National Center for Emerging and Zoonotic Infectious Diseases

Emerging Fungal Infections: Environmental Changes Bring About New Challenges

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Chief, Mycotic Diseases Branch

Hosted by Martin Kiernan
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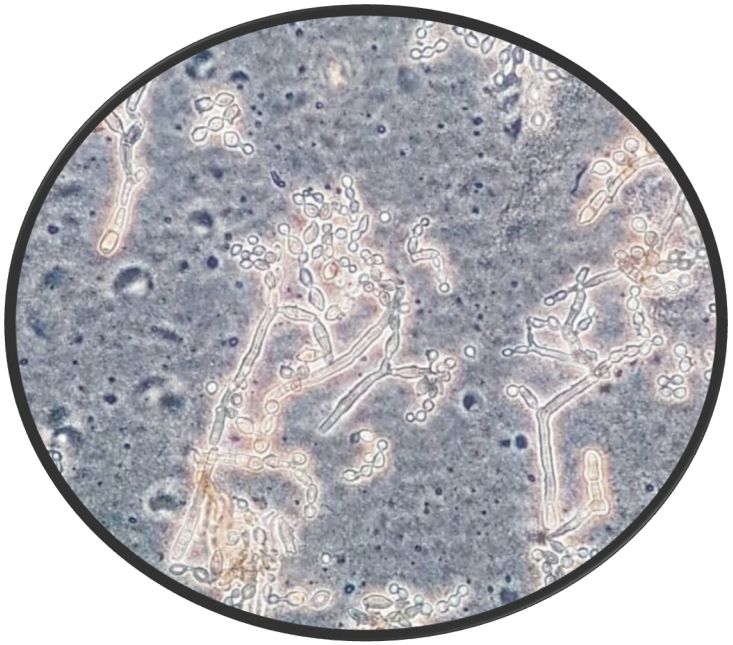
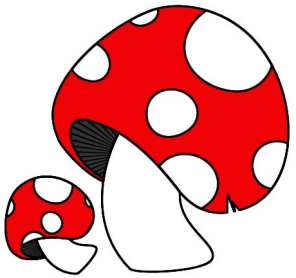
Fungal Kingdom

- ~ 5,000,000 species ~ 300 cause human disease.
- New species could emerge as pathogens, and they do every year!



We live in gentle balance with the environment




Our Risk for
Infectious Diseases
is Increasing
because of
Climate Change
CDC

Current Situation

- **This period is now the warmest in the history of modern civilization.**
- **Human activities are the dominant cause of the observed warming since the mid-20th century.**
- **Researchers around the world have published thousands of studies that document changes**

Vose, RS, DR Easterling, KE Kunkel, AN LeGrande, MF Wehner, 2017: Temperature changes in the United States.
In: Climate Science Special Report: Fourth National Climate Assessment, Volume I. pp. 185-206, DOI: 10.7930/J0N29V45

What to Expect

- By 2050, annual average temperatures in the U.S. are expected to be about 2.5˚F hotter than they were, on average, from 1976 to 2005.

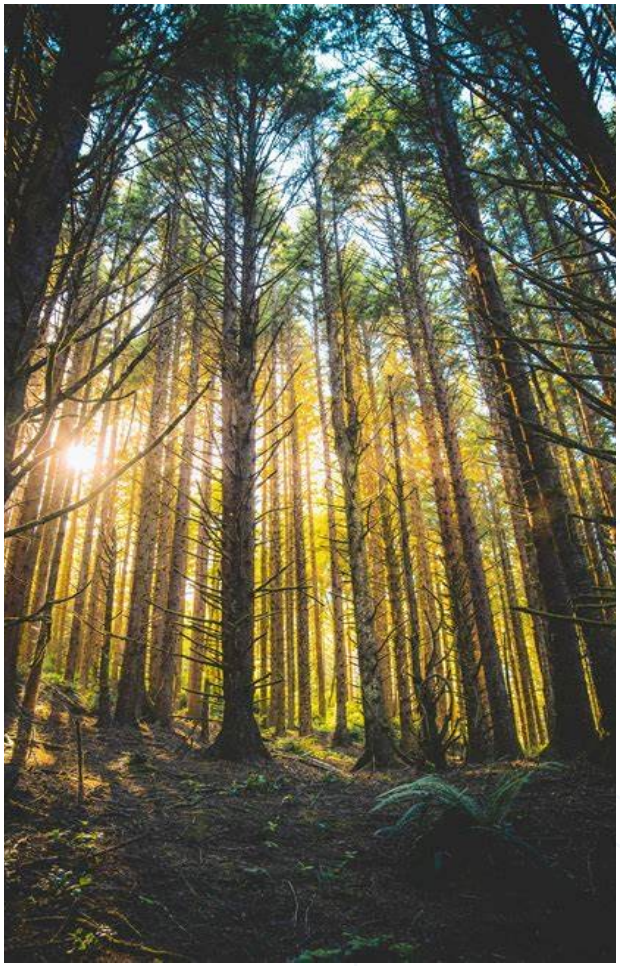
Vose, RS, DR Easterling, KE Kunkel, AN LeGrande, MF Wehner, 2017: Temperature changes in the United States.
In: Climate Science Special Report: Fourth National Climate Assessment, Volume I. pp. 185-206, DOI: 10.7930/J0N29V45

