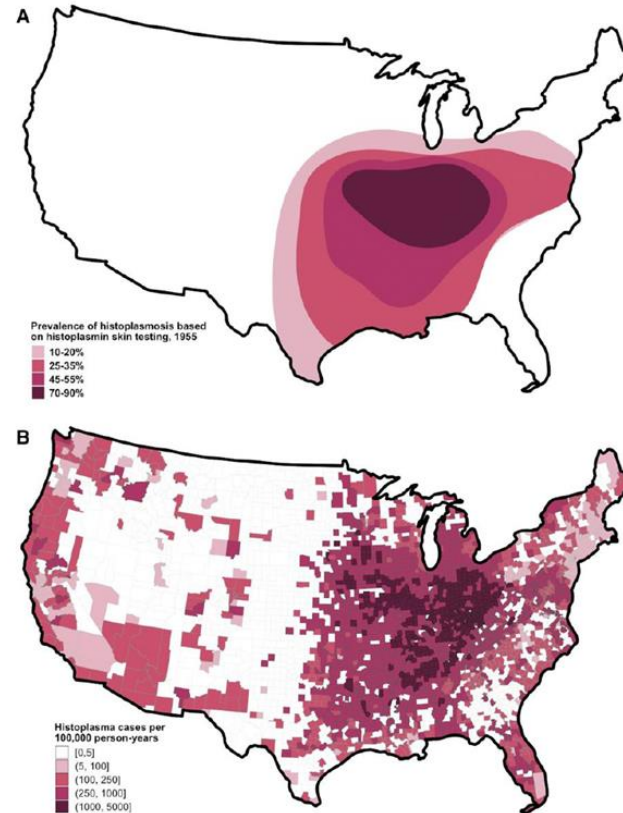


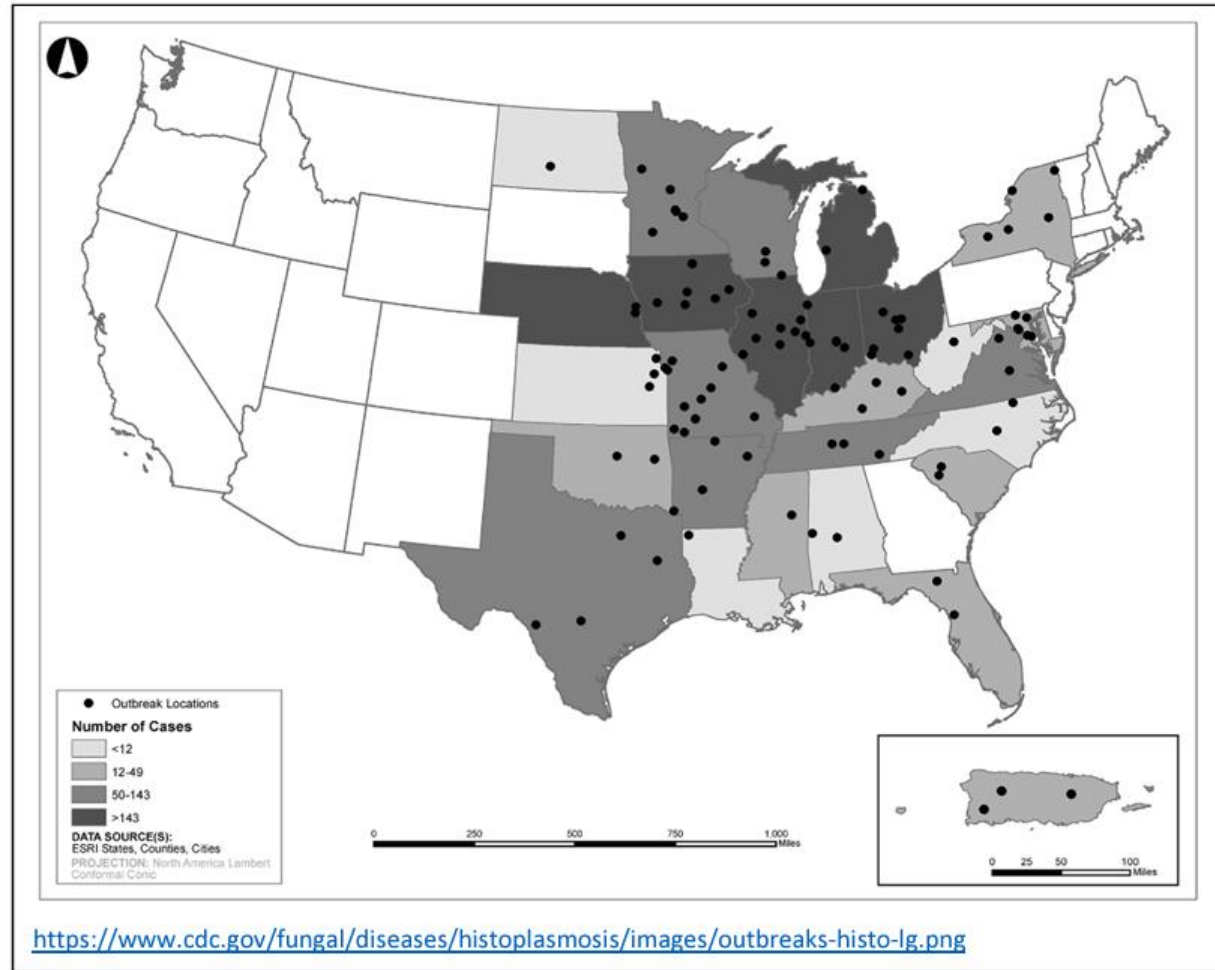
Figure 1. Geographic distribution of histoplasmosis. A, Historical geographic distribution of histoplasmosis derived from histoplasmin skin antigen testing. Map is adapted from Schwartz and Furcolow, 1955 [2]. B, Histoplasmosis incidence from 2007 through 2016 in Medicare fee-for-service beneficiaries by US county. Reported as histoplasmosis cases/100 000 person-years.

