

Update on Coccidiomycosis (Valley Fever)

Christopher M. Zimmerman, MD, MPH

Medical Epidemiologist
Deputy Medical Director, Communicable Disease Control Division

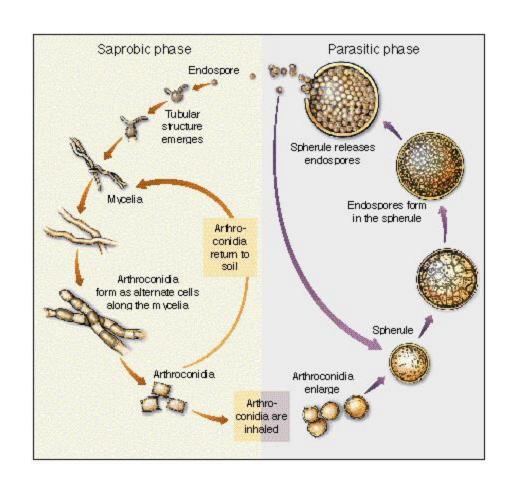


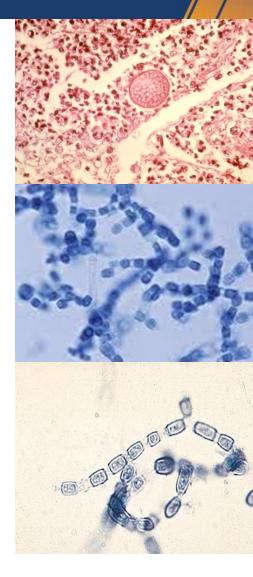
What are Coccidioides

- Coccidioides are dimorphic fungi
 - Other dimorphic fungi include
 - sporotrichosis
 - blastomycosis
 - histoplasmosis
 - coccidioidomycosis
 - paracoccidioidomycosis
 - talaromycosis
 - Candidiasis
 - Other dimorphic fungi can cause false positive clinical results



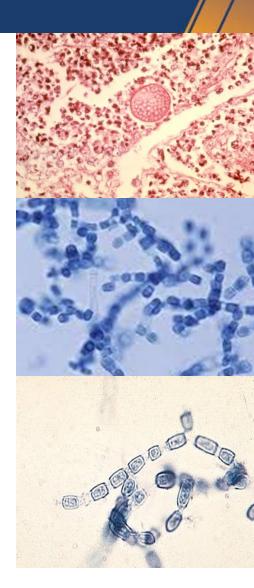
Life Cycle of Coccidioides







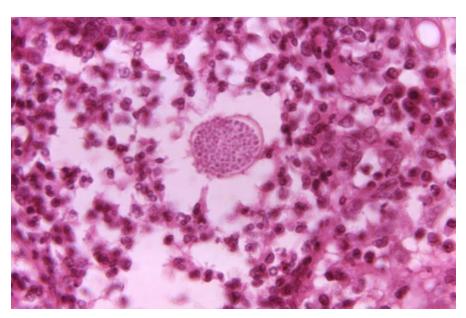
- They are endemic to the western United States also present in parts of Central and South America
- Two genetically and geographically distinct clades exist, although morphologically identical
 - Coccidioides immitis California
 - Coccidioides posadasii Arizona, the Central and South America





Ecology

- First identified in 1932
- It is thought that mammals may serve as a reservoir
- Fungal DNA has been identified in the air during dust storms





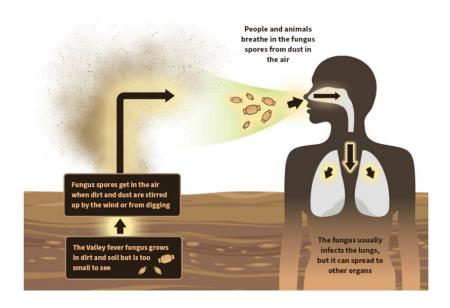


Update on Coccidiomycosis October 202

Coccidioides

- Naturally exist in soils
- Growth during rainy seasons
- Form spores

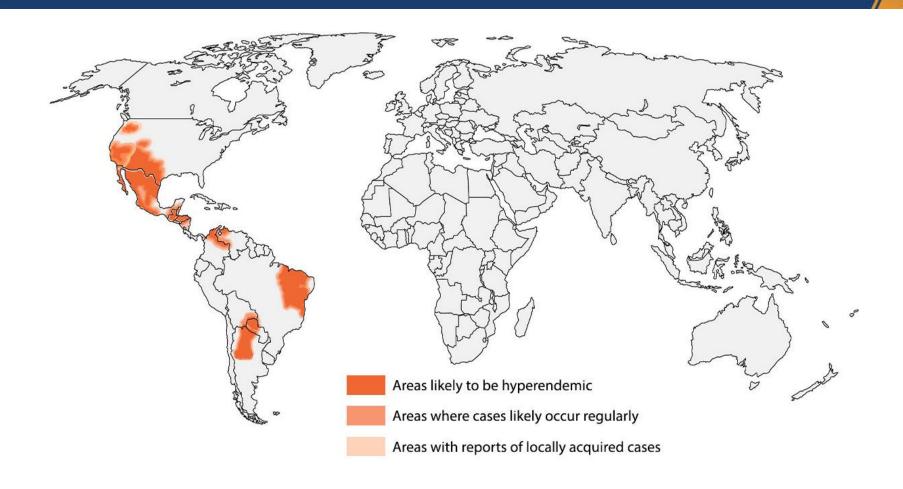
 (arthroconidia) which
 can be carried in the air
 when soil is disturbed
- As little as a single spore many lead to disease



https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Coccidioidomycosis.aspx