Anticipated Trends

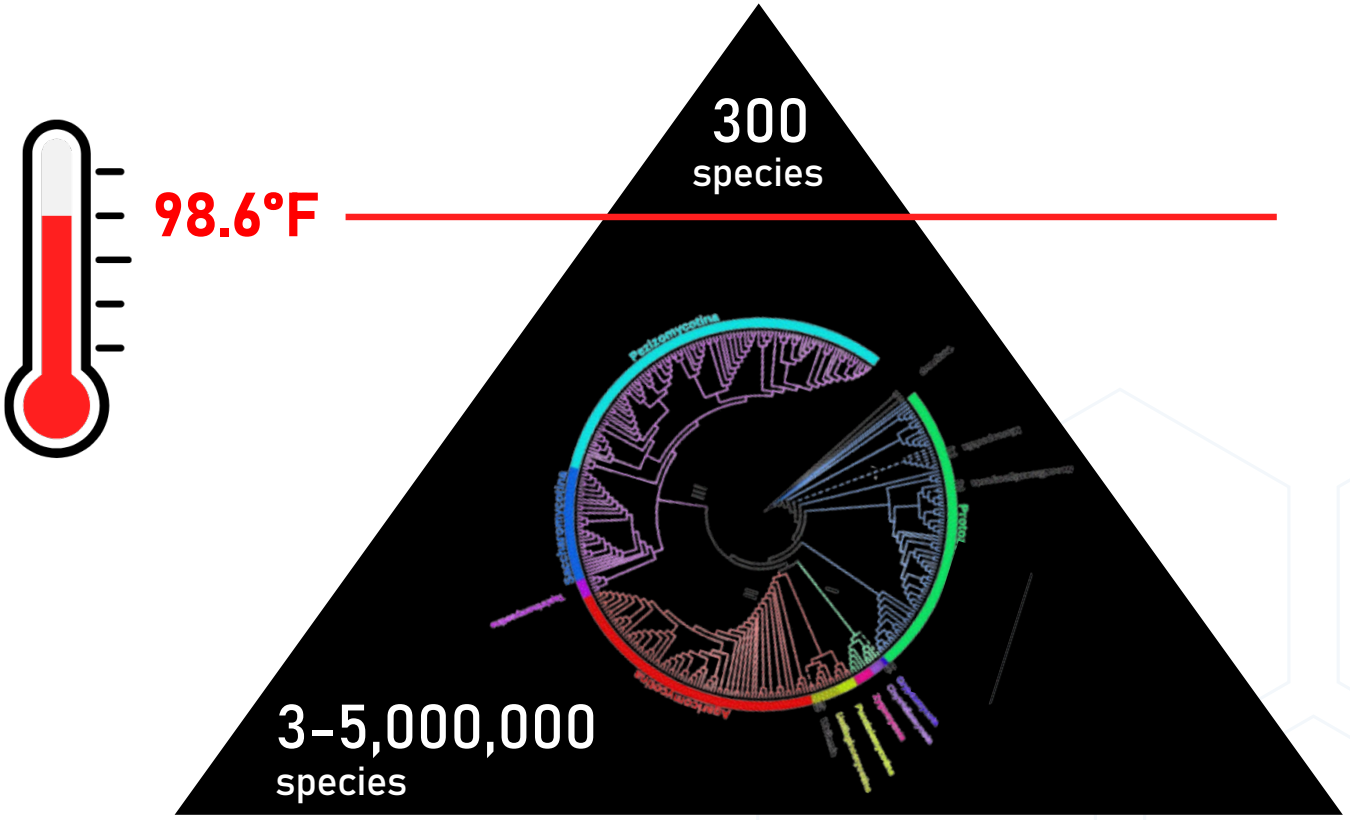
- Longer and warmer summers
- Shorter and milder winters
- Fewer frost days
- More intense heat waves; less intense cold waves
- More extreme and unpredictable weather events

