Current Topics in Coccidioidomycosis 10/21/23

Disclosures

There is no commercial support for today's activity.

None of the speakers or planners for today's meeting have disclosed any relevant financial relationships.

Coccidioidomycosis

October 21, 2023

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Zachary Rubin, MD

Los Angeles County Department of Public Health
Acute Communicable Disease Control Program

Clinical spectrum of disease

- First diagnosed in 1889 by Alejandro Posadas, medical student in Argentina who examined a 36M soldier with a lesion on his cheek→
  - "In 1891, Posadas, then a medical student, first saw the patient, who had a large purple, fungal-like mass covering much of his right cheek, several ulcerative vegetations on his nose, one on his arm resembling a cauliflower, and many papules on his extremities and trunk..
  - "…skin biopsy specimens revealed organisms resembling the protozoan *Coccidia*
  - "The patient eventually died in 1898 after 7 years of recurrent fever and progressive cutaneous lesions."

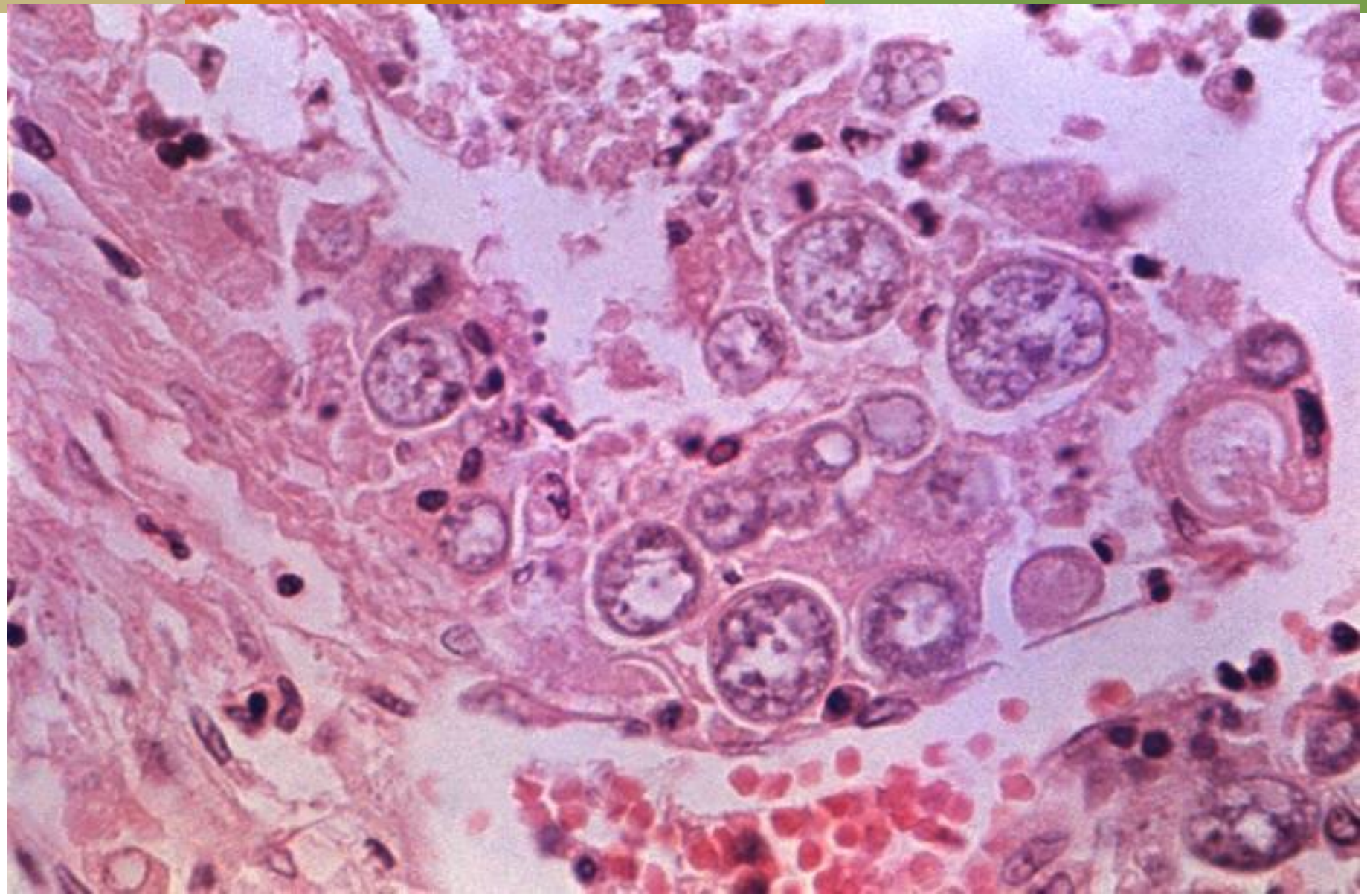
Hirschman. CID. 2007.
https://academic.oup.com/cid/article/44/9/1202/328906

Domingo Escurra

- Head discovered in a jar in 1948 in University of Buenos Aires medical school.
- Foot discovered in 1949

Deresinski Med Mycology. 2019. https://www.researchgate.net/publication/330742292_Coccidioidomycosis_What_a_long_strange_trip_it's_been.

- Biopsy findings:

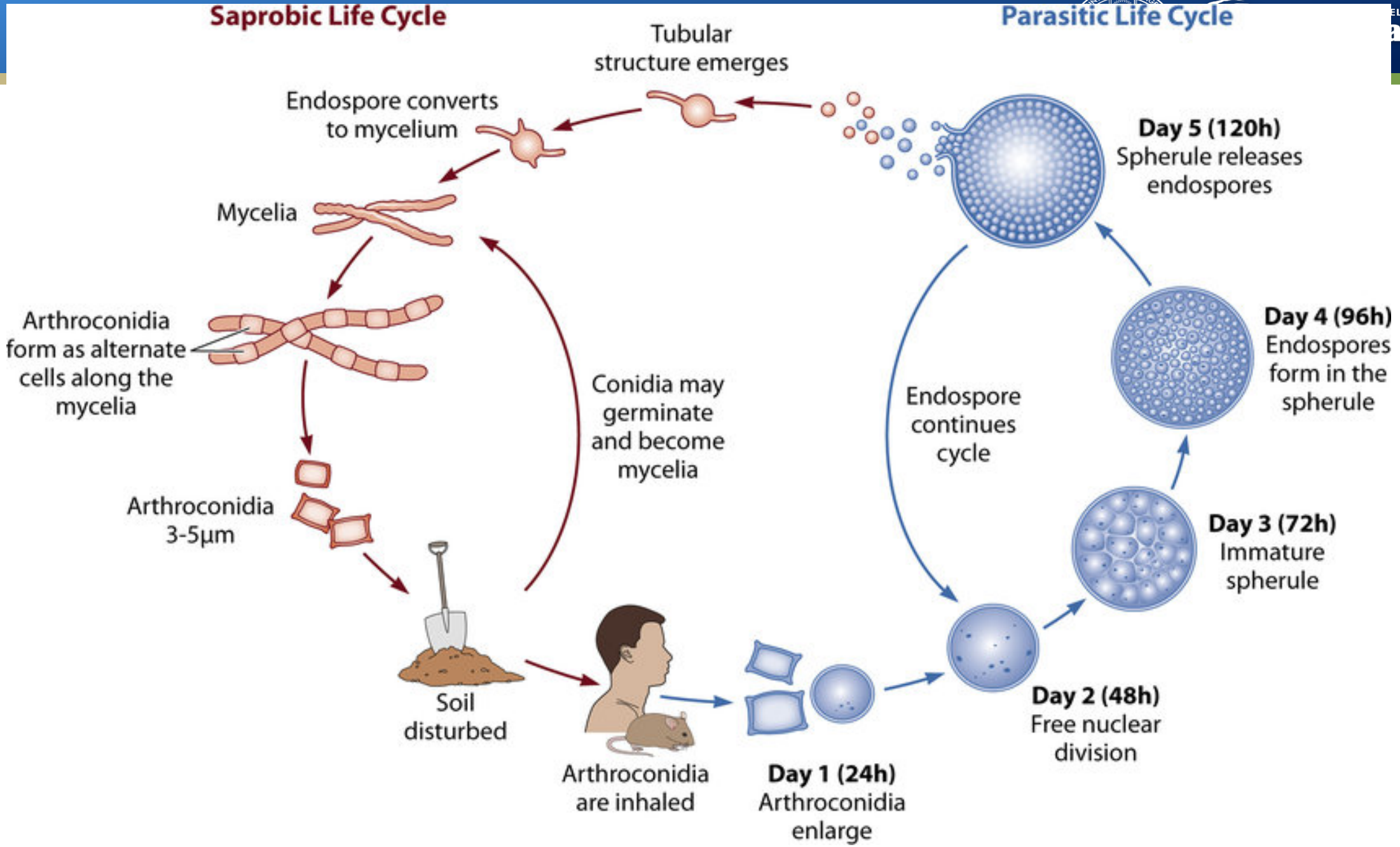


CDC. PHIL:. https://phil.cdc.gov/Details.aspx?pid=21836

Coccidiodiomycosis

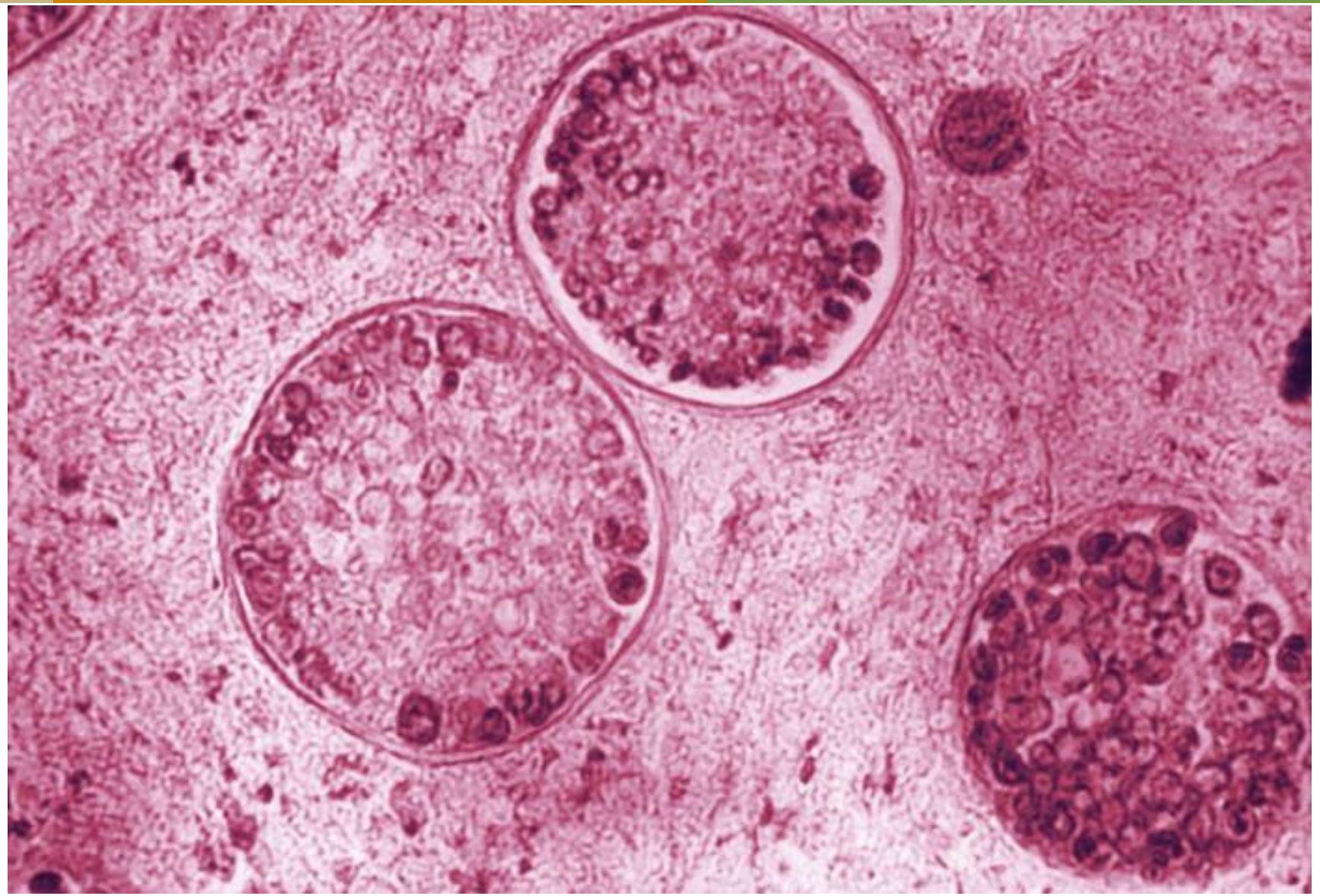
Cocci

- 2 species:
  - *C. immitis*
  - *C. posadasii*
- Southwestern US
- Dimorphic fungus (yeast form [spherule] in human tissue and mold in culture)
- Fungal transmitted via inhalation of arthroconidia spores in soil/dust.
- No person to person transmission
- Disease may be observed after inhalation of a single spore
- Rodent burrows thought to be common source
- Cocci infects humans, dogs, cats, other mammals (dolphins, sea lions)



https://www.researchgate.net/figure/Life-cycle-of-Coccidioides-Coccidioides-spp-alternate-between-saprobic-mycelia-left_fig1_336590024