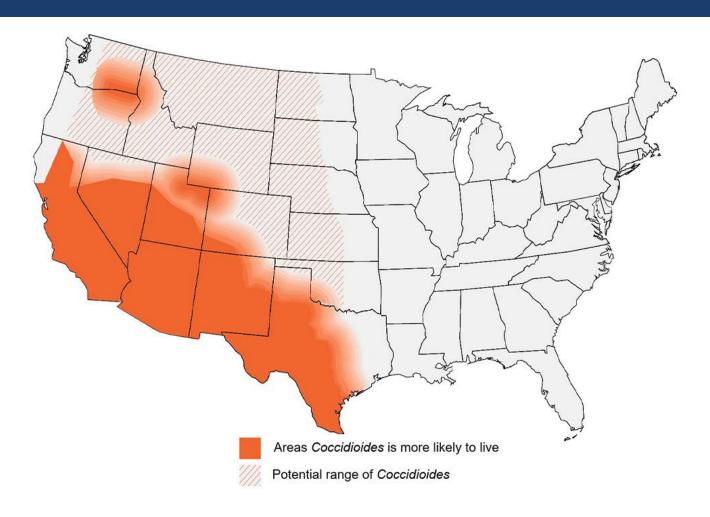
Global Distribution Coccidioides



https://www.cdc.gov/valley-fever/hcp/testing-algorithm/index.html



National Distribution of Coccidioides



https://www.cdc.gov/valley-fever/hcp/testing-algorithm/index.html



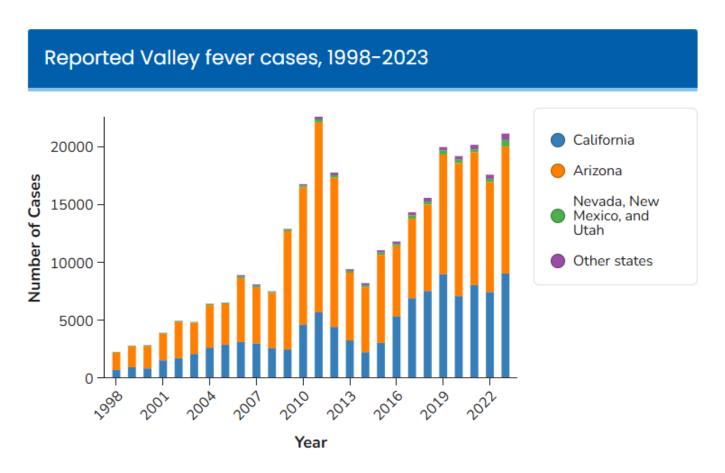
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Epidemiology Of Coccidiomycosis (CM)



National Epi 2011-2024

Reported Valley fever cases, 1998-2022



https://www.cdc.gov/valley-fever/php/statistics/index.html







Home | Programs | Center for Infectious Diseases | Division of Communicable Disease Control | Valley Fever in California Year-end Data Dashboard

VALLEY FEVER

Return to the Valley Fever Data & Publications webpage

Valley Fever in California Year-end Data Dashboard

This dashboard provides an overview of year-end surveillance data for Valley fever (coccidioidomycosis or "cocci") in California from 2001–2024. For an overview of data inclusion/exclusion criteria for this dashboard, please see the Technical Notes.

For a summary of provisional Valley fever cases in California reported so far in the current year, please see <u>CDPH Provisional Valley Fever Data Dashboard</u>.

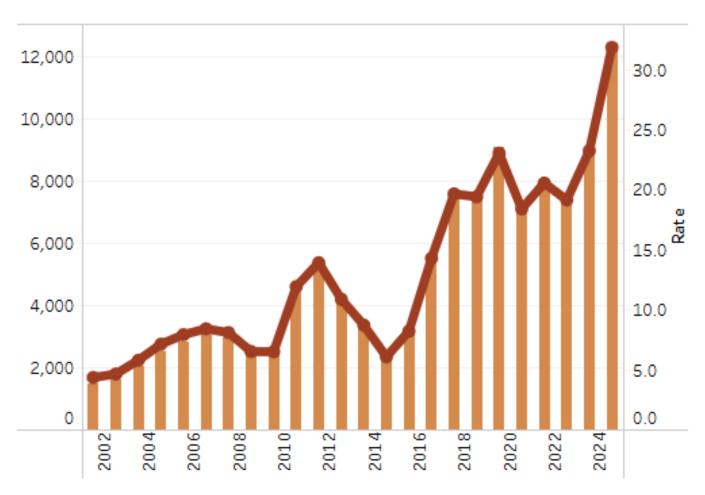
<u>Dashboard Instructions | Technical Notes (PDF) | Download Data, 2001–2024 (Excel)</u>

https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/ValleyFeverDashboard.aspx