Vose, RS, DR Easterling, KE Kunkel, AN LeGrande, MF Wehner, 2017: Temperature changesin the United States.
In: Climate Science Special Report: Fourth National Climate Assessment, Volume I. pp. 185-206, DOI: 10.7930/J0N29V45

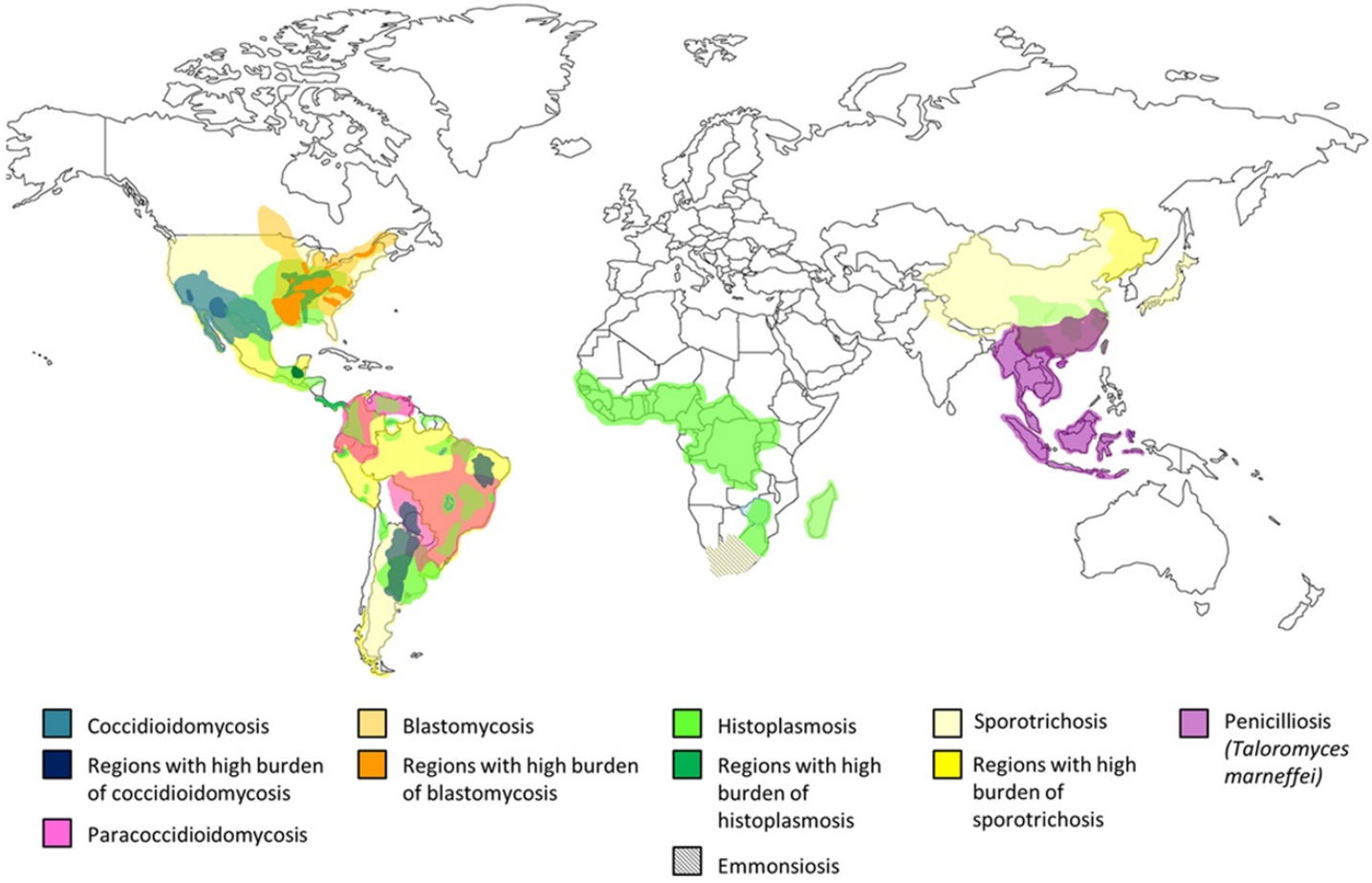
Disease-causing fungi are inextricably linked to our environment