- Characteristic spherule with endospores on microscopy

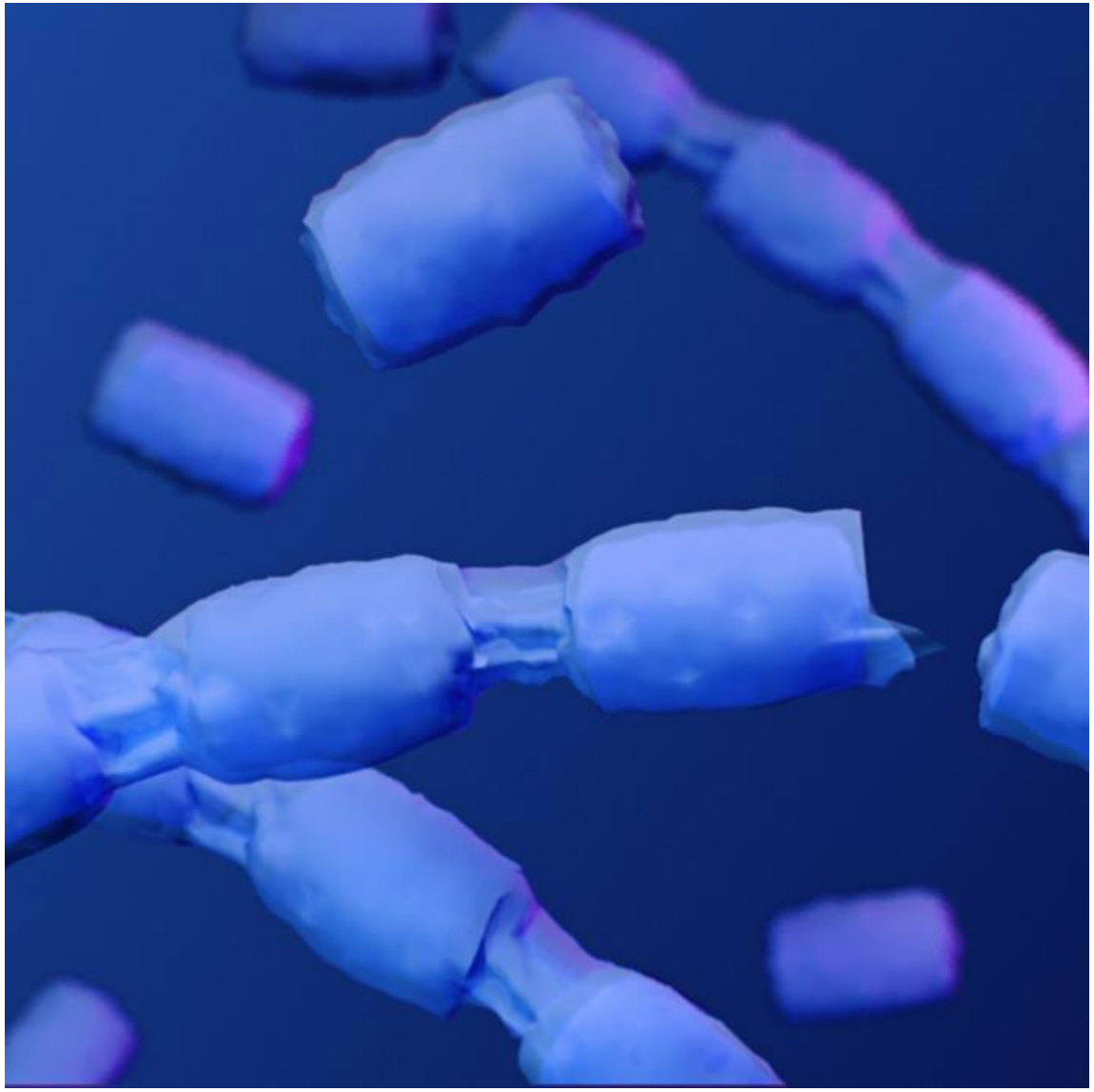


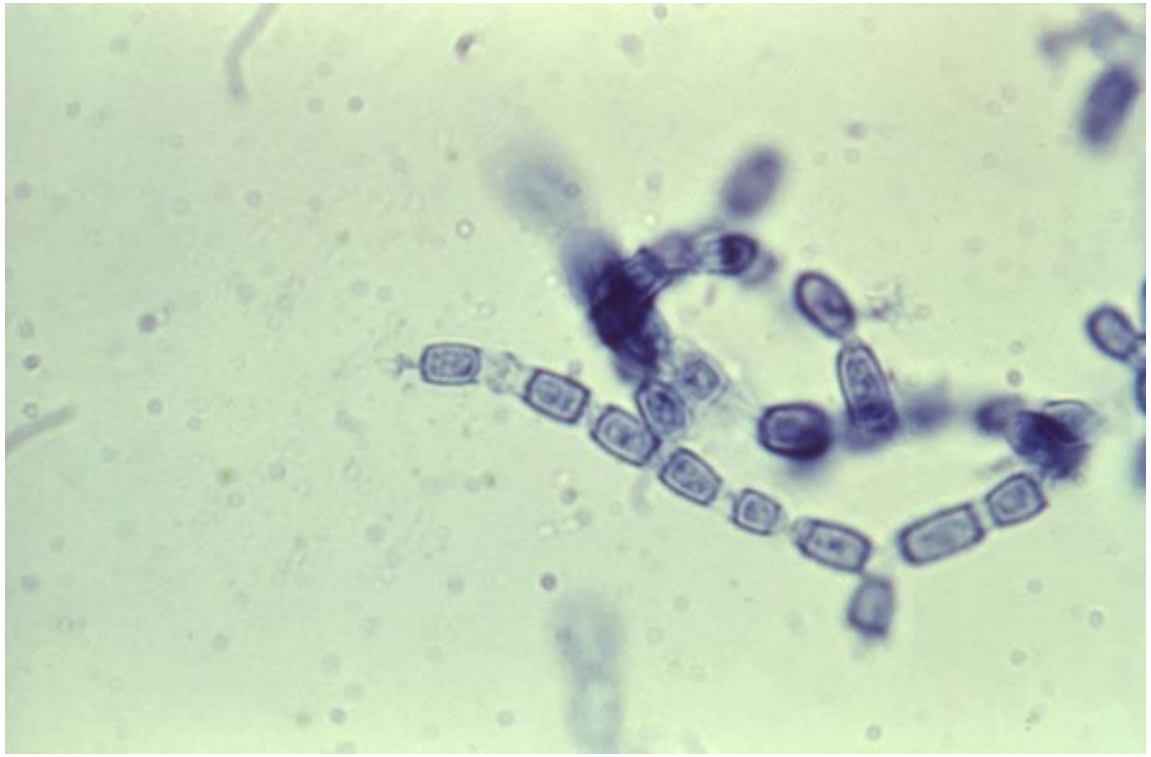
CDC. PHIL:. https://phil.cdc.gov/Details.aspx?pid=22308

- Characteristic colony appearance

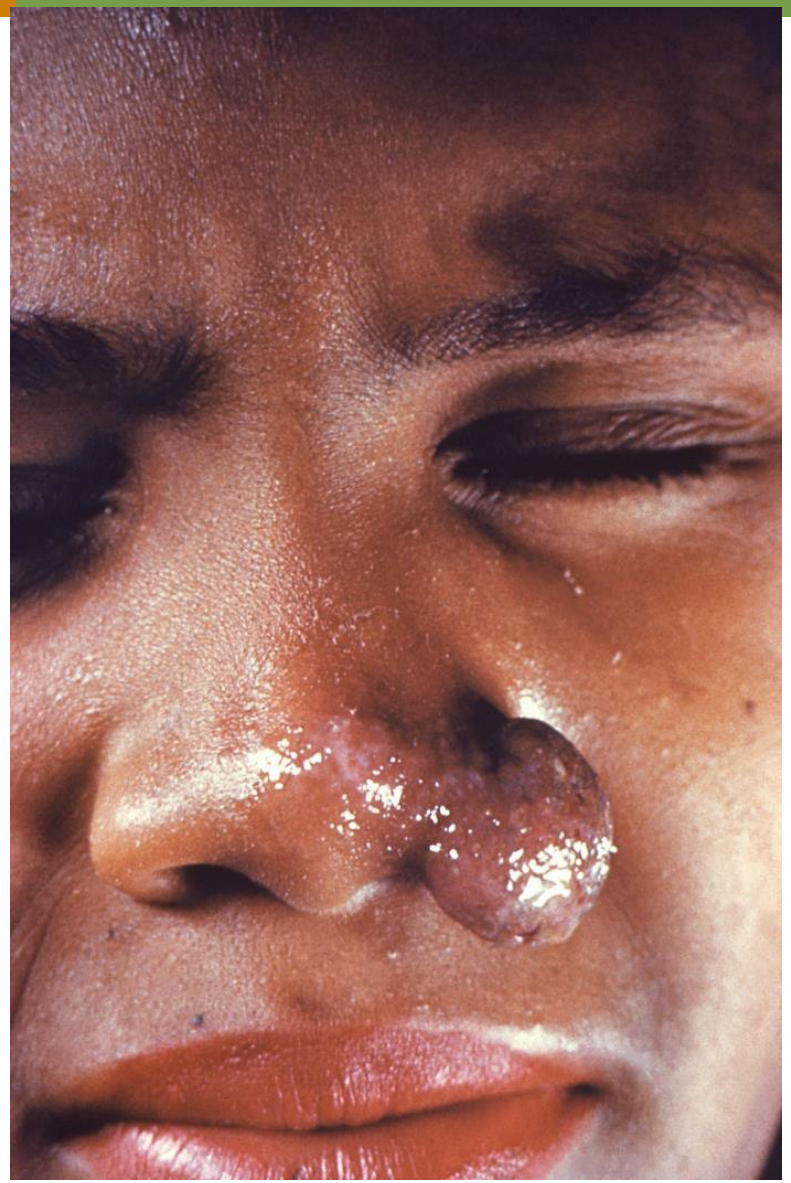
CDC. PHIL.. https://phil.cdc.gov/Details.aspx?pid=21609

Arthroconidia—infectious form





CDC. PHIL:. https://phil.cdc.gov/Details.aspx?pid=24211; https://phil.cdc.gov/Details.aspx?pid=15780



CDC. PHIL:. https://phil.cdc.gov/Details.aspx?pid=20135: https://phil.cdc.gov/Details.aspx?pid=16305

What is the mortality rate of Cocci?

- Complicated question…..
- After initial description, cases were thought to be almost universally fatal.
- In 1929, Harold Chope (26yo med student at Stanford) opened a plate with old Cocci mold and became infected with pneumonia, fever, erythema nodosum, sputum + cocci spherules, positive guinea pig test.
- Thinking he was going to die, hospital gave hm a single room, radio, reading materials.
- He survived!

Desert rheumatism

- After Chope's illness and recovery, better understanding that Cocci was likely more common than thought.
  - Desert rheumatism, San Juaquin Valley Fever, Valley Fever
  - Pneumonia + joint aches + erythema nodosum.
- Most patients spontaneously resolved
- 1936 in Kern County
  - 25% of random sample + by Coccidiodin skin test
  - 104 patients with Valley Fever
    - 94% white
    - Disseminated disease: 60% non-white

https://en.wikipedia.org/wiki/Erythema_nodosum

Hirschman. CID. 2007. https://academic.oup.com/cid/article/44/9/1202/328906

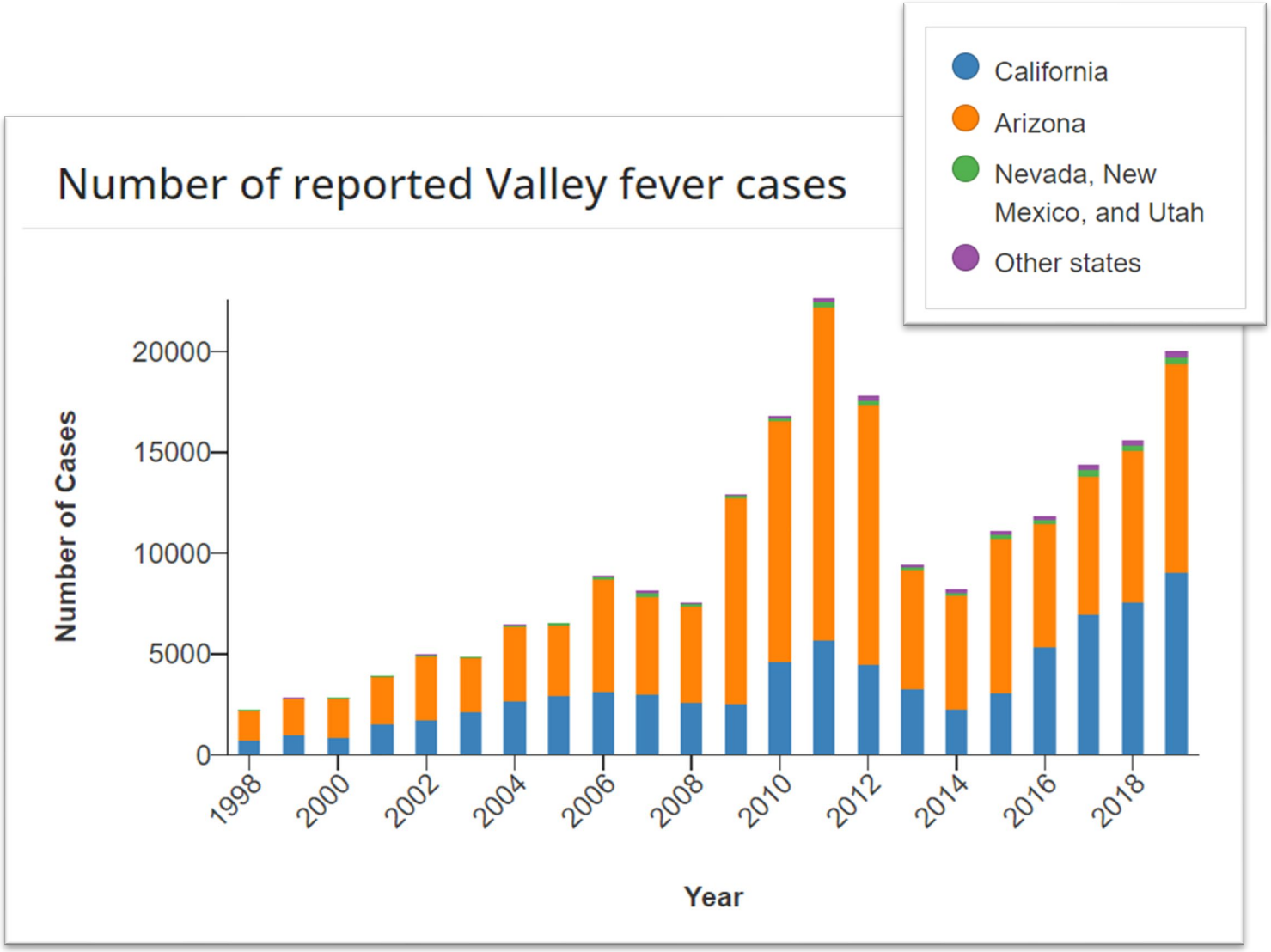
Seroprevalence studies

- Charles E. Smith at Stanford (took over after Chope graduated)
  - 1938 Kern County
  - Most cases of Valley Fever (66%)had moved to endemic area within previous 2 years
  - ~80% of school children had + skin test after 10 years, only 5% had symptoms
  - Investigated first outbreak in 1940 when Stanford students and faculty dug in rodent burrow.
  - Smith identified *C. immitis* in soil at the site and established the source of the fungus.