California CM Data

Valley Fever by Year

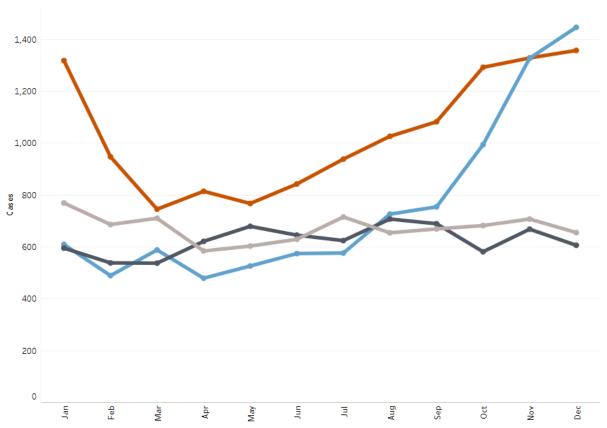




California CM Data by Month and Year

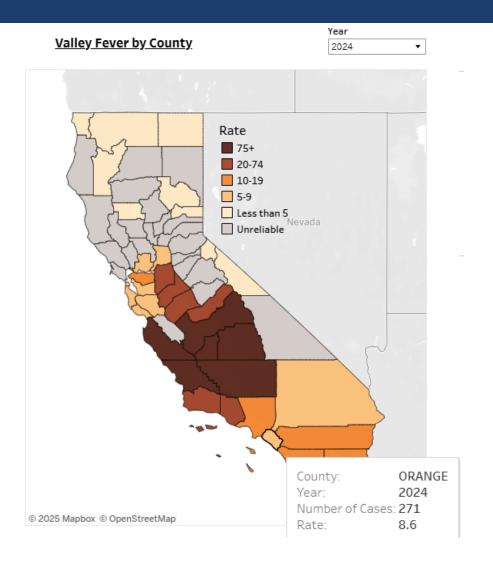


Number of Valley Fever Cases by Month of Estimated Illness Onset, California



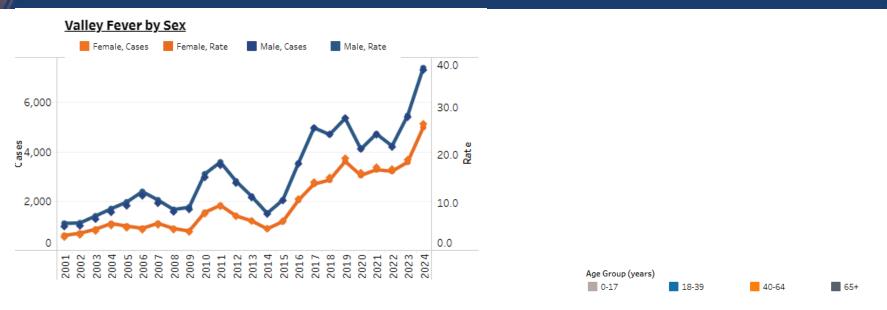


California CM Data – Rate by County

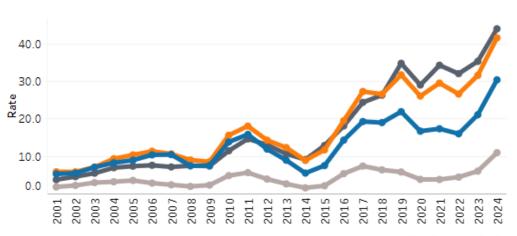




California CM Data- Sex & Age Group



Valley Fever by Age Group



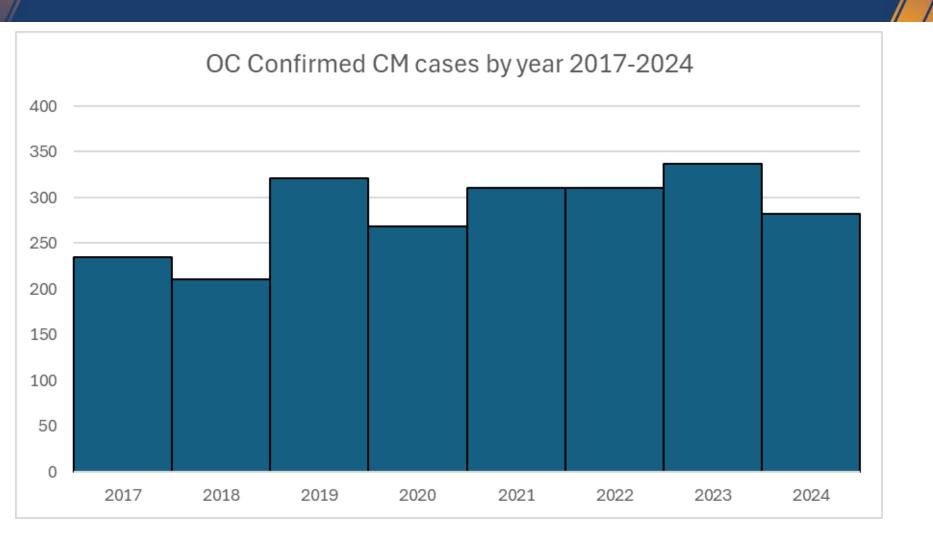


Orange County CM Data

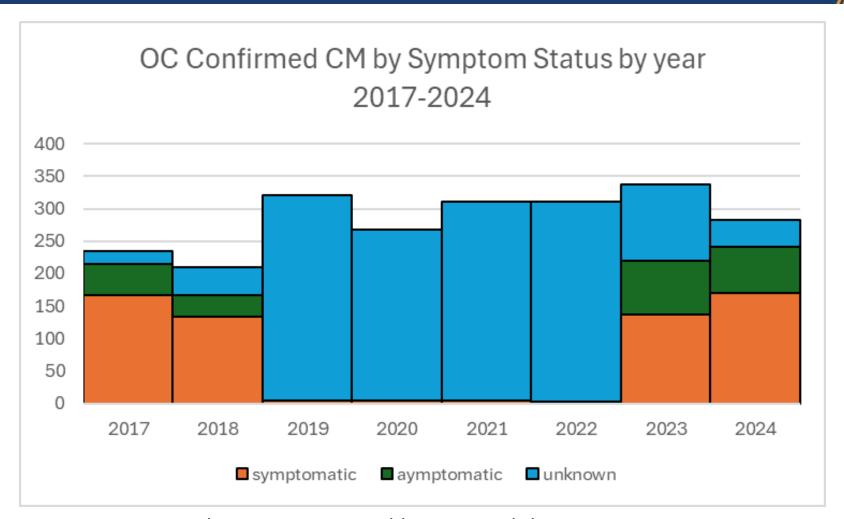
- Most disease is reported via electronic laboratory reports
- Investigation involves interview if possible and obtaining of medical records
- During the COVID-19 pandemic investigations of CM were halted temporarily



Orange County CM Epidemiology

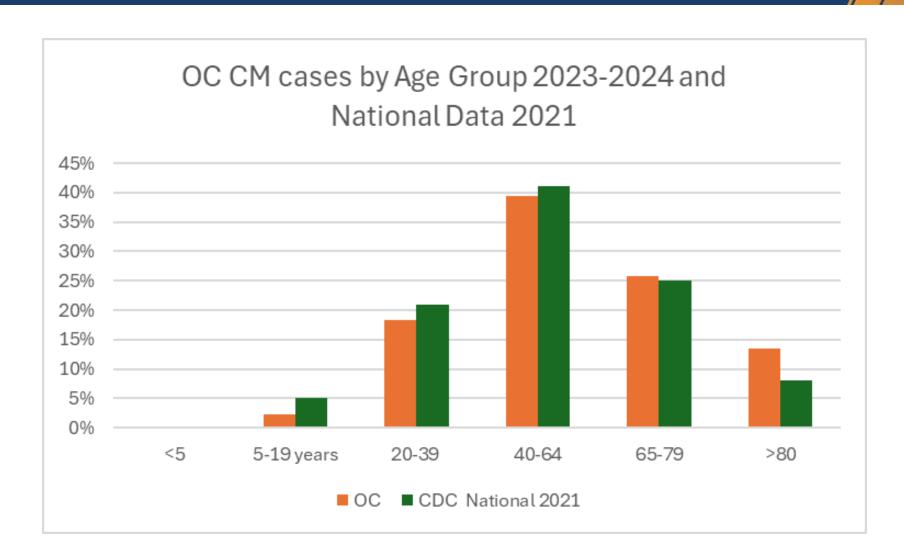




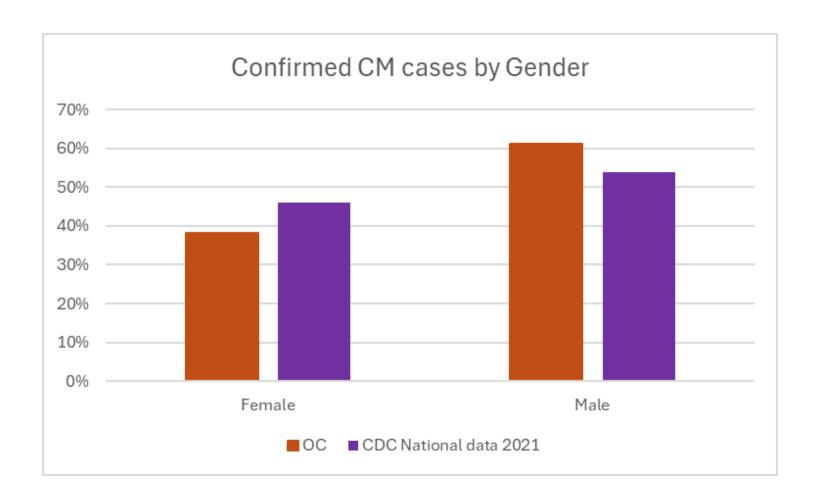


Between 2019 and 2022 Communicable Disease did not investigate CM cases





OC CM Data





OC CM Data

 Among patient we were able to interview or review records for 2023-2024

2023-2024	
Flu like symptoms	90%
Pnumonia	60%
rash	10%
Meningitis	4%
Hosptialized	51%