- 2007-2016
- >45 million Medicare recipients
- 94% of states with ≥ 1 county with > 100 cases/100,000 person-years (threshold)
- >75% of ID physicians in areas meeting threshold reported not seeing histoplasmosis

"We believe the continued use of "endemic" in the context of Histoplasma, Coccidioides, and Blastomyces contributes to the false heuristic that these DMs are not frequently encountered and diagnosed across the United States."

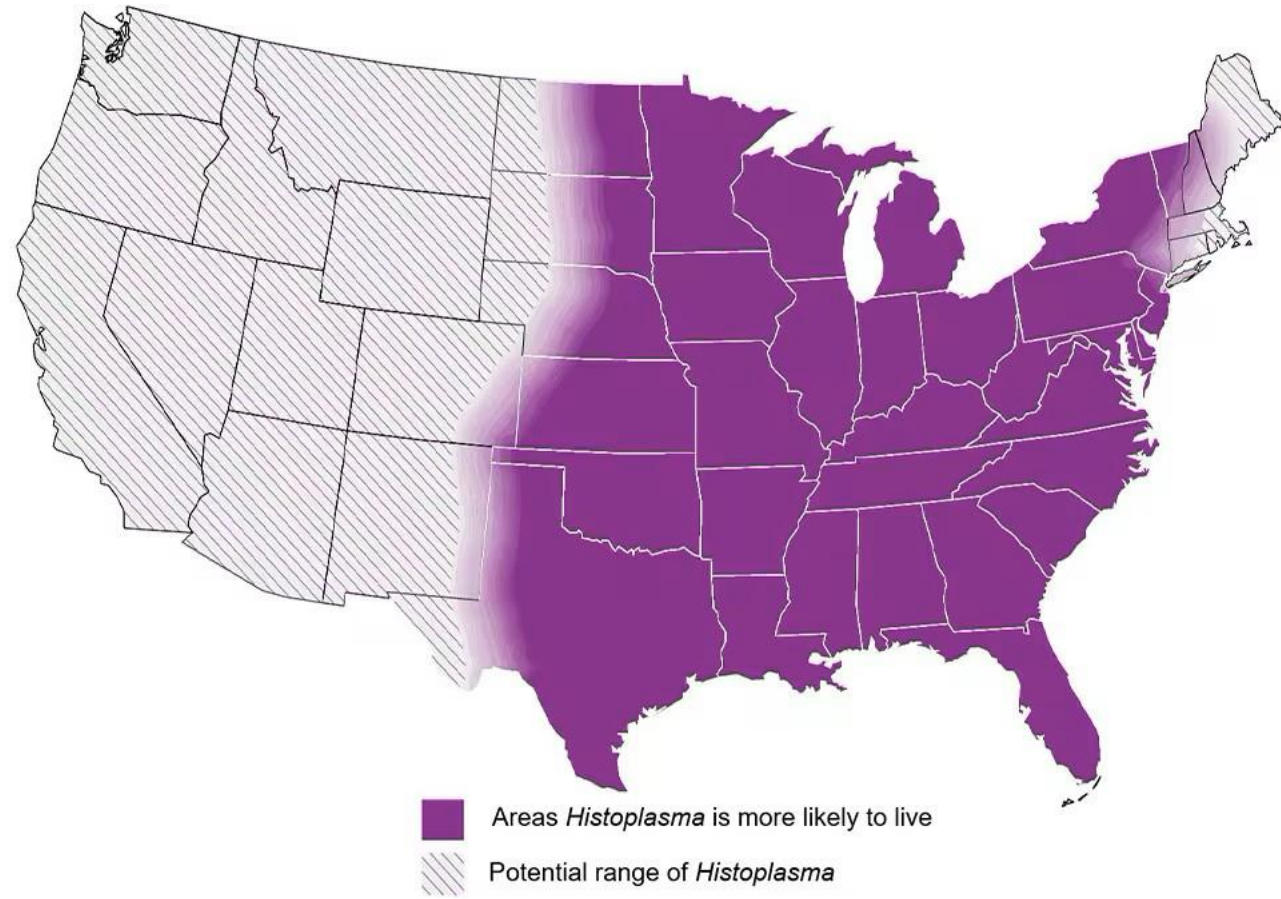
Epidemiology - US

US Histoplasmosis Outbreaks 1983-2013



Epidemiology - US

Current CDC Mapping



Epidemiology - Washington

Washington State

- Added as a notifiable disease 1/1/2023
- 2013-2022, 0-3 cases reported annually
- 2023 13 cases reported
 - Reporting bias
- No locally-acquired cases confirmed
- No surveillance activities

Epidemiology- Southeast Asia



Epidemiology

Factors Influencing Geographic Range Shifts

- Climate change
- Migratory shifts
 - Although birds are not a reservoir, it is thought that they might carry to other locations