Hirschman. CID. 2007. https://academic.oup.com/cid/article/44/9/1202/328906

Epidemiology of Cocci

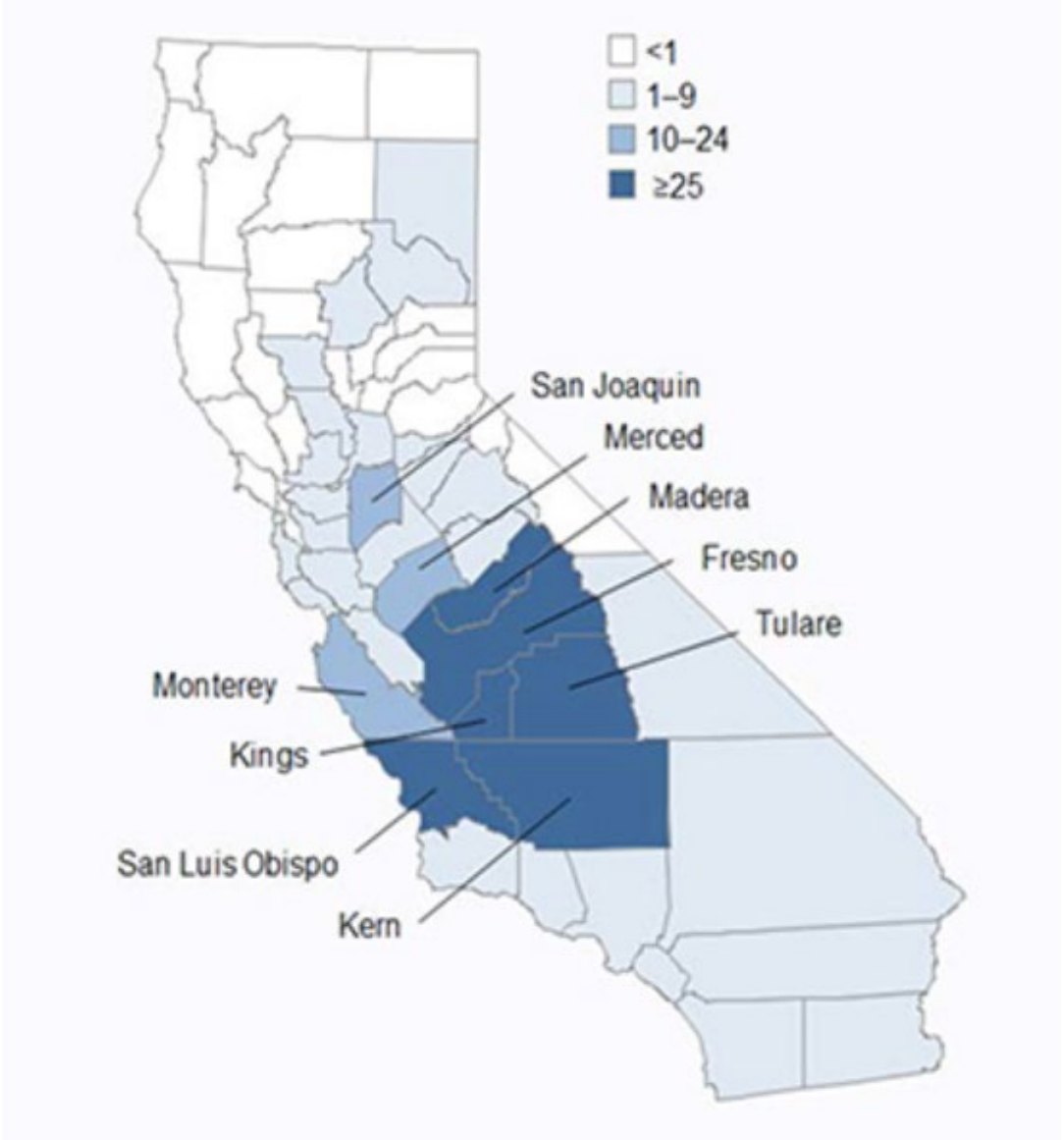
- Symptomatic cases rising
  - Population growth
  - Population growth into high risk areas
  - Increased testing
  - Increased population of immunocompromised
  - Environmental changes



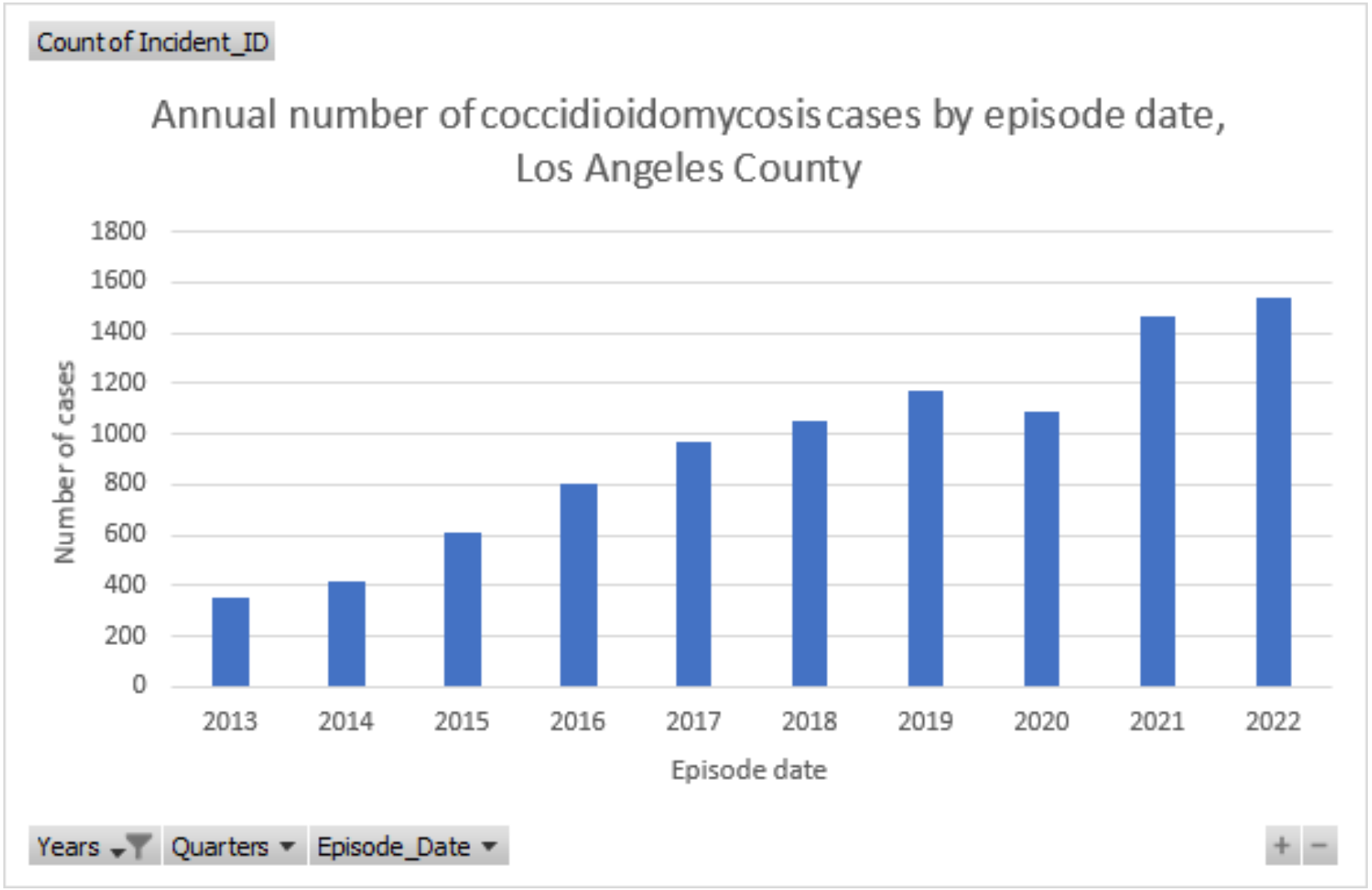
https://www.cdc.gov/fungal/diseases/coccidioidomycosis/statistics.html

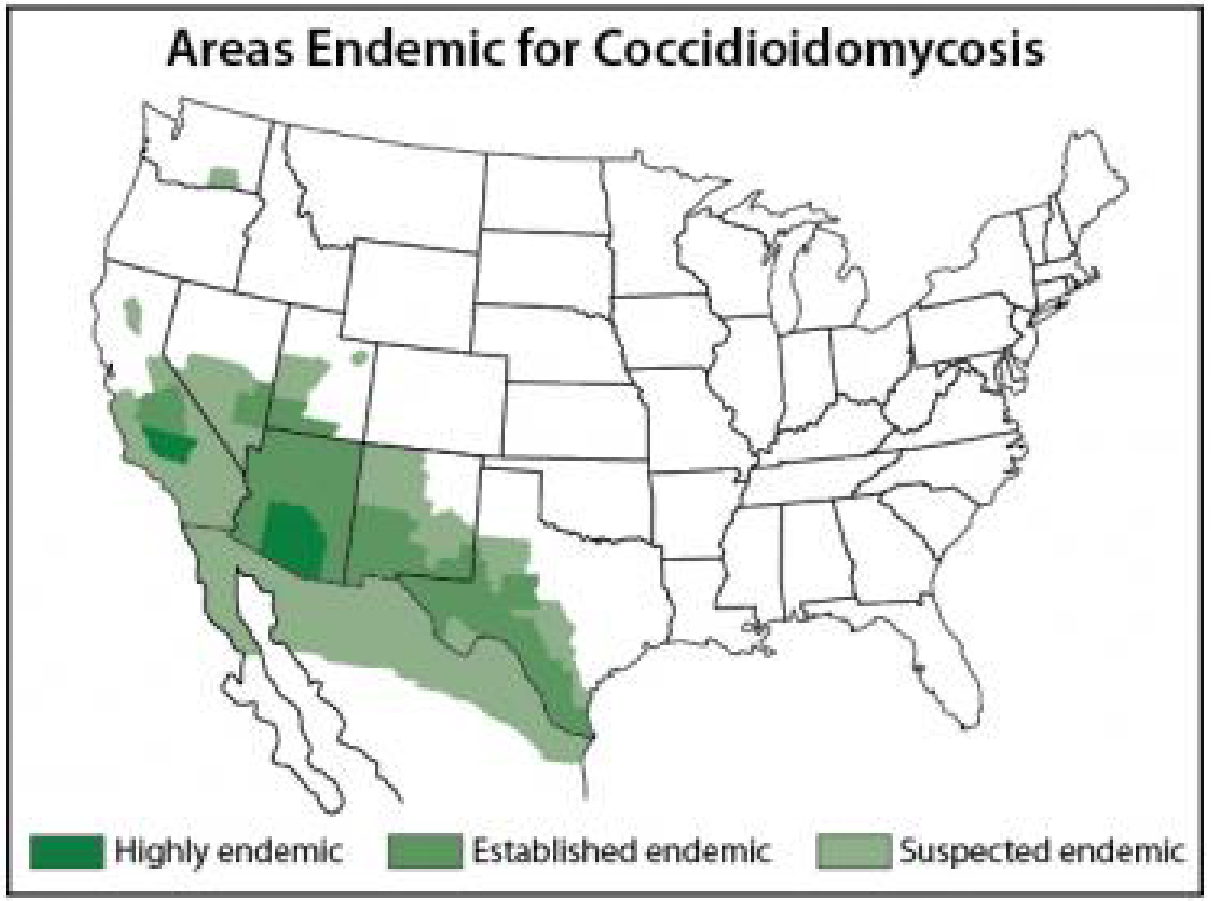
Risk factors for acquisition of Cocci

- Employment
  - Construction
  - Archaelogists
  - Geologists
  - Wildland firefighters
  - Military personnel
  - Mining
  - Agriculture workers
  - Prison