Few fungi can grow at 98.6°F (37 °C)



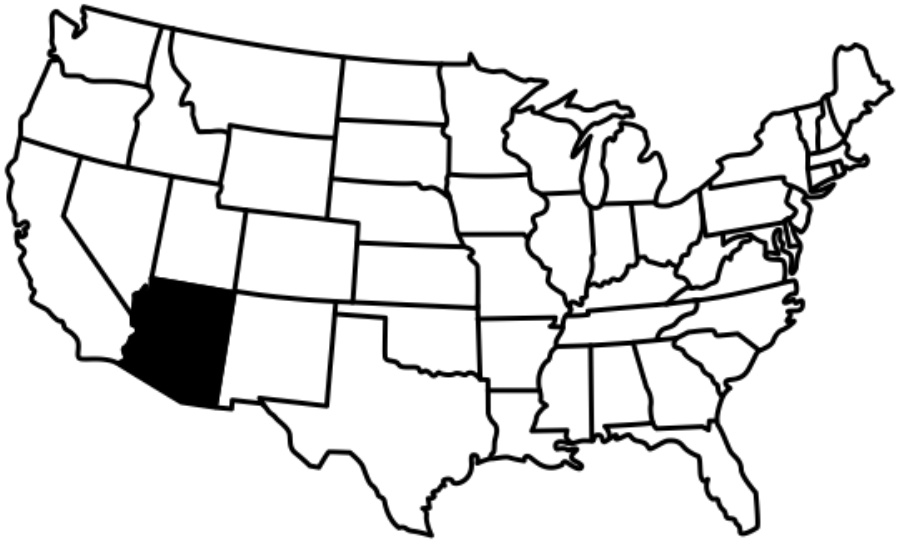
The Endemic Fungi (Geographic)



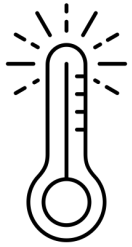
https://www.frontiersin.org/articles/10.3389/fimmu.2017.00735/full

Valley Fever

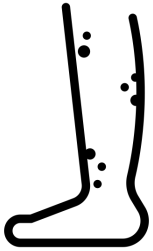
Case example: Laura in Arizona



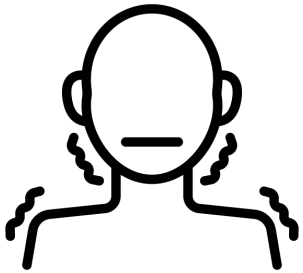
June 2020, Laura (38 and healthy) trouble breathing



Fever



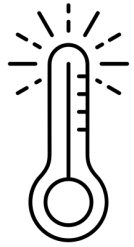
Rash



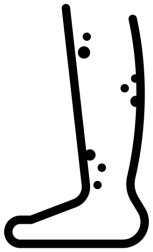
Chills

Persistent fatigue

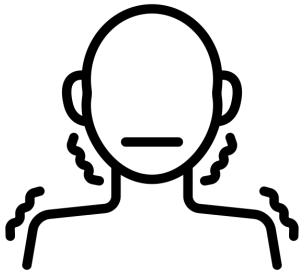
June 2020, Laura (38 and healthy) trouble breathing