Outbreaks of CM





ome | Programs | Office of Communications | CDPH Identifies Valley Fever Illness Among Five People Who Attended Kern County Music Festiva

OFFICE OF COMMUNICATIONS

Contact:

Office of Communications media@cdph.ca.gov

CDPH Identifies Valley Fever Illness Among Attendees of Kern County Music Festival

July 29, 2024 NR24-018

Contact: media@cdph.ca.gov

People who attended "Lightning in a Bottle" music festival should see a healthcare provider if they are experiencing respiratory symptoms

What You Need To Know: CDPH is notifying Californians of Valley fever cases possibly associated with an outdoor music festival near Bakersfield, California. To date, CDPH has identified five patients with Valley fever who attended the festival; three were hospitalized. Valley fever is not contagious, meaning it cannot spread from one person or animal to another. Symptoms include cough, fever, fatigue, difficulty breathing, and chest pain.



► Emerg Infect Dis. 2018 Mar;24(3):417-424. doi: 10.3201/eid2403.170623 ☑

Coccidioidomycosis Outbreaks, United States and Worldwide, 1940-2015

Michael Freedman 1,2, Brendan R Jackson 1,2, Orion McCotter 1,2, Kaitlin Benedict 1,2,™



Morbidity and Mortality Weekly Report (MMWR)

Search Q

Notes From the Field: Coccidioidomycosis Outbreak Among Wildland Firefighters — California, 2021

Weekly / August 26, 2022 / 71(34);1095-1096

Print

Marisa A.P. Donnelly, PhD^{1,2}; Dorothy Maffei, MPH^{1,3}; Gail L. Sondermeyer Cooksey, MPH¹; Thomas J. Ferguson, MD, PhD^{4,5}; Seema Jain, MD¹; Duc Vugia, MD¹; Barbara L. Materna, PhD¹; Amanda Kamali, MD¹ (VIEW AUTHOR AFFILIATIONS)

ccheddh 🔵

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Clinical Presentations of CM



Clinical Presentations of Coccidiomycosis

- 60%
 - Subclinical disease
- 30% Pulmonary disease
 - Acute pulmonary disease
 - Chronic Pulmonary disease
- 10% Disseminated disease
 - Non-central nervous system (CNS) disseminated disease
 - CNS disseminated disease



Subclinical CM

- 60% of people exposed to Coccidioides will experience no symptoms or are mildly symptomatic disease which resolves on its own.
- No need for treatment
- These people are felt to develop long standing immunity and are protected from reinfection



Skin manifestations of CM

 Erythema nodosum is a reactive inflammatory condition of the skin commonly seen with CM Erythema multiforme can also be seen as part of the presentation of CM



Erythema Nodosum James Heilman, MD, Public Domain, via Wikimedia Commons

https://pmc.ncbi.nlm.nih.gov/articles/PMC4631225/



Acute Pulmonary CM

- Incubation period
 - 1-3 weeks after exposure
- Pulmonary symptoms
 - Chest pain, dyspnea, non-productive cough
- Constitutional symptoms
 - Fever, night sweats, arthralgias, headache, conjunctivitis, skin manifestations
- Constitutional symptoms can last for weeks and months



Pulmonic Disease

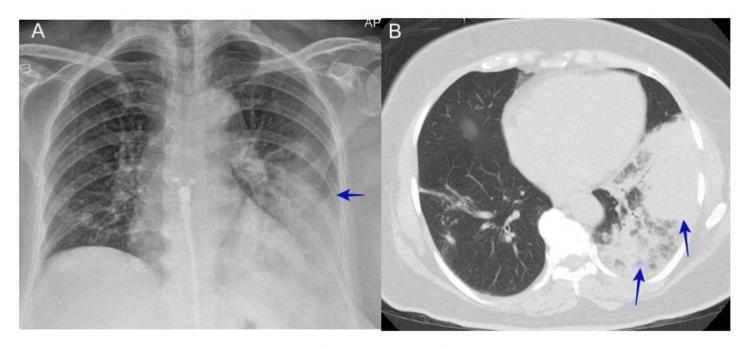


Figure 5. (**A**) A chest X-ray shows a left lower opacity (blue arrow). (**B**) A CT scan shows left lower lobe consolidation (blue arrows). The patient was a 65-year-old woman who presented with the chief complaint of a cough and dyspnea lasting for one week. She was diagnosed with community-acquired pneumonia and placed on IV antibiotics and sent home with oral antibiotics. She tested positive for coccidioidomycosis IgG.

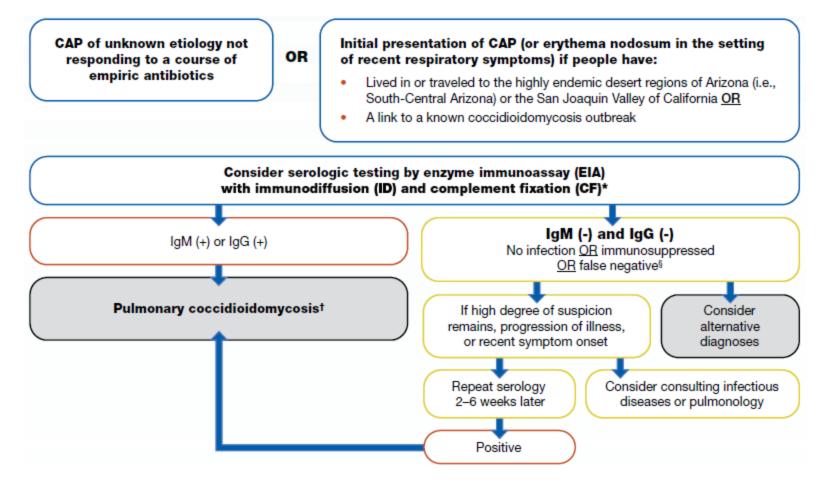


Acute Pulmonary CM & Community Acquired Pneumonia

- Can appear just as community acquired pneumonia which can lead to
 - Diagnostic delays
- CDC has put out an algorithm for considering CM in the face of CAP
 - https://www.cdc.gov/valley-fever/hcp/testingalgorithm/index.html