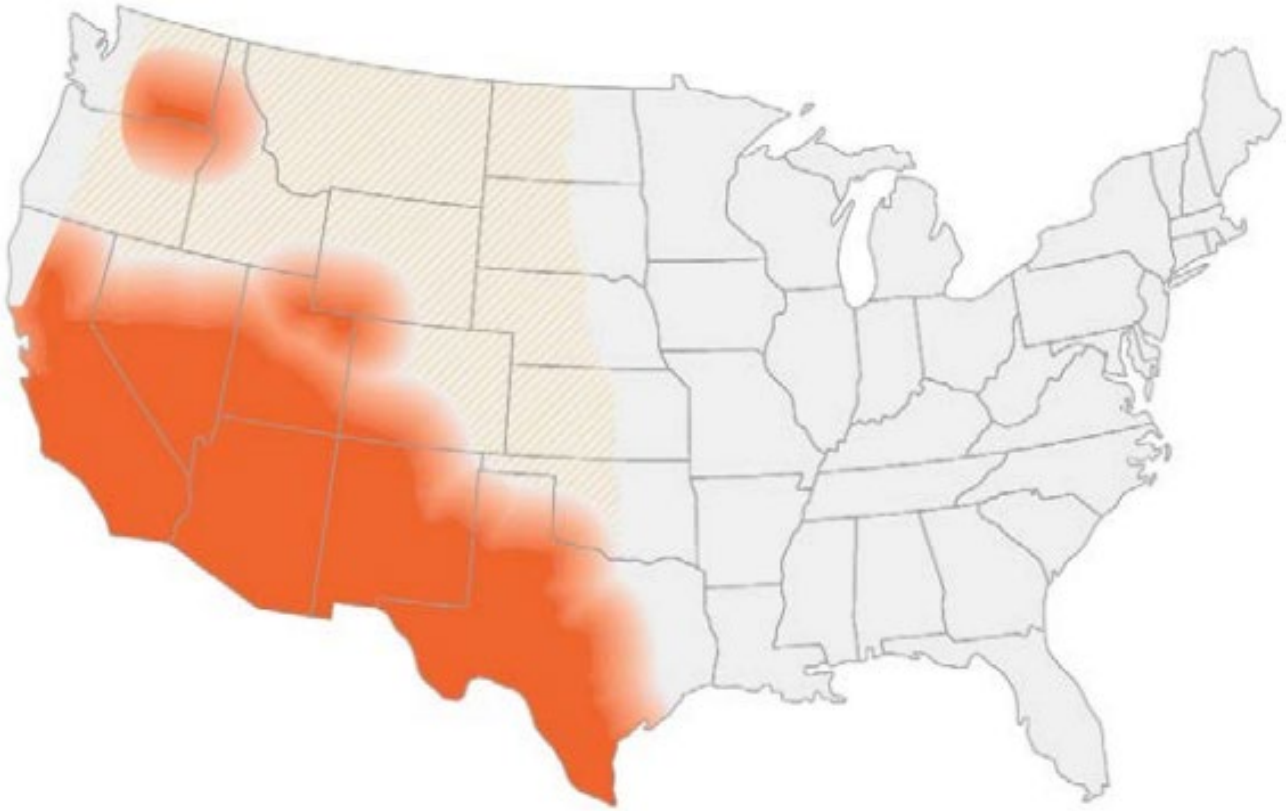
Cocci case count in LA County





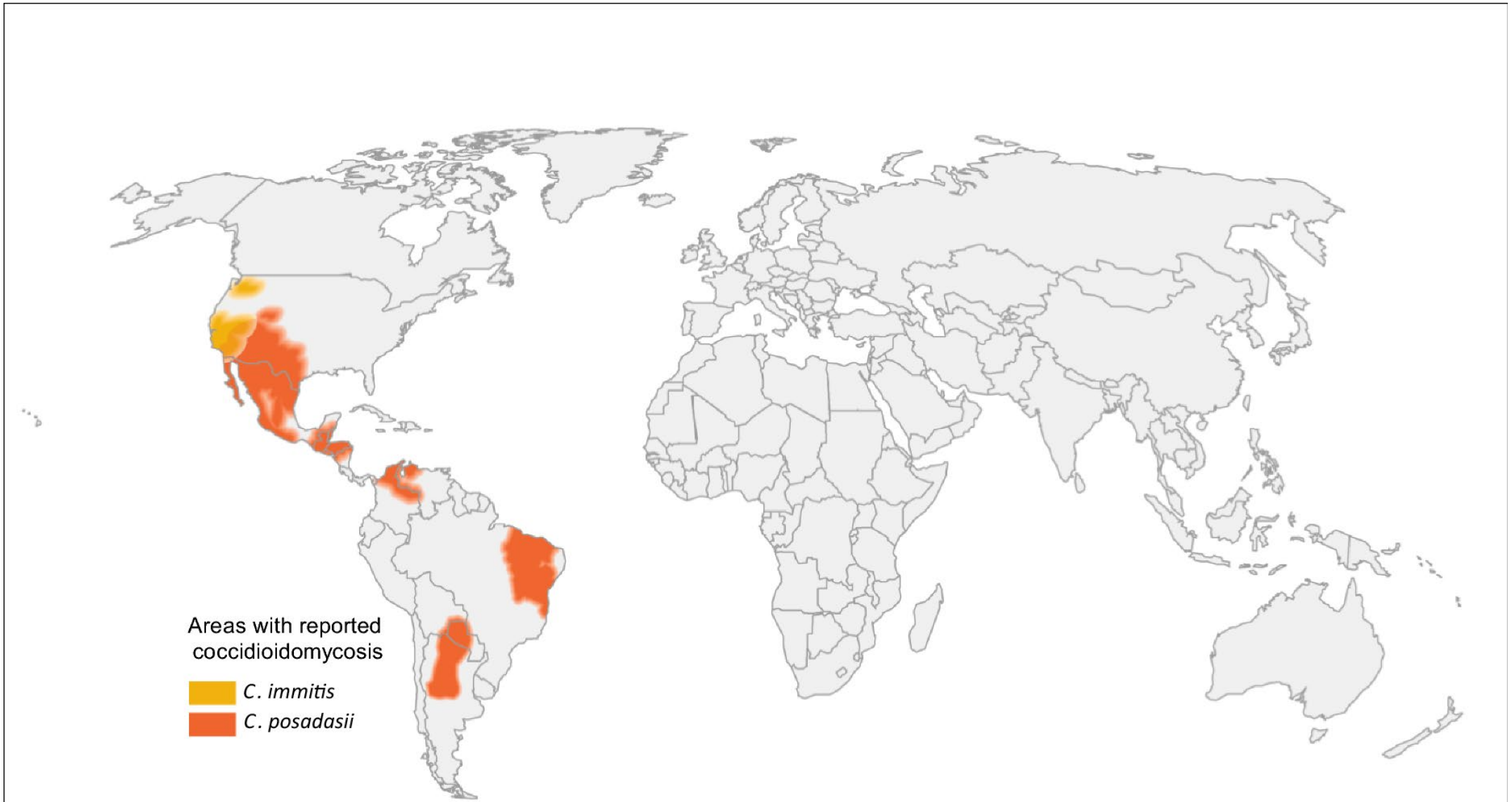
https://news.arizona.edu/valley-fever

Coccidioidomycosis (Valley fever)



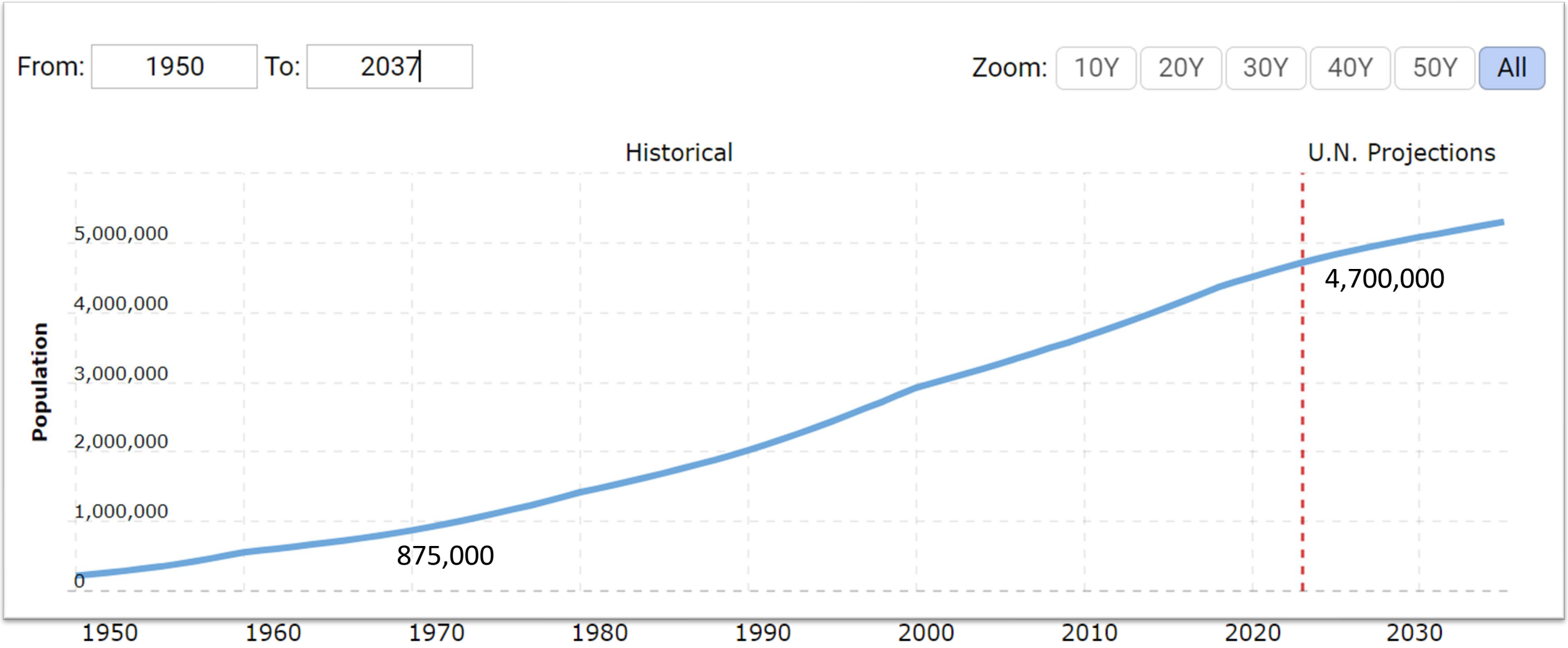
https://www.cdc.gov/fungal/pdf/more-information-about-fungal-maps-508.pdf

Cocci is an international disease



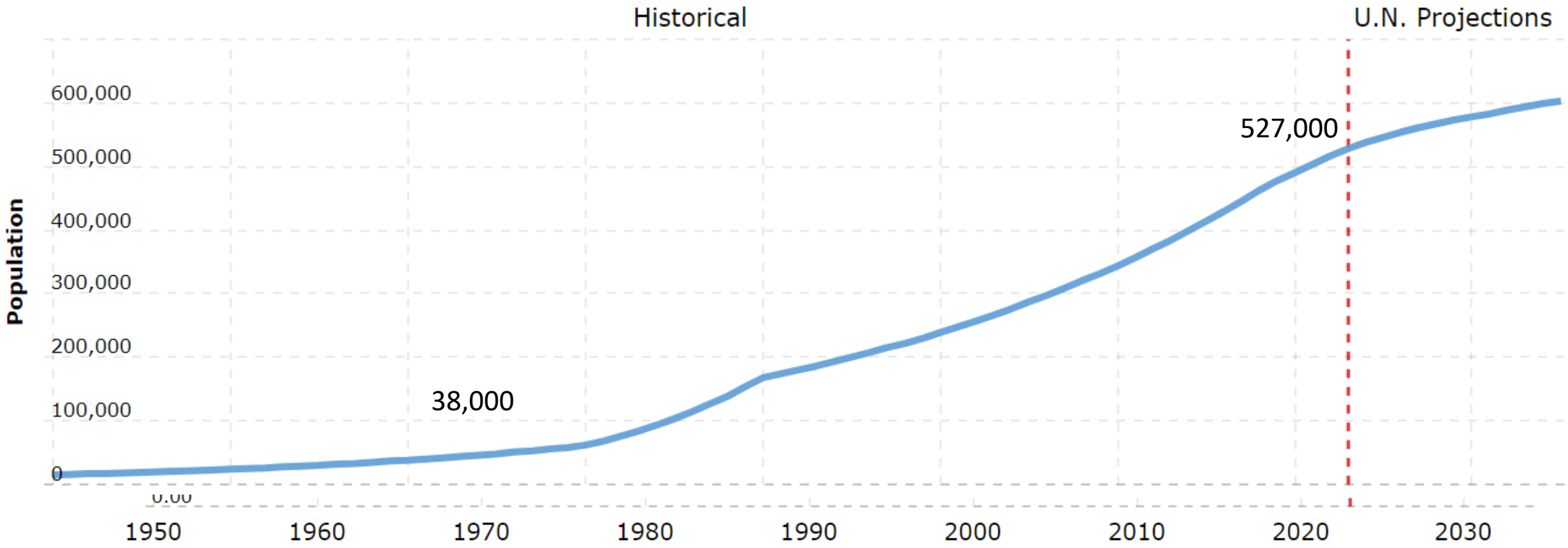
https://link.springer.com/article/10.1007/s11046-020-00431-2/figures/2

Population at risk increasing, Phoenix, AZ



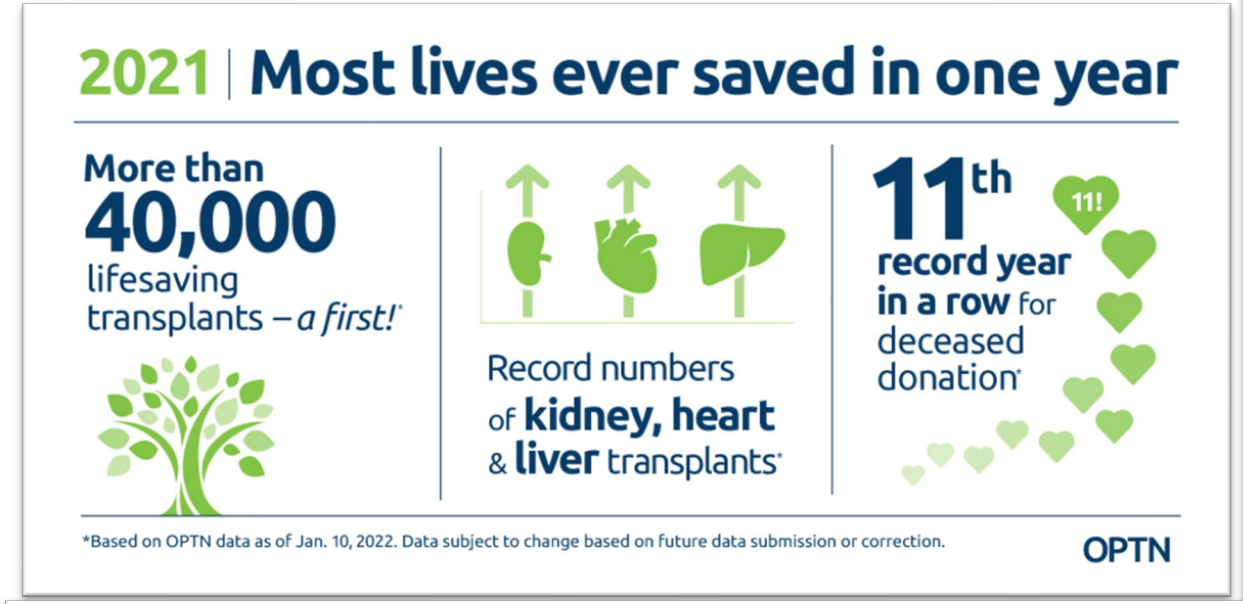
https://www.macrotrends.net/cities/23099/phoenix/population