Fever

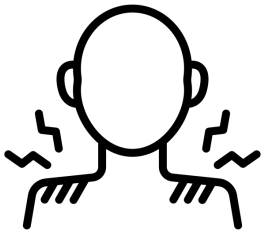


Rash

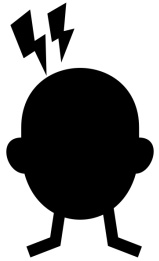


Chills

Persistent fatigue



Muscle aches

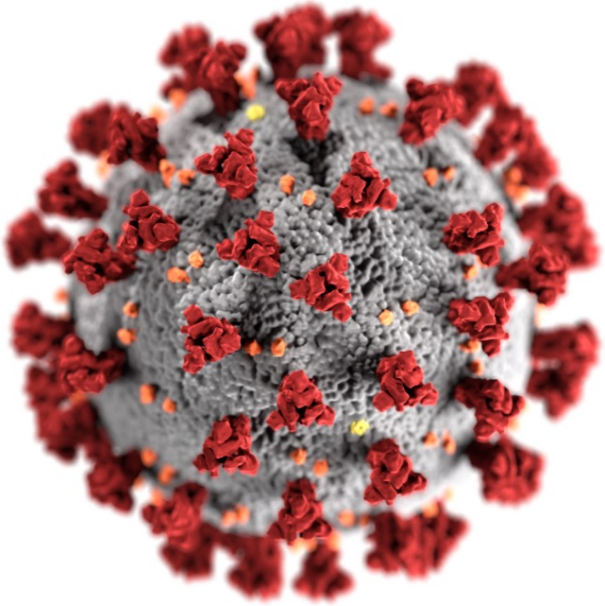


Headache

Increased pulse rate

Sweats

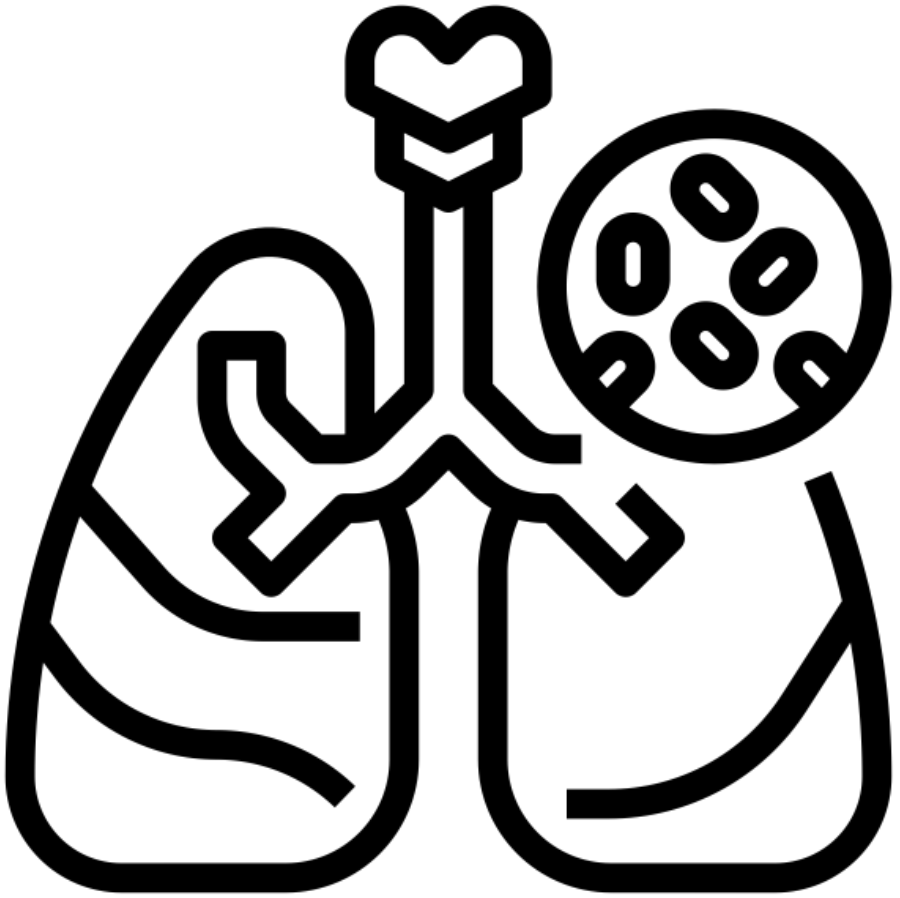
Fungal Diseases in the COVID Era: Hiding in Plain Sight



