Algorithms for Diagnosing the Endemic Mycoses Blastomycosis, Coccidioidomycosis, and Histoplasmosis

Clinician Outreach and Communication Activity (COCA) Call

Thursday, September 21, 2023

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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Describe the epidemiology of blastomycosis, coccidioidomycosis, and histoplasmosis in the United States and the impact of delayed and underdiagnosed cases.
2. Discuss diagnostic challenges associated with blastomycosis, coccidioidomycosis, and histoplasmosis.
3. Identify populations clinicians should consider testing for blastomycosis, coccidioidomycosis, and histoplasmosis.
4. Describe diagnostic tests clinicians should consider initially and after a negative test for blastomycosis, coccidioidomycosis, and histoplasmosis.
5. Discuss the implementation of the clinical diagnostic algorithms for blastomycosis, coccidioidomycosis, and histoplasmosis.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

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COCA Call: Algorithms for Diagnosing Endemic Mycoses: Blastomycosis, Coccidioidomycosis, and Histoplasmosis

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Agenda

- Case report
- Endemic mycoses overview
- Diagnostic challenges
- Impact of underdiagnosis
- Diagnostic algorithms

38-year-old previously healthy man in Indiana

- Construction worker on large-scale projects

Case reprinted with permission from the PIM/MSGERC/Terranova CE activity, ***Community-Acquired Pneumonia: When to Think Fungus***, available at http://www.funguscme.org/CAP2022/index.html

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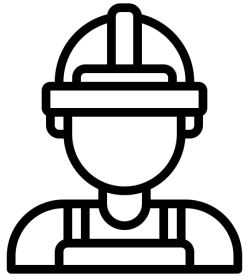
- Construction worker on large-scale projects



- No recent travel

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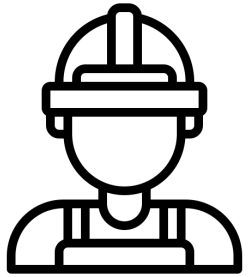
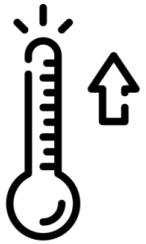


- No recent travel

- Develops fever, cough



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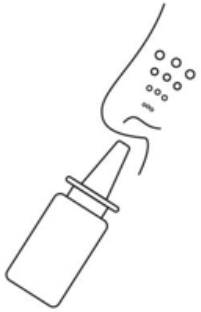
38-year-old previously healthy man in Indiana

- Cough treated with intranasal steroids and antibiotics



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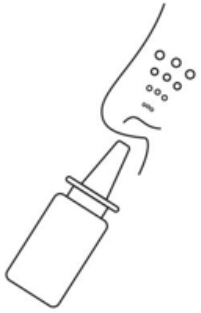
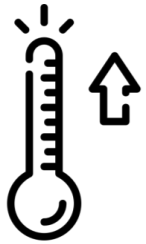


- Cough resolves, fever persists



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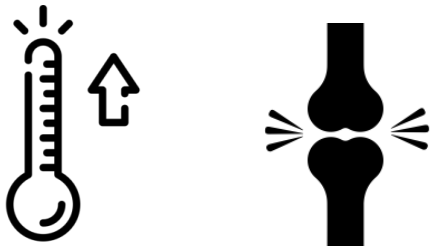
About 8 weeks after onset

- Presents at hospital

- Ongoing fevers up to 102.4° and significant joint pain



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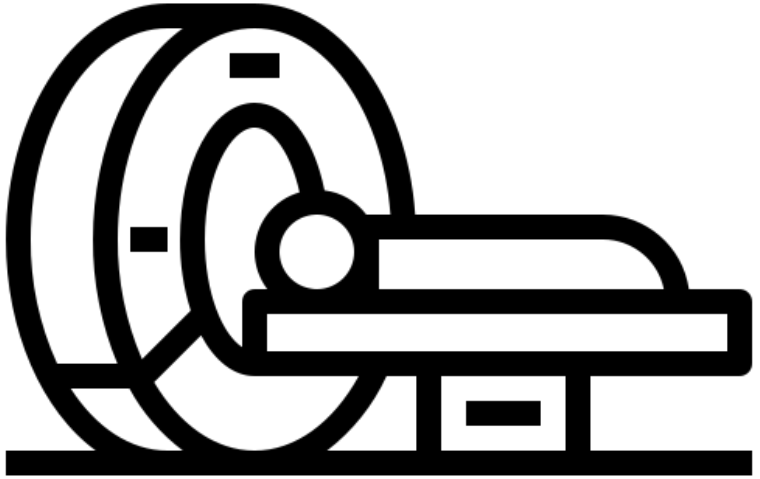
Radiologic findings revealed abnormalities

- Full-body CT positive for significant lymphadenopathy, several small lung nodules



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Patient diagnosed with adult-onset Still's disease

Rare type of inflammatory arthritis featuring fevers, rash, and joint pain

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Medications prescribed according to diagnosis

- Patient starts on steroids with transient improvement in symptoms

- Anti-inflammatory medication prescribed due to worsening arthritis

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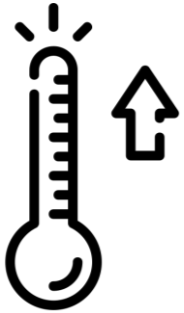
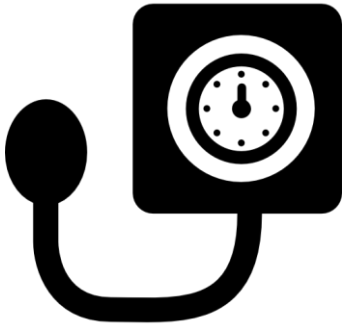
4 months later

- Patient presents at hospital with sepsis
- Condition had worsened starting 2 weeks prior

Substantial weight loss



Fever of 103°



Hypotension

Elevated heart rate

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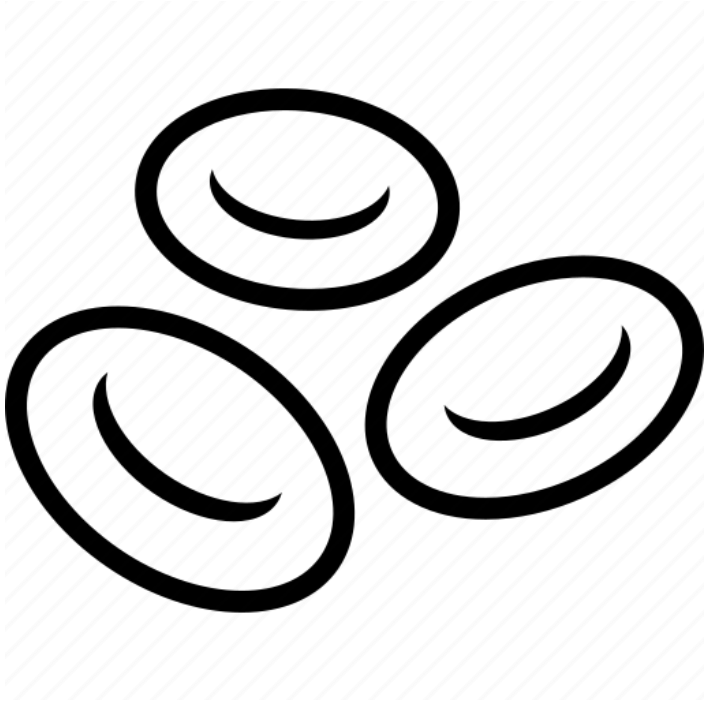
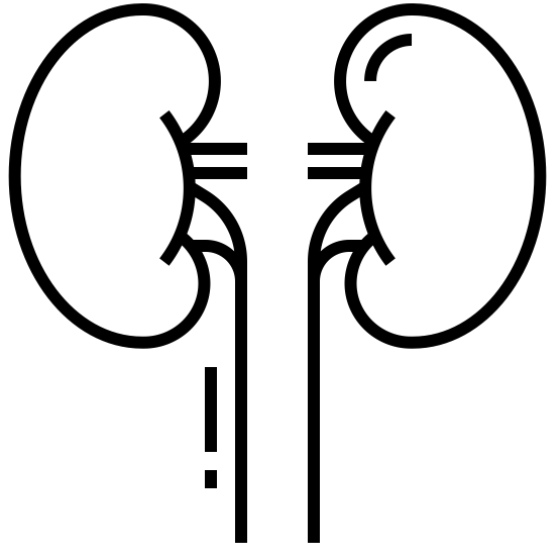
4 months later



Low blood cell count



Acute kidney injury

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4 months later

- Cultures are obtained
- Patient started on broad-spectrum antibiotics

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Hospital days 1–4

- No improvement
- Antibiotics broadened twice

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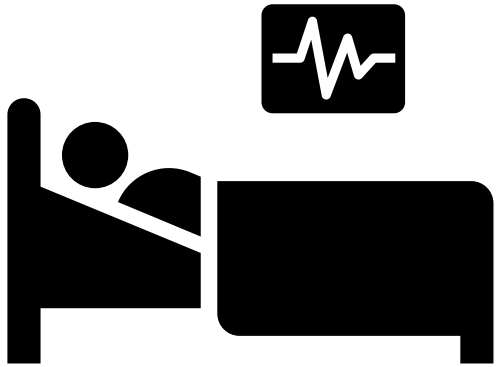
Hospital day 6

- Patient died after cardiac arrest



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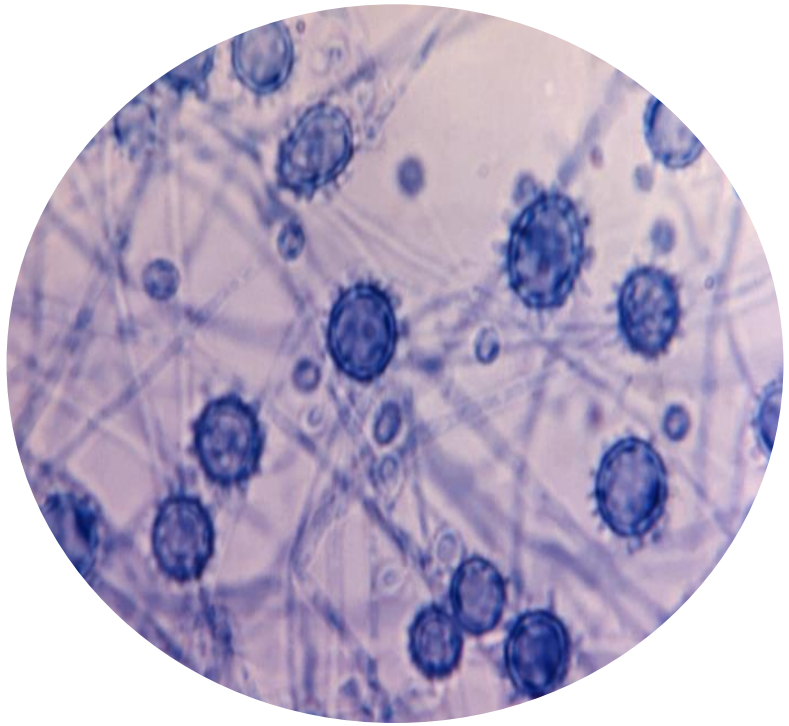
2 days later

- Blood cultures positive for *Histoplasma capsulatum*



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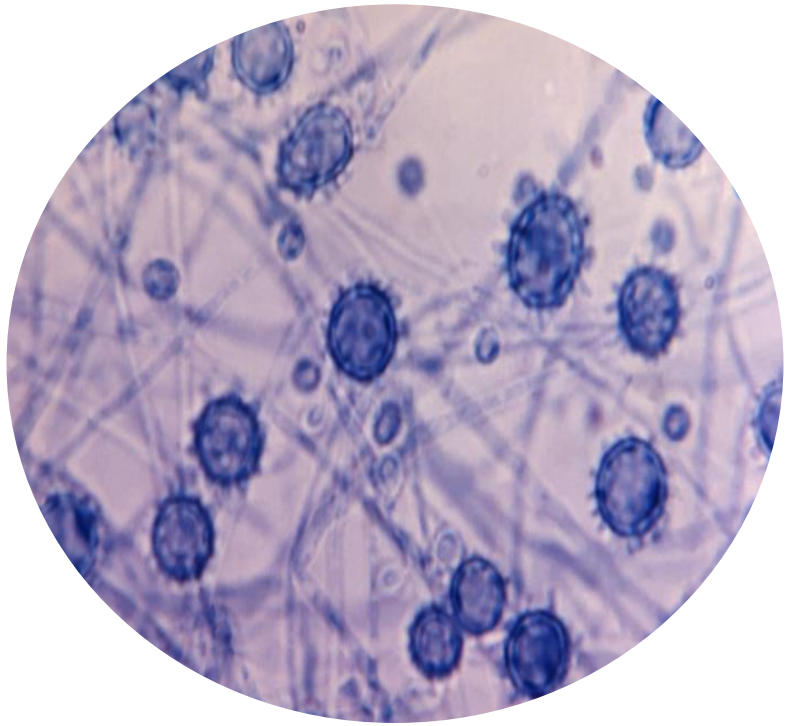
Histoplasma is the causative agent of the fungal infection, histoplasmosis



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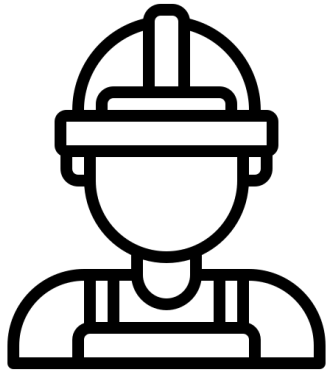
What initial factors may have suggested fungal disease?

Infection did not respond to multiple rounds of antibiotics

Residence in an endemic area for blastomycosis and histoplasmosis



High-risk occupation for environmental fungal diseases

Why might histoplasmosis not have been considered?

- No noted exposure to bird or bat guano
  - Although birds, bats, or their droppings are described in 77% of histoplasmosis outbreaks, only 25% of people with sporadic histoplasmosis recall these exposures.

Benedict K, Toda M, Jackson BR. Revising Conventional Wisdom about Histoplasmosis in the United States, *Open Forum Infect Dis*. 2021 July; 8(7): ofab306.

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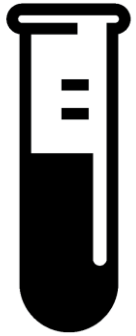
- Patient did not have HIV
  - Decline in HIV-associated histoplasmosis in recent decades in the United States. Autoimmune diseases (20%), cancer (13%), and diabetes (11%) were more common risk factors than HIV (3%).

Benedict K, Toda M, Jackson BR. Revising Conventional Wisdom about Histoplasmosis in the United States, *Open Forum Infect Dis*. 2021 July; 8(7): ofab306.

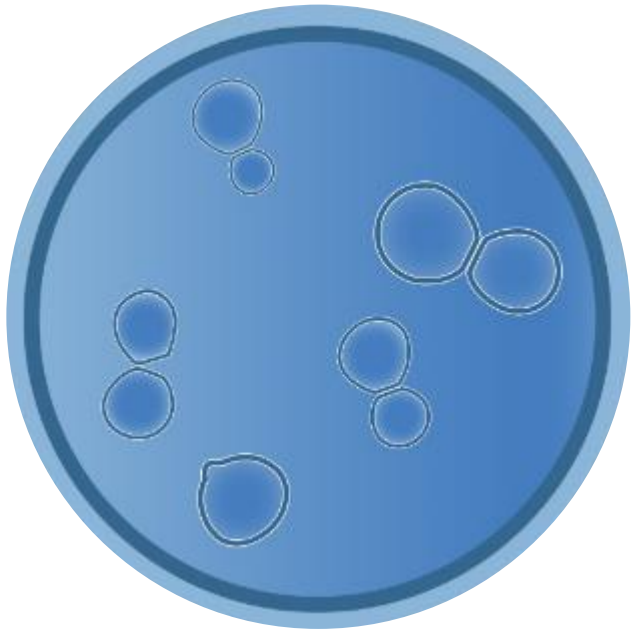
Alternate diagnostic testing approach may have improved outcome

- Turnaround time for culture results was over a week.

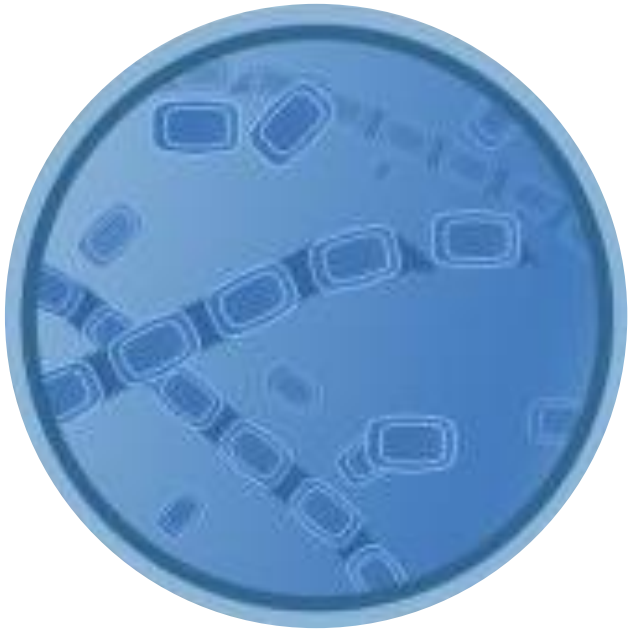
- Urine antigen or serology testing could have led to earlier diagnosis.



Histoplasma is part of a group of pathogens that are endemic in certain areas



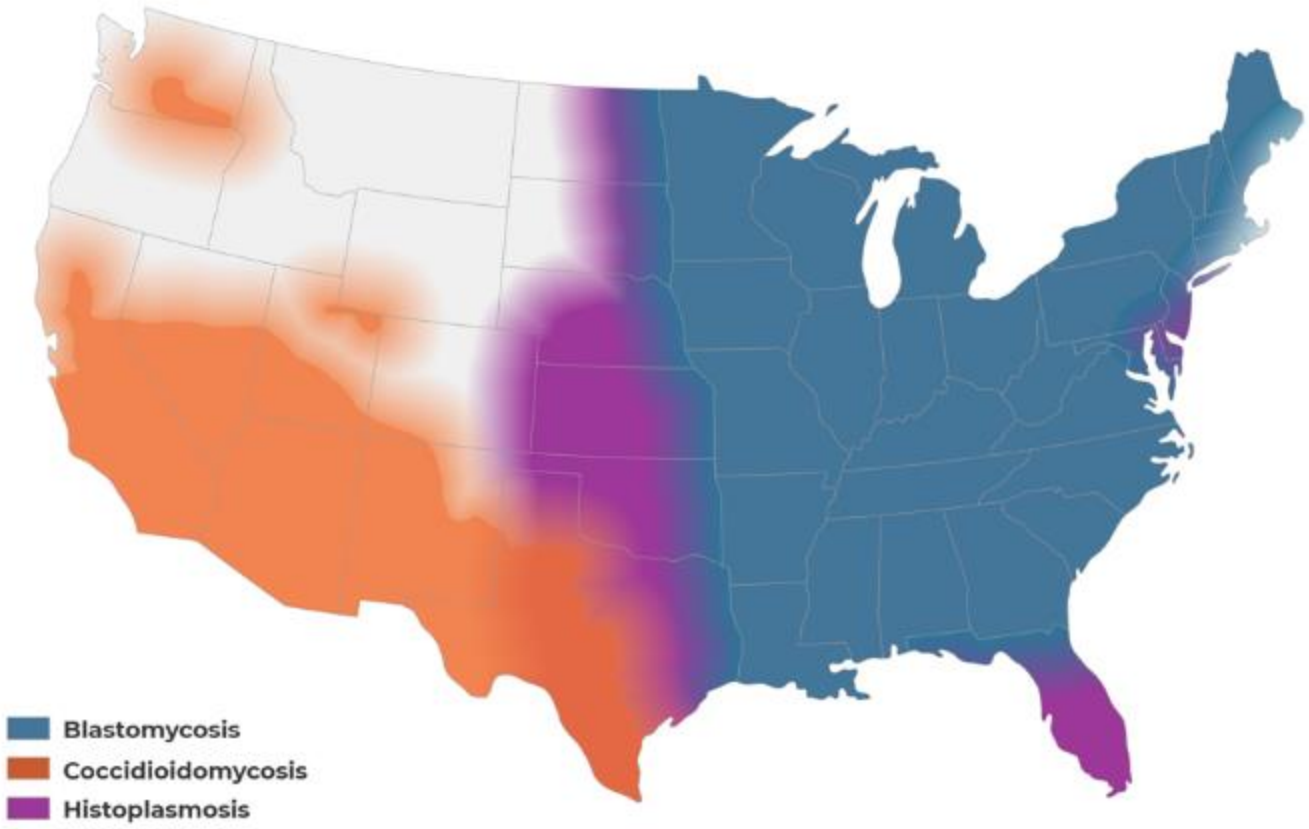
Blastomyces



Coccidioides

Histoplasma

Their combined distribution spans most of the country



Hospitalizations

- Coccidioidomycosis (~6,700)
- Histoplasmosis (~4,600)
- Blastomycosis (~1,000)

Direct medical costs

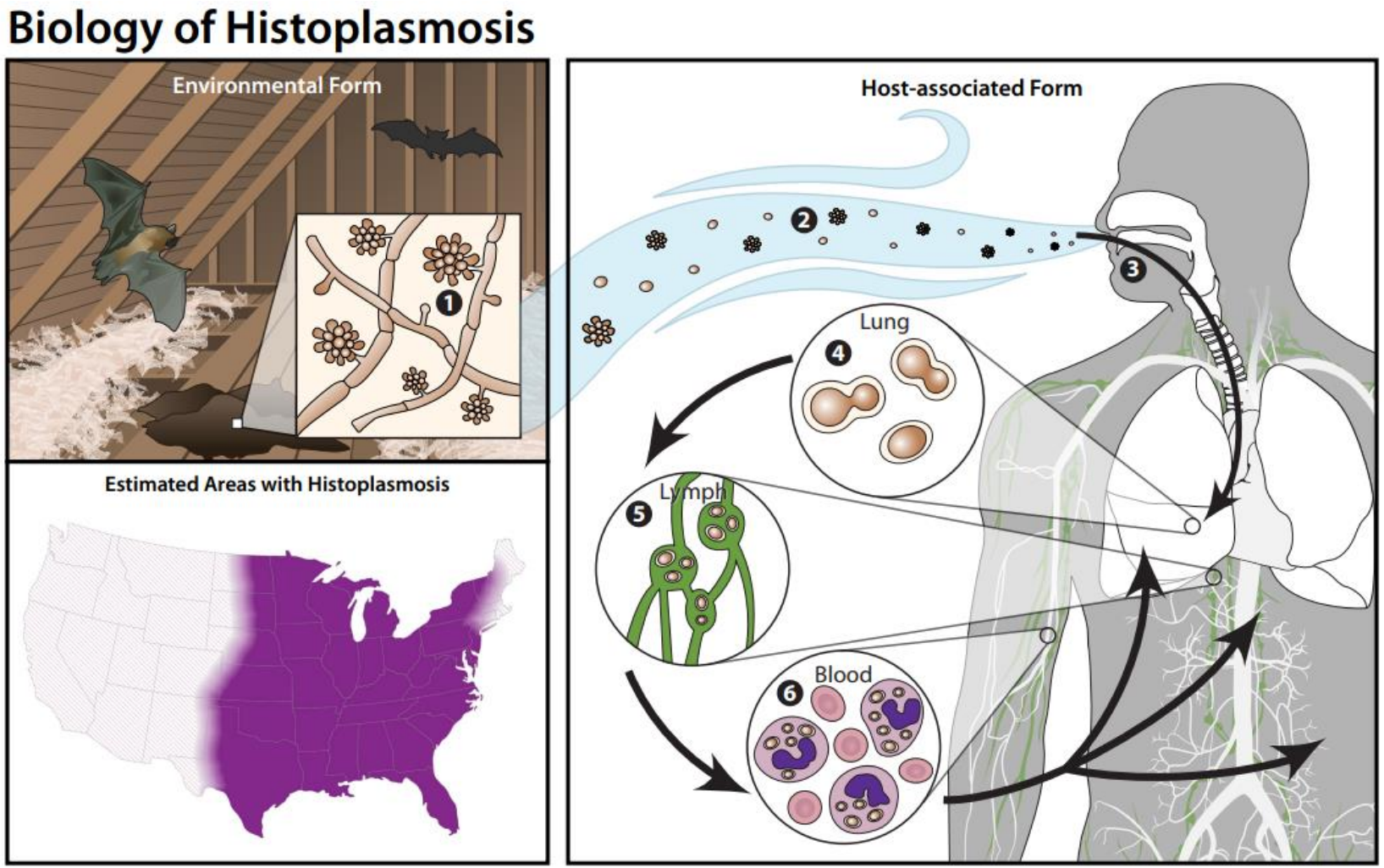
- Coccidioidomycosis (~$200m)
- Histoplasmosis (~$200m)
- Blastomycosis (~$23m)

https://www.cdc.gov/fungal/cdc-and-fungal/burden.html

Fungi that cause these diseases live in the environment, particularly in soil

Exposure typically occurs through inhalation of microscopic spores

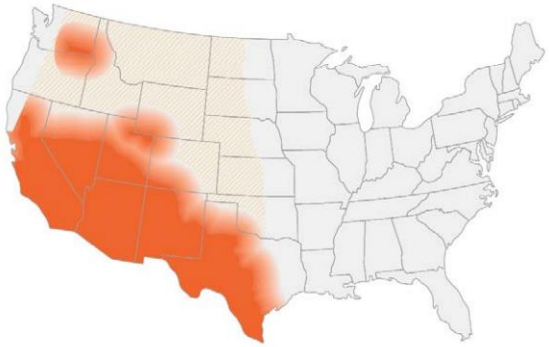
These fungi are dimorphic, with mycelial and yeast phases



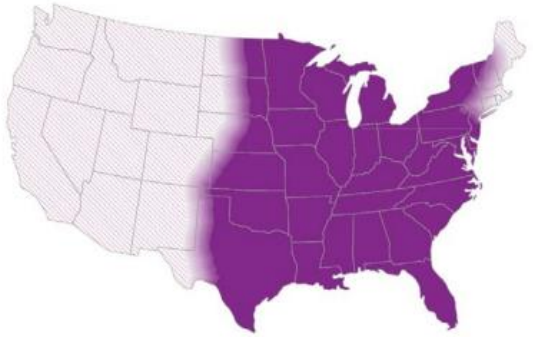
Each fungus is associated with a geographic range

Estimated areas of endemicity:

Blastomycosis



Coccidioidomycosis



Histoplasmosis

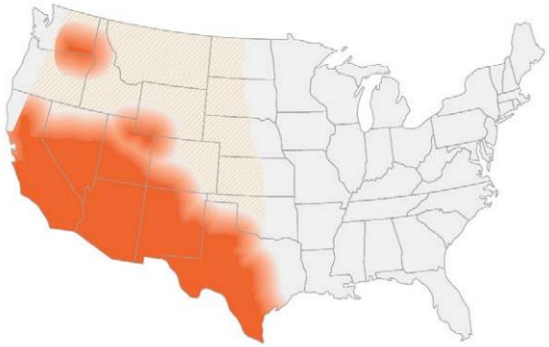
Trends are monitored through national surveillance in select states where any of these disease are reportable

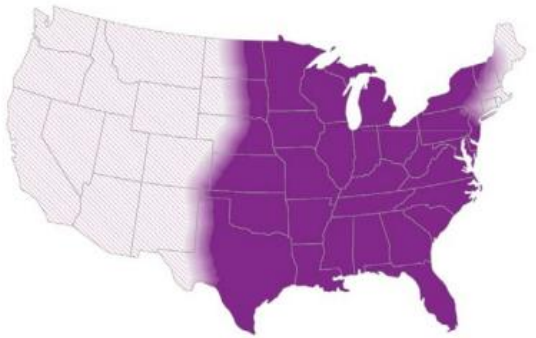
- In states where a disease is **reportable**, healthcare professionals, laboratories, hospitals, and other providers must tell public health departments when a person is diagnosed.
- Case data is **voluntarily submitted** to CDC when a patient meets standardized criteria to be classified as a case according to the Council of State & Territorial Epidemiologists case definition.