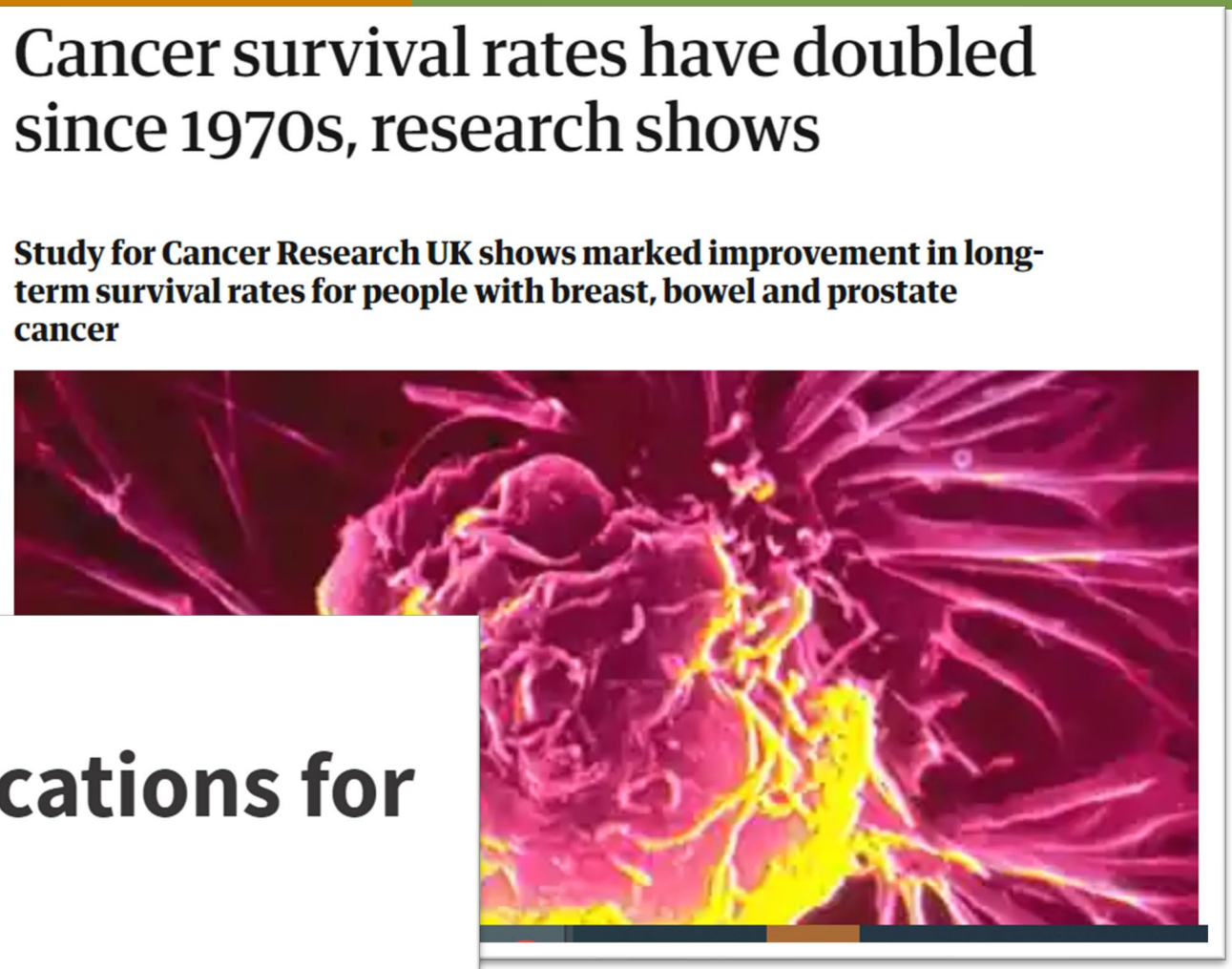
Population at risk increasing, Antelope Valley, CA

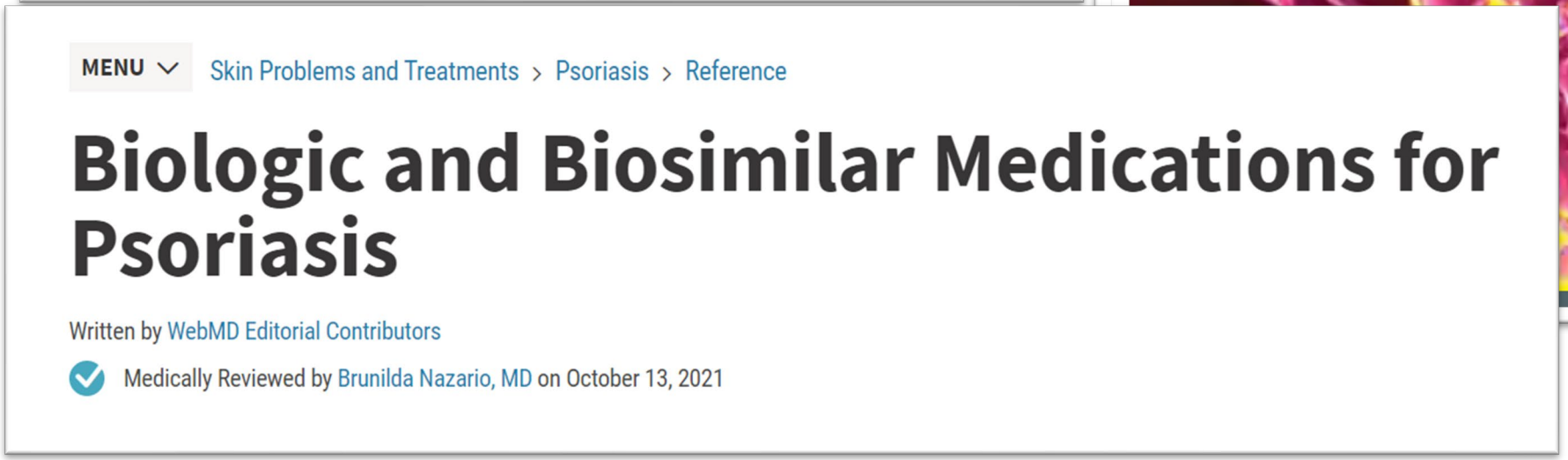


https://www.macrotrends.net/cities/23099/phoenix/population

People living with immunosuppression increasing





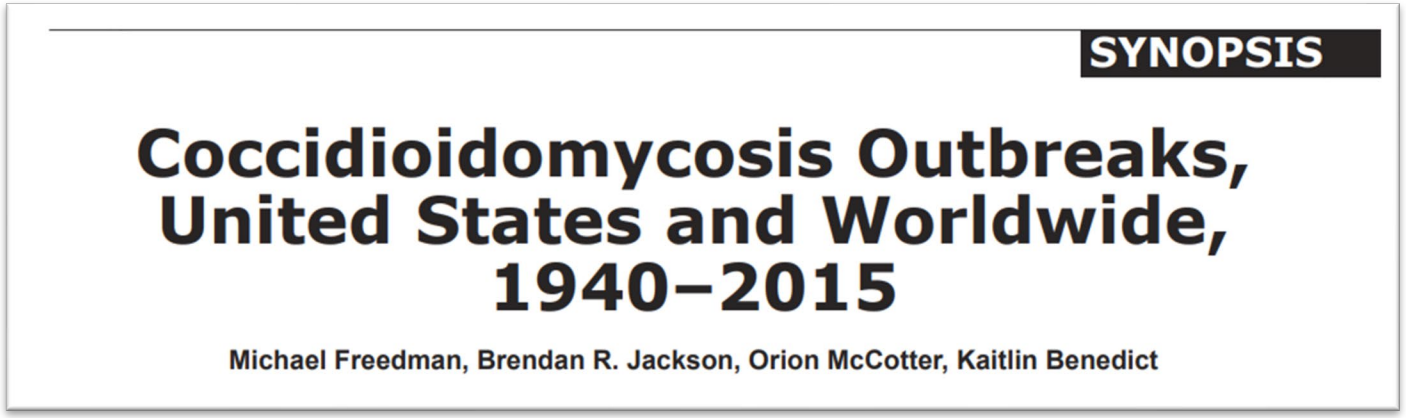


https://optn.transplant.hrsa.gov/news/all-time-records-again-set-in-2021-for-organ-transplants-organ-donation-from-deceased-donors/

https://www.theguardian.com/science/2010/jul/12/cancer-survival-rates-doubled

https://www.webmd.com/skin-problems-and-treatments/psoriasis/biologic-medications-psoriasis

Cocci Outbreaks



SYNOPSIS

Coccidioidomycosis Outbreaks, United States and Worldwide, 1940–2015

Michael Freedman, Brendan R. Jackson, Orion McCotter, Kaitlin Benedict

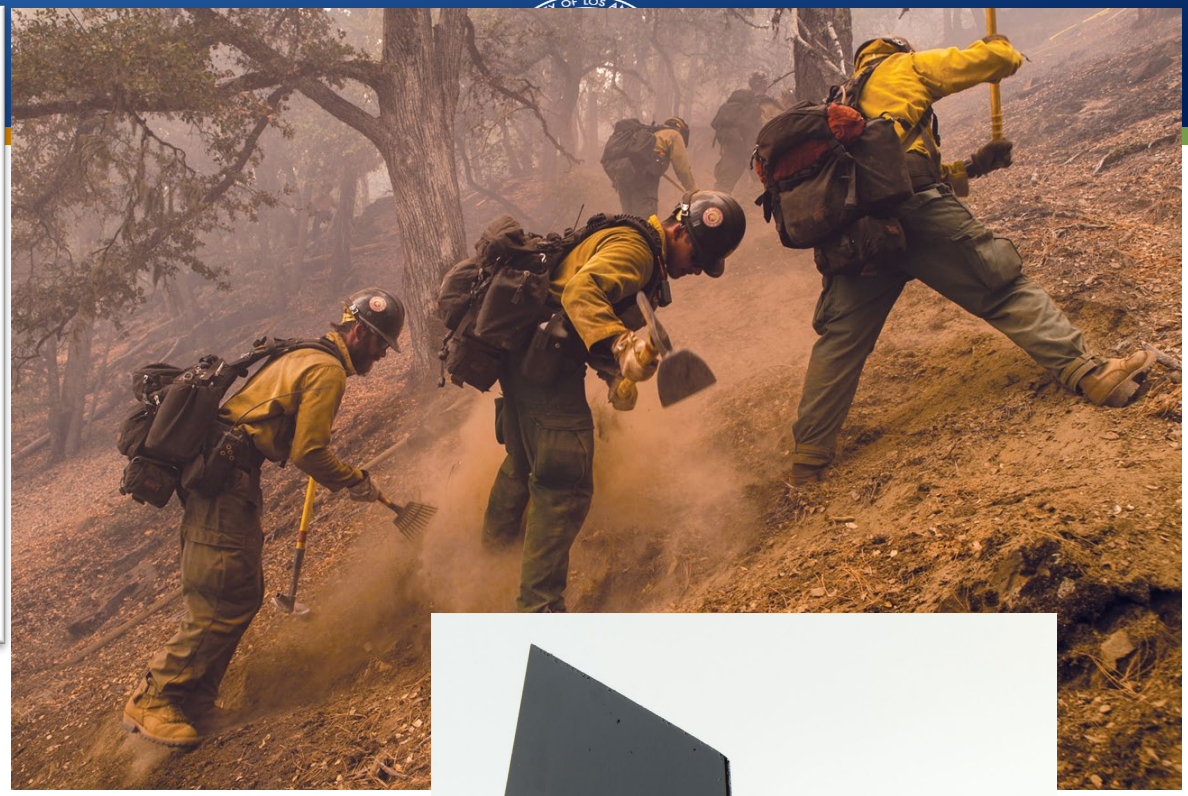
- Lit search identified 47 outbreaks (76% in CA):
  - Environmental exposure (earthquake, dust storm, etc)
  - Occupational exposure (military, archaeology, construction, lab exposure)
  - Location (travel, residential, incarceration)
  - Other (armadillo hunting in Brazil, disruption of native American site)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5823332/pdf/17-0623.pdf

Published in final edited form as:
Am J Ind Med. 2021 April ; 64(4): 266–273. doi:10.1002/ajim.23218.