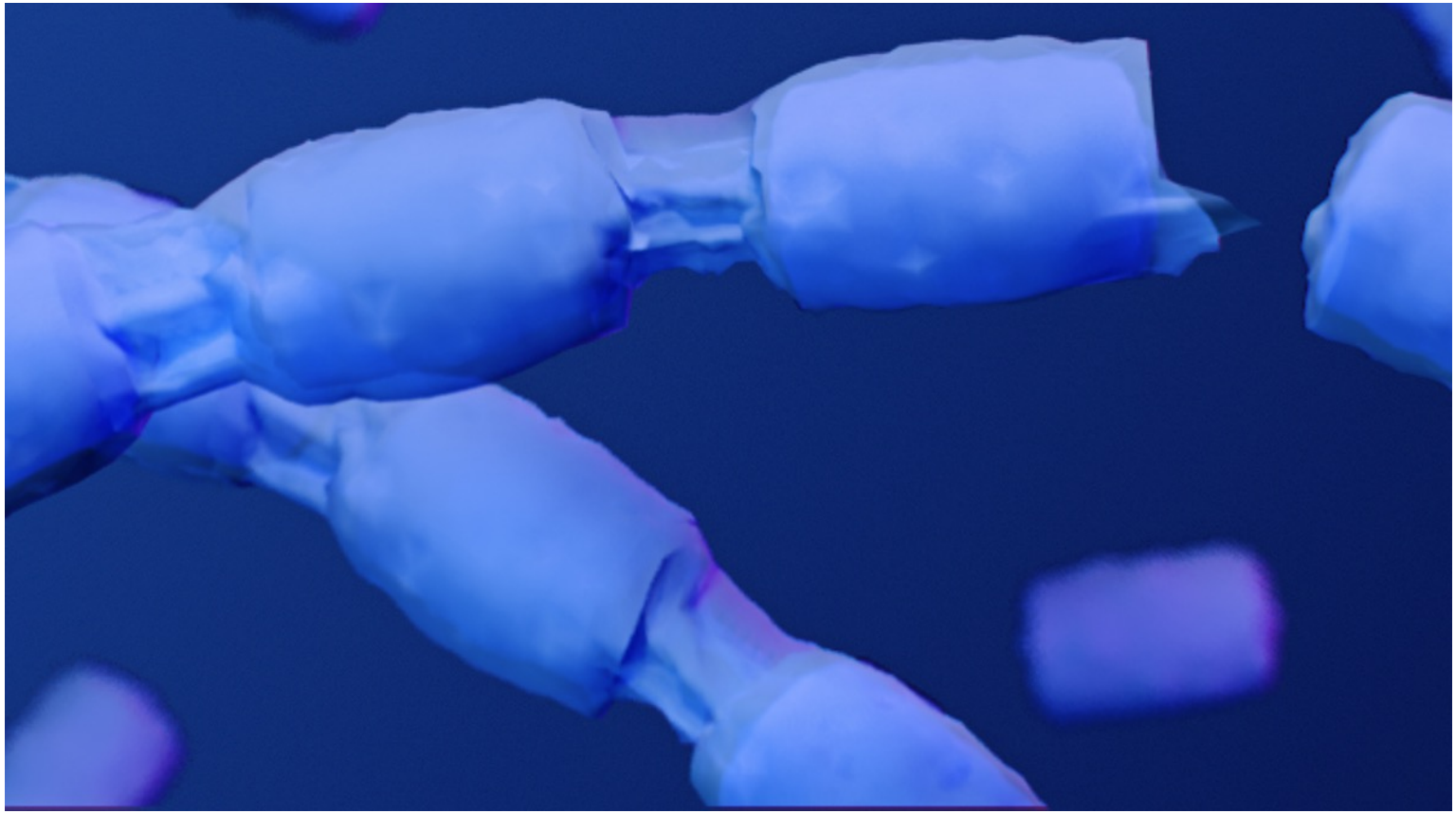
- Three negative SARS-CoV-2 tests
- Strict home isolation
- Tested negative for Valley fever

A month later, still feeling poorly

- Two courses of antibacterials didn’t help
- Physician friend in Atlanta suggested testing for Valley fever again