CDC CM Testing Algorithm



https://www.cdc.gov/valley-fever/hcp/testing-algorithm/index.html



Risk Factors



https://vfce.arizona.edu/valley-fever-people/check-risk-factors



Chronic Pulmonary CM

- More complex presentations
 - Miliary disease
 - Lung nodule
 - Cavitary disease
 - Pleural disease

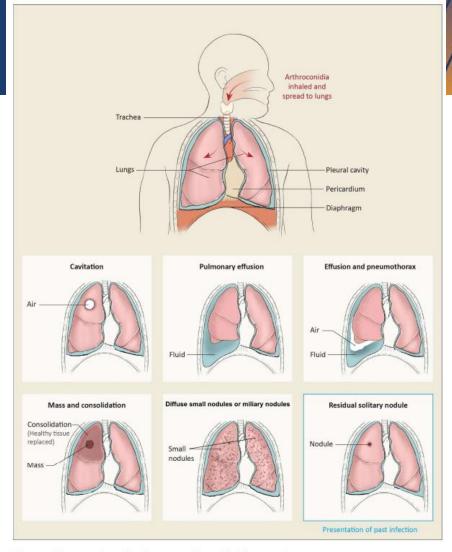


Figure 4. Presentation of pulmonary of coccidioidomycosis.



Miliary

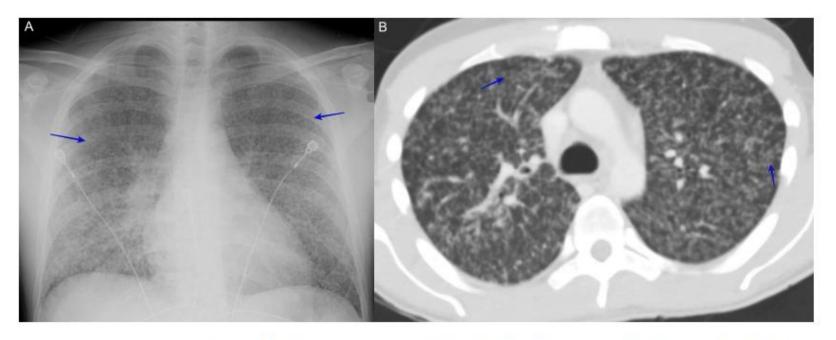


Figure 9. (**A**) A chest X-ray shows diffuse reticulonodular interstitial miliary nodules (blue arrows). (**B**) A CT scan shows diffuse reticulonodular interstitial miliary nodules (blue arrows). The patient



Cavitary Disease

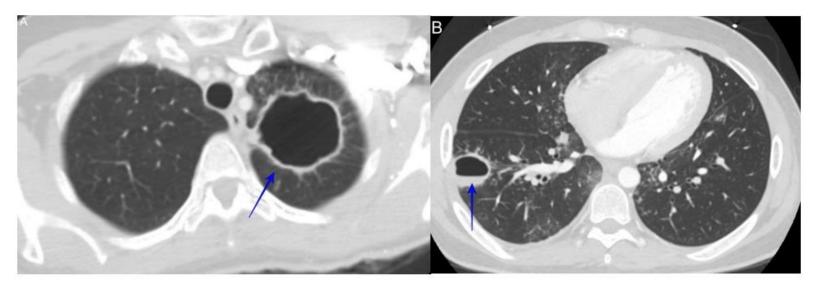


Figure 8. (**A**) shows a large left upper lobe cavitary lesion. The patient was a 48-year-old woman who had cavitary disease discovered during a shoulder pain work-up (blue arrow). She later tested positive for IgM and IgG coccidioidomycosis serology. (**B**) shows a right lower lobe cavitary lesion. The patient was a 22-year-old man with a history of diabetes who presented with hemoptysis (blue arrow). The fungal culture from bronchial washing showed *C. immitis*.



Solitary nodule

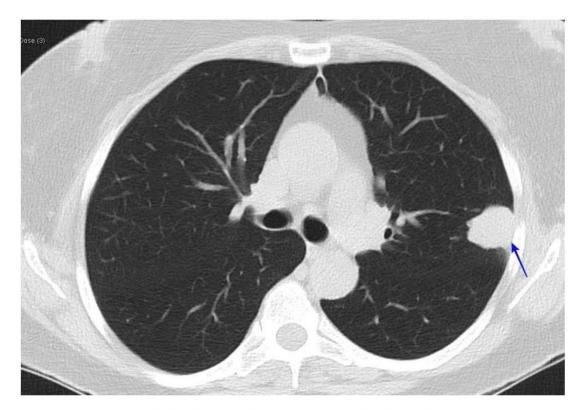
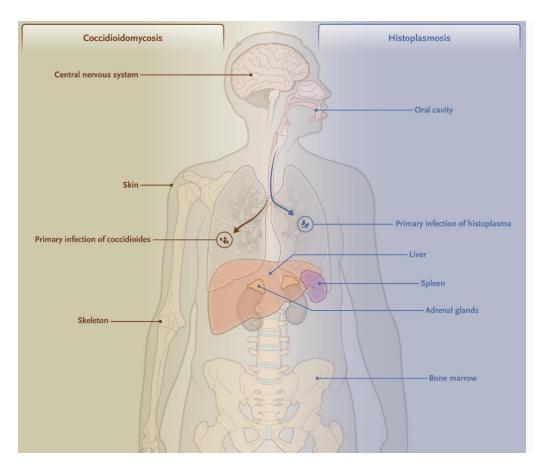


Figure 12. A CT scan with a left upper lobe nodule (blue arrow). The patient was a 64-year-old woman who presented with an incidental 2.5 cm left upper lobe nodule. She underwent a bronchoscopy with a biopsy, which was not diagnostic. Then, she underwent a CT guided biopsy, which showed necrotizing granuloma with fungal spherules consistent with coccidioidomycosis.



Disseminated CM Disease



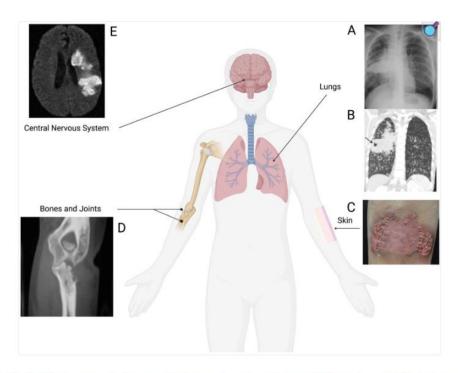
- Meningeal disease
- Bone
- Skin

https://www.nejm.org/doi/full/10.1056/NEJMra2306821



Disseminated Disease

Figure 1.