NNDSS
National Notifiable Diseases Surveillance System

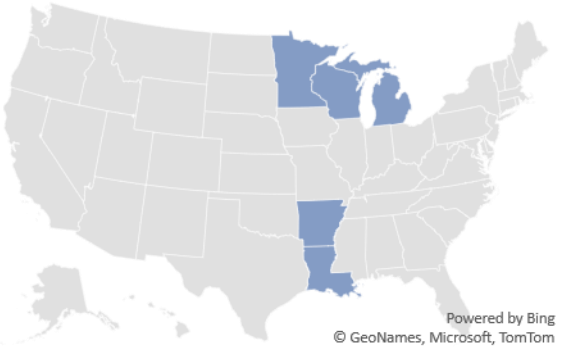
Endemic mycoses are not reportable in all states

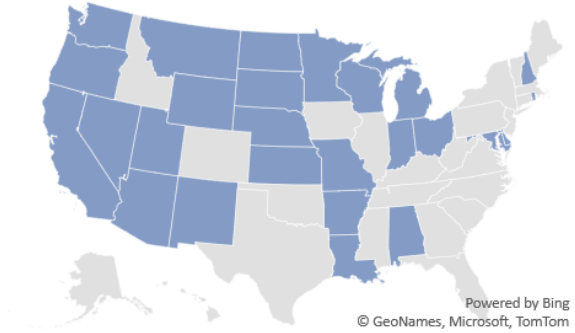
Estimated areas of endemicity:

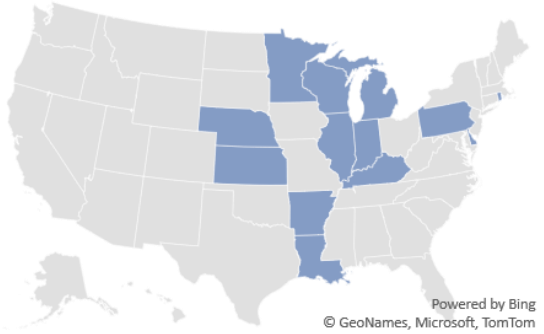




States where disease is reportable:







Blastomycosis

Coccidioidomycosis

Histoplasmosis

Self-knowledge Check

- The fungi that causes blastomycosis is thought to be endemic to:

A. The Pacific Northwest

B. Hawaii and Alaska

C. Midwest States

D. A and B only

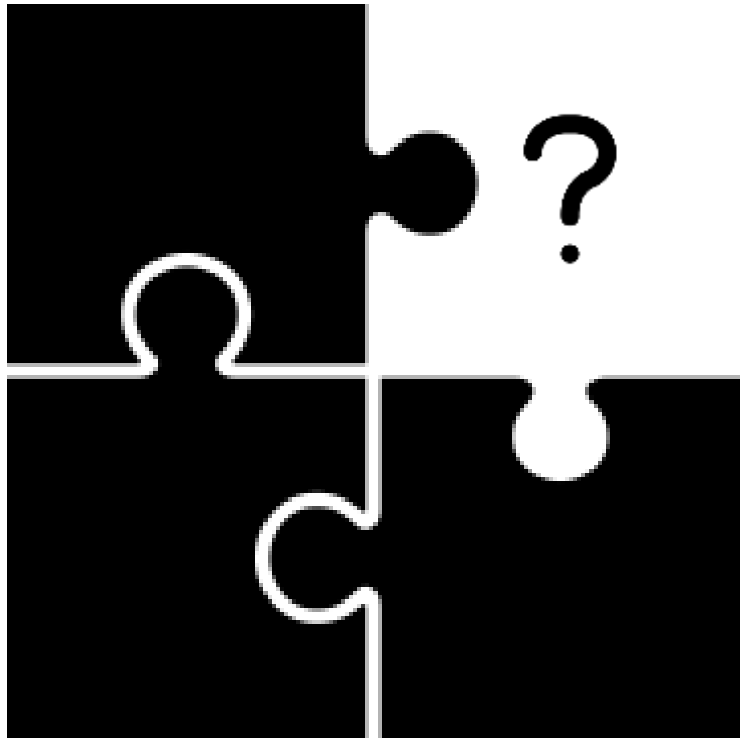
E. All of the above

Self-knowledge Check

- The correct answer is: C

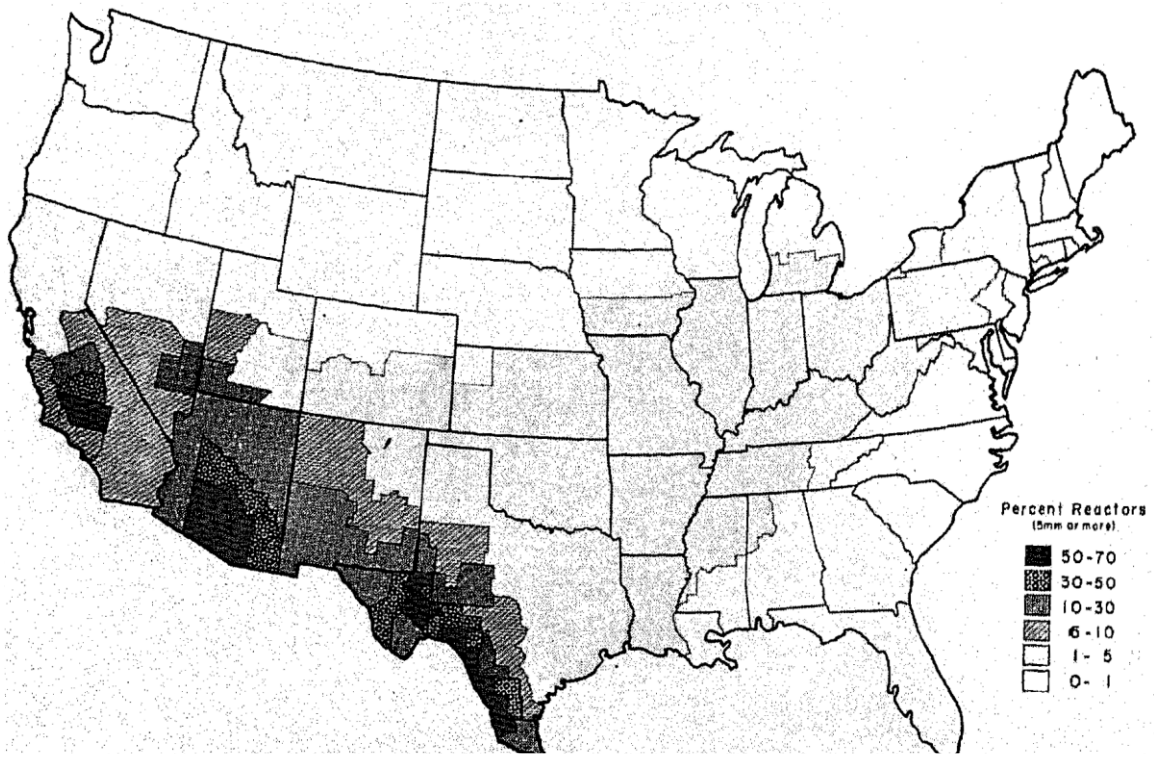
- In the United States, the fungus mainly lives in the midwestern, south-central, and southeastern states, particularly in areas surrounding the Ohio and Mississippi River valleys, the Great Lakes, and the Saint Lawrence River.
  - However, clinicians can diagnose these fungal infections anywhere in the United States due to travel-associated disease.

Surveillance limitations result in incomplete understanding of disease



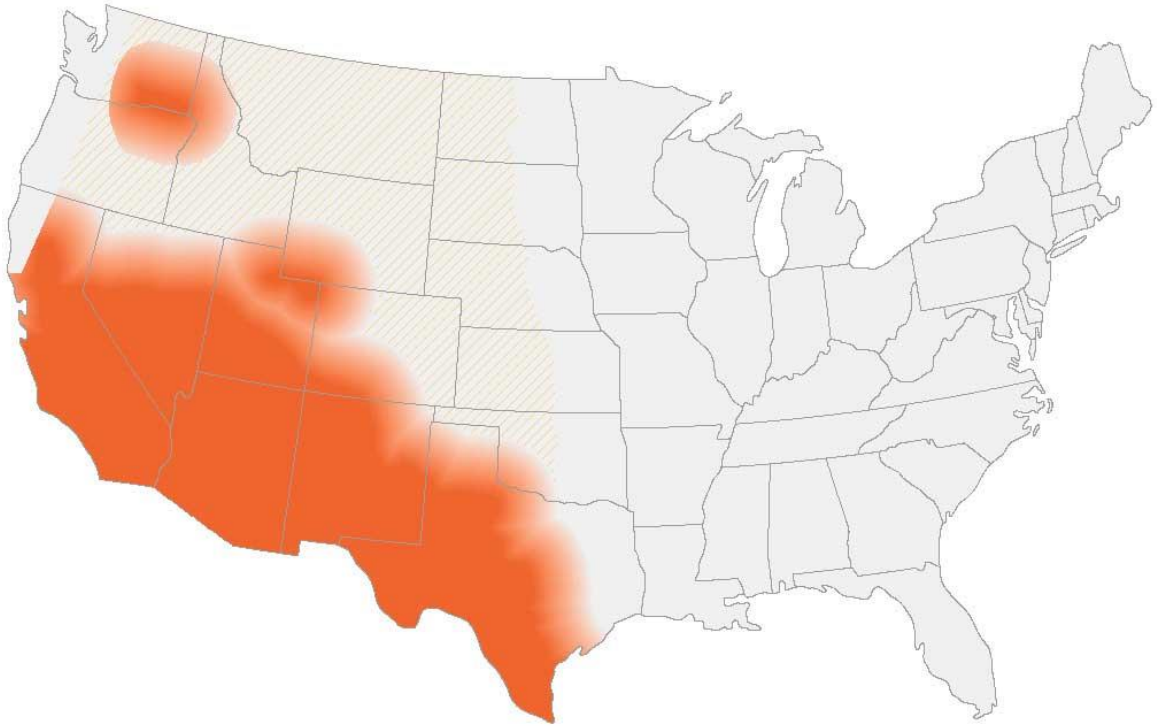
Geographic range likely wider than currently recognized

Coccidioidomycosis skin testing in 1940s-1950s



Distribution of counties and groups of counties by frequency of coccidioidin reactors in 48,676 young adults. *Edwards et al* 1957.

New map of coccidioidomycosis endemicity



https://www.cdc.gov/fungal/diseases/coccidioidomycosis/maps.html

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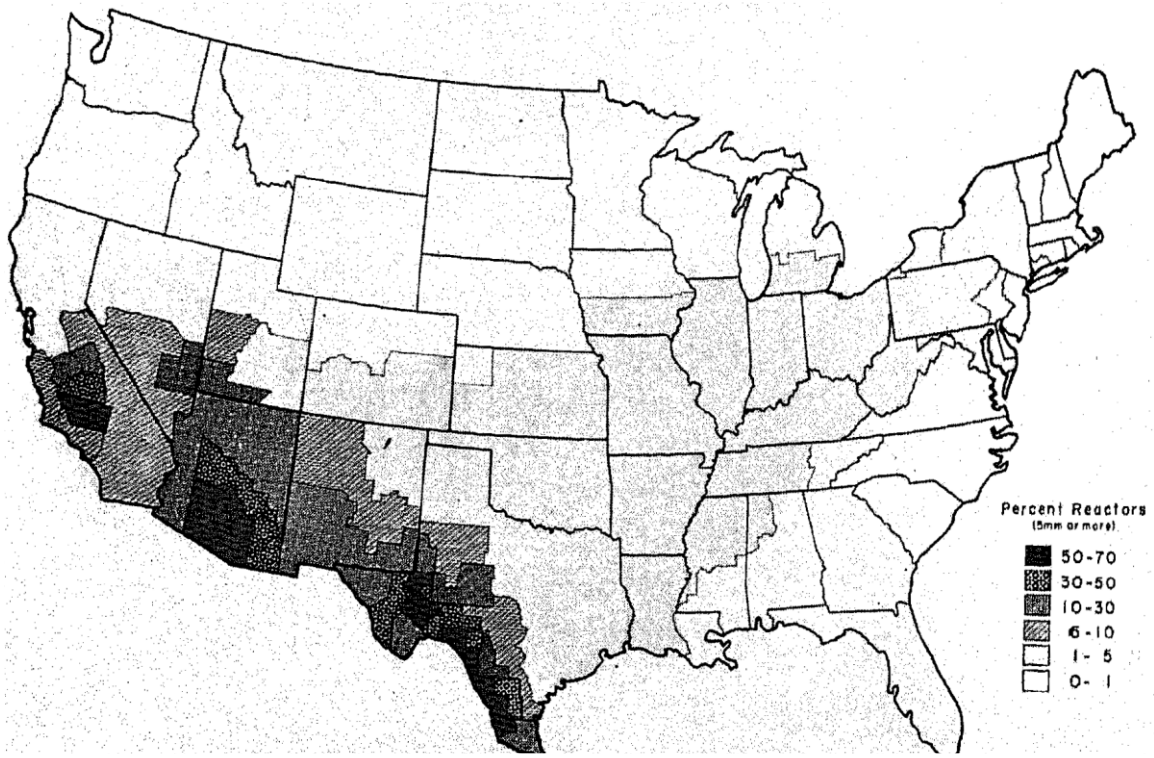

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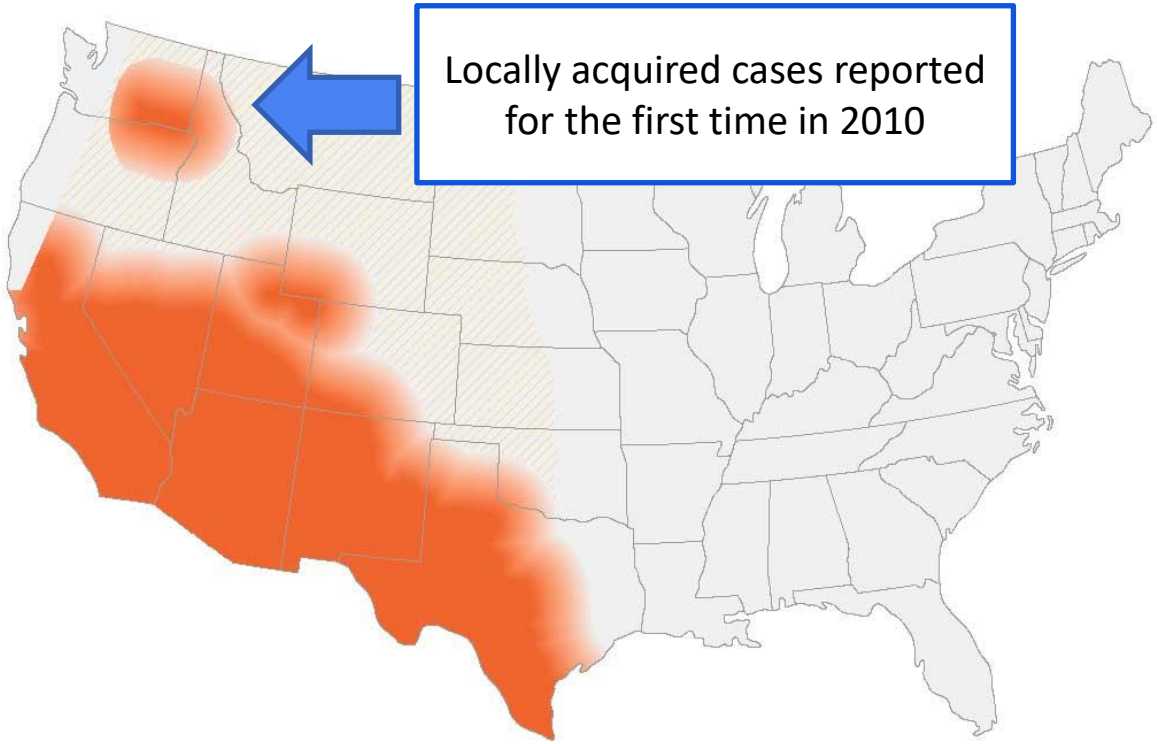

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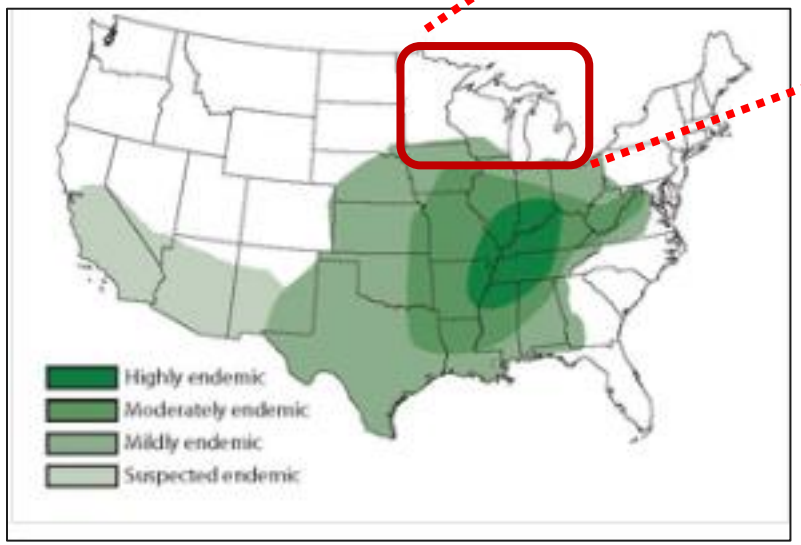
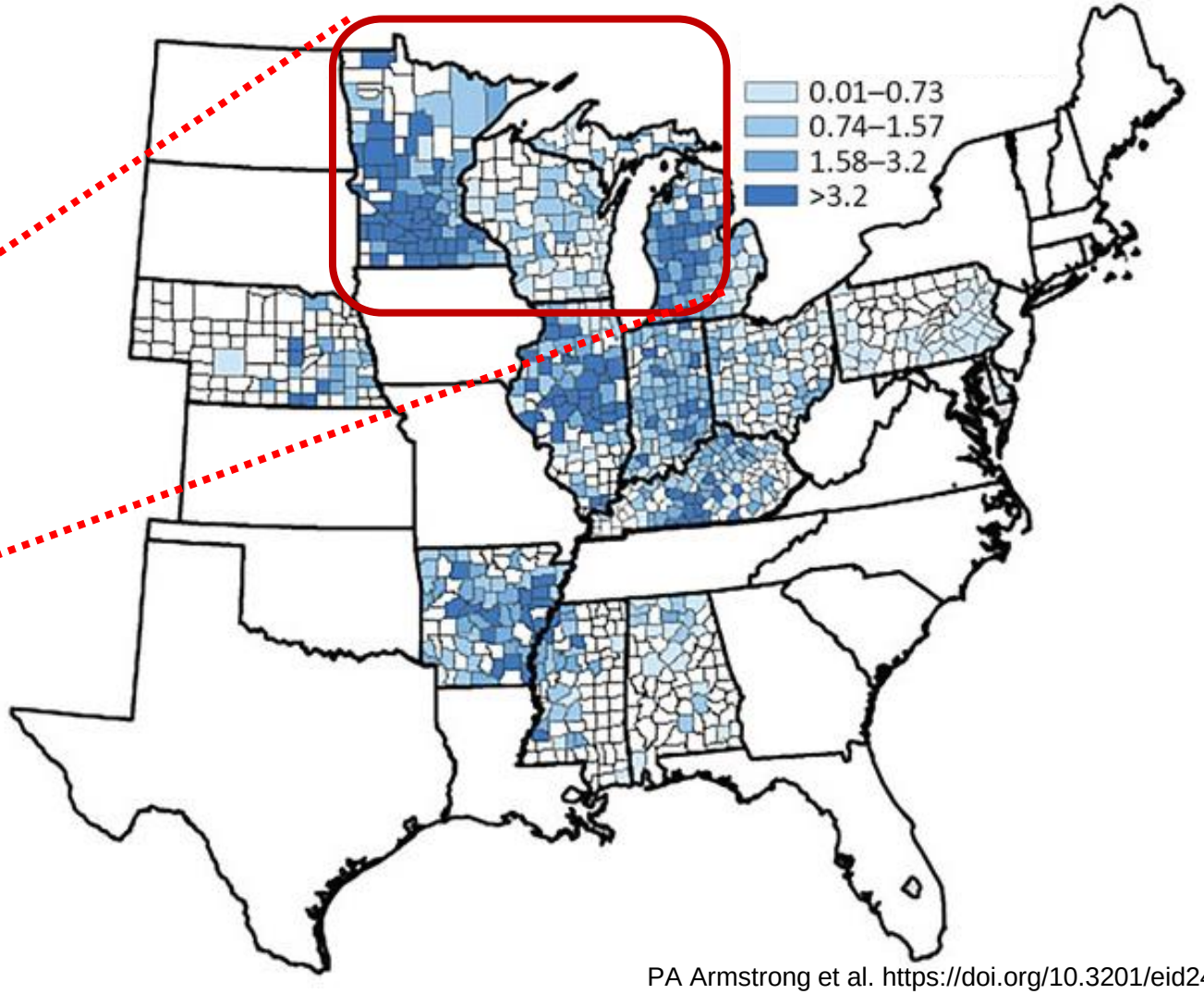
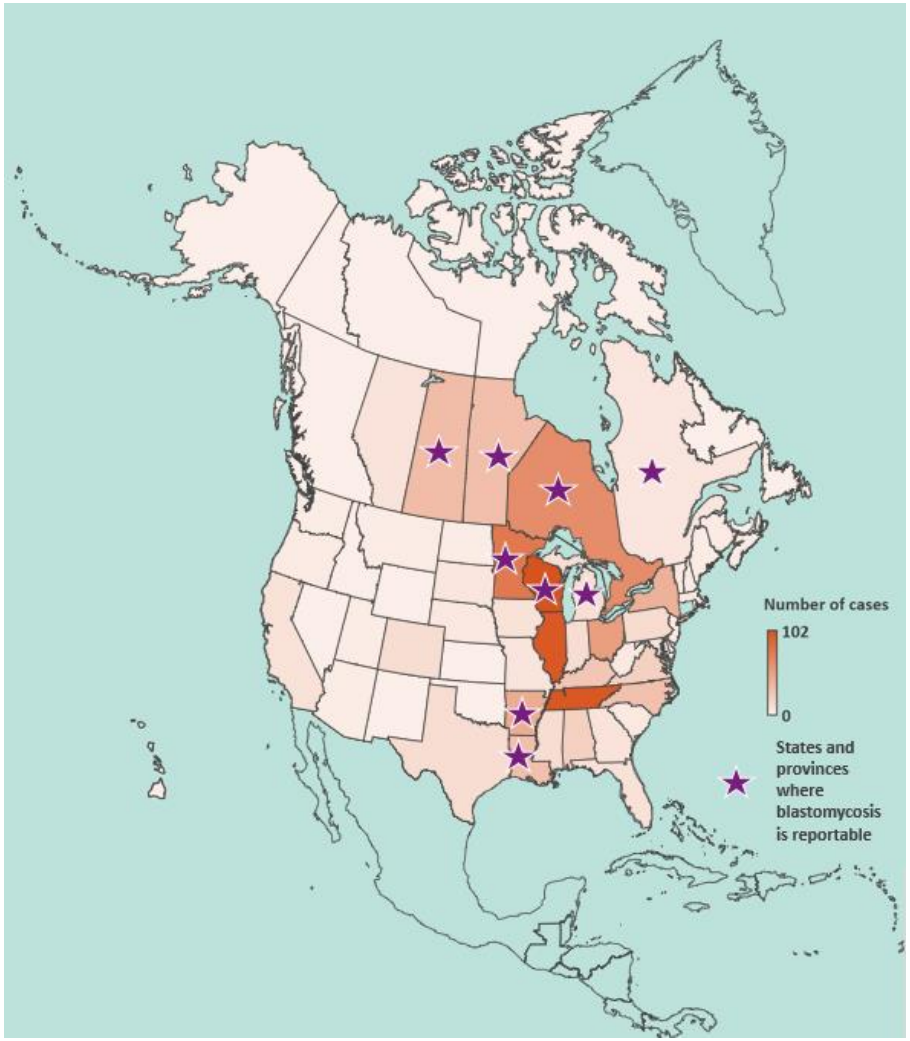


Histoplasmosis incidence, 2011-2014



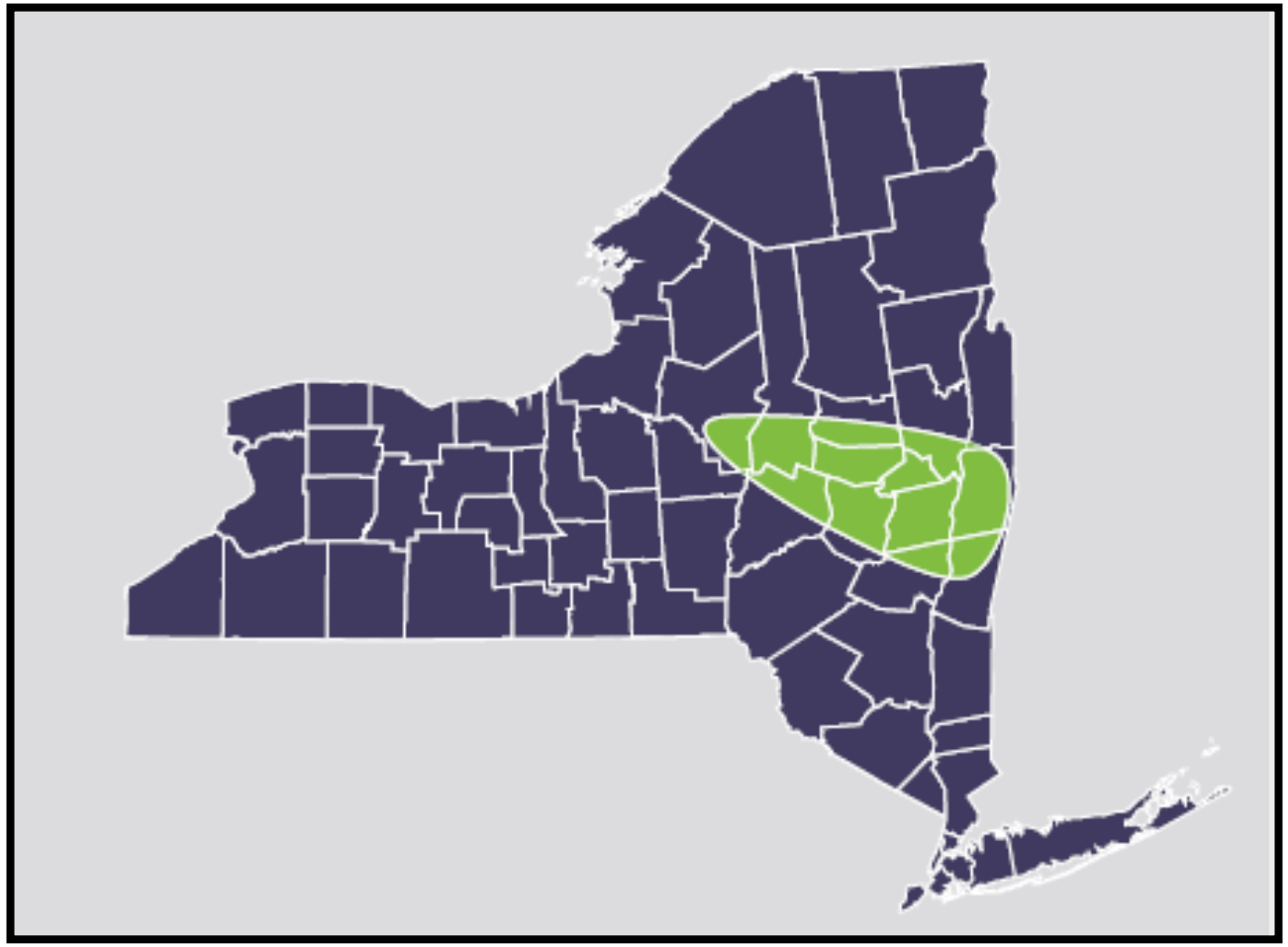
PA Armstrong et al. https://doi.org/10.3201/eid2403.171258

Limited blastomycosis surveillance hinders ability to assess geographic trends



- Reviewed blastomycosis case reports from 1970-2020, mapped where cases were diagnosed.
- Most published blastomycosis cases were diagnosed within the estimated endemic range.
- Over half of published cases occurred in jurisdictions without public health surveillance.