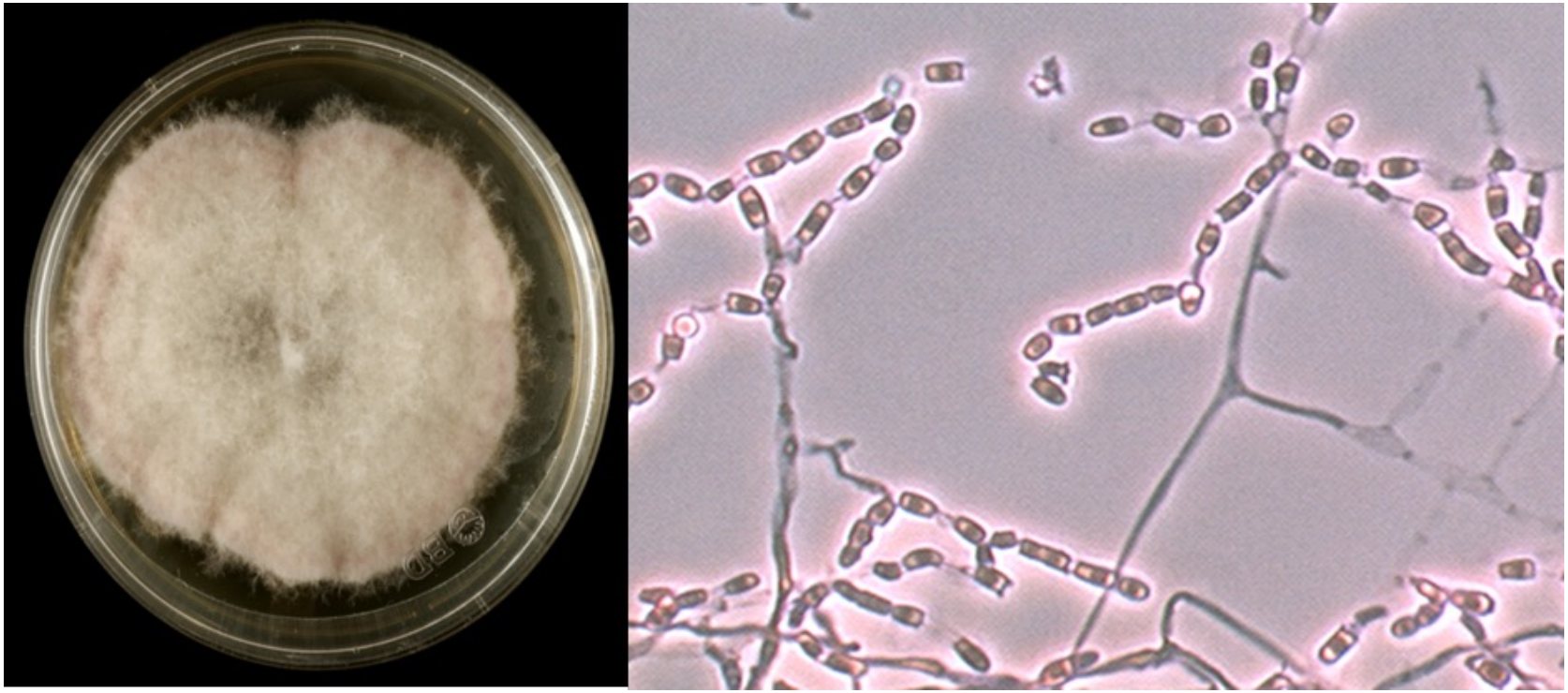
Laura had Valley fever



https://www.cdc.gov/fungal/personalstories/laura.html

Not all that coughs is COVID

Coccidioides immitis and Coccidioides posadasii



Dimorphic Fungi
Two Forms
"Valley Fever"