Common sites of *Coccidioides* infection. From the lung, coccidioidomycosis can spread to many different sites, as highlighted above. Chest radiograph and CT image of a patient with pulmonary coccidioidomycosis infection (A,B), respectively (reproduced from Adam et al. with permission [6]). The arrow in (B) points to cavitation where fungal infection is present. Skin infection appearing as verrucous plaques on a Coccidioidomycosis patient (C) (reproduced from Garcia et al. with permission [2]). CT image of the patient's right elbow with eroded ulna due to *Coccidioides* dissemination (D) (reproduced from Capoor et al. with permission [11]). MR image showing coccidioidomycosis-induced cerebral infarction (E) (reproduced from Lammering et al. with permission [12]). Created using BioRender.com, accessed on 2 February 2023.

https://pmc.ncbi.nlm.nih.gov/articles/PMC10607509/



Skin Infection

- Skin infection is due to dissemination of disease
- Primary skin infection is extremely rare



Disseminated coccidioidomycosis presenting as an erythematous, crusted plaque in the upper extremity

https://pmc.ncbi.nlm.nih.gov/articles/PMC4631225/



CNS CM

- Symptoms of CNS CM
 - Headache
 - Blurry vision
 - Photophobia
 - Meningismus
 - Decline in cognition
 - Hearing changes
 - Focal neurologic deficit
- Treatment for CNS disease is life-long treatment



MAJOR ARTICLE







Challenges in the Long-term Management of Patients With Coccidioidal Meningitis: A Retrospective Analysis of Treatment and Outcomes

Geetha Sivasubramanian, Saurin Kadakia, Jani M. Kim, Sarah Pervaiz, Yueqi Yan, and Robert Libke 1

¹Division of Infectious Disease, University of California, San Francisco, Fresno, California, USA, ²Department of Internal Medicine, University of California, San Francisco, Fresno, California, USA, and ³HSRI Biostatistics and Data Support Core, University of California, Merced, California, USA

Background. Coccidioidal meningitis (CM) is the most severe form of disseminated coccidioidomycosis. Despite years of clinical experience, it remains a difficult condition to treat, often requiring surgical procedures, such as placement of a ventriculoperitoneal shunt, in addition to lifelong antifungal therapy.

Methods. We performed a retrospective analysis of patients with CM seen in a large referral center in Central Valley, California, from 2010 to 2020. Data pertinent to CM were collected and analyzed.

Results. Among 133 patients with CM identified in the 10-year period, nonadherence to antifungal therapy was noted in 43% of patients. Of the 80 patients who underwent ventriculoperitoneal shunt placement for management of intracranial pressure, shunt failure requiring revision surgery occurred in 42 (52.5%). Rehospitalizations due to CM-related reasons occurred in 78 of 133 patients (59%). Twenty-three percent of patients (n = 29) died due to complications from CM, on an average 22 months after the diagnosis of CM. Encephalopathy at presentation was associated with a significantly higher risk of death.

Conclusions. Patients with CM in central California are predominantly rural agricultural workers with elevated levels of poverty and low health literacy and many barriers to care, leading to high rates of medication nonadherence and loss to follow-up outpatient care. Management challenges are frequent, such as failure of antifungal therapy, high rates of rehospitalization, and the need for repeated shunt revision surgeries. In addition to the development of curative new antifungal agents, understanding the barriers to patient adherence to care and antifungal therapy and identifying means to overcome such barriers are of paramount importance.

https://pmc.ncbi.nlm.nih.gov/articles/PMC10270562/pdf/ofad243.pdf

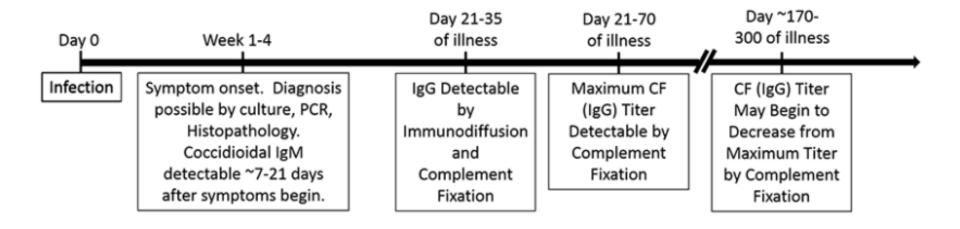


Risks for Disseminated CM

- Immunocompromised
- African or Filipino ancestry
- Age beyond puberty
- Pregnancy
- Most disseminated CM occurs in people without an identified risk factor



Immune Response to CM



https://health.ucdavis.edu/valley-fever/about-valley-fever/coccidioides-diagnostic-testing/index.html



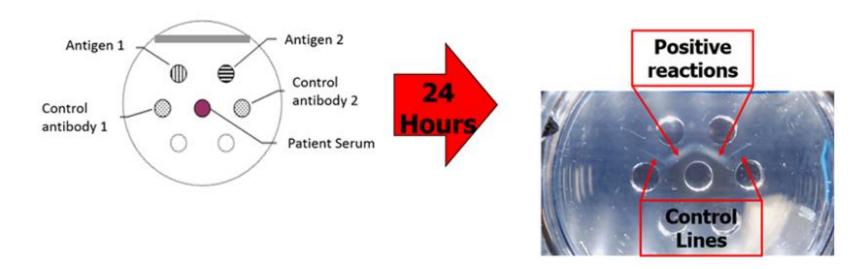
Testing for CM

Test	Sensitivity	Specificity	Population studied
Antibody tests			
EIA (IgM & IgG) antibody	59%–88%	68%–96% (Cross reacts with other dimorphic fungi)	General patient population, immunocompromised population, patients with disseminated disease
Complement fixation (CF) antibody	65%–83%	High	General patient population, immunocompromised population, patients with disseminated disease
Immunodiffusion (ID) antibody	60%	99%	General patient population, immunocompromised population, patients with disseminated disease
Lateral flow assay (LFA) antibody	31%	92%	General patient population



Immunodiffusion Testing

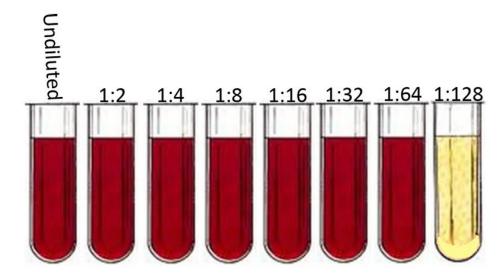
Immunodiffusion is a serum-based diagnostic that identifies specific antibodies in a patient's serum. The test relies on the ability of antibodies and antigens in different wells of a gellan plate to diffuse into the gel and form a visible precipitation band at their intersection point. When performed in an experienced lab, this test is highly sensitive for the detection of *Coccidioides*-specific antibodies and thus the diagnosis of Valley Fever. We use this test to detect both coccidioidal IgM (sometimes referred to as coccidioidal precipitins) and IgG (sometimes referred to as coccidioidal CF or Complement Fixation) antibodies.