- Human activity
 - Travel
 - Development
 - Interstate commerce
- Increased availability/use of immune suppression

Additional Data

Donor-related

Mate kidney recipient urine histo Ag neg
Donor kidney █/24 biopsy histo PCR neg
x2
Donor from █, no known endemic
exposures, served in military, travel
history incomplete

Review of prior imaging:

- no granulomas
- no LAD
- no calcified lymph nodes

No immune suppression:

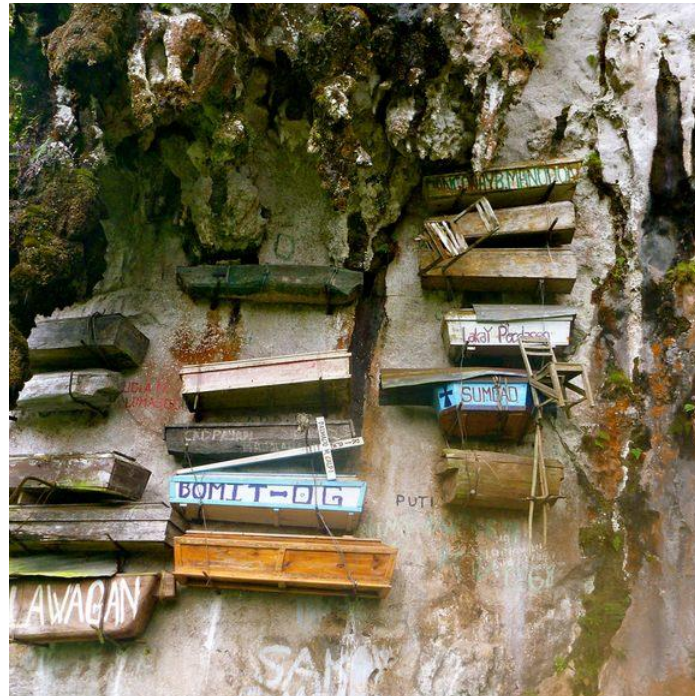
- birth to 2015

Immune suppressed:

- 2015-2024
- █/2024-█/2024 pred+ MMF+tac
- █/2024-█/2024 pred+tac

Social History/Exposures

- Traveled to Philippines early 2023,
visited Sagada Caves
(did not go inside)



- Avid gardener, developed his own
fertilizer with rotten vegetables
and water, buried meat and
compost from compost bins

Thank You!

- [REDACTED] and [REDACTED] family for letting us learn from their tragedy
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

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