New York investigation indicated potential local acquisition of blastomycosis

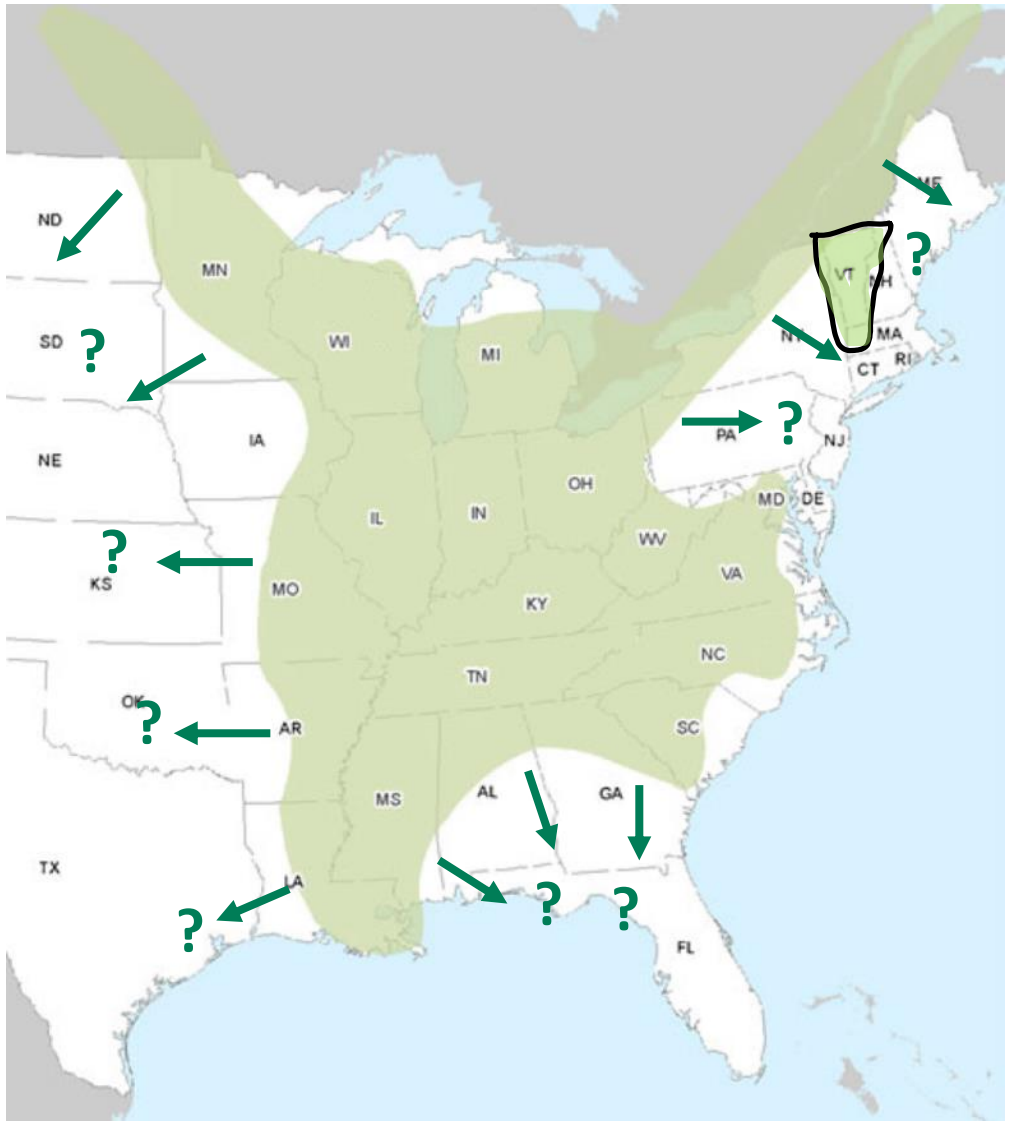


McDonald R, Dufort E, Jackson BR, Tobin EH, Newman A, Benedict K, Blog D. Notes from the Field: Blastomycosis Cases Occurring Outside of Regions with Known Endemicity - New York, 2007-2017. *MMWR Morb Mortal Wkly Rep*. 2018 Sep 28;67(38):1077-1078

Recent analyses suggest *Blastomyces* may be endemic in Vermont

Borah B, EIS Conference, 2023
Benedict et al., 2012, *Current Fungal Infection Reports*

Endemicity may extend beyond historical regions

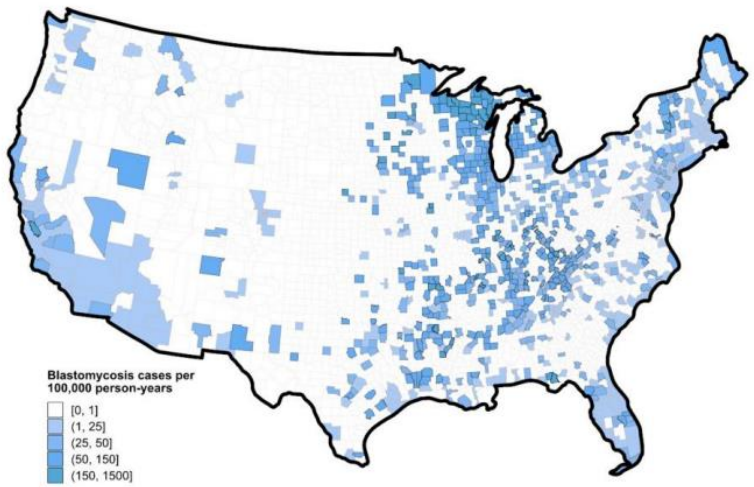


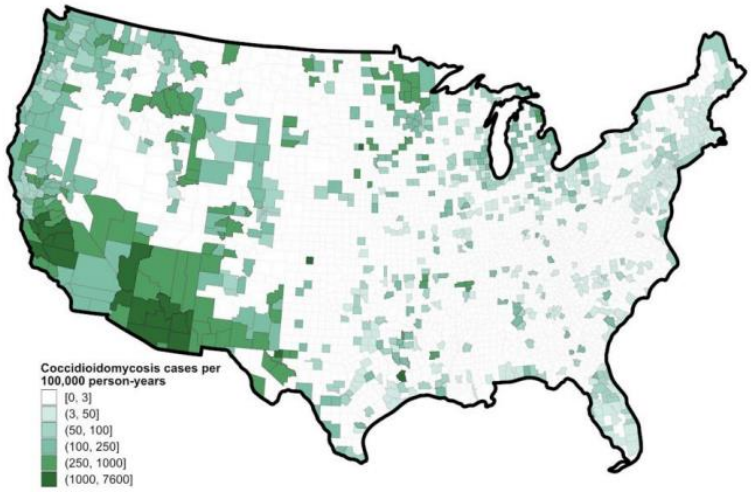
Borah B, EIS Conference, 2023

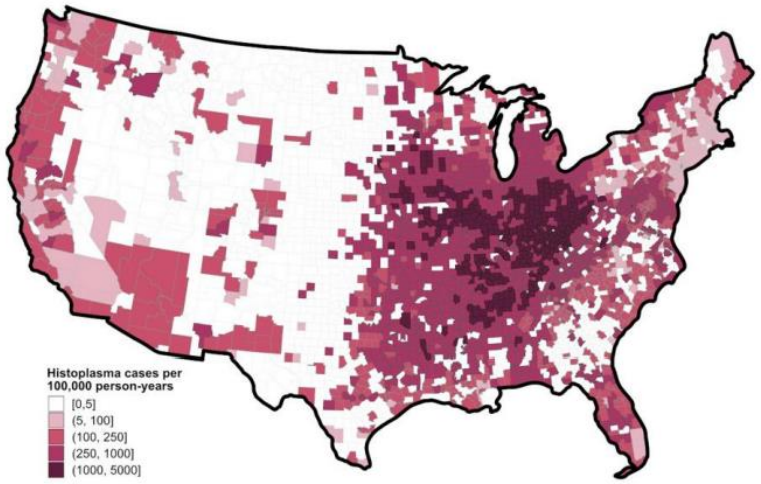
Benedict et al., 2012, *Current Fungal Infection Reports*

Cases are identified outside of traditionally established endemic regions

Incidence from 2007–2016 in Medicare fee-for-service beneficiaries by U.S. county
Reported as cases per 100,000 person-years





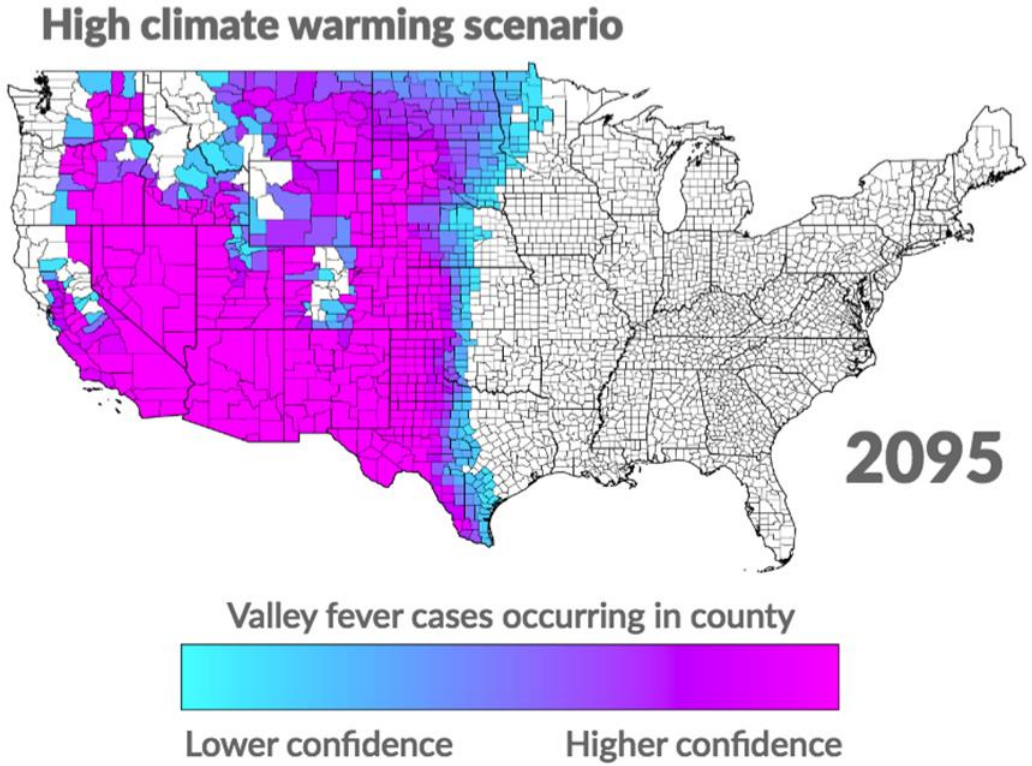


Blastomycosis **Coccidioidomycosis** **Histoplasmosis**

Mazi, P. B., Sahrmann, J. M., Olsen, M. A., et al., (2022). The Geographic Distribution of Dimorphic Mycoses in the United States for the Modern Era. *Clinical infectious diseases,* https://doi.org/10.1093/cid/ciac882

Climate change may further impact the geographical distribution of coccidioidomycosis

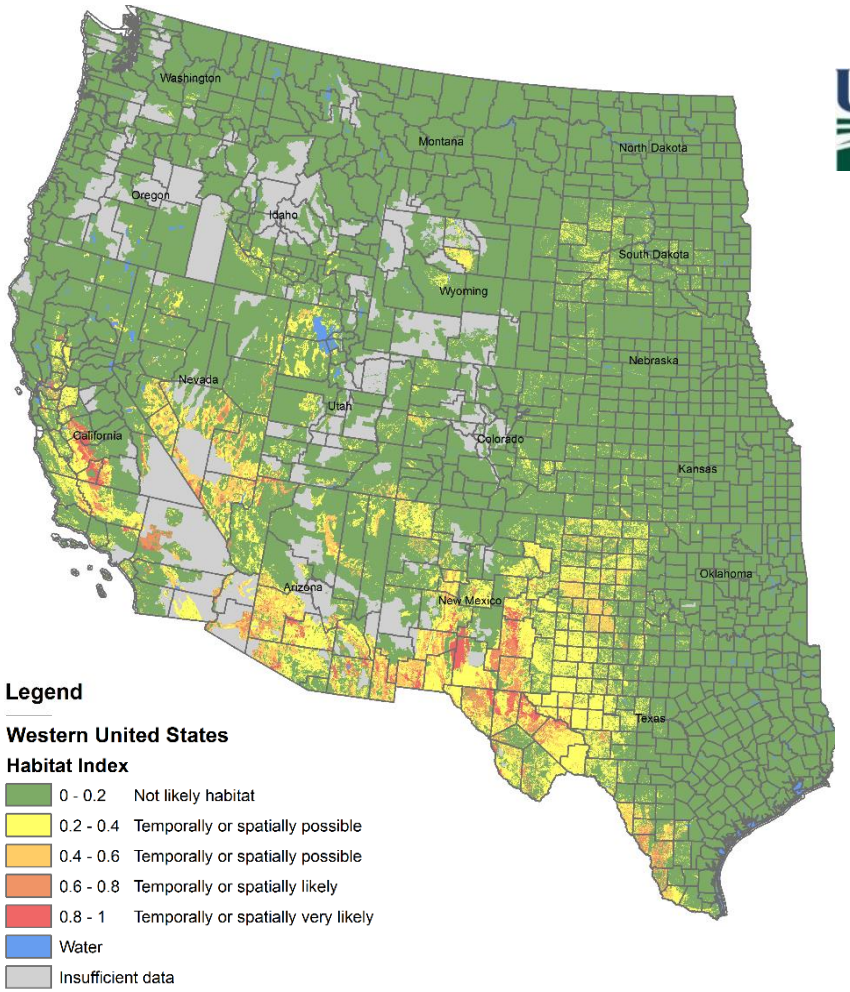
- Climate niche model for coccidioidomycosis based on temperature and precipitation
- Predicted areas affected by coccidioidomycosis under different climate warming scenarios



Estimated ranges of coccidioidomycosis
(Gorris et al, GeoHealth 2019)

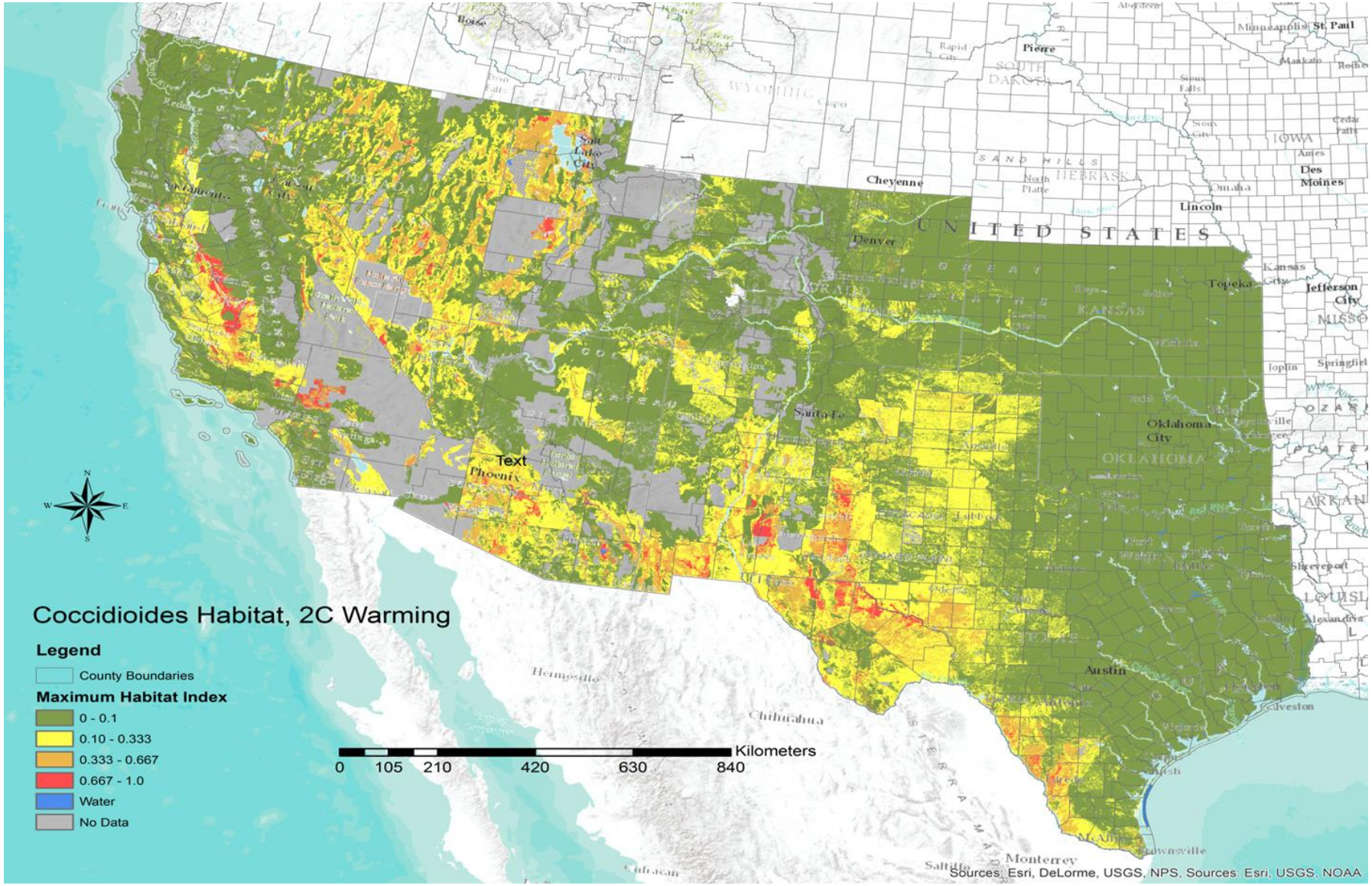
Climate change may further impact the geographical distribution of coccidioidomycosis, continued

- Model predicted suitable soil habitat for coccidioidomycosis based on USDA data
  - Electrical conductivity, pH, temperature, precipitation, organic matter, water holding capacity, surface morphology.



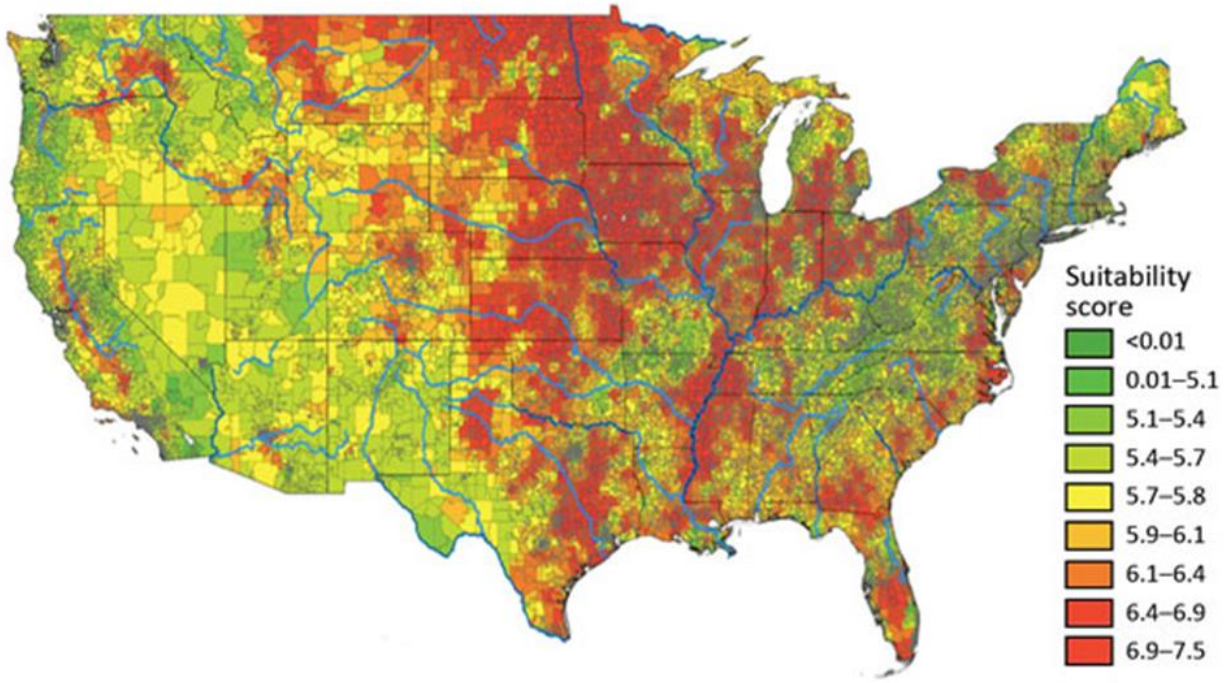
https://doi.org/10.1371/journal.pone.0247263

What if we impose a 2^{o} Celsius warming?



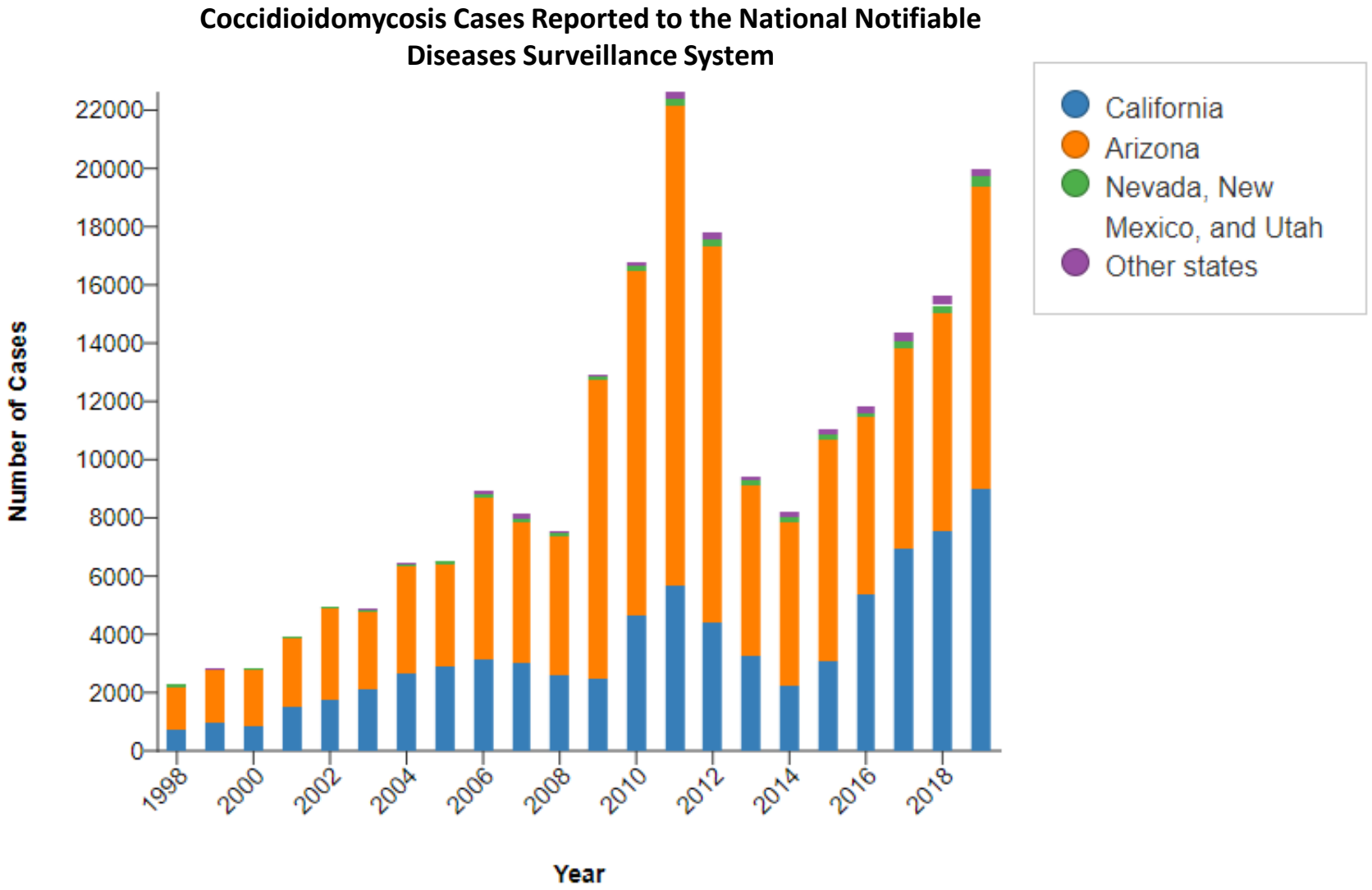
Climate change may further impact the geographic suitability for *Histoplasma*

- Geographic suitability model to predict areas favorable to *Histoplasma* presence
  - Land cover use
  - Distance to water
  - Soil pH



Estimated ranges of histoplasmosis
(Maiga et al, EID 2018)

Reported coccidioidomycosis cases have increased since 2014



Steady rise in histoplasmosis hospitalization rates

Open Forum Infectious Diseases

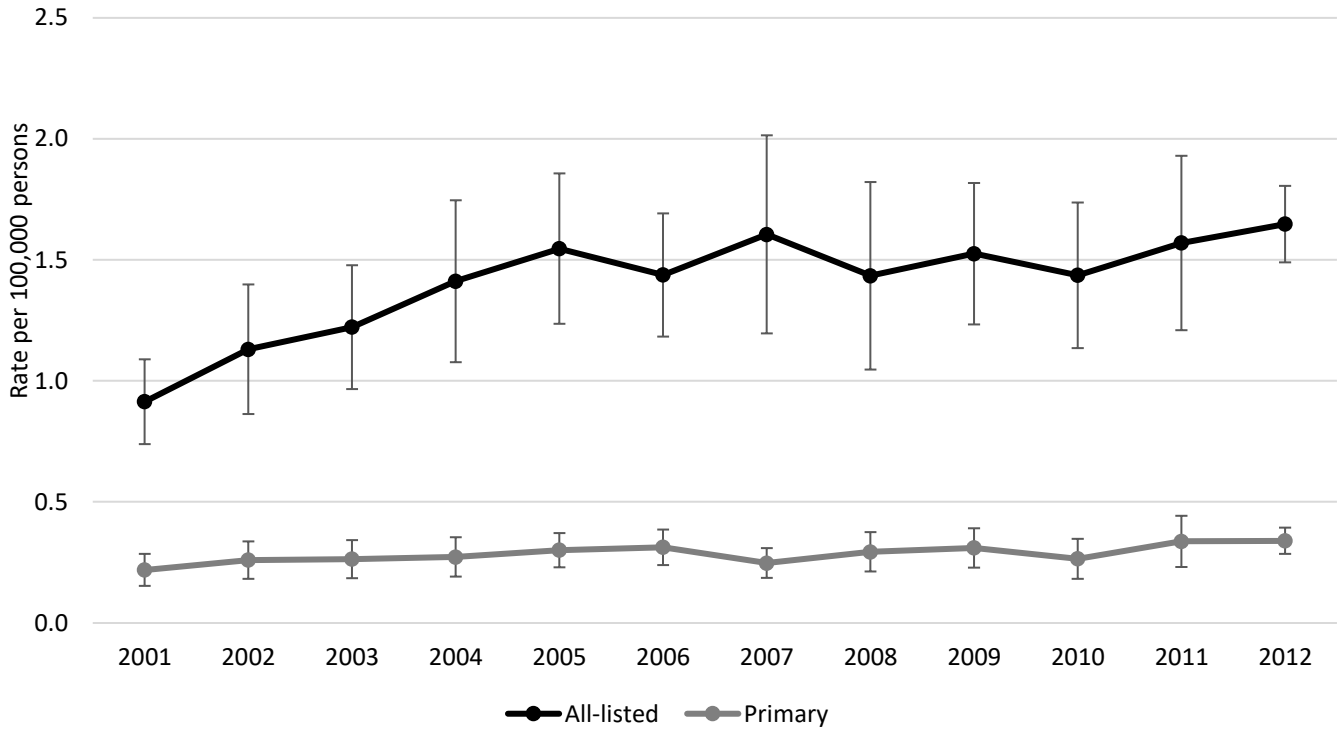
BRIEF REPORT

Histoplasmosis-Associated Hospitalizations in the United States, 2001–2012

Kaitlin Benedict,[1] Gordana Derado,[2] and Rajal K. Mody[1]

[1]Mycotic Diseases Branch and [2]Biostatistics and Information Management Office, Division of Foodborne, Waterborne and Environmental Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Annual rates of all-listed and primary histoplasmosis-associated hospitalizations per 100,000 persons



Reported case counts are likely a substantial underestimation of true disease burden

Several factors limit the ability to detect cases of endemic mycoses

Underreporting

Underdiagnosis

Care-seeking Behavior

Reported case counts are likely a substantial underestimation of true disease burden

Several factors limit the ability to detect cases of endemic mycoses

Underreporting

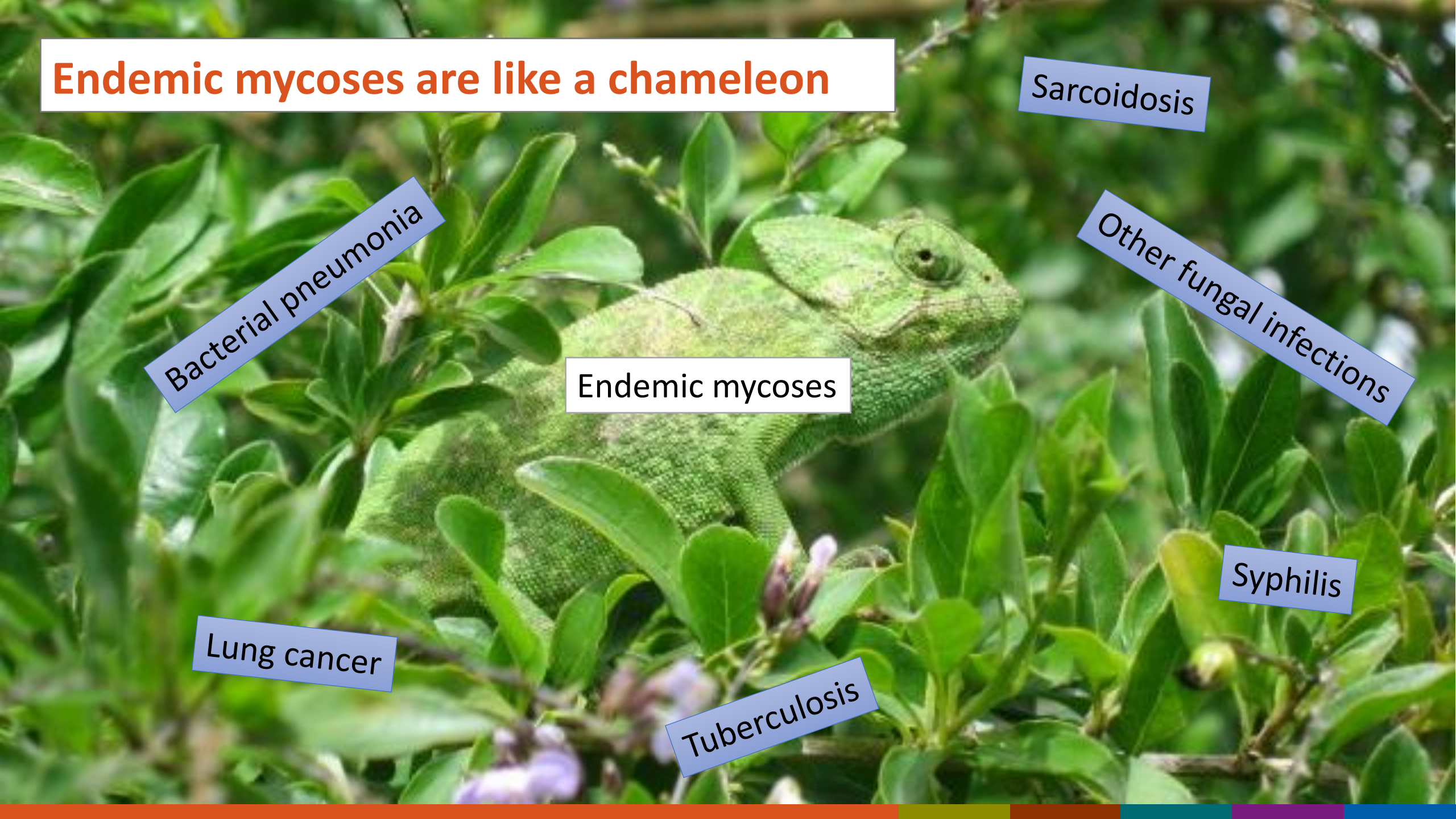
Underdiagnosis

Care-seeking Behavior

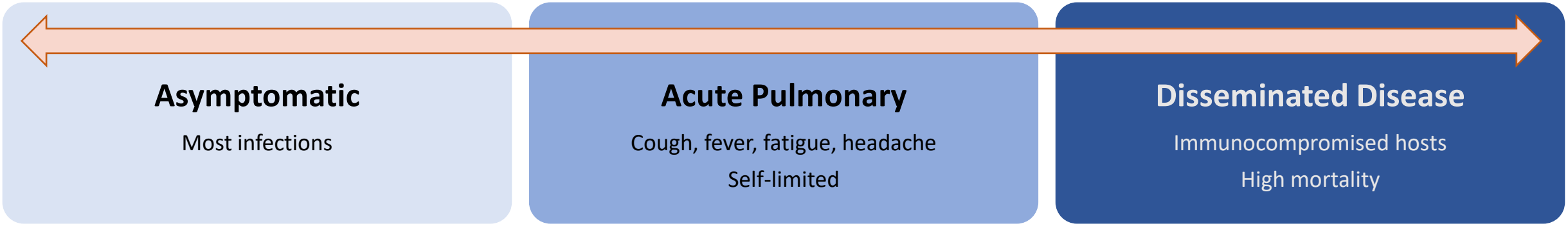
Missed or delayed diagnosis can have wide-reaching implications.