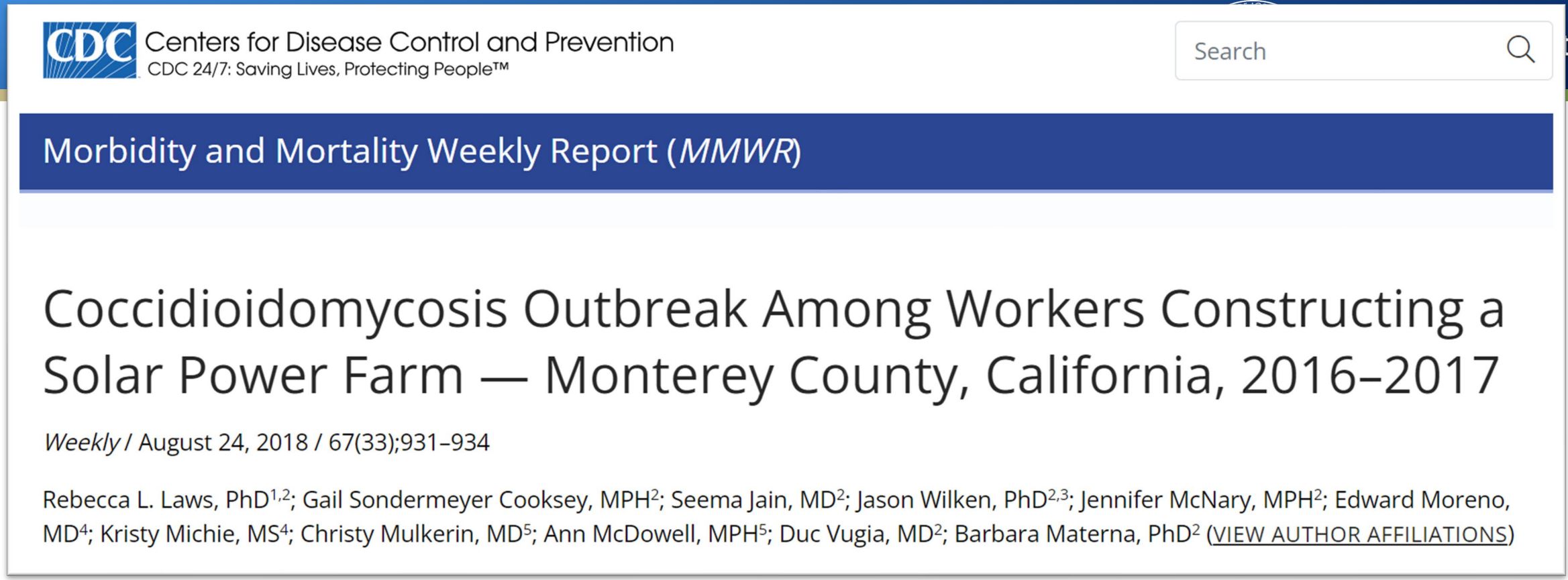
Coccidioidomycosis outbreak among inmate wildland firefighters: California, 2017

Rebecca L. Laws, PhD, MPH[1,2], Seema Jain, MD[2], Gail Sondermeyer Cooksey, MPH[2], Janet Mohle-Boetani, MD[3], Jennifer McNary, MPH[2], Jason Wilken, PhD, MPH[2,4,5], Robert Harrison, MD[2], Bruce Leistikow, MD[3], Duc J. Vugia, MD, MPH[2], Gayle C. Windham, PhD[2], Barbara L. Materna, PhD[2]



- 12 case out of 198 exposed inmates (identified by survey from symptoms)
- 2 hospitalizations
- Cutting fire lines with a McLoed tool main risk factor
- No firefighters wore respiratory protection
- Only 2 of 112 interviewed had Cocci training

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8935635/pdf/nihms-1778588.pdf
https://www.formula4media.com/articles/a-wildland-firefighter-weighs-in
https://www.wildlandwarehouse.com/shop/mcleod-tool/



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Search

Morbidity and Mortality Weekly Report (*MMWR*)

Coccidioidomycosis Outbreak Among Workers Constructing a Solar Power Farm — Monterey County, California, 2016–2017

Weekly / August 24, 2018 / 67(33);931–934

Rebecca L. Laws, PhD[1,2]; Gail Sondermeyer Cooksey, MPH[2]; Seema Jain, MD[2]; Jason Wilken, PhD[2,3]; Jennifer McNary, MPH[2]; Edward Moreno, MD[4]; Kristy Michie, MS[4]; Christy Mulkerin, MD[5]; Ann McDowell, MPH[5]; Duc Vugia, MD[2]; Barbara Materna, PhD[2] (VIEW AUTHOR AFFILIATIONS)

- 9 cases of 2410 exposed, identified clinically (no testing of asymptomatic pts done)
- Heavy dust exposure
- Jobs: biologist, paleontologist, electrician, truck driver, iron worker, general laborer
- Inconsistent respiratory protection
- 7/9 cases had some prior training

https://www.cdc.gov/mmwr/volumes/67/wr/mm6733a4.htm

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 63 / No. 15
April 18, 2014

Coccidioidomycosis Among Cast and Crew Members at an Outdoor Television Filming Event — California, 2012

Jason A. Wilken, PhD[1,2], Patricia Marquez, MPH[3], Dawn Terashita, MD[3], Jennifer McNary, MPH[1], Gayle Windham, PhD[1], Barbara Materna, PhD[1] (Author affiliations at end of text)

- 10 cases (5 confirmed) of 655 exposed
- Unexpected industry (film and television)
- Identified using Doctor's First Reports of Occupational Injury or Illness (DFR)

- Donor: AMS with unknown history
- Hydrocephalus of unknown etiology
- No cocci screening
- Postmortem antibody positive
- May influence prophylaxis or early treatment

	Recipient 1—kidney	Recipient 2—heart	Recipient 3—kidney/liver
Transplanted	Jan 19	Jan 19 (elective)	Jan 19
Discharged	Jan 23 (4)	Jan 28 (9)	N/A
Symptom onset	Jan 31 (11) Fever	Feb 3 (14) Pericardial effusion	Feb 1 (12) Fever
Readmitted	Feb 1 (12)	Feb 4 (15)	N/A
Antifungal Treatment	Voraconazole Feb 4 (15)	Caspofungin Feb 6 (17) Voraconazole Feb 8	Voraconazole Feb 1 (12)
Disposition	Died Feb 6 (17)	Died Feb 9 (20)	D/C Mar 28

Prevention of Cocci

The Guardian

‘It took everything’: the disease that can be contracted by breathing California’s air

Valley fever, derived from a fungus that lives in the US south-west's soil, is on the rise as climate crisis dries out the landscape.

Aug 29, 2022

Prevention strategies

- Earlier diagnosis & treatment
- Mitigation of transmission
  - High-risk
  - Work
- Chemoprophylaxis

High-risk individuals

On windy and dusty days, stay inside and keep windows and doors closed.

When driving through a dusty area, keep car windows closed and use recirculating air.

Control dust in your yard by covering open dirt areas around your house with grass, plants, or other ground cover (like gravel).

When digging

Before digging, wet down dirt to reduce dust.

While digging, face away from the direction that the wind is blowing.

Consider wearing an N95 mask if you must be around outdoor dust. Cloth masks and medical masks do not provide the same level of protection against dust as N95 masks.

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

Chemoprophylaxis recommended by IDSA Guidelines

RECOMMENDATIONS FOR PREEMPTIVE STRATEGIES FOR COCCIDIOIDOMYCOSIS IN SPECIAL AT-RISK POPULATIONS

XXVI. For Organ Transplant Recipients Without Active Coccidioidomycosis, Which Primary Prevention Strategy Is Preferred: Observation or Oral Azole?

Recommendation

53. For all patients undergoing organ transplantation in the endemic area without active coccidioidomycosis, we recommend the use of an oral azole (eg, fluconazole 200 mg) for 6–12 months (*strong, low*).

JOURNAL ARTICLE

Universal Lifelong Fungal Prophylaxis and Risk of Coccidioidomycosis in Lung Transplant Recipients Living in an Endemic Area

Get access >

Clover N Truong, Michael D Nailor, Rajat Walia, Lauren Cherrier, Aasya Nasar, Kellie J Goodlet ✉

Clinical Infectious Diseases, Volume 74, Issue 11, 1 June 2022, Pages 1966–1971, https://doi.org/10.1093/cid/ciab752

Published: 31 August 2021 **Article history** ▾

Galgiana. CID> 2016. https://academic.oup.com/cid/article/63/6/e112/2389093?login=false
https://academic.oup.com/cid/article-abstract/74/11/1966/6360397?redirectedFrom=fulltext&login=false

Vaccine development

Vaccine Protection of Mice With Primary Immunodeficiencies Against Disseminated Coccidioidomycosis

Daniel A. Powell[1,2], Amy P. Hsu[3], Christine D. Butkiewicz[1], Hien T. Trinh[1], Jeffrey A. Frelinger[1], Steven M. Holland[3], John N. Galgiani[1,4] and Lisa F. Shubitz[1]*

[1] Valley Fever Center for Excellence, University of Arizona, Tucson, AZ, United States, [2] Department of Immunobiology, University of Arizona, Tucson, AZ, United States, [3] Laboratory of Clinical and Infectious Diseases, National Institutes of Allergy and Infectious Disease, Bethesda, MD, United States, [4] Department of Medicine, University of Arizona, Tucson, AZ, United States

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8777018/pdf/fcimb-11-790488.pdf

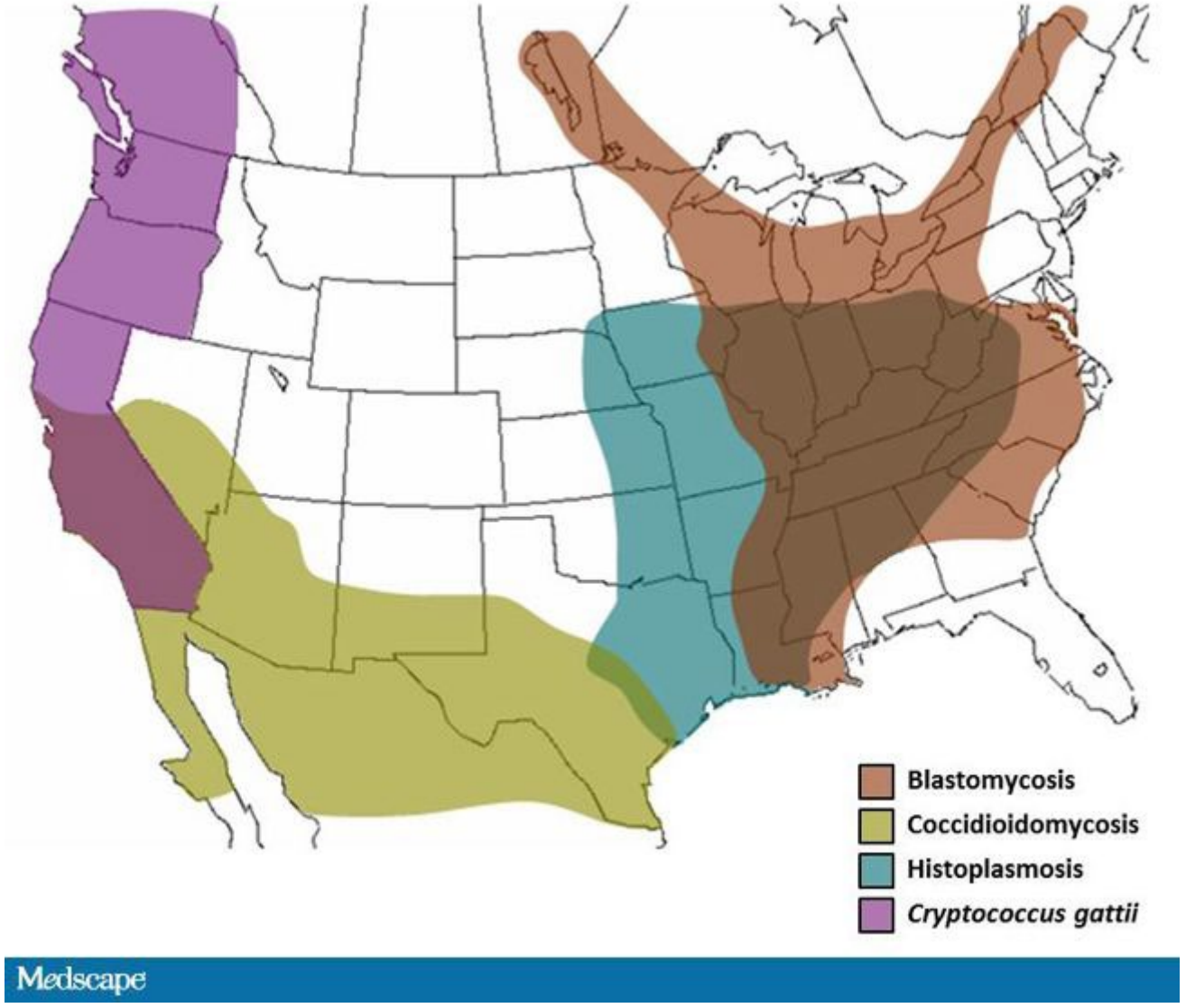
Thank You!

Questions?