Complement Fixation

Complement fixation provides titers that can be followed over time

To arrive at a titer, positive serum samples can then be serially diluted and subjected to the same test to find the highest concentration of serum that fails to lyse red blood cells. The following is an illustration of a complement fixation test performed on 2-fold dilutions of a single serum specimen. The final 'positive' reaction (i.e. the last tube without lysed red blood cells) is 1:64, so the coccidioidal IgG antibody titer would be reported as 1:64.





Non-serology testing for CM

Test Antigen tests	Sensitivit	y Specificity	Population studied
EIA urine antigen	37%–71%	High (but does cross-react with other dimorphic fungi)	General patient population, immunocompromised population, patients with disseminated disease
EIA serum antigen	51%–73%	High (but does cross-react with other dimorphic fungi)	General patient population, immunocompromised population, patients with disseminated disease
Other tests			
Histopathology	23%–84%	High	General patient population, patients with diabetes, patients with disseminated disease
Cytology	15%–75%	High	General patient population, patients with diabetes, patients with disseminated disease
PCR	56%–75%	99%–100%	General patient population



Guidelines for Treatment

Clinical Infectious Diseases

IDSA GUIDELINE







2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis

John N. Galgiani, Neil M. Ampel, Janis E. Blair, Antonino Catanzaro, Francesca Geertsma, Susan E. Hoover, Royce H. Johnson, Shimon Kusne, Jeffrey Lisse, Joel D. MacDonald, Shari L. Meyerson, Patricia B. Raksin, John Siever, David A. Stevens, Rebecca Sunenshine, And Nicholas Theodore Sunenshine, Antonino Catanzaro, Francesca Geertsma, Susan E. Hoover, Royce H. Johnson, Shimon Kusne, Nicholas Theodore Sunenshine, Antonino Catanzaro, Francesca Geertsma, Susan E. Hoover, Royce H. Johnson, Shimon Kusne, Sh

¹Valley Fever Center for Excellence, and ²Division of Infectious Diseases, University of Arizona, Tucson, and ³Division of Infectious Diseases, Mayo Clinic, Scottsdale, Arizona; ⁴Division of Pulmonary and Critical Care, University of California, San Diego, and ⁵Department of Pediatrics, Infectious Diseases, Stanford University School of Medicine, California; ⁶Division of Sanford Health, Sioux Falls, South Dakota; ⁷David Geffen School of Medicine at UCLA, Department of Medicine, Kern Medical Center, Bakersfield, California; ⁸Department of Rheumatology, University of Arizona, Tucson; ⁹Department of Neurosurgery School of Medicine, University of Utah, Salt Lake City; ¹⁰Division of Thoracic Surgery, Northwestern University, Feinberg School of Medicine, and ¹¹Division of Neurosurgery, John H. Stroger Jr Hospital of Cook County, Chicago, Illinois; ¹²Arizona Pulmonary Specialists, Ltd, Phoenix; ¹³Division of Infectious Diseases, Stanford University School of Medicine, California; ¹⁴Career Epidemiology Field Officer Program, Division of State and Local Readiness, Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention; ¹⁵Maricopa County Department of Public Health, and ¹⁶Department of Neurosurgery, Barrow Neurological Institute, Phoenix, Arizona

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

Coccidioidomycosis, also known as San Joaquin Valley fever, is a systemic infection endemic to parts of the southwestern United States and elsewhere in the Western Hemisphere. Residence in and recent travel to these areas are critical elements for the accurate recognition of patients who develop this infection. In this practice guideline, we have organized our recommendations to address actionable questions concerning the entire spectrum of clinical syndromes. These can range from initial pulmonary infection, which eventually resolves whether or not antifungal therapy is administered, to a variety of pulmonary and extrapulmonary complications. Additional recommendations address management of coccidioidomycosis occurring for special at-risk populations. Finally, preemptive management strategies are outlined in certain at-risk populations and after unintentional laboratory exposure.

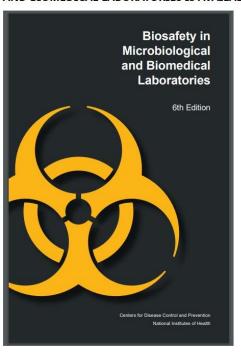
https://www.idsociety.org/practice-guideline/coccidioidomycosis/



Infection Control

- CM is not transmissible person to person
- Laboratory exposures have occurred

THE 6TH EDITION OF THE BIOSAFETY IN MICROBIOLOGY AND BIOMEDICAL LABORATORIES IS AVAILABLE



While culture evaluation can occur in a biosafety cabinet under biosafety level 2 (BSL-2) conditions, the 6th edition of *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) recommends BSL-3 practices when propagating and manipulating sporulating *Coccidioides* cultures (10).

https://doi.org/10.1128/jcm.01581-22

Expert Opinion: What To Do When There Is *Coccidioides* Exposure in a Laboratory

David A. Stevens,^{1,2,3,4,5} Karl V. Clemons,^{1,4,5} Hillel B. Levine,⁴ Demosthenes Pappagianis,⁷ Ellen Jo Baron,^{5,6} John R. Hamilton,³ Stanley C. Deresinski,^{1,5} and Nancy Johnson²

Departments of 'Medicine and 'Infection Control and 'Clinical Microbiology Laboratory, Santa Clara Valley Medical Center, and 'California Institute for Medical Research, San Jose, 'Division of Infectious Diseases and Geographic Medicine and 'Clinical Microbiology Laboratory, Stanford University Medical School, Stanford, and 'Department of Medical Microbiology, University of California, Davis, California

https://doi.org/10.1086/605441



Estimated Burden of CM





Original Investigation | Infectious Diseases

Estimated Burden of Coccidioidomycosis

Samantha L. Williams, MPH; Kaitlin Benedict, MPH; Brendan R. Jackson, MD; Malavika Rajeev, PhD; Gail Cooksey, MPH; Irene Ruberto, PhD; Thomas Williamson, MPH; Rebecca H. Sunenshine, MD; BreAnne Osborn, MPH; Hanna N. Oltean, PhD; Rebecca R. Reik, MPH; Michael S. Freedman, MD; Andrej Spec, MD; Adrienne Carey, MD; Ilan S. Schwartz, MD; Luis Medina-Garcia, MD; Nathan C. Bahr, MD; Rasha Kuran, MD; Arash Heidari, MD; George R. Thompson III, MD; Royce Johnson, MD; John N. Galgiani, MD; Tom Chiller, MD; Mitsuru Toda, PhD

conclusions and reporting are needed to improve patients of coccidioidomycosis epidemiology.