Diagnostic challenges

Endemic mycoses are like a chameleon



Clinical manifestations vary substantially



Severity of illness depends principally on:

1. Fungal inoculum
2. Host immunity

Goodwin et al. Medicine (Baltimore) 1981; 60: 231-66

Hospitalization and mortality rates are of concern

Morbidity and Mortality Weekly Report (*MMWR*)

Surveillance for Coccidioidomycosis, Histoplasmosis, and Blastomycosis — United States, 2019

Surveillance Summaries / August 19, 2022 / 71(7);1–14

Dallas J. Smith, PharmD[1,2]; Samantha L. Williams, MPH[2]; Endemic Mycoses State Partners Group; Kaitlin M. Benedict, MPH[2]; Brendan R. Jackson, MD[2]; Mitsuru Toda, PhD[2] (VIEW AUTHOR AFFILIATIONS)

54% of **histoplasmosis** patients were hospitalized and **5%** died

65% of **blastomycosis** patients were hospitalized and **9%** died

Symptoms may be mild and are generally nonspecific

Fever

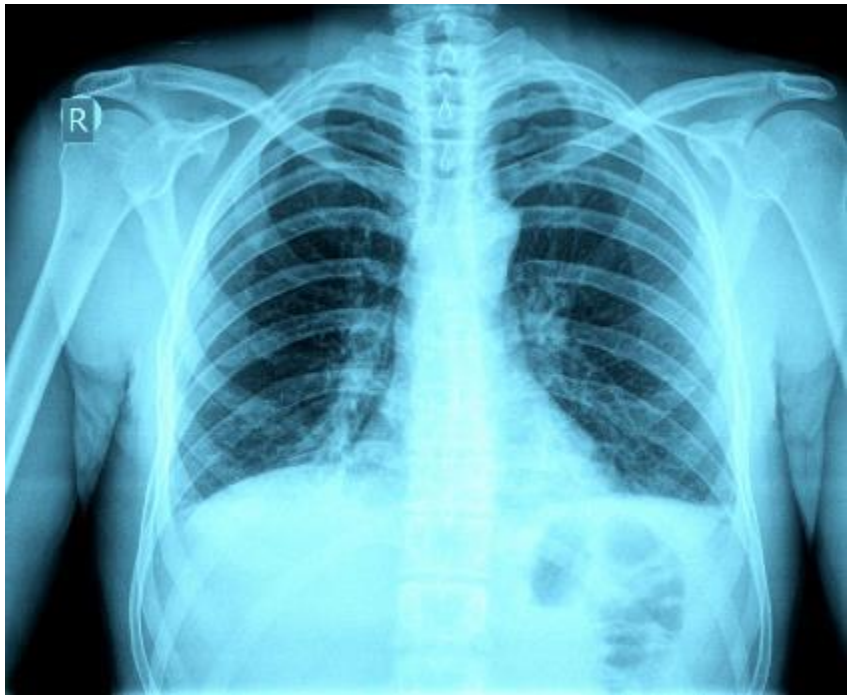
Cough

Fatigue

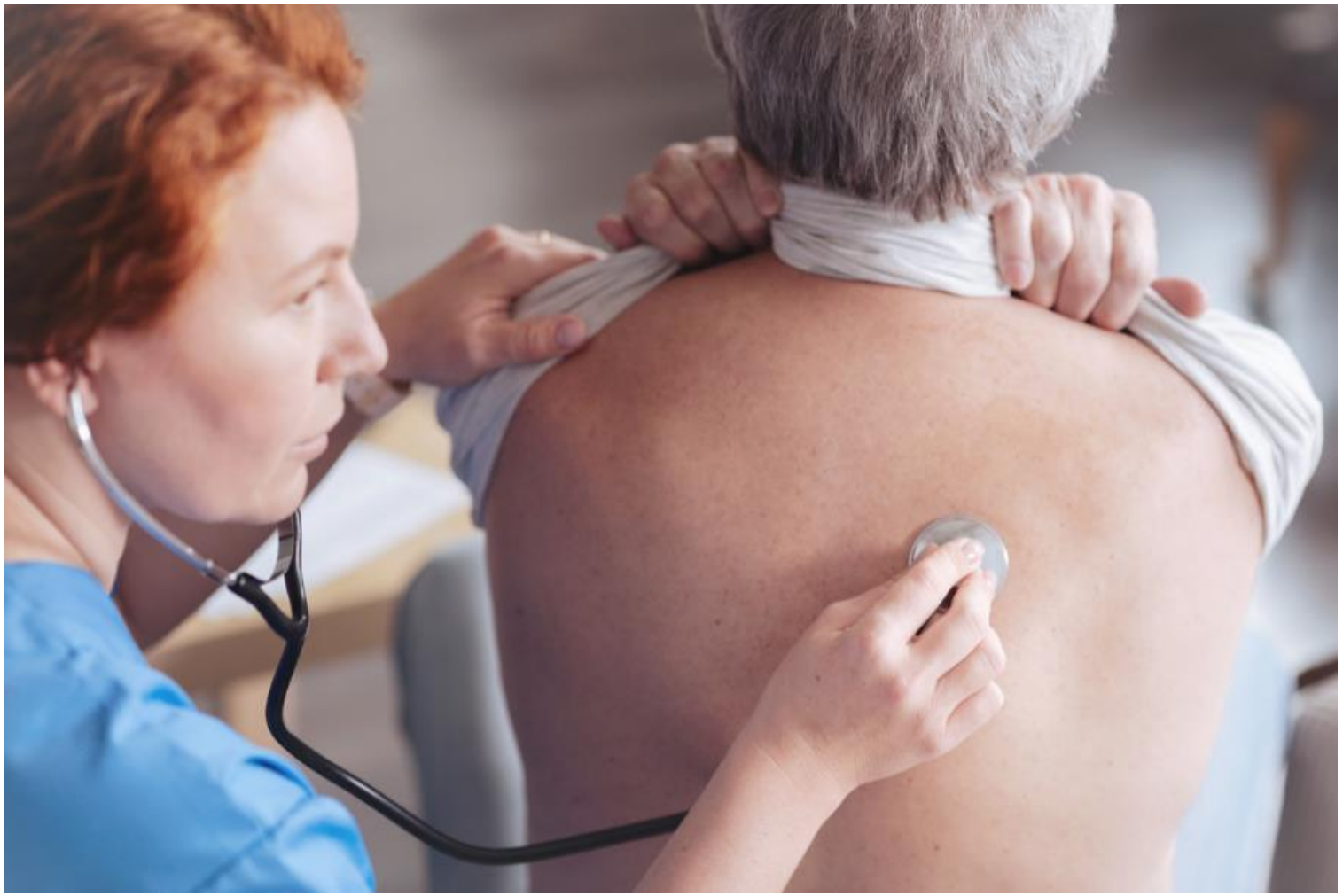
Headache

Night sweats

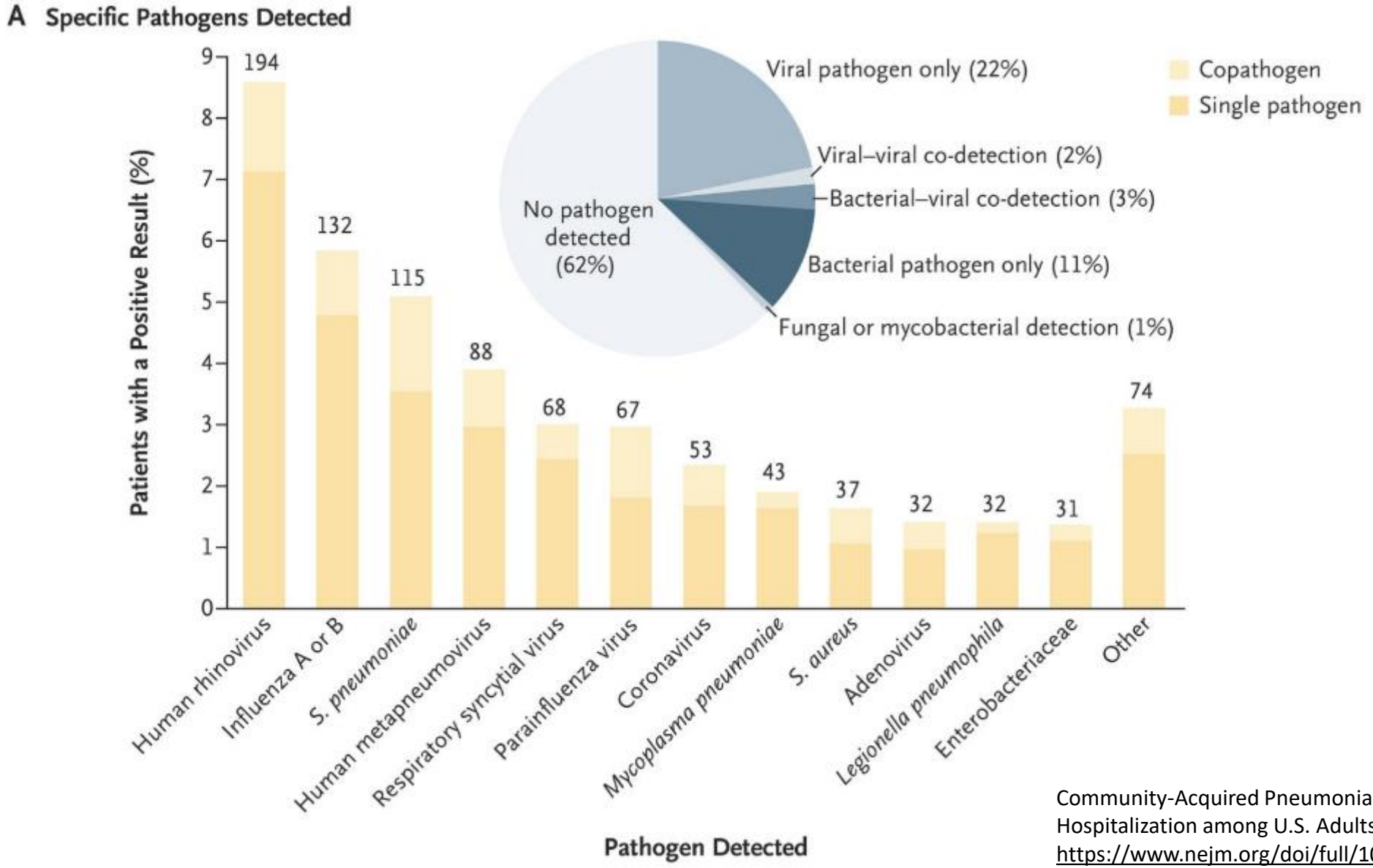
Muscle aches



The endemic mycoses are often misdiagnosed as community-acquired pneumonia (CAP) of bacteria or viral etiology

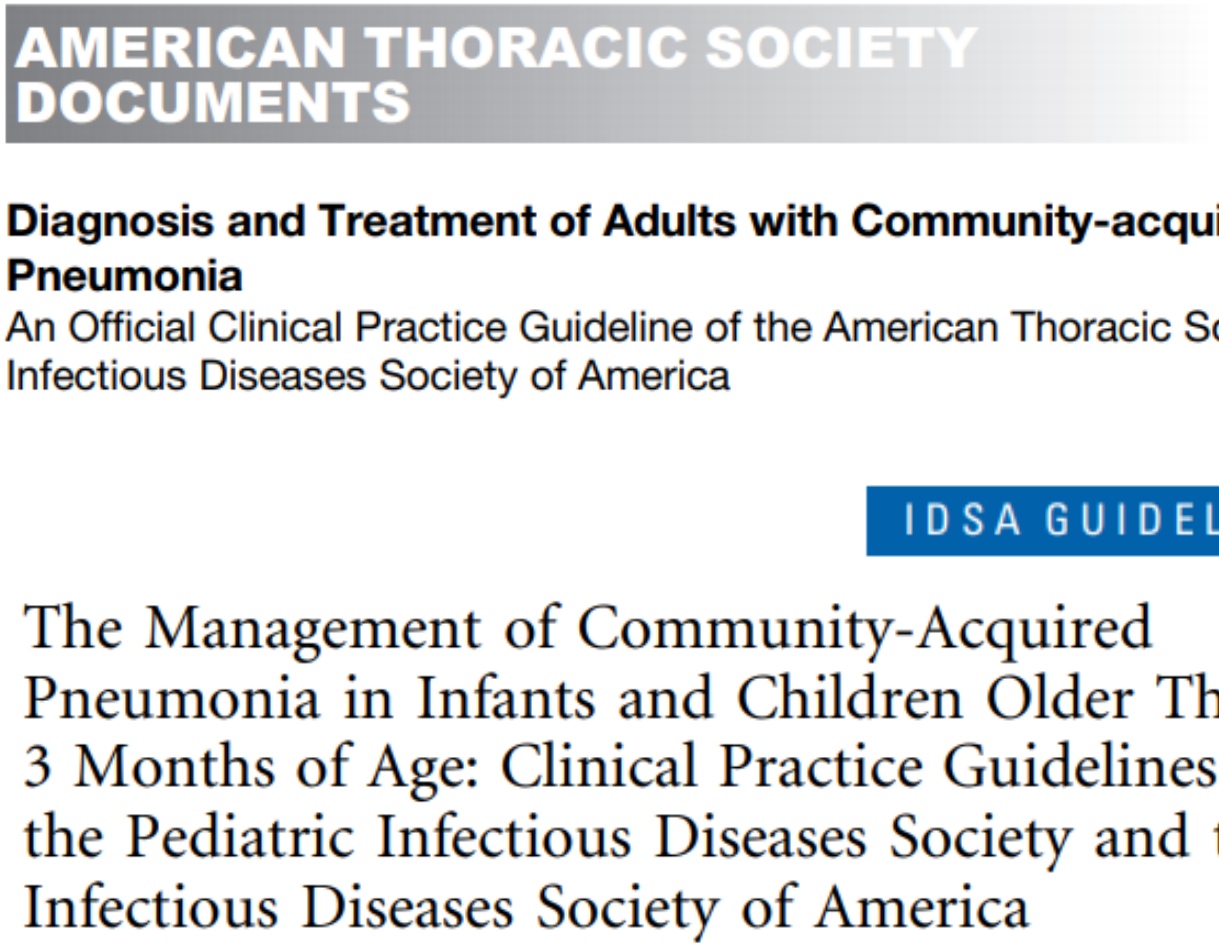


Etiology of pneumonia in the community (EPIC)



Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults | NEJM. https://www.nejm.org/doi/full/10.1056/nejmoa1500245

Current clinical practice guidelines for CAP do not recommend testing for endemic mycoses



- Guidelines state that endemic mycoses are uncommon pathogens
- True burden likely higher

Survey of healthcare providers asked frequency of testing for endemic mycoses with CAP

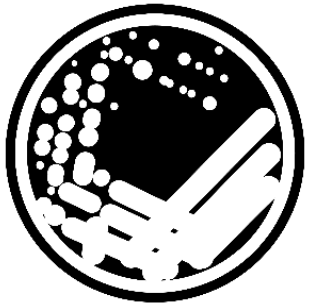
	Primary care providers sometimes or frequently	**Infectious disease physicians** sometimes or frequently
Blastomycosis	Not surveyed	35%
Coccidioidomycosis	19%	36%
Histoplasmosis	22%	58%

Open Forum Infectious Diseases, Volume: 8, Issue: 2, First published: 18 January 2021, DOI: (10.1093/ofid/ofab020)
Journal of Fungi, Volume: 7, Issue: 8, First published 27 July 2021, DOI: (10.3390/jof7080605)

Selecting the optimal laboratory test(s) is complex and nuanced

Antibody/Antigen detection

Culture



Molecular methods

Histopathology

Pros and cons of laboratory methods

Methods	Pros	Cons
Antibody/ Antigen 	• Quick turnaround times • Antigen testing useful early in disease progression	• Cross-reactivity • Sensitivity dependent on host immune status and disease course

Pros and cons of laboratory methods, continued

Methods	Pros	Cons
Antibody/ Antigen	• Quick turnaround times • Antigen testing useful early in disease progression	• Cross-reactivity • Sensitivity dependent on host immune status and disease course
Molecular 	• Quick turnaround times	• Not widely available • Few performance-related studies

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Molecular	• Quick turnaround times	• Not widely available • Few performance-related studies
Culture	• Highly specific	• Long turnaround times • Requires invasive procedures • Personnel training • Specialized facilities
Histopathology 	• Highly specific • Relatively quick turnaround times	• Requires invasive procedures • Personnel training

Test performance varies based on specimen, disease course, and immune status

Sensitivities and specificities of histoplasmosis diagnostic tests

Test	Sensitivity	Specificity	Population Studied
Antigen tests			
EIA Urine antigen[7]	79%	99%	Adult population, people living with HIV
EIA Serum antigen[7]	82%	97%	Adult population, people living with HIV
Antibody tests			
EIA antibody[8]	98%	97% (high cross-reactivity with *Blastomyces*)	Immunocompromised & healthy populations
Complement fixation (CF) antibody[9,10]	66%–95%	70%–80%	Adult populations
Immunodiffusion (ID) antibody[9,10]	63%–95%	100%	Adult populations
Other tests			
Culture[11]	15%–85%	100%	Acute or subacute, disseminated disease
Microscopy/histopathology[11]	9%–43%	100%	Acute or subacute, disseminated disease

Self-knowledge Check

Blastomycosis, coccidioidomycosis, and histoplasmosis are most often diagnosed by:

A. Primary Care Providers
B. Infectious Disease Physicians
C. Urgent Care Providers
D. A and B
E. A and C

Self-knowledge Check

The correct answer is: B

Most blastomycosis, coccidioidomycosis, and histoplasmosis diagnoses are made by pulmonologists and infectious disease physicians

Impact of underdiagnosis

Unresolved illness, repeat healthcare visits

23–38 days (median time between seeking healthcare and diagnosis)

Benedict K, Ireland M, Weinberg MP, Gruninger R, Weigand J, Chen L, et al. Enhanced Surveillance for Coccidioidomycosis, 14 U.S. States, 2016. *Emerging Infectious Diseases*. 2018 Aug; 24(8).
Alpern JD, Bahr NC, Vazquez-Benitez G, Boulware DR, Sellman JS, Sarosi GA. Diagnostic Delay and Antibiotic Overuse in Acute Pulmonary Blastomycosis. *Open Forum Infect Dis*. 2016 Apr 19;3(2):ofw078.
Benedict K, McCracken S, Signs K, Ireland M, Amburgey V, et al. Enhanced Surveillance for Histoplasmosis–9 States, 2018–2019 . *Open Forum Infect Dis*. 2020 Sept; 7(9):ofaa343.

Unresolved illness, repeat healthcare visits

23–38 days (median time between seeking healthcare and diagnosis)

56%–70% receive **another diagnosis** before being tested for an endemic fungal infection

Benedict K, Ireland M, Weinberg MP, Gruninger R, Weigand J, Chen L, et al. Enhanced Surveillance for Coccidioidomycosis, 14 U.S. States, 2016. *Emerging Infectious Diseases*. 2018 Aug; 24(8).
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Unresolved illness, repeat healthcare visits

23–38 days (median time between seeking healthcare and diagnosis)

56%–70% receive **another diagnosis** before being tested for an endemic fungal infection

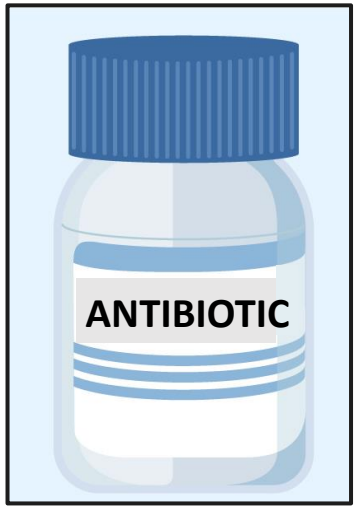
54%–60% see provider **≥3 times** before tested for an endemic fungal infection

Benedict K, Ireland M, Weinberg MP, Gruninger R, Weigand J, Chen L, et al. Enhanced Surveillance for Coccidioidomycosis, 14 U.S. States, 2016. *Emerging Infectious Diseases*. 2018 Aug; 24(8).
Alpern JD, Bahr NC, Vazquez-Benitez G, Boulware DR, Sellman JS, Sarosi GA. Diagnostic Delay and Antibiotic Overuse in Acute Pulmonary Blastomycosis. *Open Forum Infect Dis*. 2016 Apr 19;3(2):ofw078.
Benedict K, McCracken S, Signs K, Ireland M, Amburgey V, et al. Enhanced Surveillance for Histoplasmosis–9 States, 2018–2019 . *Open Forum Infect Dis*. 2020 Sept; 7(9):ofaa343.

Overuse of unnecessary antibiotics

>50% receive **antibiotics** before diagnosis of histoplasmosis or coccidioidomycosis

Most patients receive **≥2** rounds of **antibiotics** before being tested for an endemic fungal infection



Chi GC, Benedict K, Beer KD, Jackson B, et al. Antibiotic and antifungal treatment among persons with confirmed coccidioidomycosis – Southern California, 2011. *Medical Mycology.* 2020, 58, 411–413. doi: 10.1093/mmy/myz073

Alpern JD, Bahr NC, Vazquez-Benitez G, Boulware DR, Sellman JS, Sarosi GA. Diagnostic Delay and Antibiotic Overuse in Acute Pulmonary Blastomycosis. *Open Forum Infect Dis*. 2016 Apr 19;3(2):ofw078.