Additional Slides

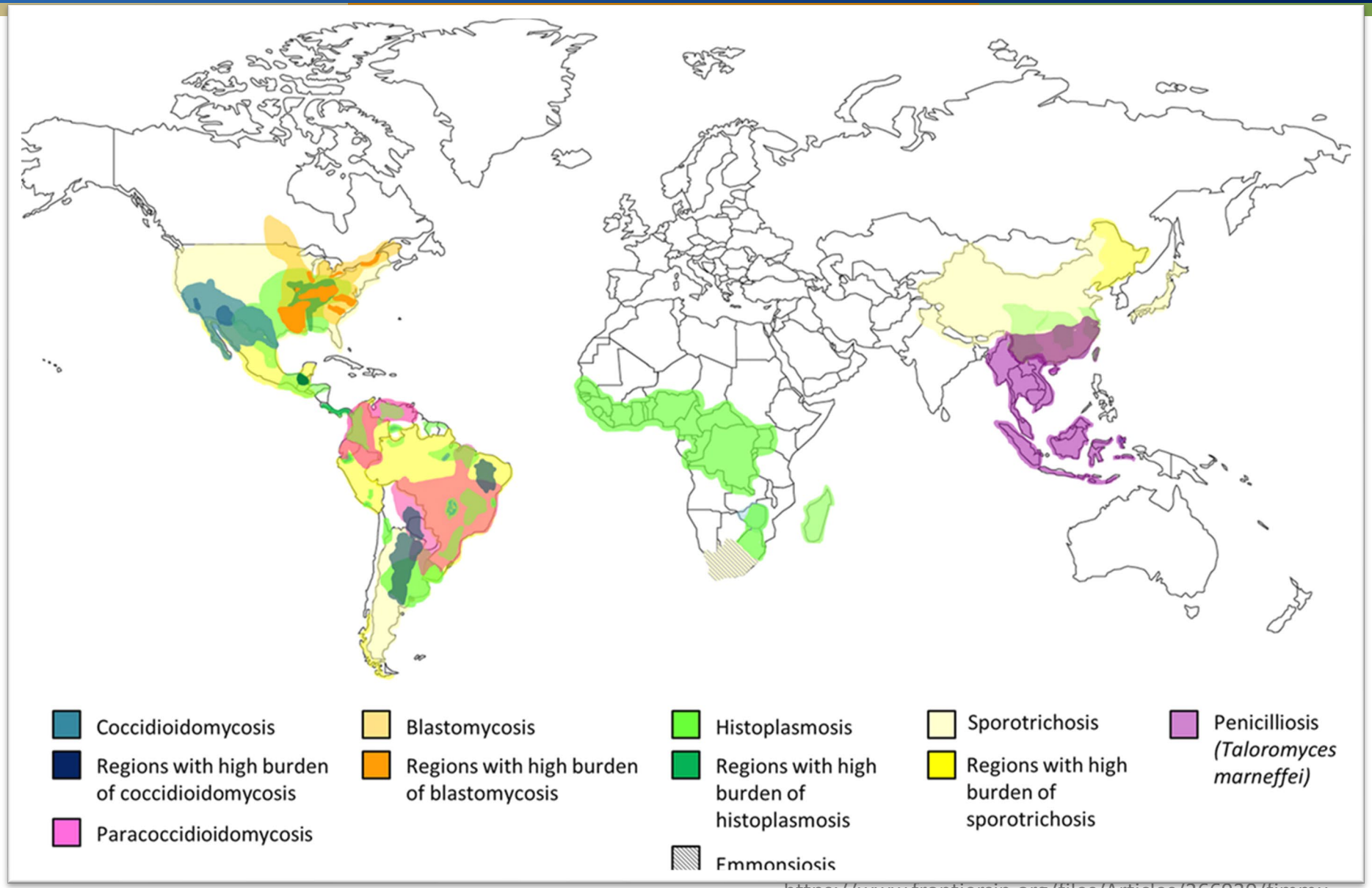
I am only going to school in CA temporarily, why worry?

Endemic Fungi in US



https://ldh.la.gov/page/2856

Endemic fungi worldwide



https://www.frontiersin.org/files/Articles/266920/fimmu-08-00735-HTML/image_m/fimmu-08-00735-g001.jpg

Endemic Fungi Worldwide

	Phylum	Order	Endemic regions	Animal hosts	Disease in human
Coccidioides immitis, C. posadasii	Ascomycota	Onygenales	Southwestern USA, northern Mexico, Central and South America	Non-human primates, domesticated or wide mammals, dogs, cats, horses, llamas, snakes	Coccidioidomycosis
Paracoccidioides brasiliensis, P. lutzii	Ascomycota	Onygenales	South America	Domesticated and wild animals (monkeys and armadillos), dogs	Paracoccidioidomycosis
Histoplasma capsulatum	Ascomycota	Onygenales	Worldwide; hyperendemic in Mississippi and Ohio river valleys in USA	Cattle, sheep, horses	Histoplasmosis
Blastomyces dermatitidis	Ascomycota	Onygenales	Worldwide (endemic in North America, autochthonous in Africa, South America, and Asia)	Dogs, cats, horses, marine mammals	Blastomycosis
Emmonsia spp.	Ascomycota	Onygenales	South Africa	Wild rodents	Emmonsiosis
Sporothrix schenckii, S. brasiliensis	Ascomycota	Ophiostomales	Worldwide	Cats, occasionally dogs, horses, cows, goats, mules, pigs, rats, armadillos, camels, dolphins, birds	Sporotrichosis
Talaromyces (Penicillium) marneffei	Ascomycota	Eurotiales	Southwest and southern China; Southeast Asia	Bamboo rats, domestic animals such as dogs and cats	Penicilliosis

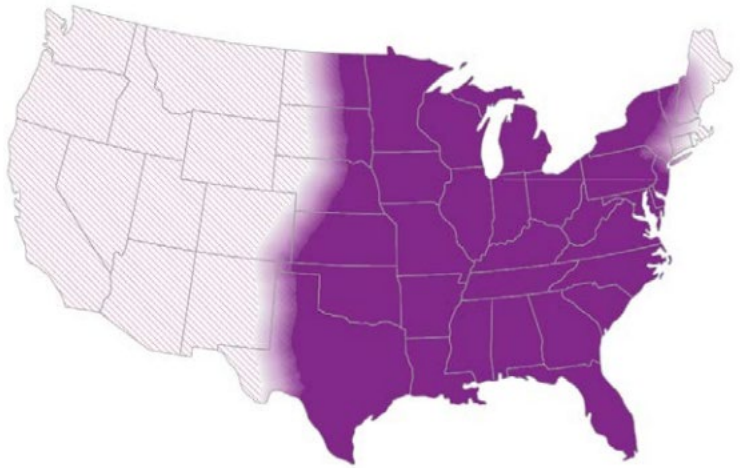
https://www.frontiersin.org/files/Articles/266920/fimmu-08-00735-HTML/image_m/fimmu-08-00735-t001.jpg

Questions?

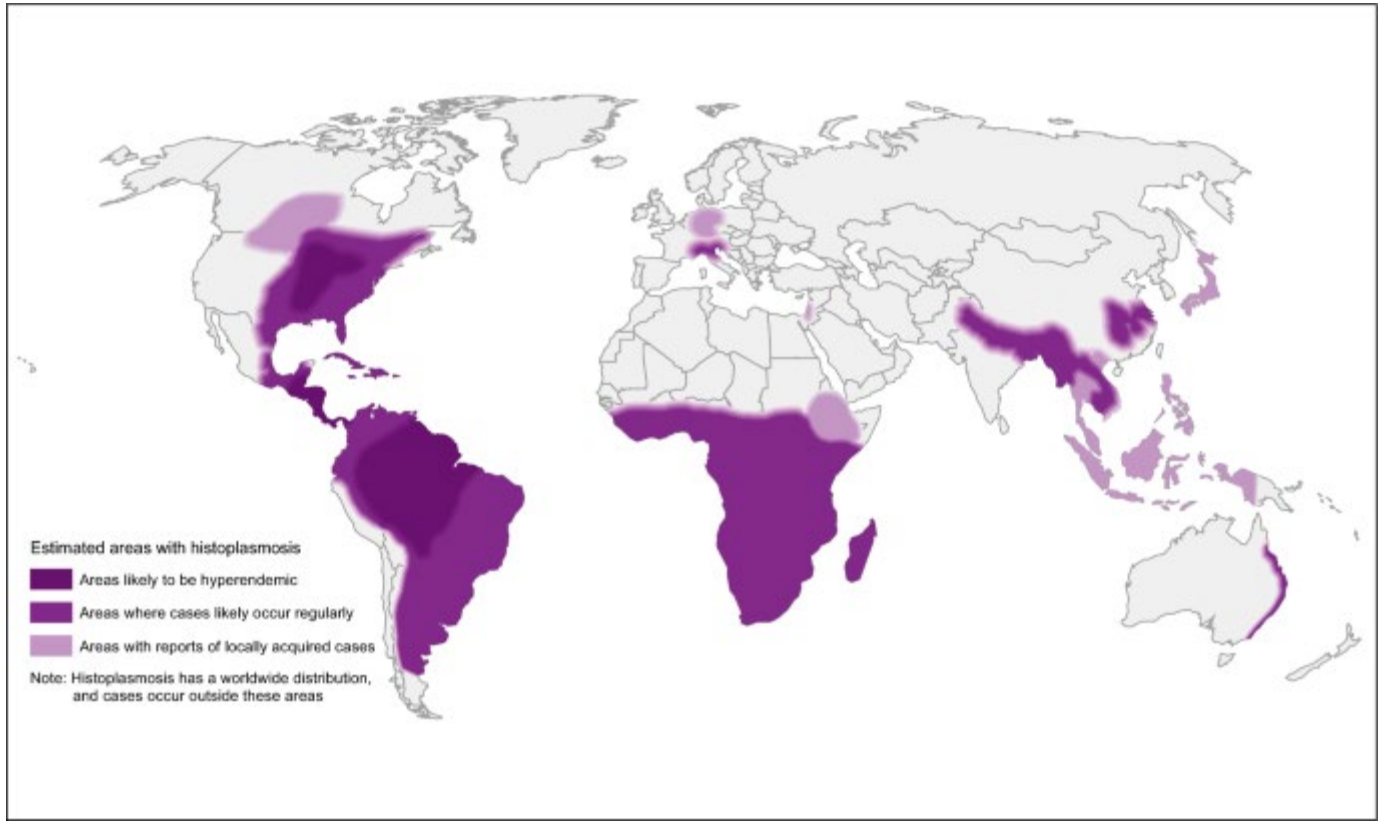
By Aaron Siirila, CC BY-SA 2.5, https://commons.wikimedia.org/w/index.php?curid=6164873

	Main endemic regions	Other areas	Natural habitat	Human activities/ conditions associated with increased risk of exposure	Occupations associated with increased risk of exposure
Coccidioidomycosis	Arizona and California in the US	Other parts of Southwestern US: New Mexico, Nevada, Utah and Texas Central America: Mexico, Guatemala, Honduras South America: Venezuela, Brazil, Argentina, Paraguay	Alkaline soils in dry desert climates	Soil excavations Dust storms, earthquakes	Construction site workers, farmers, military personnel, excavators, archeologists, inmates, and officers in correctional facilities
Histoplasmosis	*Histoplasma capsulatum var. capsulatum*: Ohio and Mississippi River Valleys in the Upper Midwest and Southeastern US *H. capsulatum var. duboisii* (African histoplasmosis): between 20° North and 20° South of the equator, and Madagascar	Southern Mexico Central and South America, e.g., Brazil, Uruguay, Paraguay, Argentina, Venezuela Mainland China: provinces along the Yangtze River (Yunnan, Sichuan, Hubei, Hunan, Jiangsu, Zhejiang) Southeast Asia, e.g., Thailand India, especially West Bengal and Uttar Pradesh along the Gangetic plains Europe: Italy (Po River Valley), Spain, Germany	Soil contaminated by bird and chicken excreta, or bat guano; bat caves	Walking on contaminated grounds, setting up tents Excavation, clearing foliage in a bird-roosting site	Miners, cave explorers, guano workers, farmers, beekeepers, archeologists
Paracoccidioidomycosis	*Paracoccidioides brasiliensis*: Brazil, Columbia, Venezuela, Paraguay *P. lutzii*: Center-West of Brazil	Central America and Mexico	Acid soils in area of coffee and sugar cane plantations	Soil exposure	Farmers, outdoor workers Women are less likely to develop clinical disease as estrogens inhibit conidial transformation to yeast cells
Blastomycosis	US: Mississippi and Ohio River valleys, Midwestern states Canada: provinces that border the Great Lakes and the Saint Lawrence Riverway, including Manitoba and northwestern Ontario	Middle and East Africa India	Warm, moist soil with high organic content, e.g., animal droppings	Occupational, residential, or recreational exposures to wildlife, soil, or bodies of freshwater	Occupational, residential, or recreational exposures that occur in close proximity to bodies of freshwater
Talaromyces marneffei infection	Thailand, Vietnam, Southern China	Laos, Malaysia, Myanmar, Cambodia, Hong Kong, Taiwan, Northeastern India	Soil, particularly burrows of bamboo rats	Soil exposure during rainy season	Agricultural workers
Sporotrichosis	Peru, Brazil, Mexico (Jalisco and Puebla mountain ranges)	Worldwide distribution in temperate and tropical regions—US, Asia (China, India, Japan), Australia	Soil and decaying vegetation, e.g., dead wood, sphagnum moss, cornstalks, hay	Cutaneous trauma with wound contamination by plants or soil; contact with reeds after flooding, bites from mice, armadillos, squirrels, cats, and dogs	Farming, gardening, flower vending, handling hay, animal husbandry, armadillo hunting (in Uruguay), mining

Histoplasmosis



https://www.cdc.gov/fungal/pdf/more-information-about-fungal-maps-508.pdf



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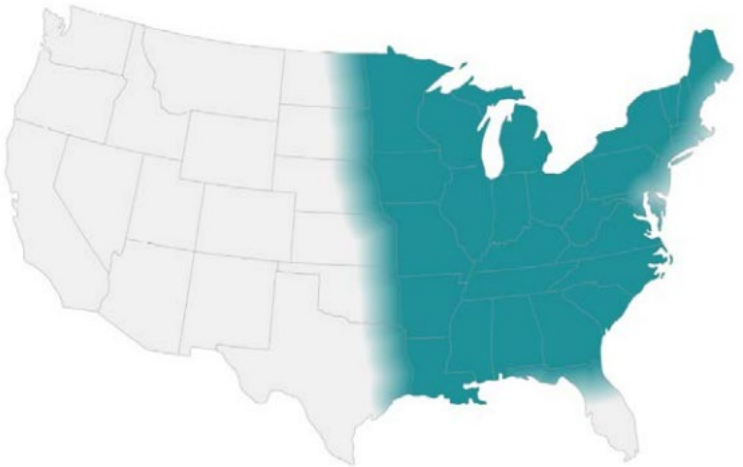
Blastomycosis