Estimated true burden of Valley fever

206,000–360,000 symptomatic cases; 10-18 times more cases than reported.

18,000–28,000 hospitalizations; 2-3 times more than found in national data.

700–1,100 deaths; 5-6 times more deaths than reported.

JAMA Network Open. 2025;8(6):e2513572.doi:10.1001/jamanetworkopen.2025.13572



Changing Epidemiology

- A number of factors may be driving the increasing number of cases identified
 - Provider awareness
 - Greater use of diagnostics
 - Increasing population in highly endemic areas
 - Changing climate



GeoHealth

₽

RESEARCH ARTICLE

10.1029/2019GH000209

Key Points:

- We created a niche model to estimate climate limits on the spatial extent of Valley fever endemicity in the United States
- For a high warming scenario, the area of climate-limited endemicity will more than double by 2100, expanding northward into dry western states
- Our predictive model of Valley fever endemic regions may help mitigate disease impacts as the disease spreads into new regions

Supporting Information:

· Supporting Information S1

Correspondence to:

M. E. Gorris, mgorris@uci.edu

Citation:

Gorris, M. E., Treseder, K. K., Zender, C. S., & Randerson, J. T. (2019). Expansion of coccidioidomycosis endemic regions in the United States in response to climate change. *GeoHealth*, 3, 308–327. https://doi.org/10.1029/ 2019GH000209

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Expansion of Coccidioidomycosis Endemic Regions in the United States in Response to Climate Change

Morgan E. Gorris¹, Kathleen K. Treseder², Charles S. Zender¹, and James T. Randerson¹

¹Department of Earth System Science, University of California, Irvine, CA, USA, ²Department of Ecology and Evolutionary Biology, University of California, Irvine, CA, USA

Abstract Coccidioidomycosis (Valley fever) is a fungal disease endemic to the southwestern United States. Across this region, temperature and precipitation influence the extent of the endemic region and number of Valley fever cases. Climate projections for the western United States indicate that temperatures will increase and precipitation patterns will shift, which may alter disease dynamics. We estimated the area potentially endemic to Valley fever using a climate niche model derived from contemporary climate and disease incidence data. We then used our model with projections of climate from Earth system models to assess how endemic areas will change during the 21st century. By 2100 in a high warming scenario, our model predicts that the area of climate-limited endemicity will more than double, the number of affected states will increase from 12 to 17, and the number of Valley fever cases will increase by 50%. The Valley fever endemic region will expand north into dry western states, including Idaho, Wyoming, Montana, Nebraska, South Dakota, and North Dakota. Precipitation will limit the disease from spreading into states farther east and along the central and northern Pacific coast. This is the first quantitative estimate of how climate change may influence Valley fever in the United States. Our predictive model of Valley fever endemicity may provide guidance to public health officials to establish disease surveillance programs and design mitigation efforts to limit the impacts of this disease.

Plain Language Summary Valley fever is a fungal disease most common in the southwestern United States. Generally, the disease is limited to areas that are hot and dry. Climate change will cause the western United States to become hotter and may change the location, timing, and amount of rain. This is likely to change which counties are affected by Valley fever. We used climate observations to estimate which counties in the United States have a higher risk for Valley fever. Then, we used predictions of future climate to map which counties may become affected by Valley fever during the remainder of the 21st century. By 2100, our model predicts that the area affected by Valley fever will more than double and the number of people who become sick will increase by 50%. The area affected by Valley fever will expand north into drier states in the western US, including Idaho, Wyoming, Montana, Nebraska, South Dakota, and North Dakota. Our estimate may help public health officials develop more effective plans so less people suffer from this disease.

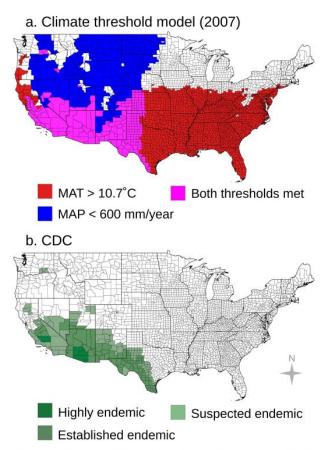


Figure 3. (a) Counties our climate-constrained niche model identify as endemic (with a mean annual temperature greater than or equal to 10.7°C and a mean annual precipitation level less than or equal to 600 mm/year) are colored in magenta. (b) There is reasonable agreement between this set of counties and the endemic region identified by the CDC. Counties shown in red in panel a have a mean annual temperature greater than or equal to 10.7°C but unsuitable mean annual precipitation (greater than 600 mm/year). Counties shown in blue have a mean annual precipitation level less than or equal to 600 mm/year but unsuitable mean annual temperature (less than 10.7°C). Counties in white our model defines as unsuitable according to both thresholds.

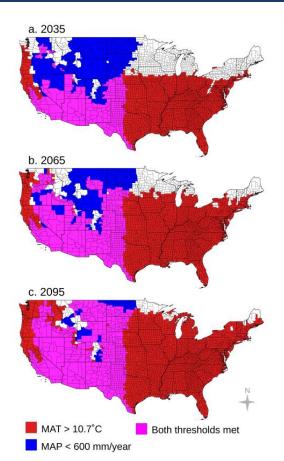


Figure 4. For the representative concentration pathway (RCP) 8.5 climate change scenario, areas where climate will permit Valley fever endemicity are shown for the years (a) 2035, (b) 2065, and (c) 2095. Areas where mean annual temperature will permit endemicity are shown in red, areas where mean annual precipitation will permit endemicity are shown in blue, and areas where both temperature and precipitation will permit endemicity are shown in magenta, following the color scheme used in Figure 3. The area endemic to Valley fever will extend farther north in future decades, especially in the rain shadows of the Sierra Nevada and Rocky Mountain Ranges. Precipitation will play a key role in determining which areas become endemic through time, as greater rainfall and moisture availability will limit the eastward extent of Valley fever as well as its presence in the Pacific Northwest and in western counties at higher elevations.

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Future Directions- Vaccines

- There are clinical trials being done for a veterinary vaccine for use in dogs
- In humans may modify disease but not prevent infections
- Decisions about who to target
- How to measure effectiveness



Thank you, Questions?

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