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Limits accurate surveillance

- Hinders the true understanding of disease epidemiology, with downstream effects on messaging and risk mitigation

Resources are needed to improve provider awareness and testing practices to promote early diagnosis

Diagnostic algorithms

Diagnostic algorithms were developed

In partnership with the Mycoses Study Group, CDC created diagnostic algorithms for blastomycosis, coccidioidomycosis, and histoplasmosis in patients with CAP to:

- **Increase levels of testing**, particularly among primary care and outpatient providers

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- Aid in the **accurate interpretation** of diagnostic test results

Diagnostic algorithms were developed

In partnership with the Mycoses Study Group, CDC created diagnostic algorithms for blastomycosis, coccidioidomycosis, and histoplasmosis in patients with CAP to:

- **Increase levels of testing**, particularly among primary care and outpatient providers
- Aid in the **accurate interpretation** of diagnostic test results
- Offer a **standard** diagnostic approach for the endemic mycoses

Focus on improving awareness and testing among primary care and outpatient providers

Considerable testing gap for patients presenting with CAP between primary care providers and infectious disease physicians

	Primary care providers Test sometimes or frequently	**Infectious disease physicians** Test sometimes or frequently
Coccidioidomycosis	19%	36%
Histoplasmosis	22%	58%

Open Forum Infectious Diseases, Volume: 8, Issue: 2, First published: 18 January 2021, DOI: (10.1093/ofid/ofab020)
Journal of Fungi, Volume: 7, Issue: 8, First published 27 July 2021, DOI: (10.3390/jof7080605)

Focus on improving awareness and testing among primary care and outpatient providers

Clinician Practice Patterns That Result in the Diagnosis of Coccidioidomycosis Before or During Hospitalization

Jie Pu, Fariba M Donovan, Kate Ellingson, Gondy Leroy, Jeff Stone, Edward Bedrick, John N Galgiani ✉

Clinical Infectious Diseases, ciaa739, https://doi.org/10.1093/cid/ciaa739

- **Less than one-third** of new diagnoses occurred outside the hospital
  - 73% of during hospitalization
  - Only 22% at ambulatory clinics, 3% in emergency departments, and 0.5% in urgent care

Focus on improving awareness and testing among primary care and outpatient providers, continued

Enhanced Surveillance for Histoplasmosis—9 States, 2018–2019

Kaitlin Benedict ✉, Stephanie McCracken, Kimberly Signs, Malia Ireland, Victoria Amburgey, Jose Antonio Serrano, Natalie Christophe, Suzanne Gibbons-Burgener, Sara Hallyburton, Kimberly A Warren, Alison Keyser Metobo, Racheal Odom, Matthew R Groenewold, Brendan R Jackson

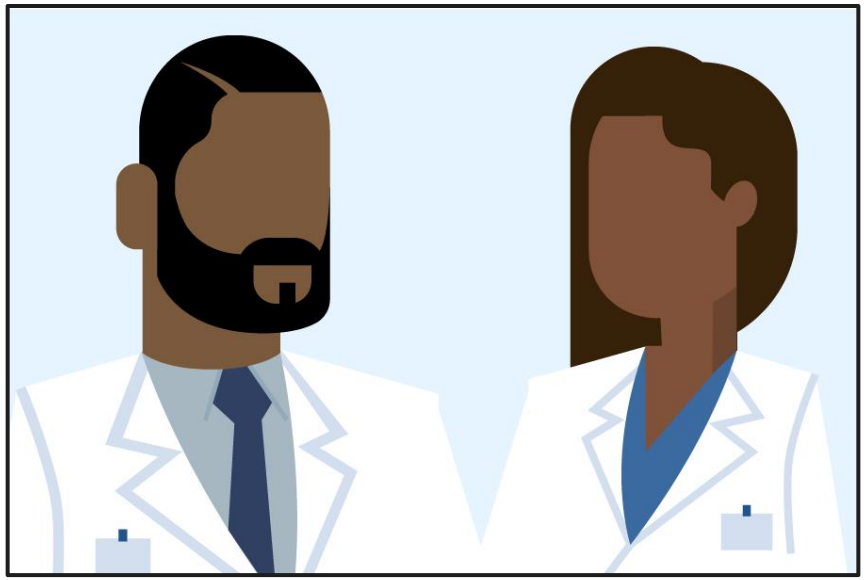
Author Notes

Open Forum Infectious Diseases, Volume 7, Issue 9, September 2020, ofaa343,

- **43%** of patients first sought care in a primary care facility
- Primary care providers made up just **11%** of providers who first tested for histoplasmosis

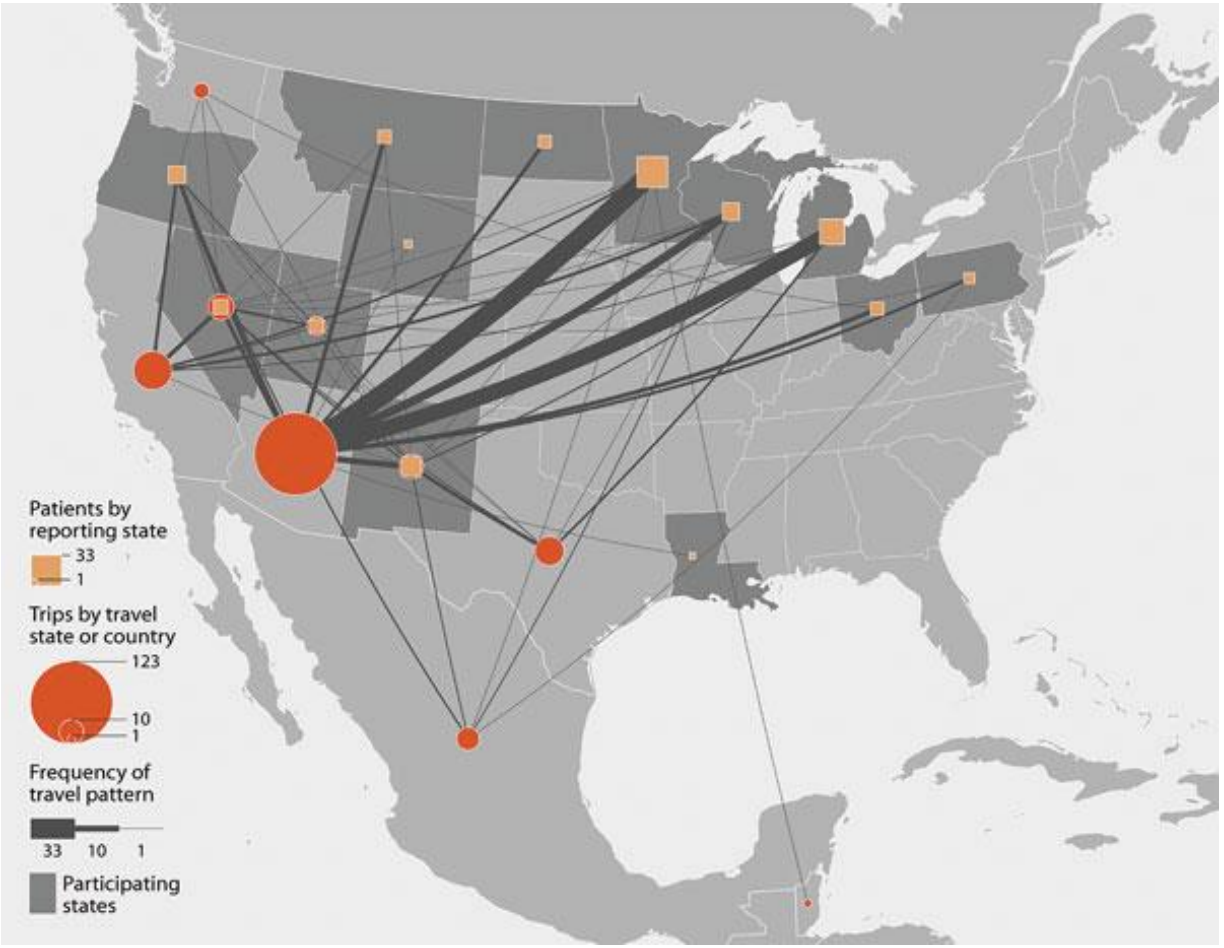
Reach providers across the United States, not just endemic areas

- Providers who live or train in low or non-endemic areas may have less awareness of disease
- Providers may move to practice in endemic areas



Travel-associated infections occur regularly

Reported cases of coccidioidomycosis related to travel, 2016



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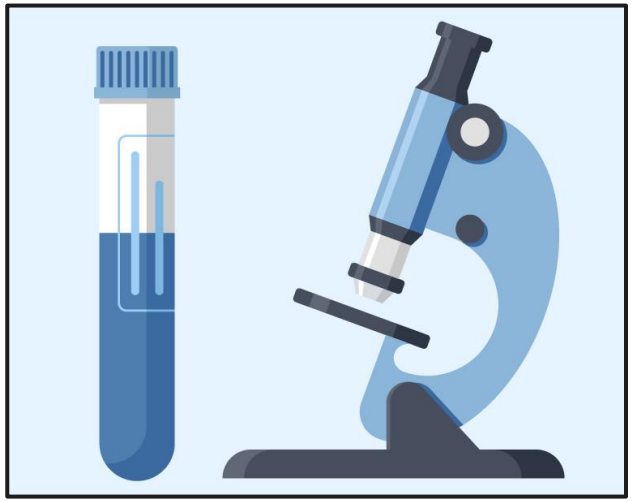
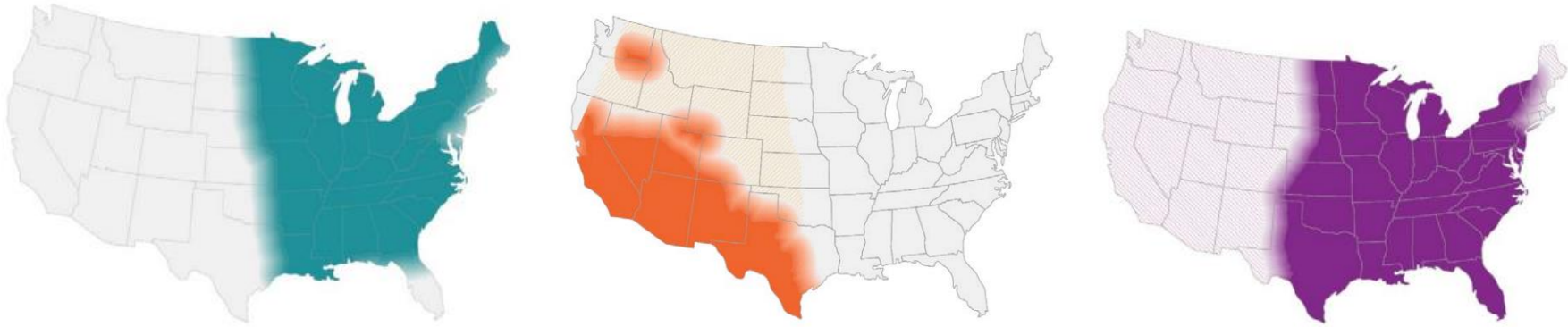
Algorithm development process

1. In consultation with experts, reviewed performance characteristics of available diagnostic tests
2. Synthesized learnings into a draft diagnostic algorithms
3. Presented to specialty groups and experts both within and external to CDC to solicit feedback
4. Revised algorithms accordingly and finalized



Consideration for testing

Patient living in or having traveled to a disease endemic area
(although note that the disease can also occur at lower levels worldwide)



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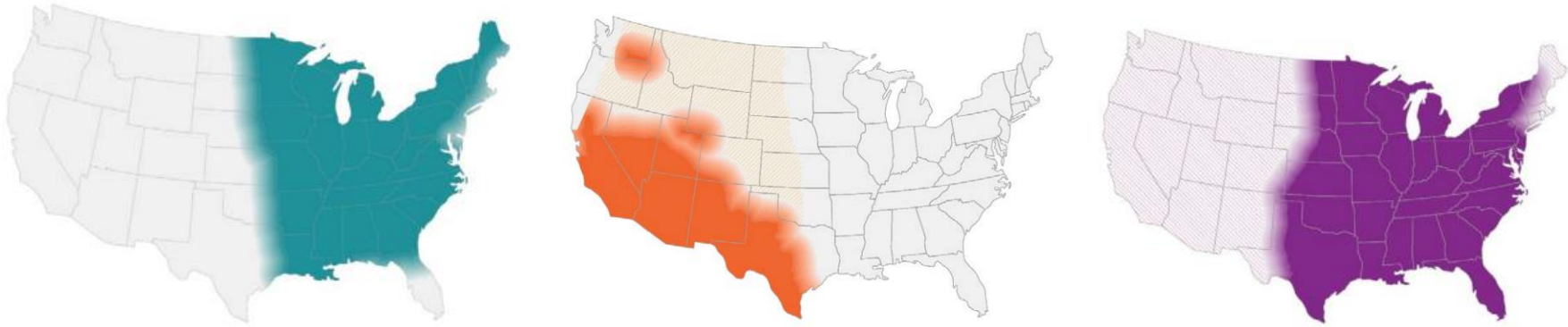

CAP of unknown etiology not responding to a course of empiric antibiotics

Consideration for testing

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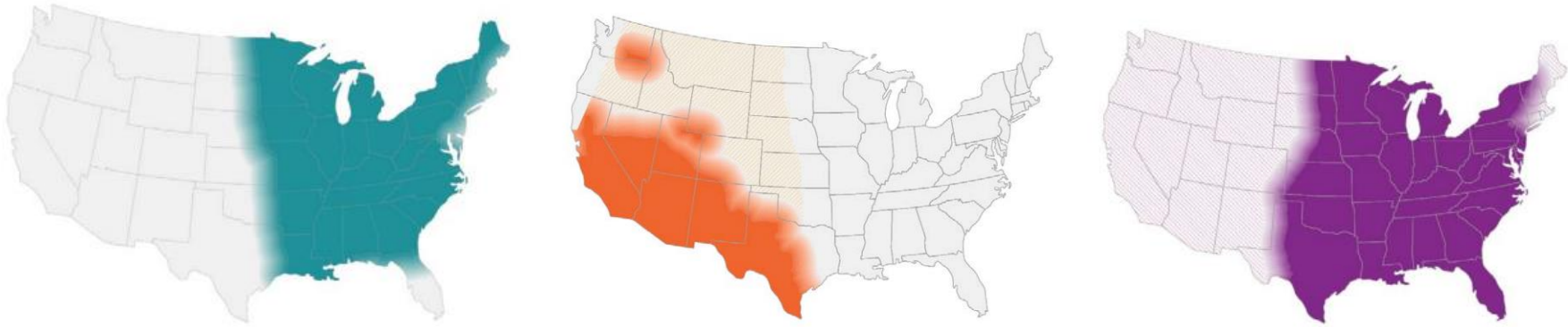

AND

Consideration for testing

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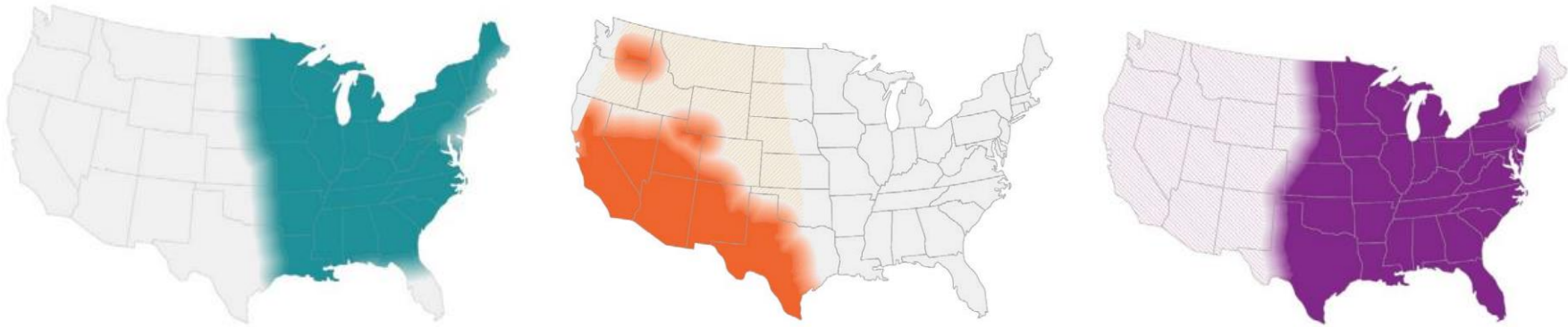


Blastomycosis

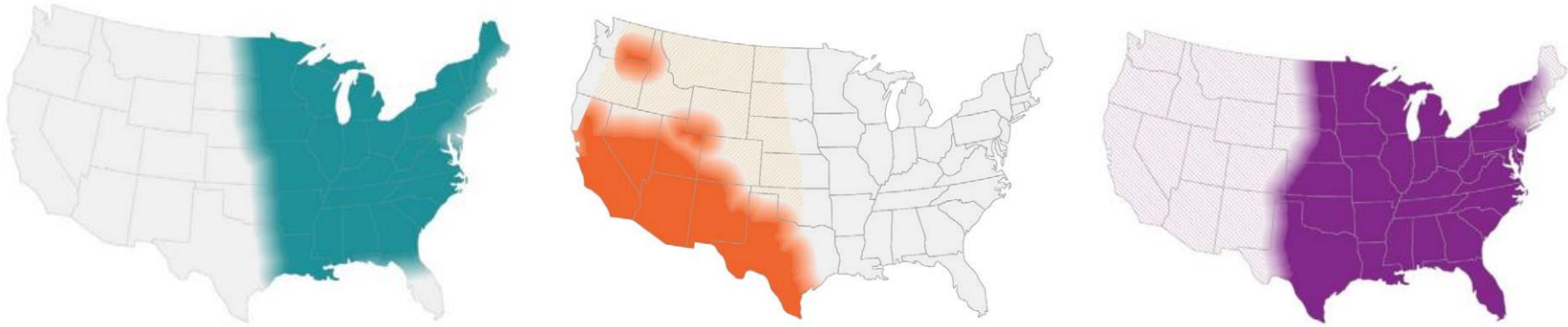
Initial CAP visit if:

- **Skin lesions present* OR**
- **Link to known blastomycosis outbreak**

***Skin lesions could be indicative of late disease or traumatic inoculation rather than acute pulmonary blastomycosis**

Consideration for testing

Patient living in or having traveled to a disease endemic area
(although note that the disease can also occur at lower levels worldwide)



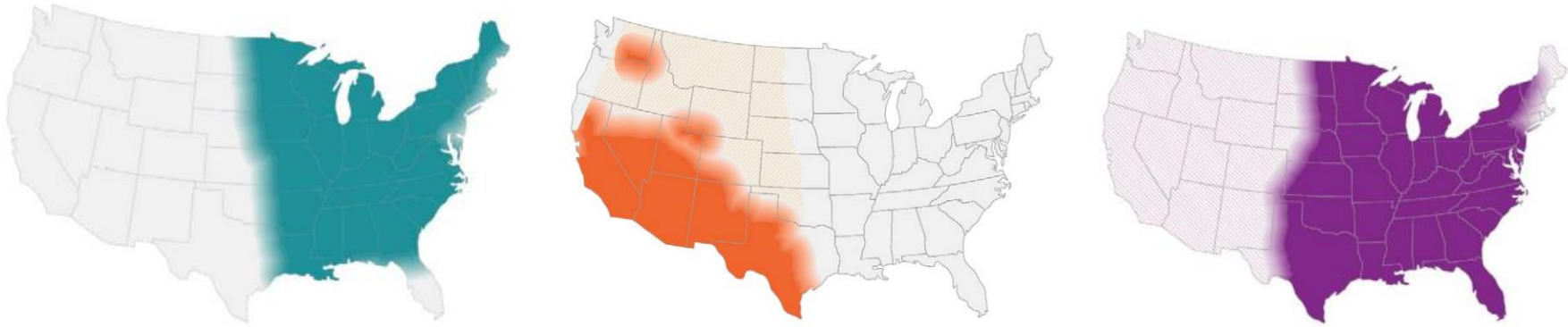
Coccidioidomycosis

Initial presentation of CAP (or erythema nodosum in the setting of recent respiratory symptoms if people have:

- **Lived in or traveled to the highly endemic desert regions of Arizona (i.e., South-Central Arizona) or the San Joaquin Valley of California OR**
- **Link to known coccidioidomycosis outbreak**

Consideration for testing

Patient living in or having traveled to a disease endemic area
(although note that the disease can also occur at lower levels worldwide)



Histoplasmosis

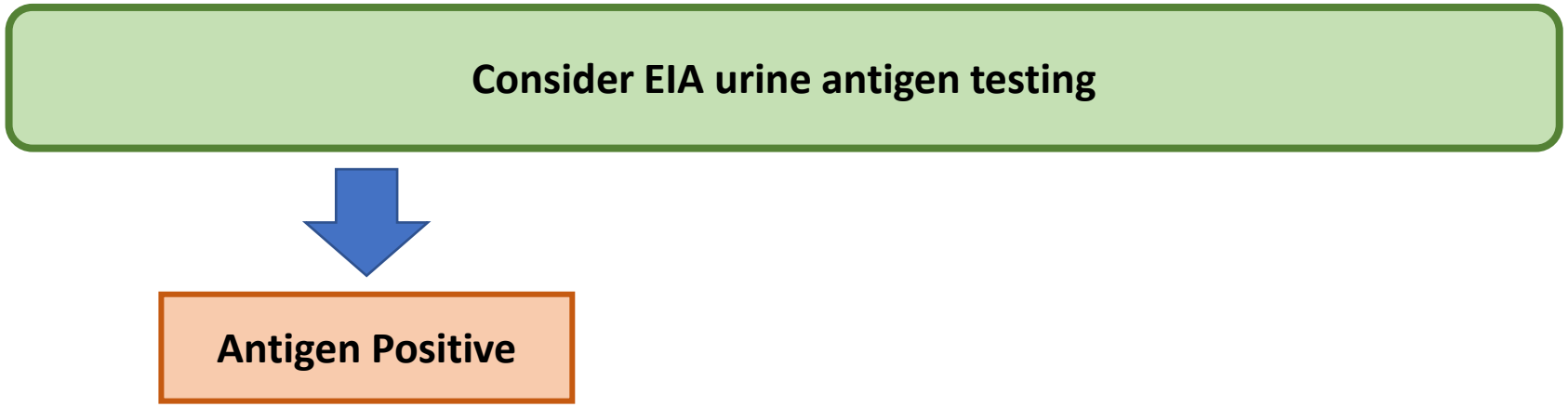
Initial CAP visit if:

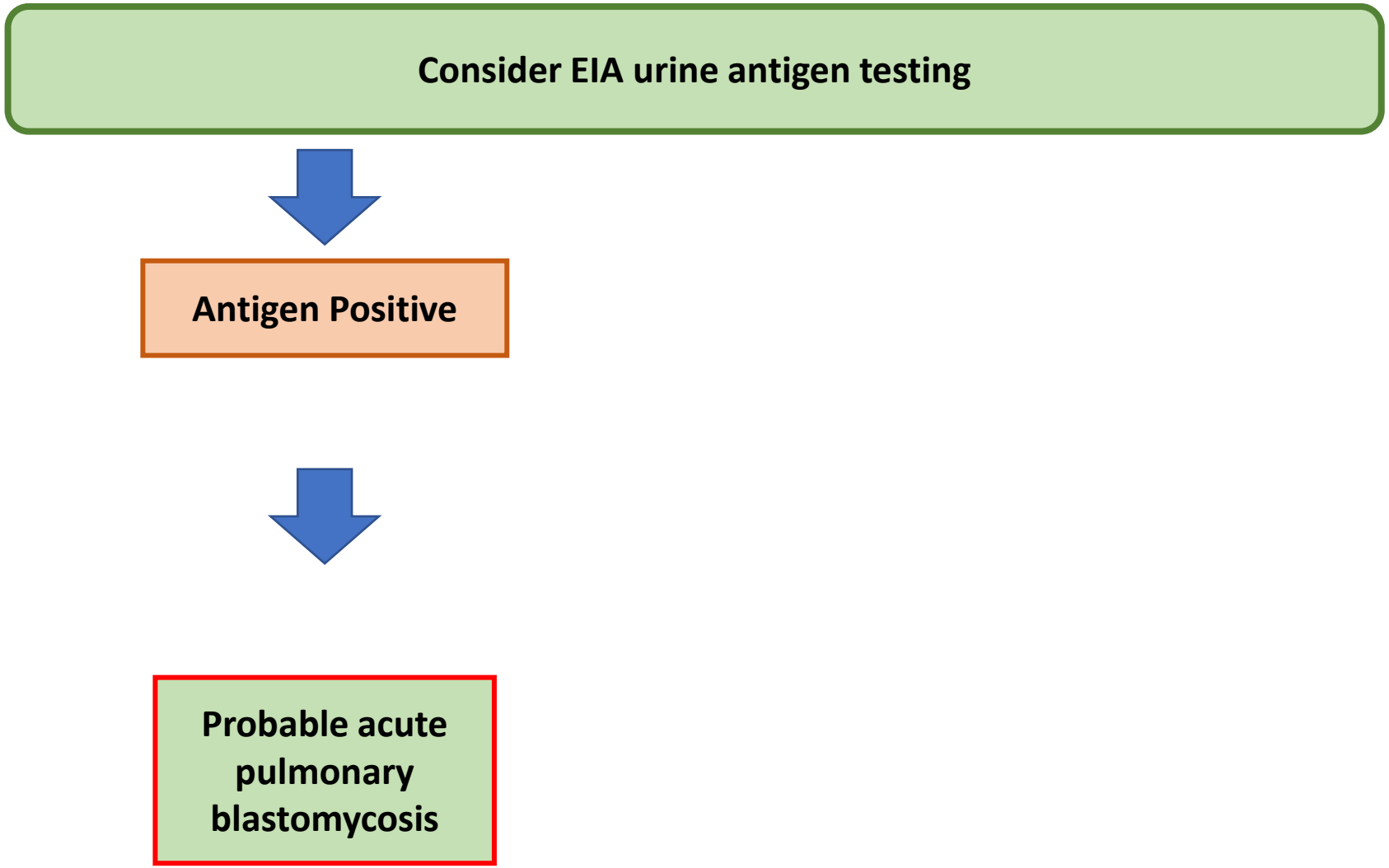
- **Notable exposure to bird or bat droppings (cave or demolition/ remodeling exposure; note that many patients do not recall a specific exposure) OR**
- **Chest x-ray showing new nodules or lymphadenopathy OR**
- **Link to known histoplasmosis outbreak**