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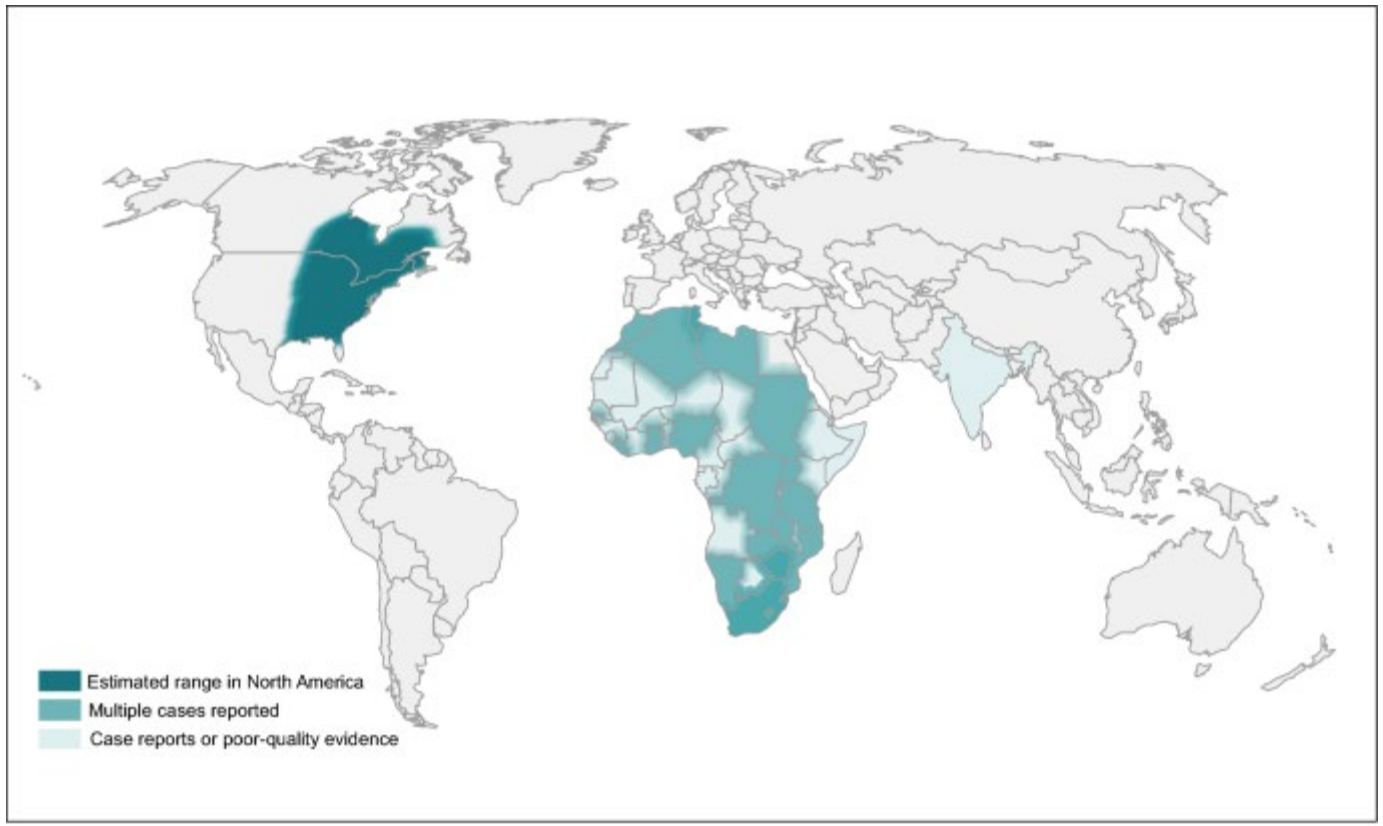
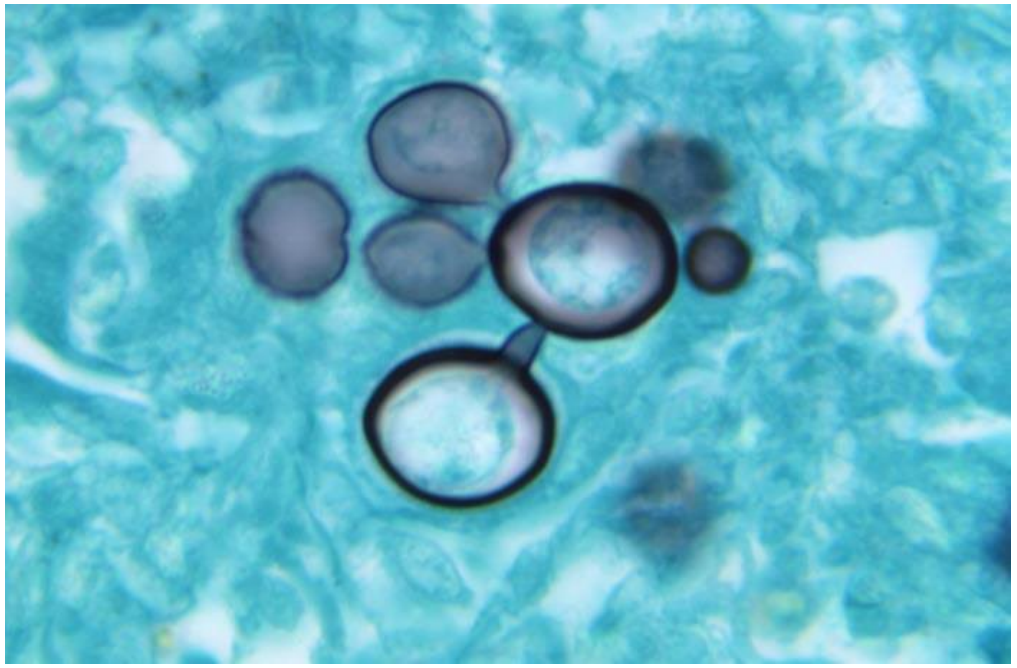
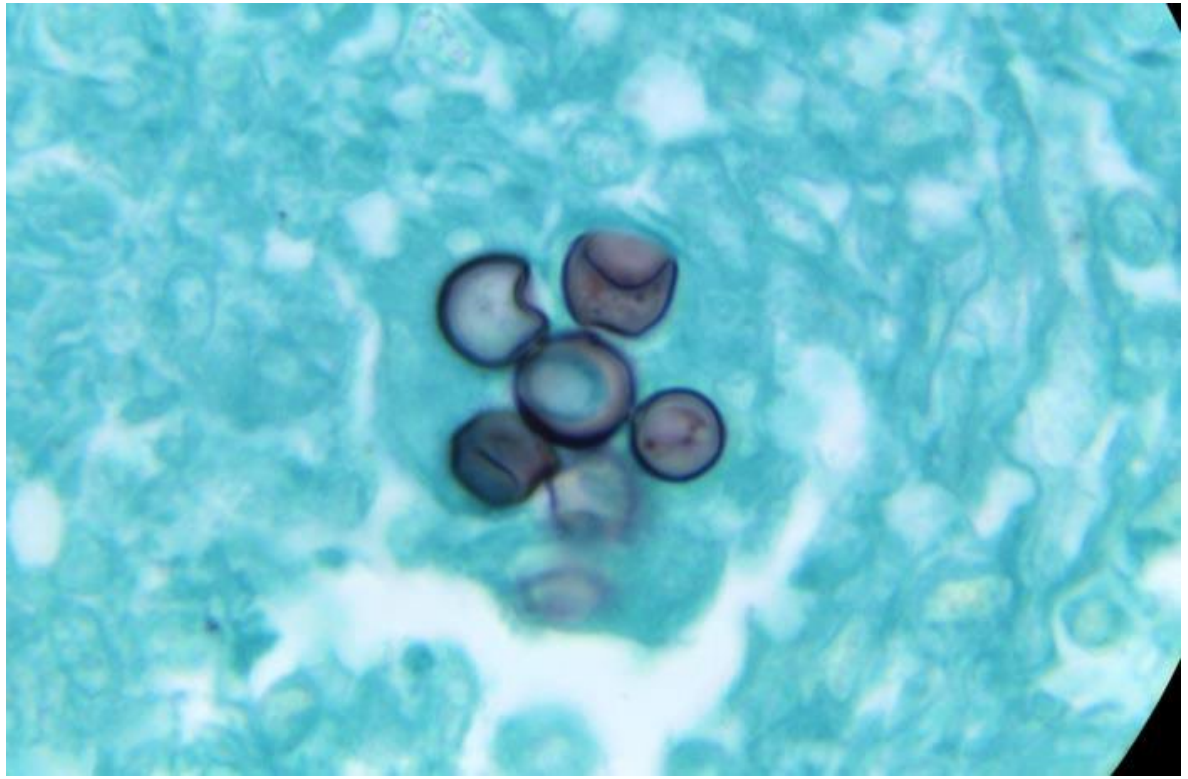


*Not that this map is specific to *Blastomyces dermatitidis* complex; other species, such as *Blastomyces helicus* are not included.

https://link.springer.com/article/10.1007/s11046-020-00431-2/figures/2

Paracocci





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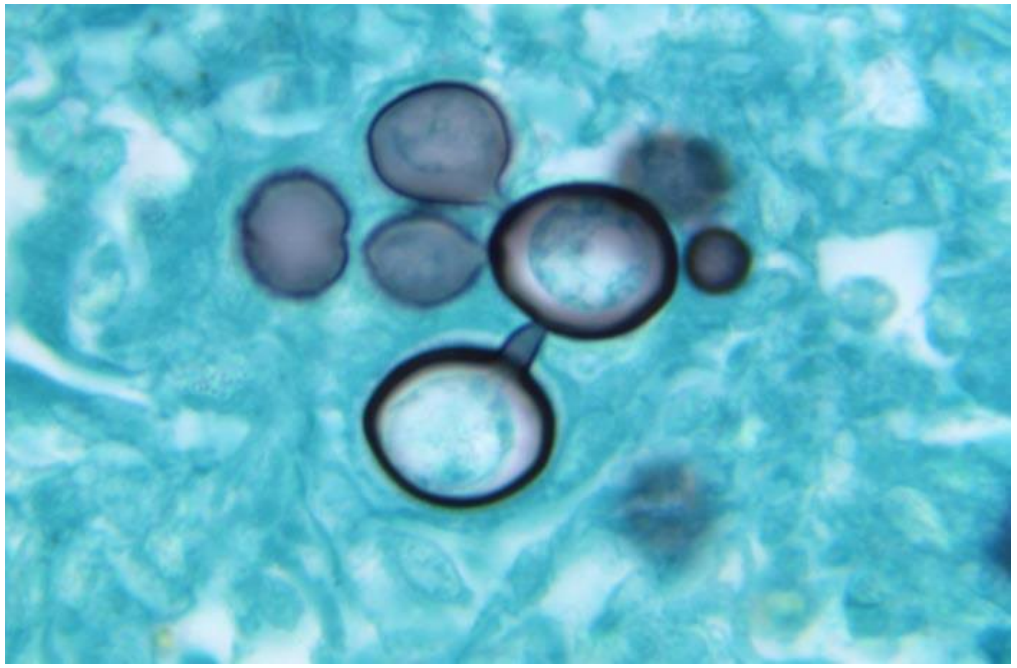

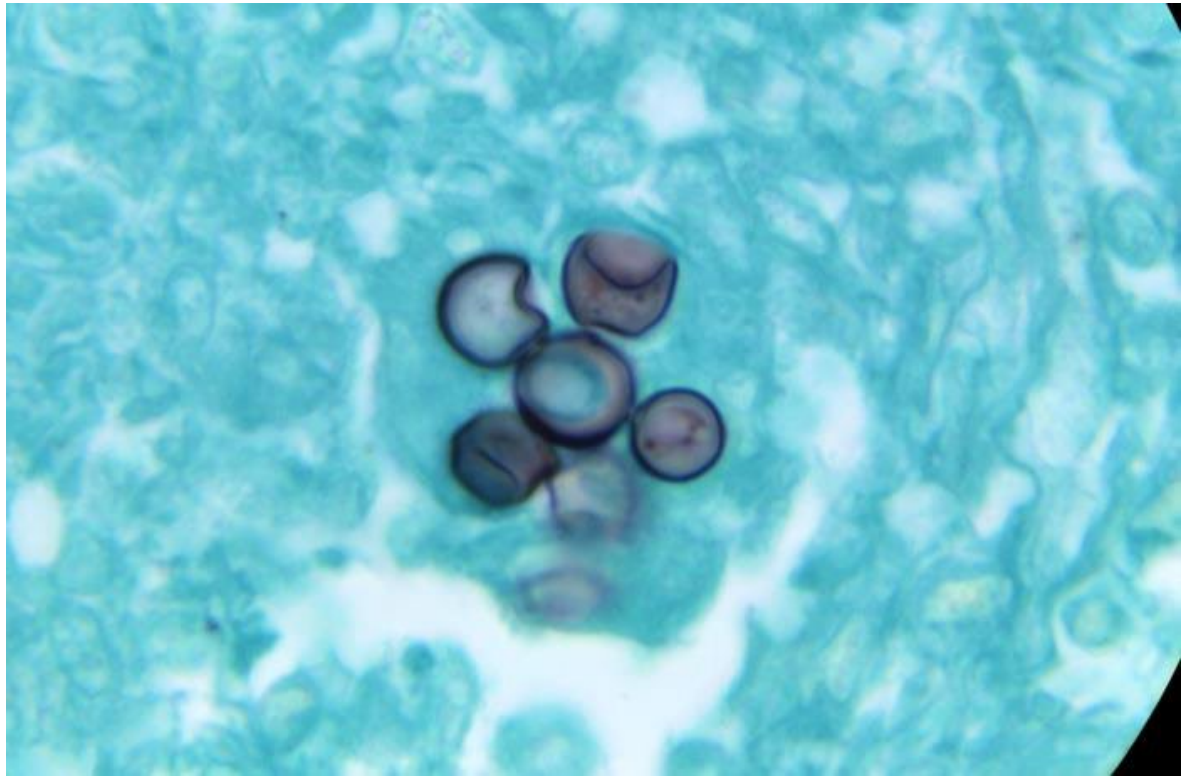

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