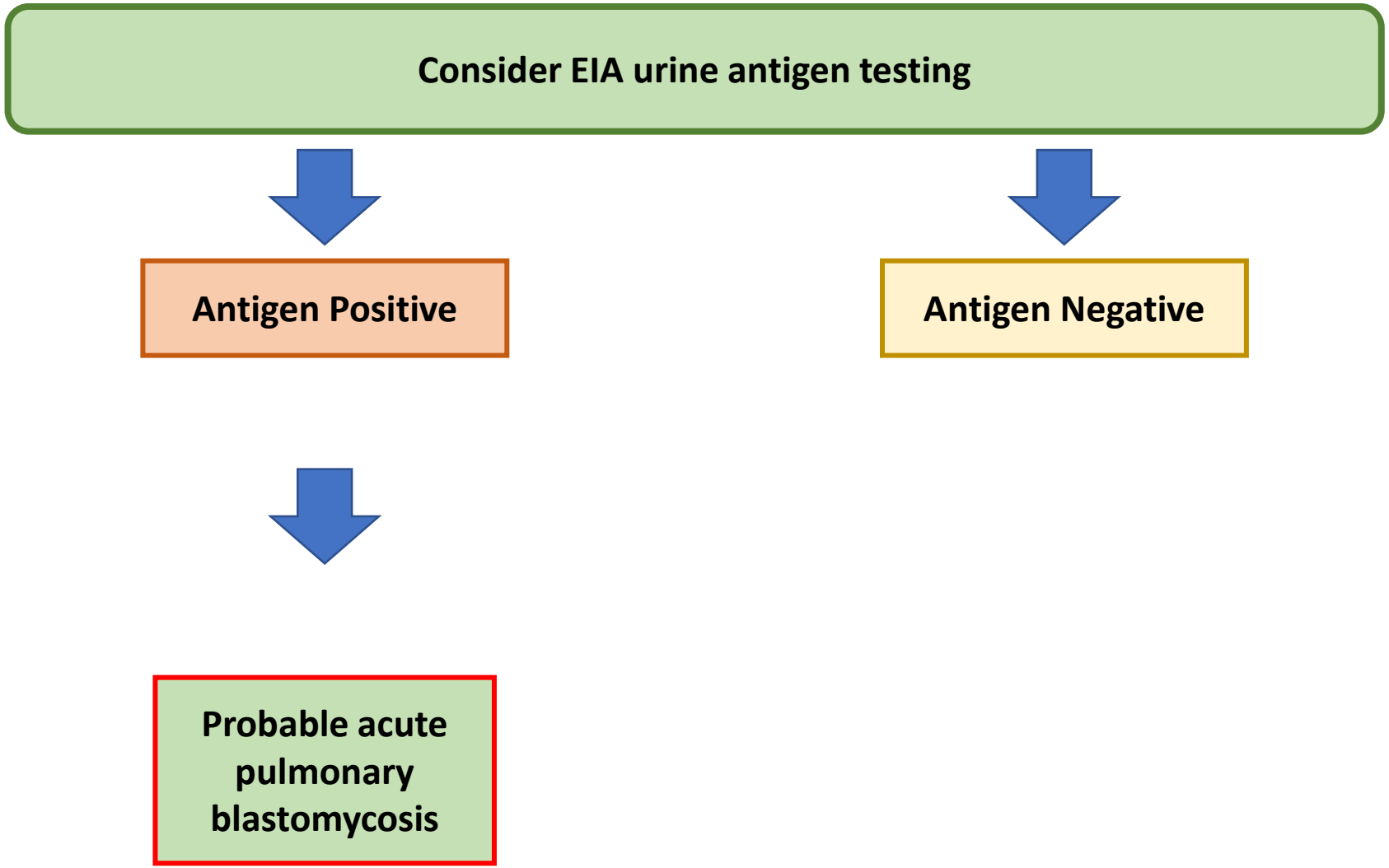
Blastomycosis Algorithm

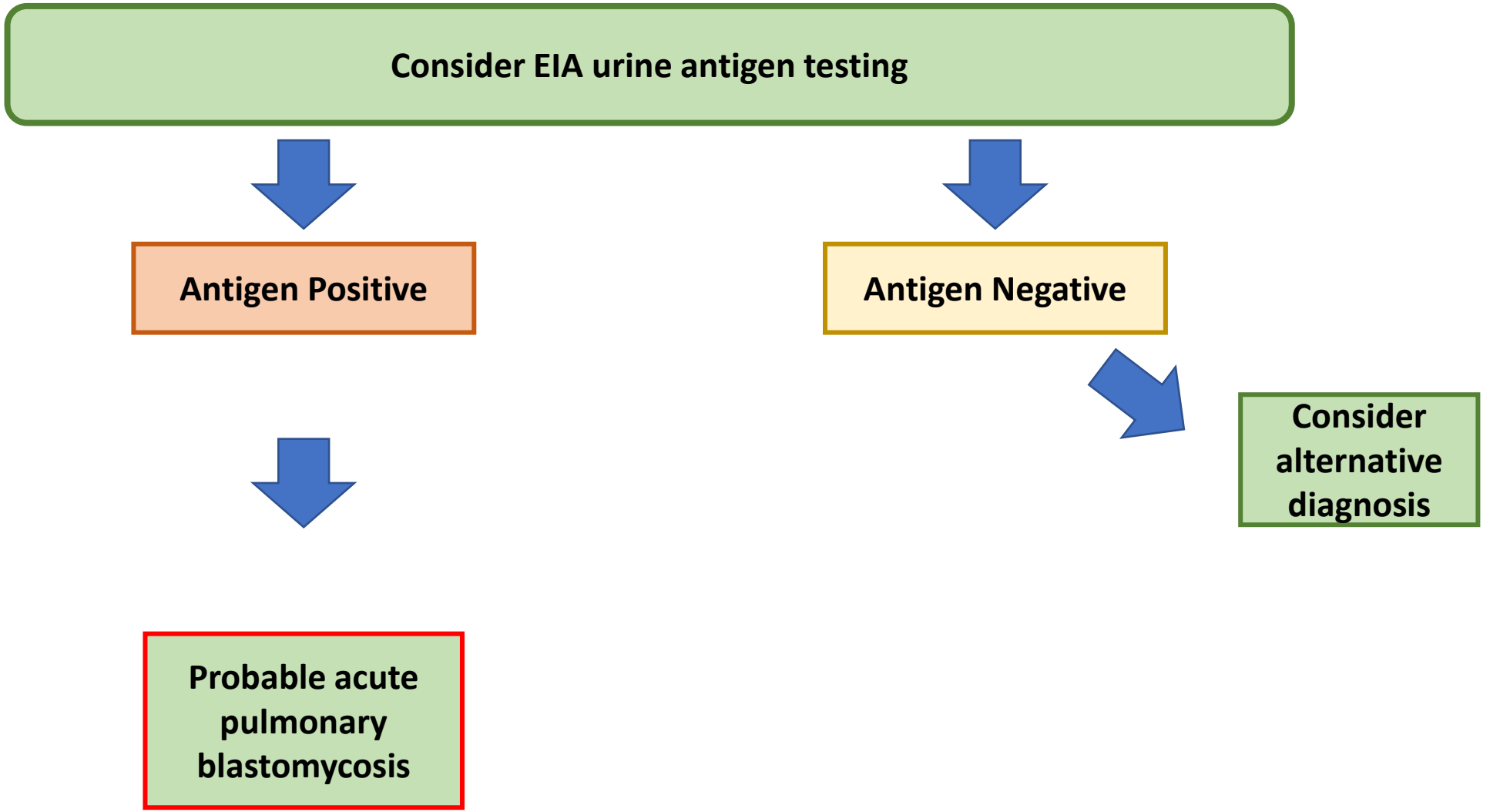
Consider EIA urine antigen testing

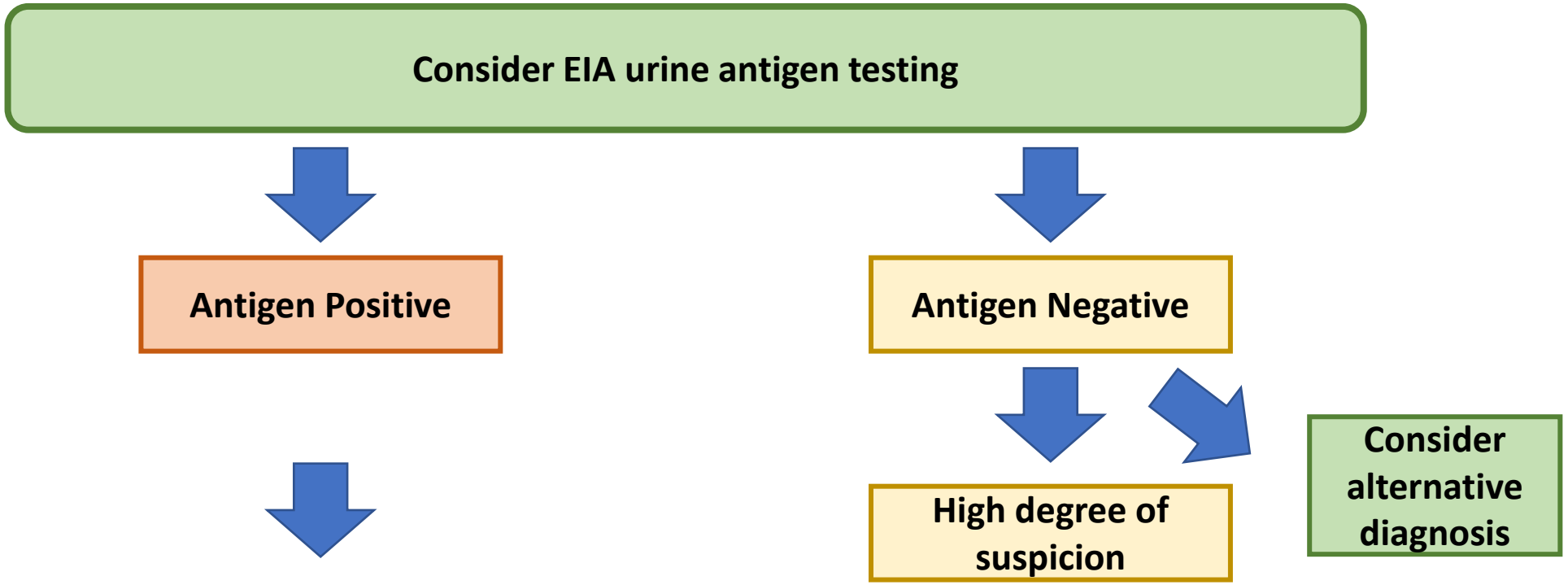
EIA = enzyme immunoassay

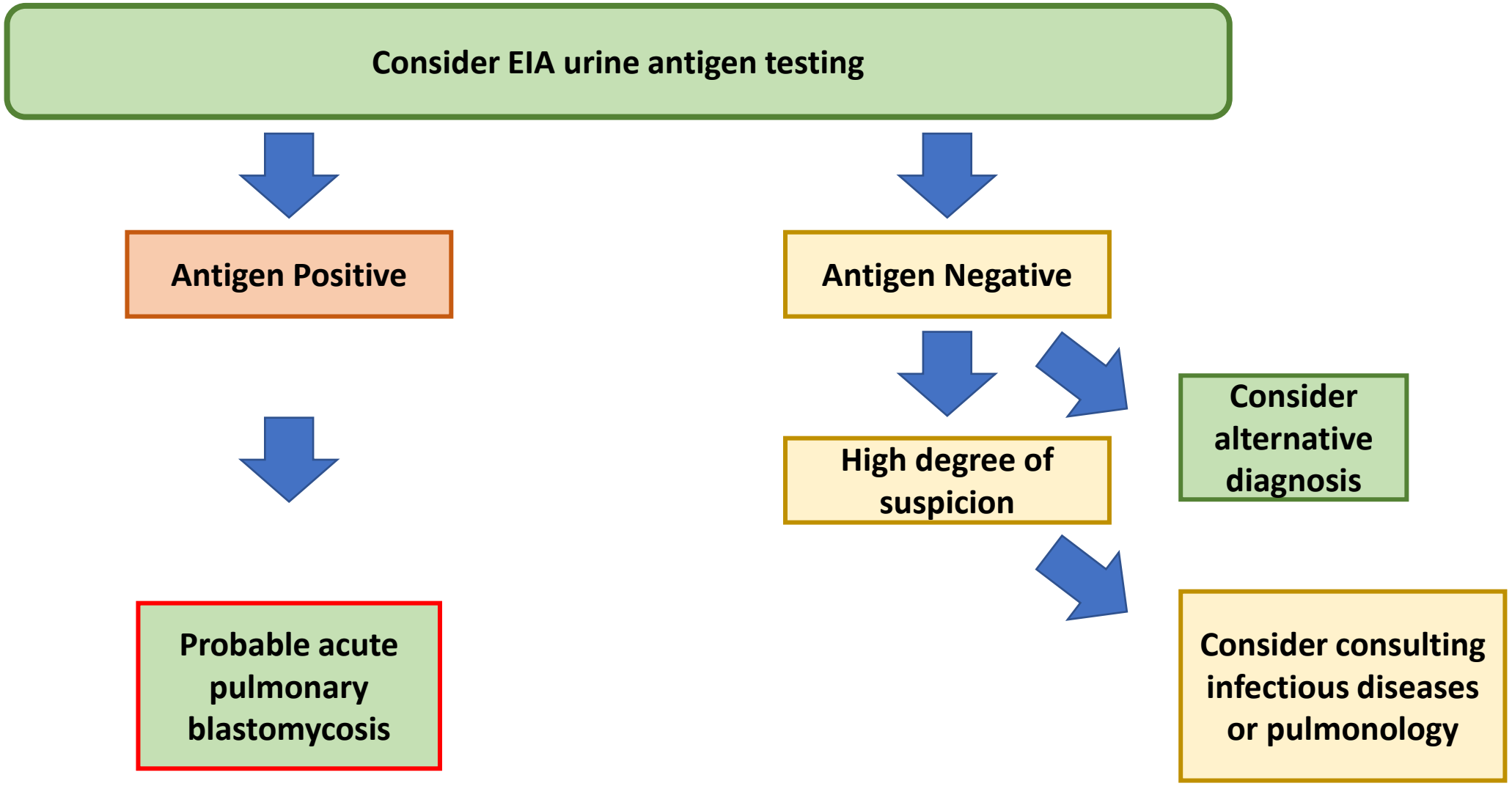

Consider EIA urine antigen testing
Antigen Positive

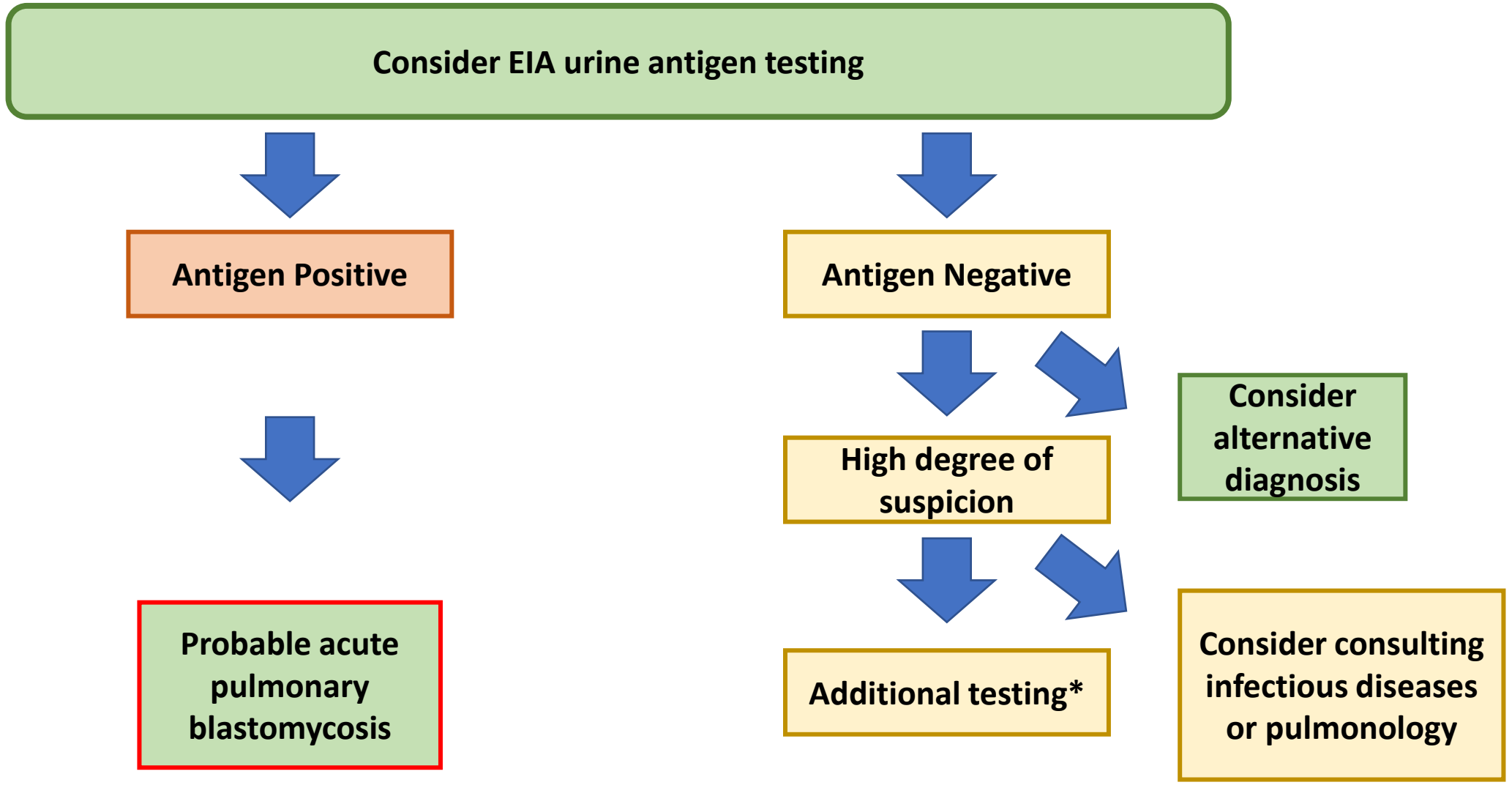

Consider EIA urine antigen testing
Antigen Positive
Probable acute pulmonary blastomycosis


Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
Probable acute pulmonary blastomycosis

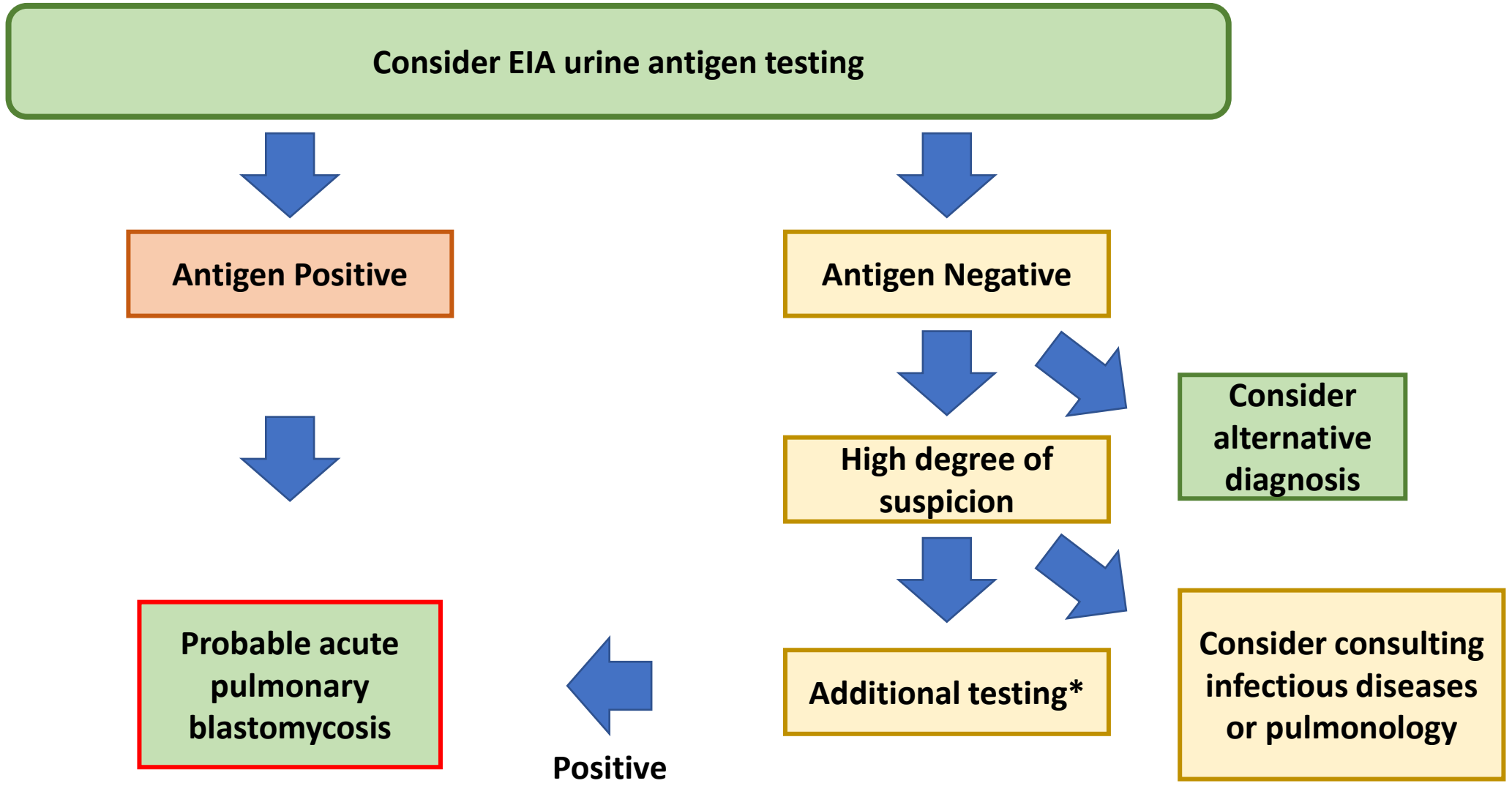

Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
Consider alternative diagnosis
Probable acute pulmonary blastomycosis

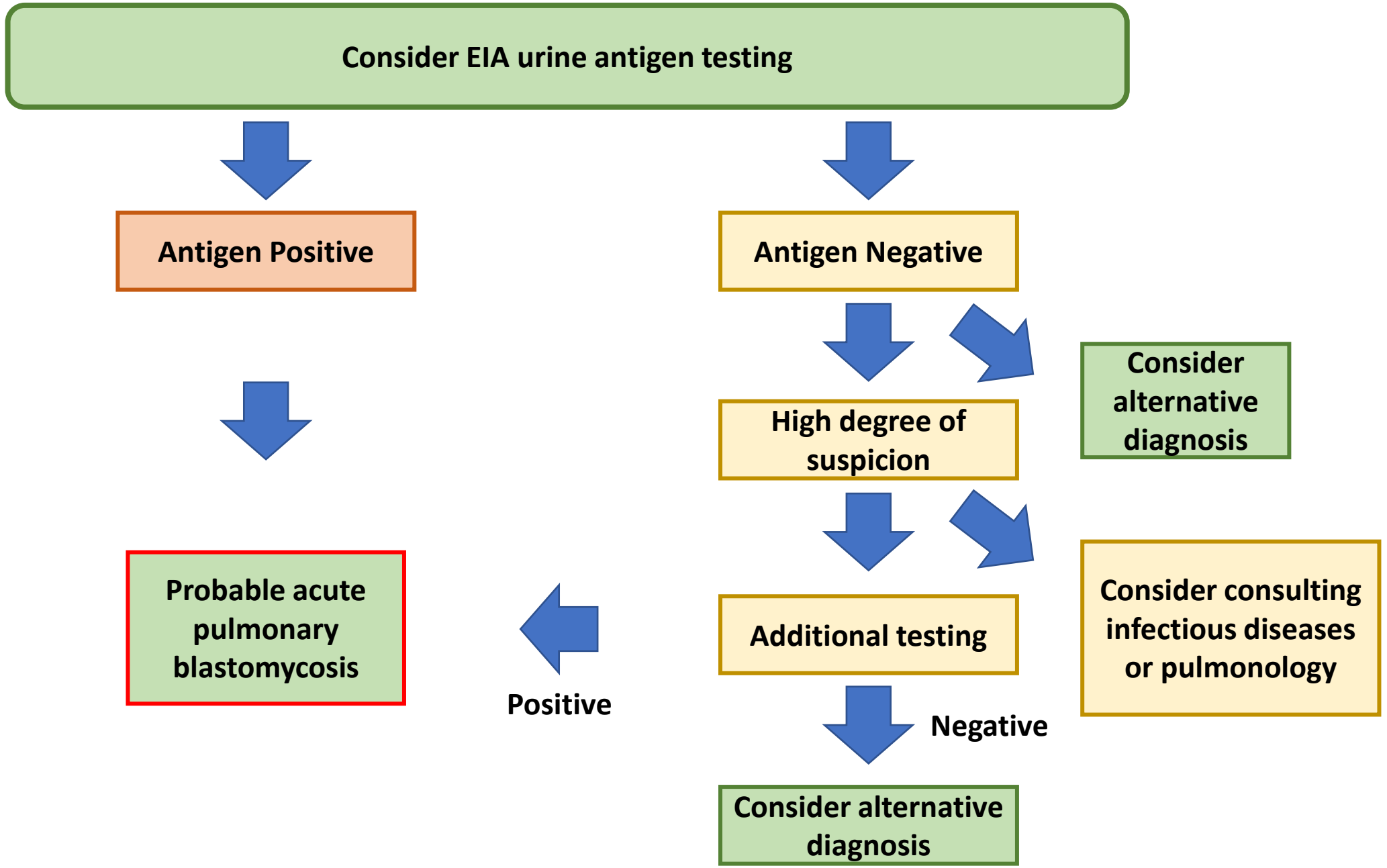

Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
High degree of suspicion
Consider alternative diagnosis
Probable acute pulmonary blastomycosis


Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
Probable acute pulmonary blastomycosis
High degree of suspicion
Consider alternative diagnosis
Consider consulting infectious diseases or pulmonology



*Sputum or bronchoalveolar lavage culture and microscopy, skin biopsy (if lesion exists), serologic antibody testing


Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
High degree of suspicion
Consider alternative diagnosis
Additional testing*
Consider consulting infectious diseases or pulmonology
Positive
Probable acute pulmonary blastomycosis


Consider EIA urine antigen testing
Antigen Positive
Antigen Negative
High degree of suspicion
Consider alternative diagnosis
Additional testing
Consider consulting infectious diseases or pulmonology
Negative
Consider alternative diagnosis
Positive
Probable acute pulmonary blastomycosis

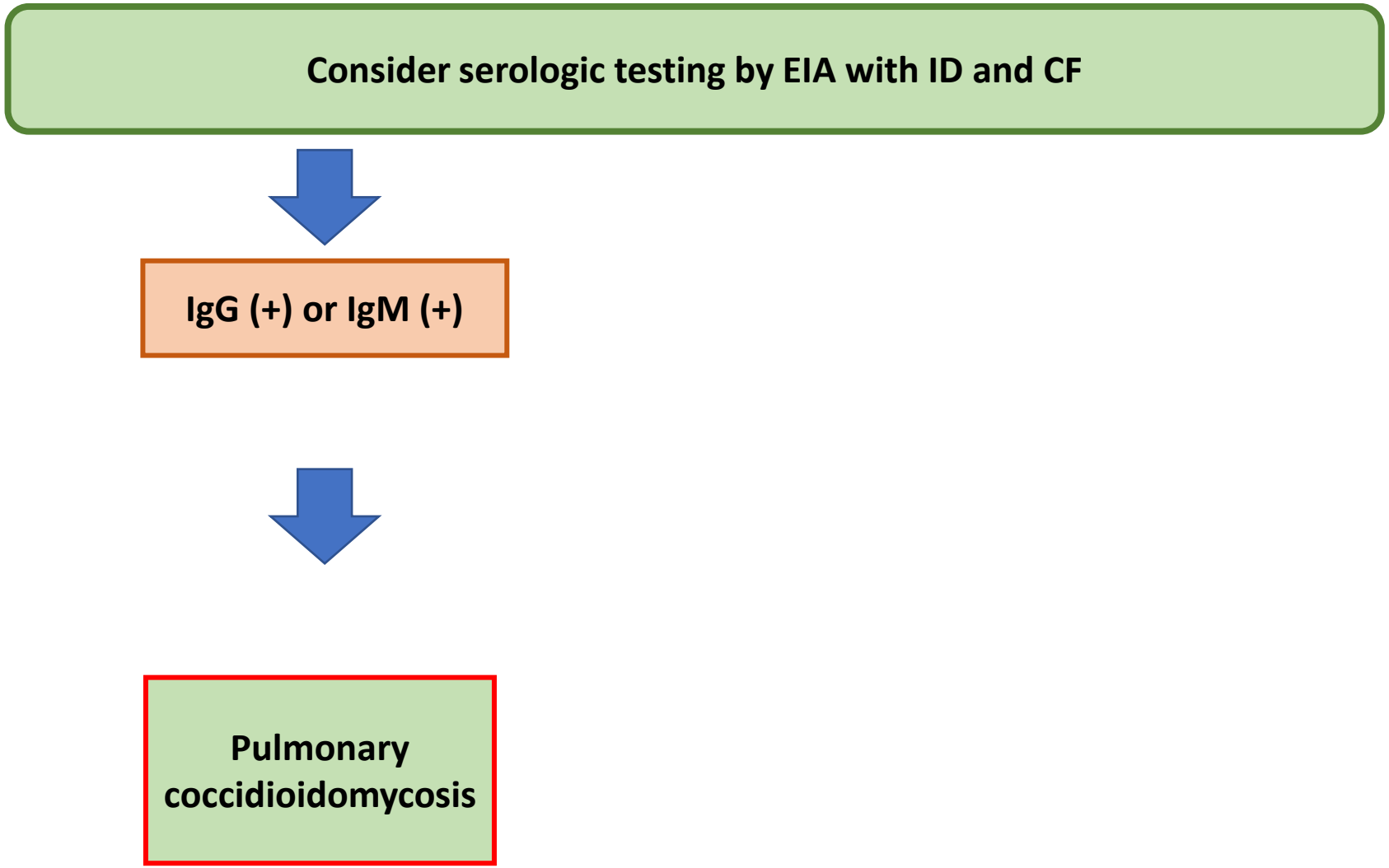
Coccidioidomycosis Algorithm

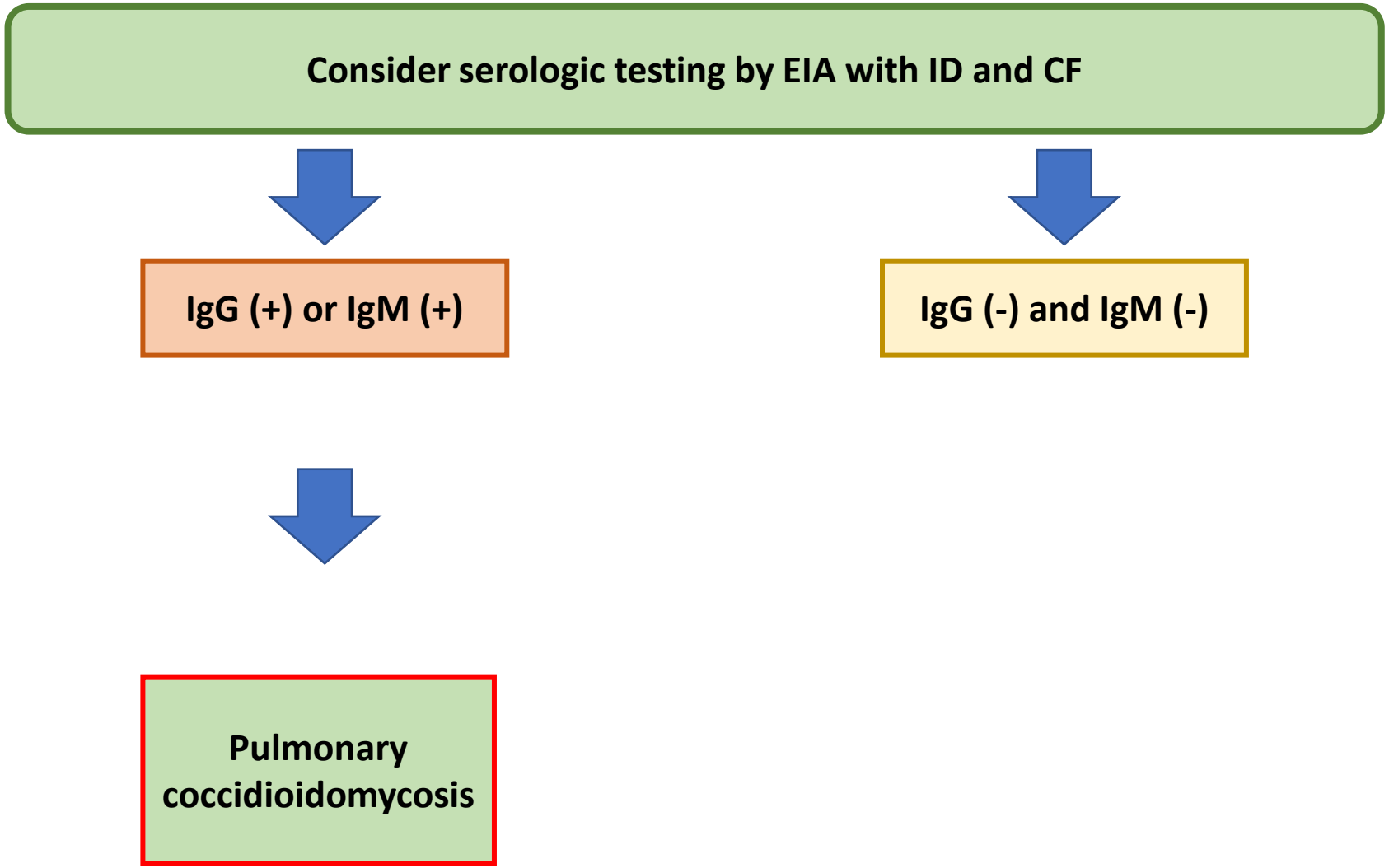
Consider serologic testing by EIA with ID and CF

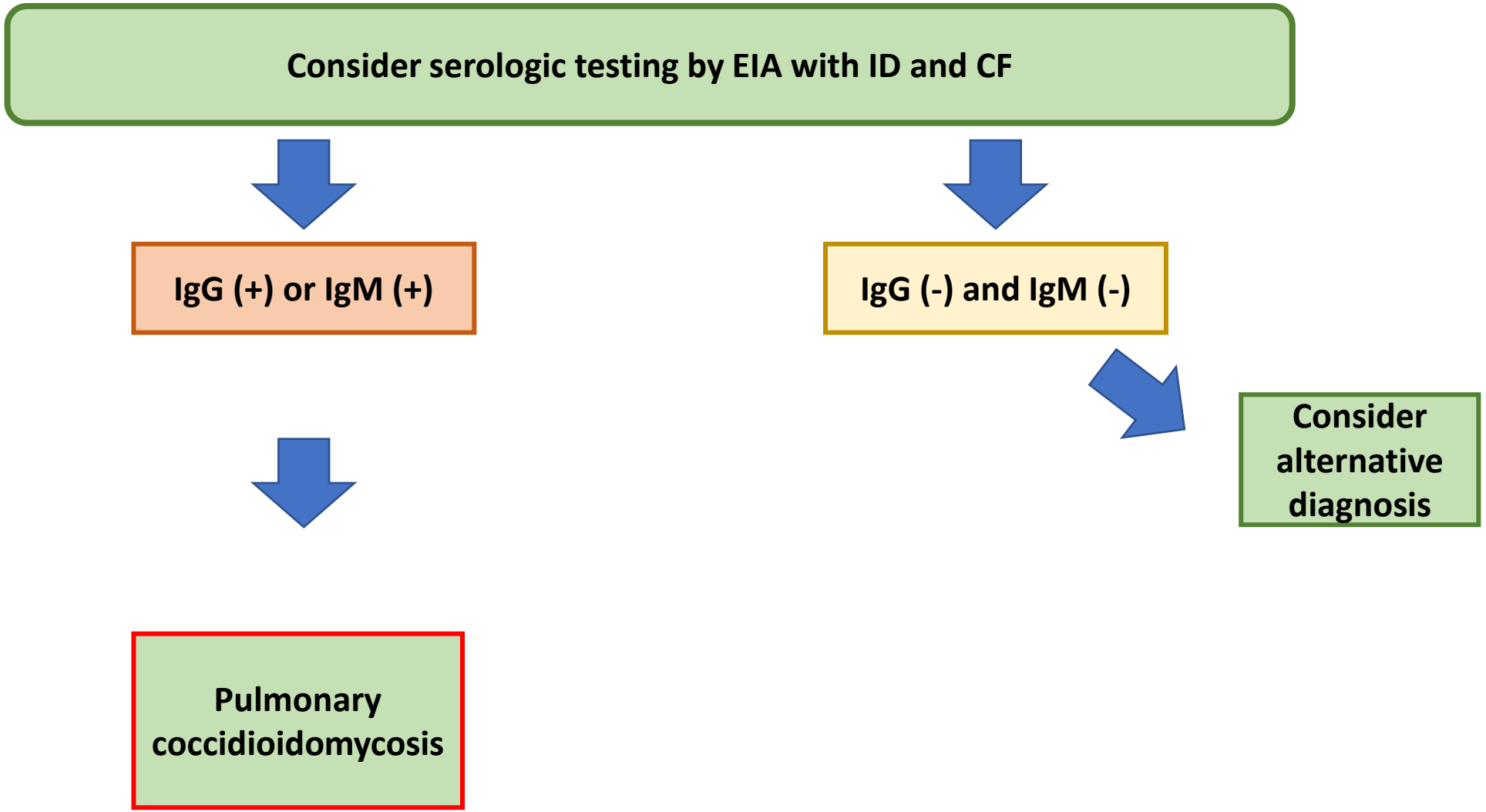
EIA = enzyme immunoassay
ID = immunodiffusion
CF = complement fixation

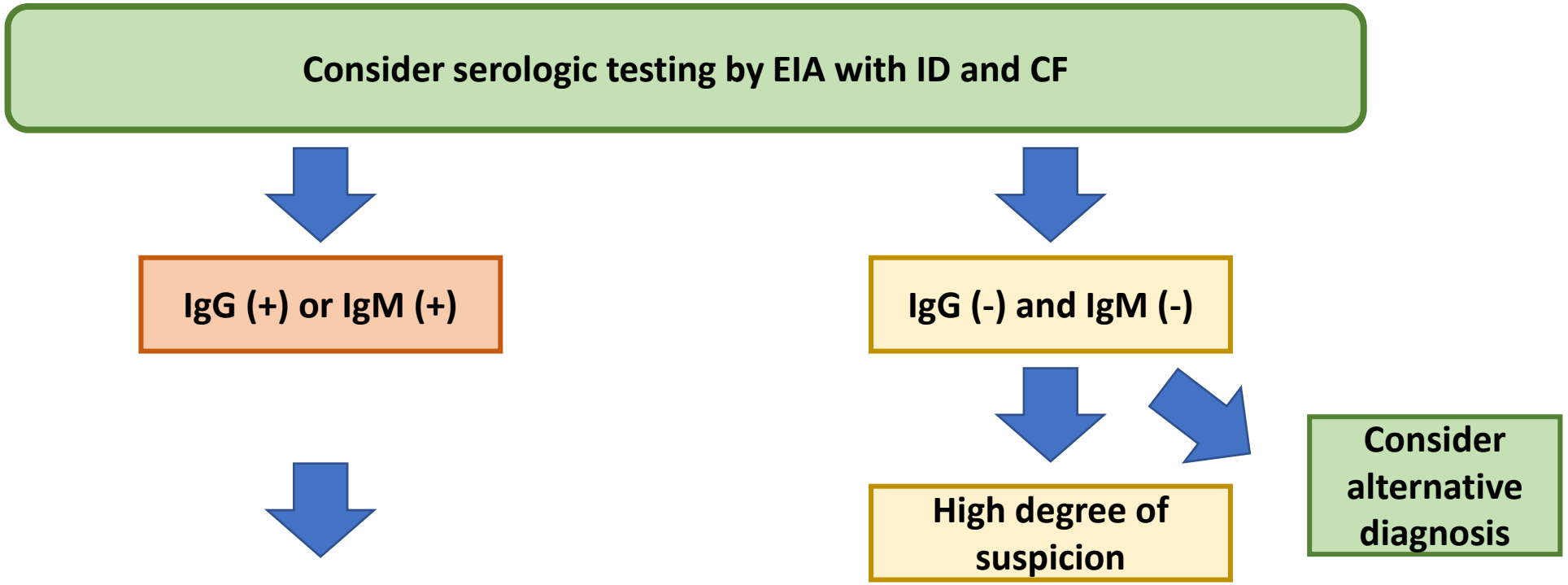
Consider serologic testing by EIA with ID and CF

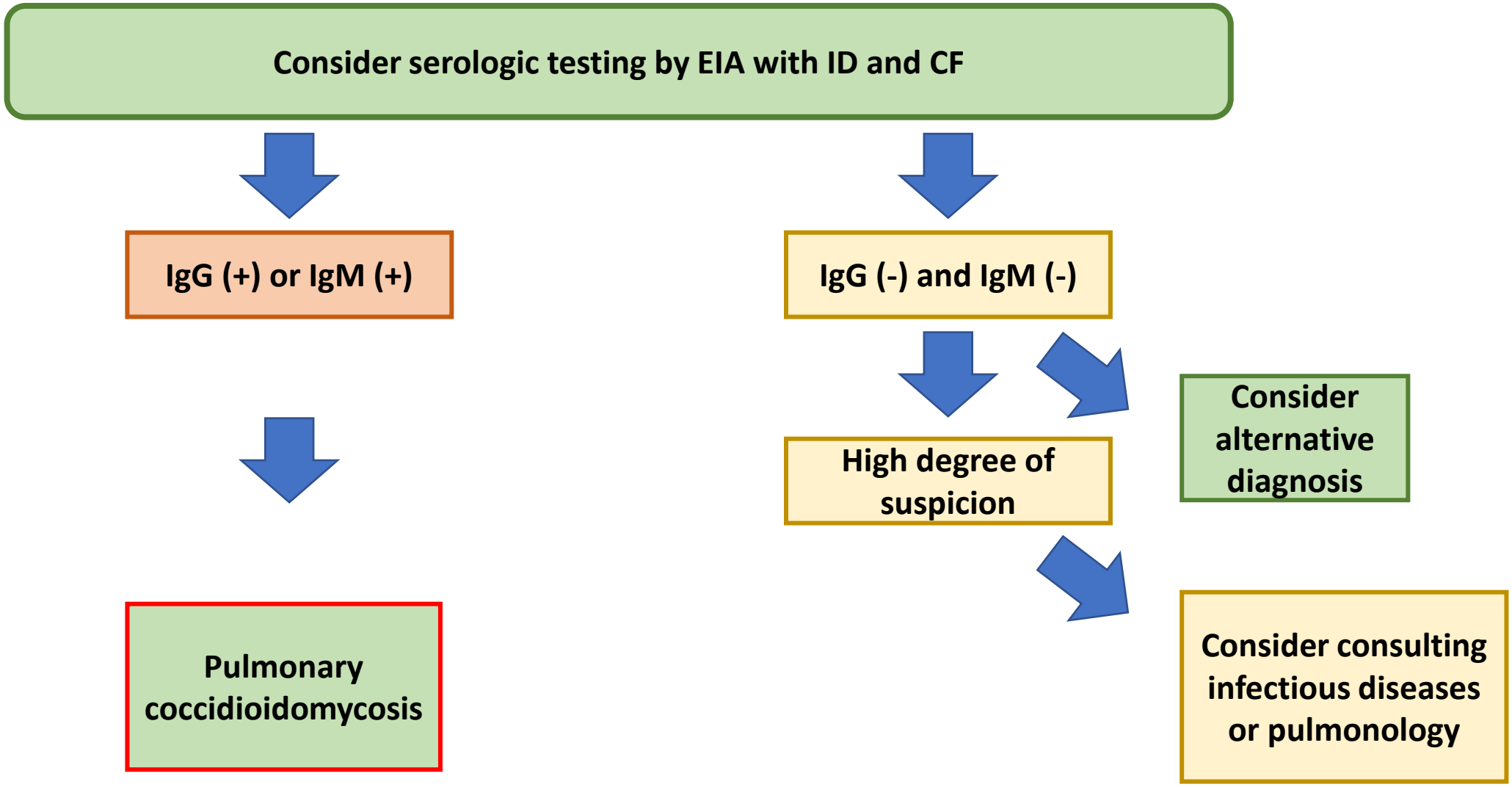
IgG (+) or IgM (+)

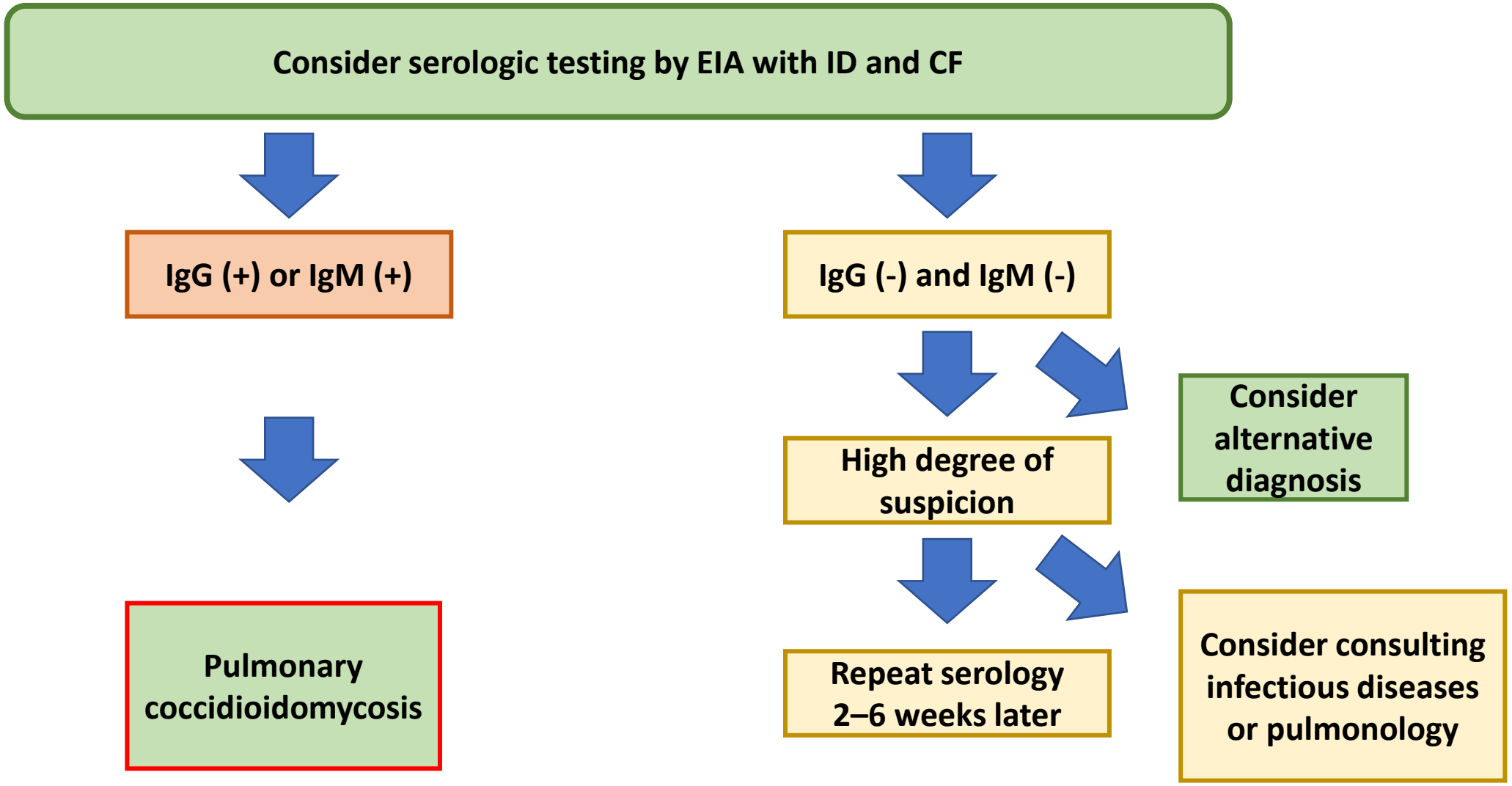

Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
Pulmonary coccidioidomycosis

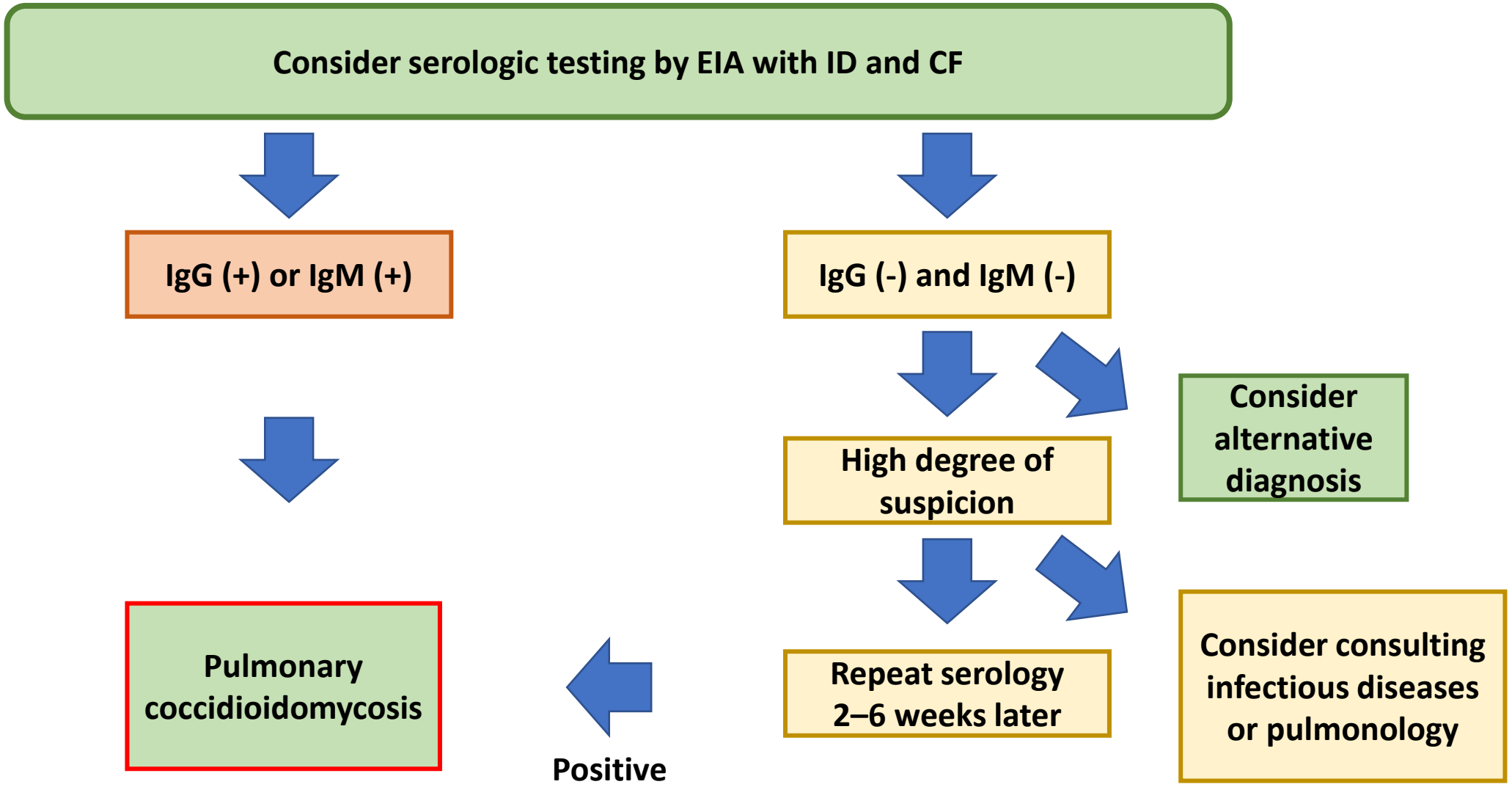

Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
Pulmonary coccidioidomycosis

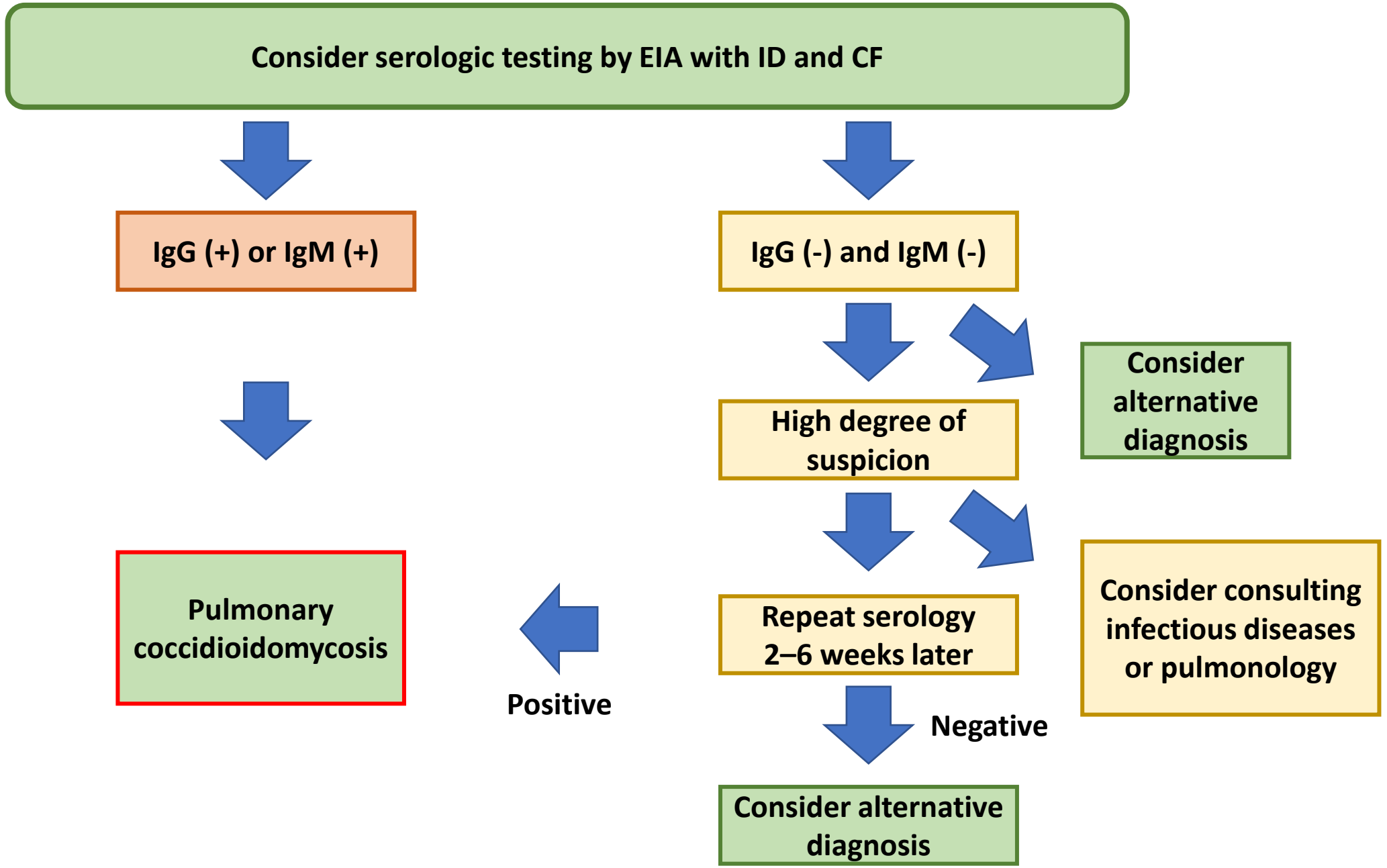

Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
Consider alternative diagnosis
Pulmonary coccidioidomycosis


Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
High degree of suspicion
Consider alternative diagnosis
Pulmonary coccidioidomycosis


Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
High degree of suspicion
Consider alternative diagnosis
Pulmonary coccidioidomycosis
Consider consulting infectious diseases or pulmonology


Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
Pulmonary coccidioidomycosis
IgG (-) and IgM (-)
High degree of suspicion
Consider alternative diagnosis
Repeat serology 2–6 weeks later
Consider consulting infectious diseases or pulmonology


Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
High degree of suspicion
Consider alternative diagnosis
Repeat serology 2–6 weeks later
Consider consulting infectious diseases or pulmonology
Positive
Pulmonary coccidioidomycosis


Consider serologic testing by EIA with ID and CF
IgG (+) or IgM (+)
IgG (-) and IgM (-)
High degree of suspicion
Consider alternative diagnosis
Repeat serology 2–6 weeks later
Consider consulting infectious diseases or pulmonology
Negative
Consider alternative diagnosis
Positive
Pulmonary coccidioidomycosis

Self-knowledge Check

The clinical diagnostic algorithm for coccidioidomycosis recommends which diagnostic test initially?

A. Enzyme immunoassay antibody test
B. Polymerase chain reaction test
C. Immunodiffusion
D. A and C
E. B and C

Self-knowledge Check

- **The correct answer is: D**

- **We recommend ordering an enzyme immunoassay (EIA) antibody test with immunodiffusion (ID) or complement fixation (CF) antibody test initially for coccidioidomycosis diagnosis.**
  - Initial testing with EIA or ID and CF may depend on availability and performance characteristics of test at facility.
  - EIAs have a quicker turnaround time than ID and CF antibody testing.
  - If the EIA is positive, clinicians may consider follow-up testing with ID and CF to rule out false positives and confirm the diagnosis.

Histoplasmosis Algorithm

Consider EIA urine antigen and ID or CF serum antibody testing

EIA = enzyme immunoassay
ID = immunodiffusion
CF = complement fixation

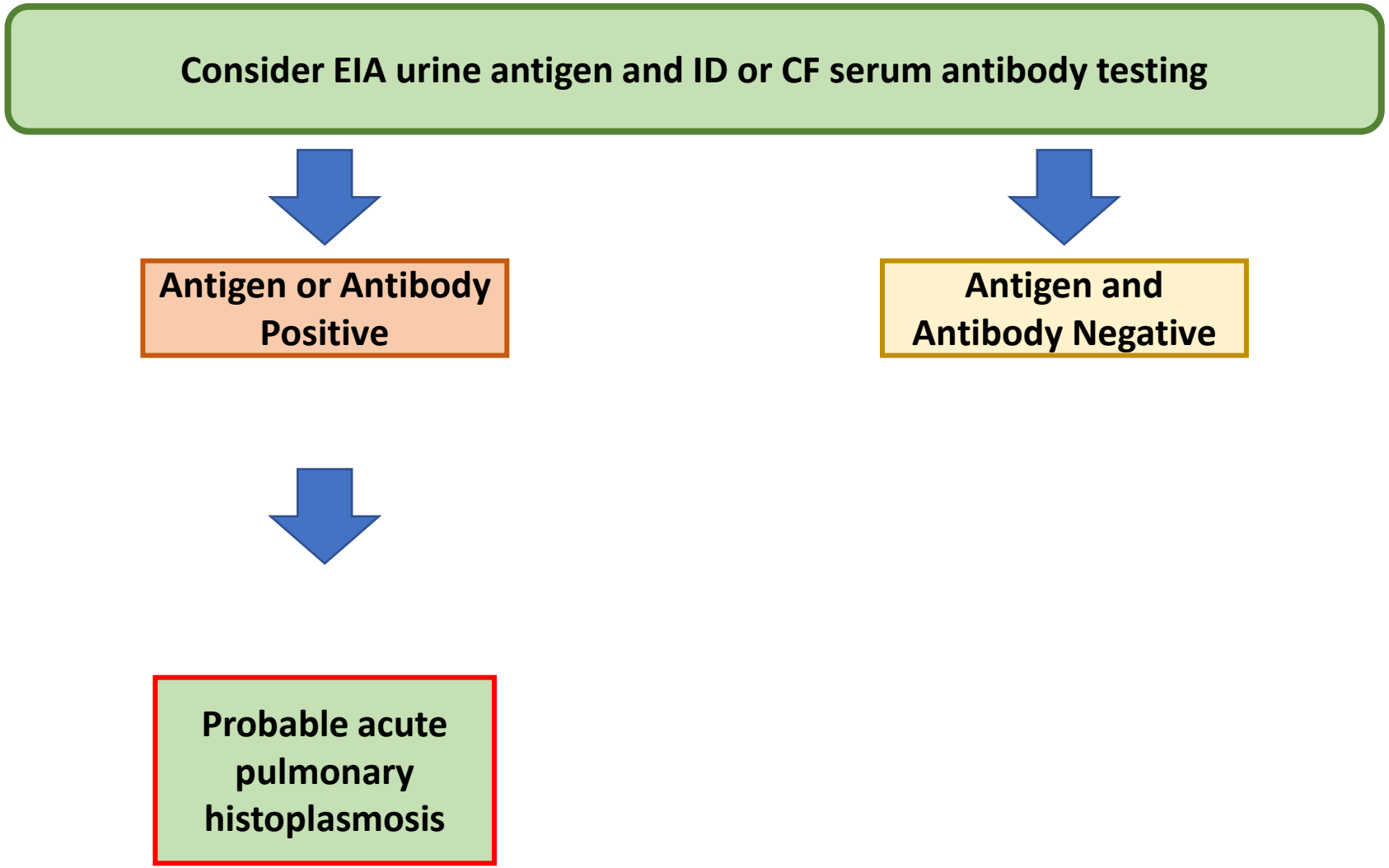
Consider EIA urine antigen and ID or CF serum antibody testing

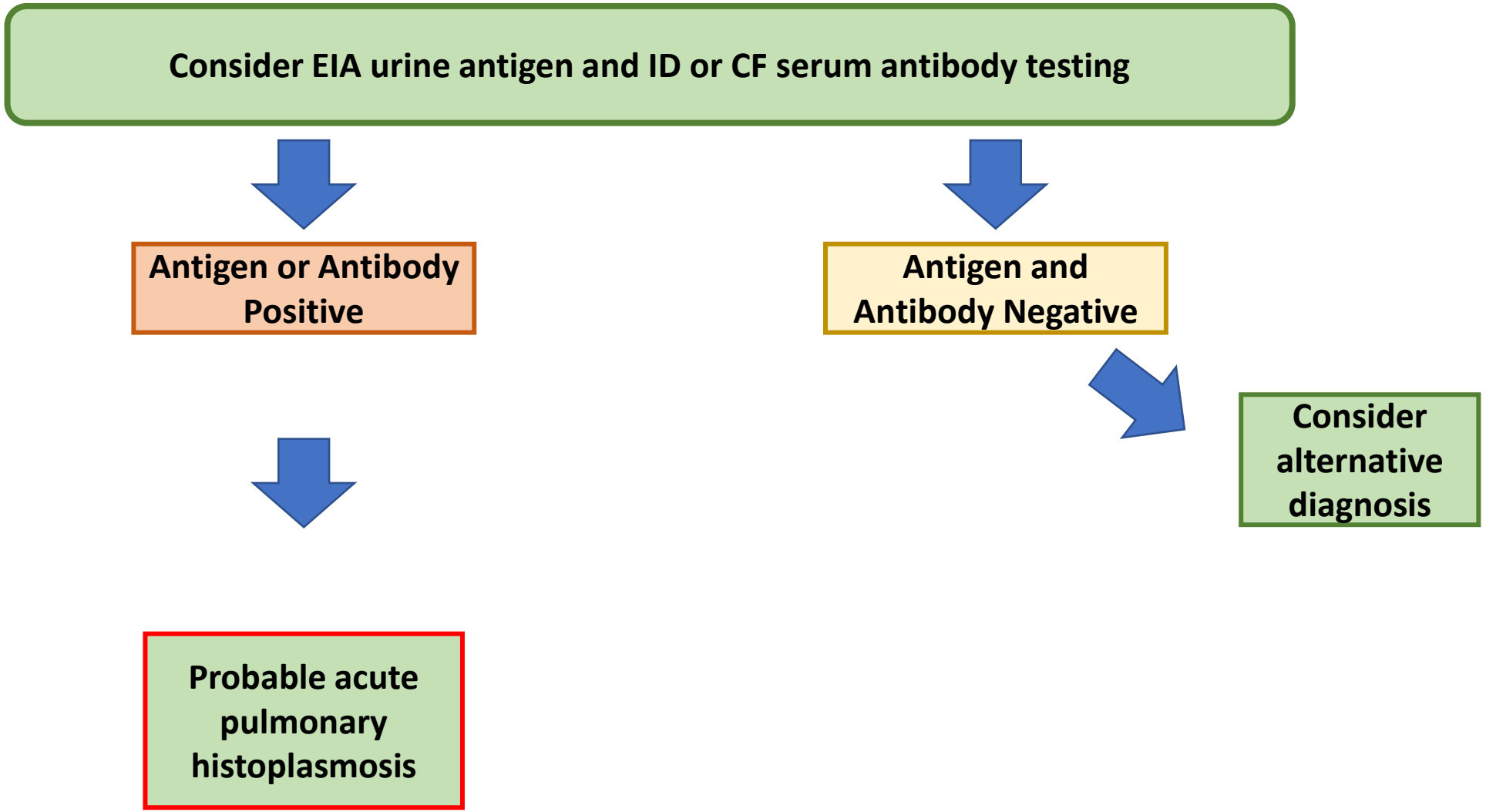
Antigen or Antibody Positive

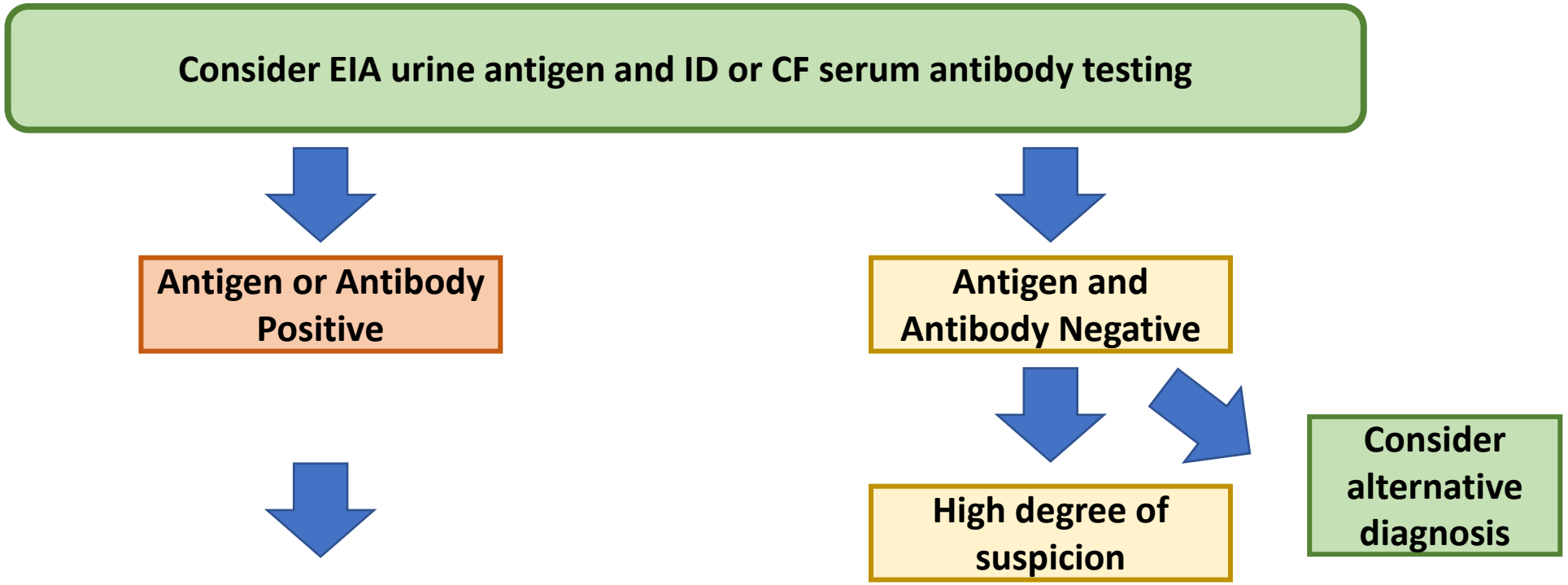
Consider EIA urine antigen and ID or CF serum antibody testing

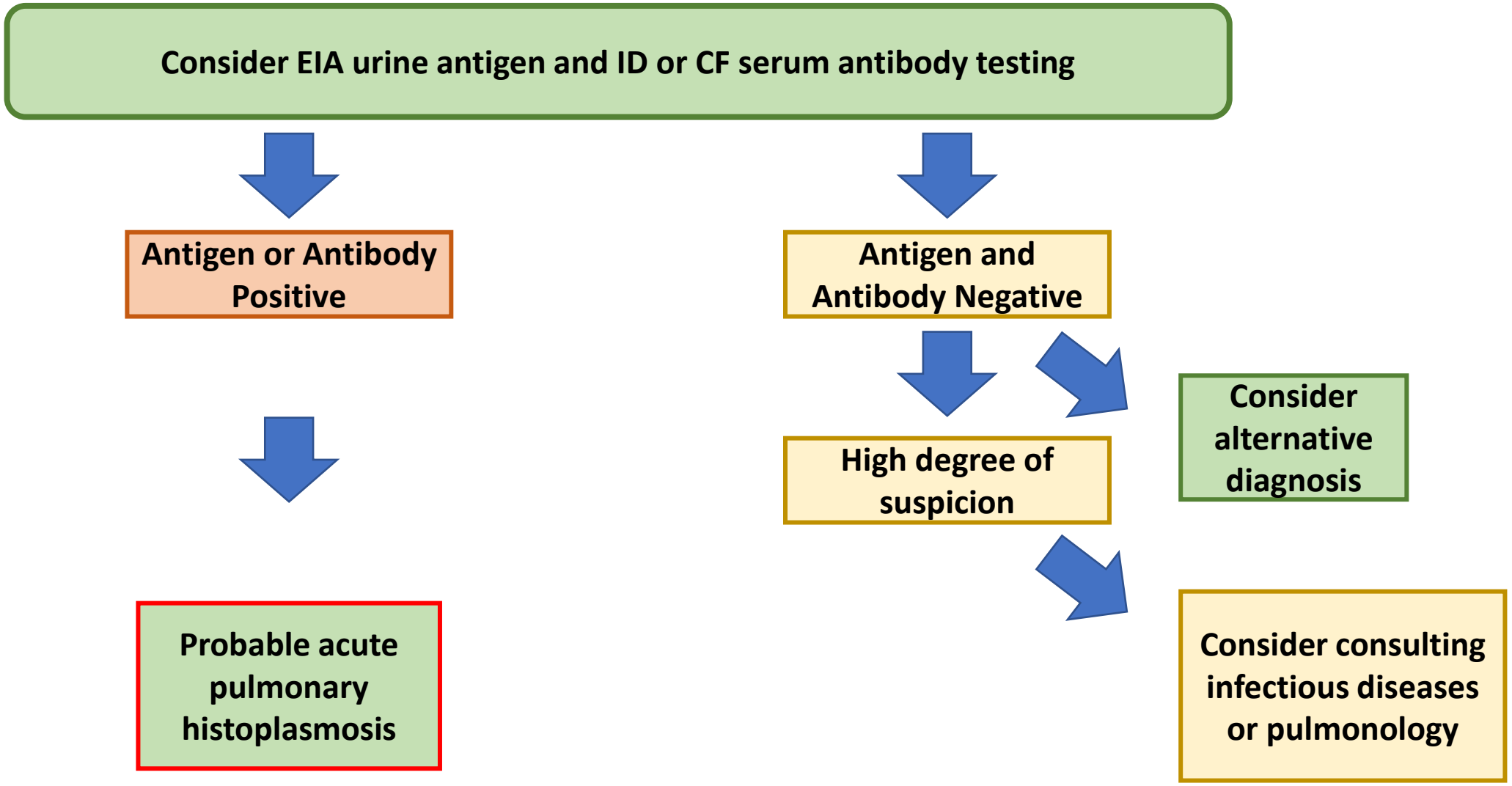
Antigen or Antibody Positive

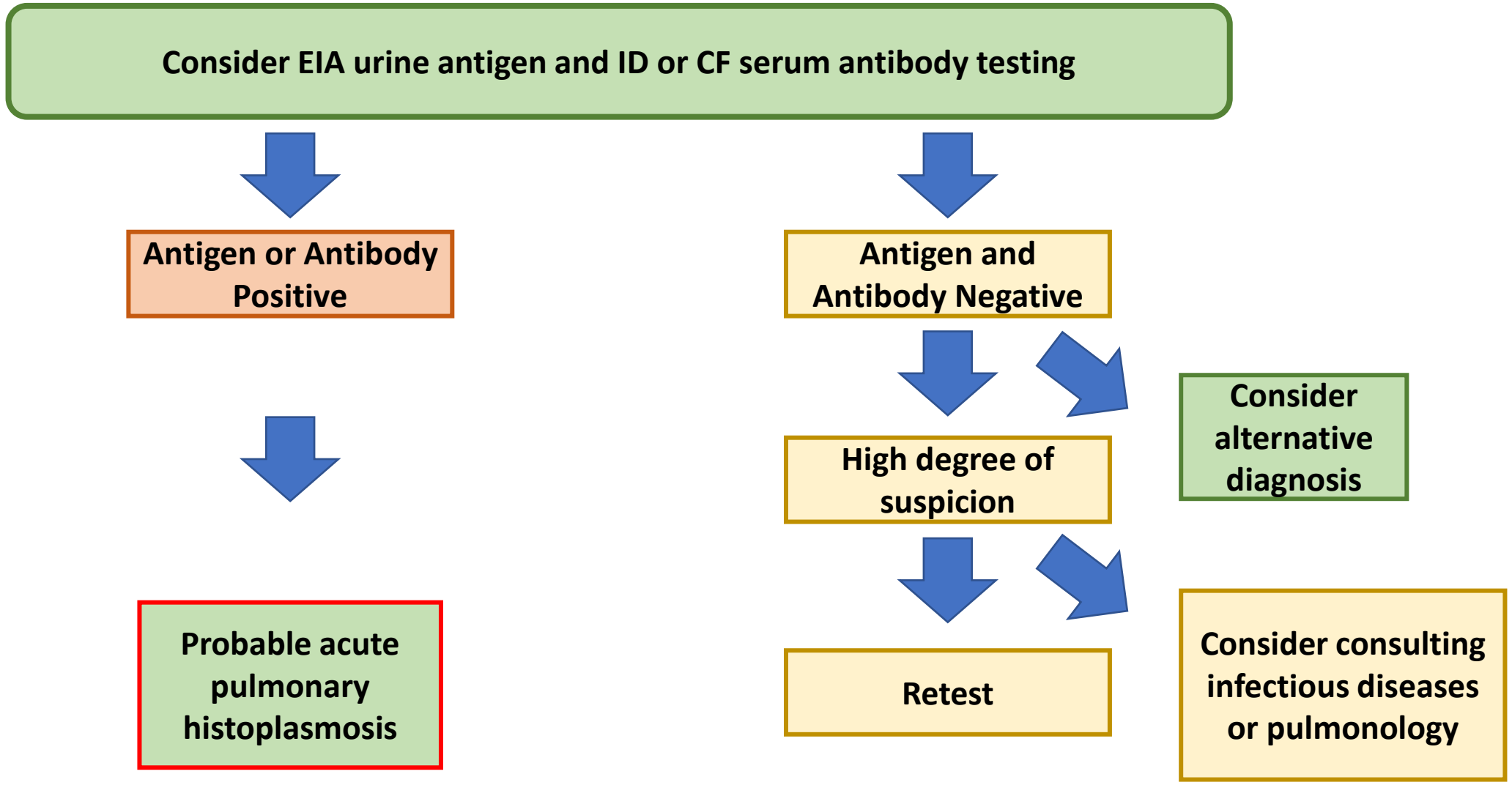
Probable acute pulmonary histoplasmosis

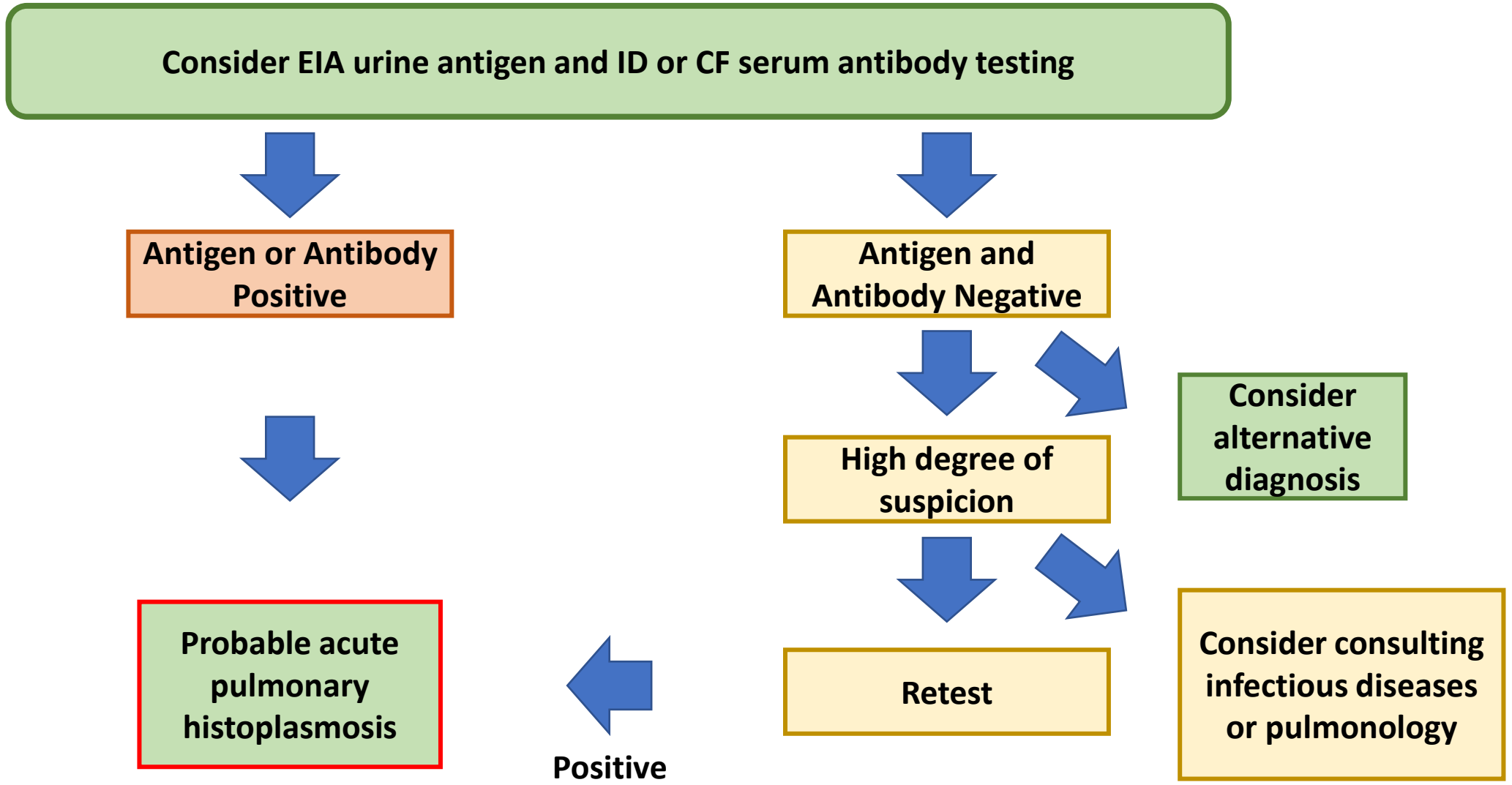

Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
Probable acute pulmonary histoplasmosis


Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
Consider alternative diagnosis
Probable acute pulmonary histoplasmosis


Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
High degree of suspicion
Consider alternative diagnosis
Probable acute pulmonary histoplasmosis


Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
High degree of suspicion
Consider alternative diagnosis
Probable acute pulmonary histoplasmosis
Consider consulting infectious diseases or pulmonology


Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
Consider alternative diagnosis
High degree of suspicion
Probable acute pulmonary histoplasmosis
Retest
Consider consulting infectious diseases or pulmonology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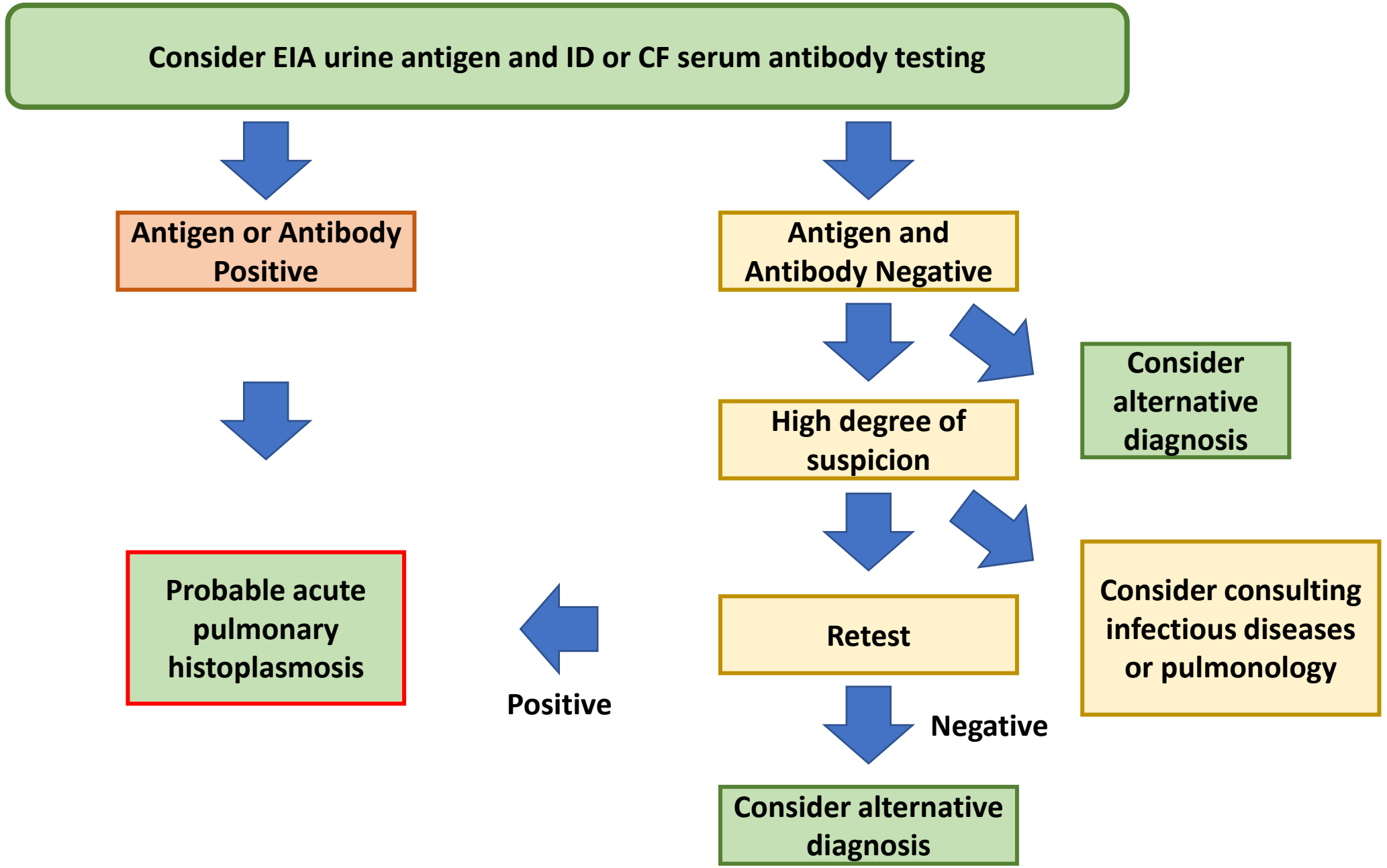
Antigen and Antibody Negative
Consider alternative diagnosis
High degree of suspicion
Probable acute pulmonary histoplasmosis
Positive
Retest
Consider consulting infectious diseases or pulmonology


Consider EIA urine antigen and ID or CF serum antibody testing
Antigen or Antibody Positive
Antigen and Antibody Negative
Consider alternative diagnosis
High degree of suspicion
Consider consulting infectious diseases or pulmonology
Retest
Probable acute pulmonary histoplasmosis
Positive
Negative
Consider alternative diagnosis

Diagnostic algorithms aim to:

1. Improve early diagnosis and reduce misdiagnoses
2. Reduce unnecessary antibacterial use
3. Improve patient outcomes

Algorithms are available on CDC's website

- **Community-Acquired Pneumonia (CAP): Clinical Testing Algorithm for Blastomycosis | Fungal Diseases | CDC**
- **Community-Acquired Pneumonia (CAP): Clinical Testing Algorithm for Coccidioidomycosis | Fungal Diseases | CDC**
- **Community-Acquired Pneumonia (CAP): Clinical Testing Algorithm for Histoplasmosis | Fungal Diseases | CDC**
- Continuing Medical Education activity jointly provided by Postgraduate Institute for Medicine; Terranova Medica, LLC; and the Mycoses Study Group Education & Research Consortium

http://www.funguscme.org/CAP2022/index.html

Future directions

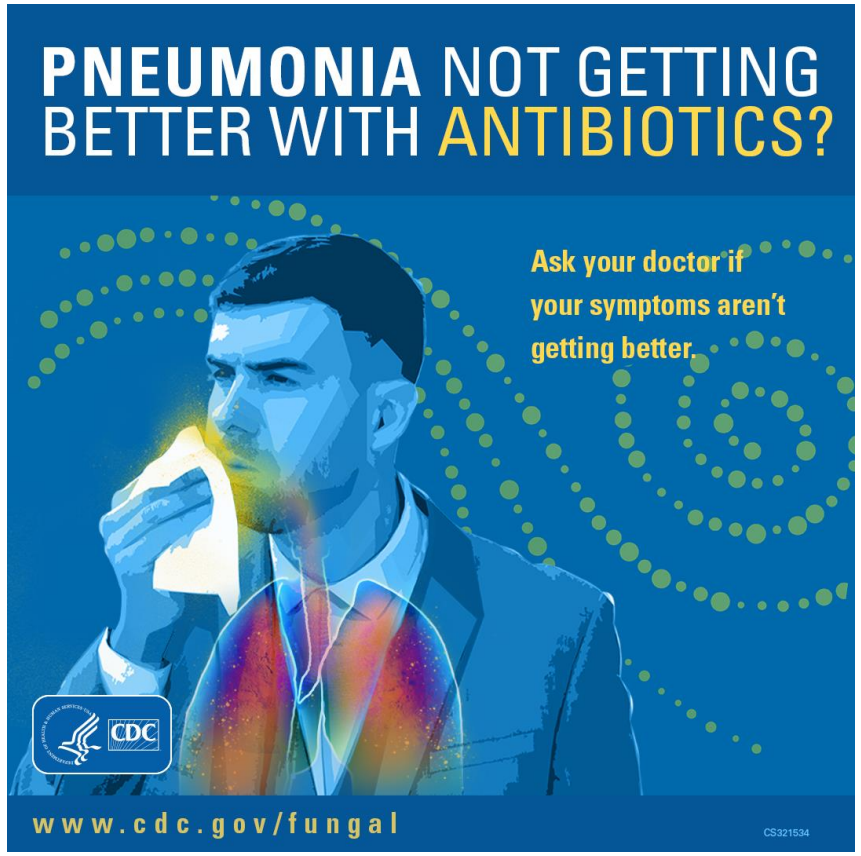
- Assess uptake and impact of diagnostic algorithms
- Incorporate new diagnostic methods as available
- Quantify proportion of CAP and other lower respiratory infections attributable to these endemic mycoses
- Further assess test performance (i.e. inter-laboratory and inter-manufacturer)
- Consider development of guidelines for diagnosis of CAP of various etiologies that do not respond to initial antibiotics

Coccidioidomycosis, histoplasmosis, and blastomycosis are fungal diseases known to be endemic to the United States

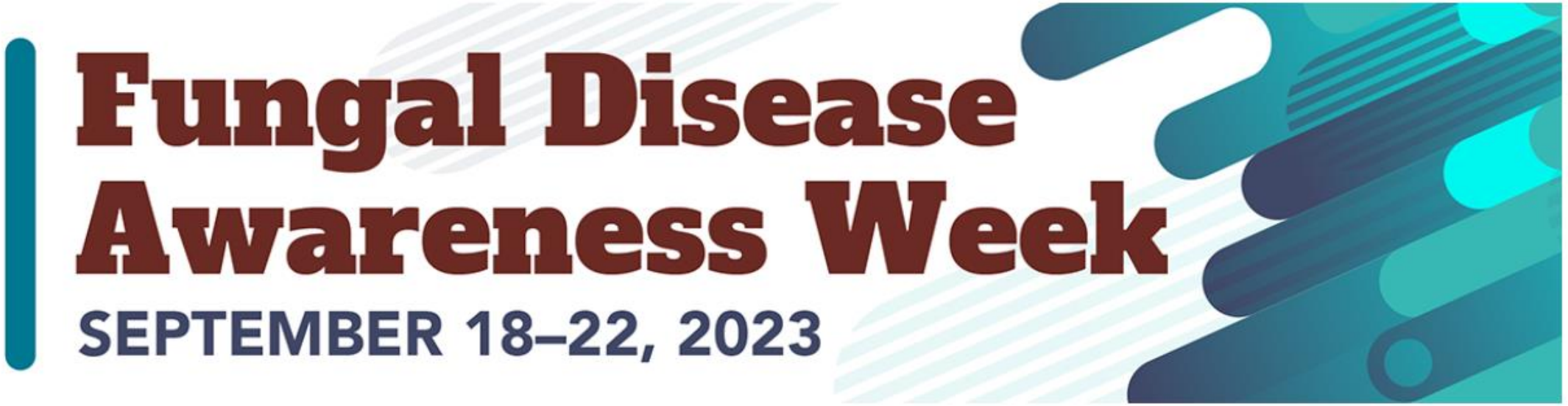
Increased awareness and testing practices can improve health outcomes

Early diagnosis and treatment can help prevent severe disease

If a patient is experiencing symptoms consistent with the endemic mycoses and does not improve on antibiotics, consider fungal testing



Celebrate Fungal Disease Awareness Week with the Mycotic Diseases Branch



[Fungal Disease Awareness Week 2023 | CDC]

Thank you

CDC’s fungal disease webpage:
https://www.cdc.gov/fungal/index.html

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Continuing Education

- All continuing education for COCA Calls is issued online through the CDC Training & Continuing Education Online system at https://tceols.cdc.gov/.

- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **Monday, October 23, 2023,** with the course code **WC4520-092123**. The access code is **COCA092123.**

- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **October 24, 2023,** and **October 24, 2025,** and use course code **WD4520-092123.** The access code is **COCA092123.**

- Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CEs obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Today's COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage https://emergency.cdc.gov/coca/calls/2023/callinfo_092123.asp

**A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*

Upcoming COCA Calls & Additional Resources

- Continue to visit https://emergency.cdc.gov/coca/ to get more details about upcoming COCA Calls.
- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at emergency.cdc.gov/coca/subscribe.asp.

Thank you for joining us today!

emergency.cdc.gov/coca