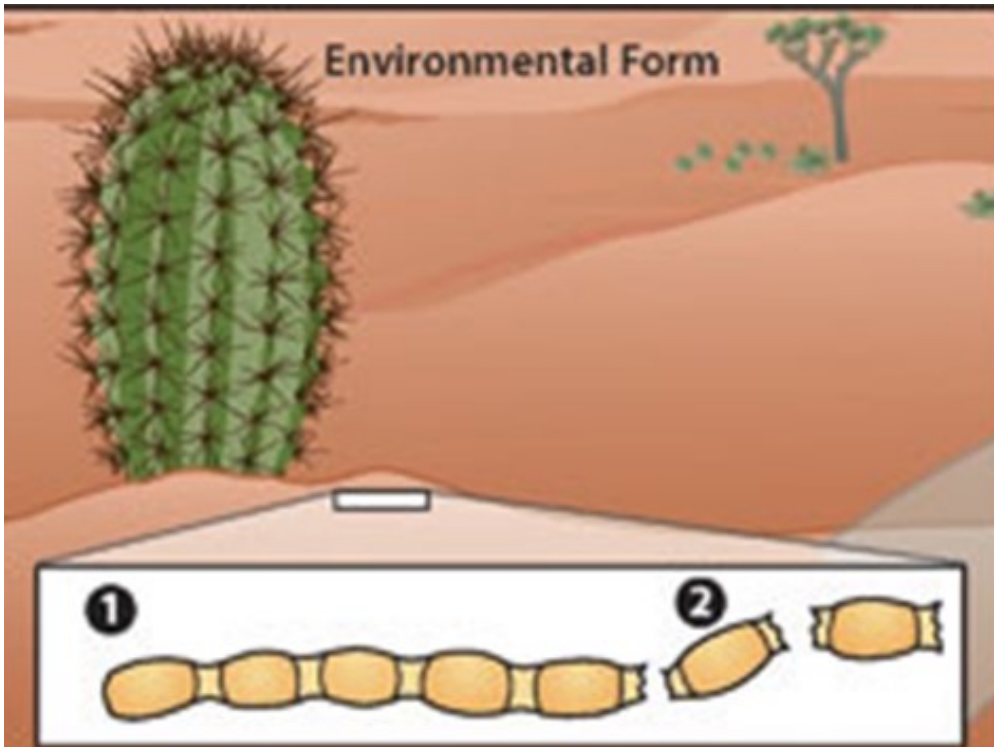
25°

Infectious

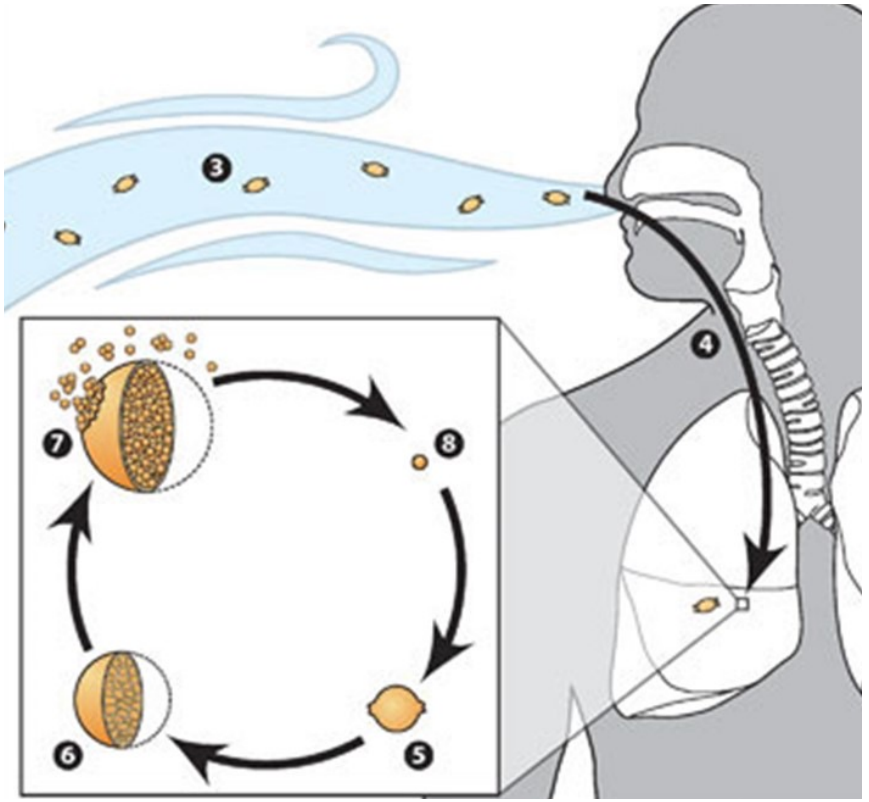
37°

Not infectious

Biology of *Coccidioides*



Environmental form



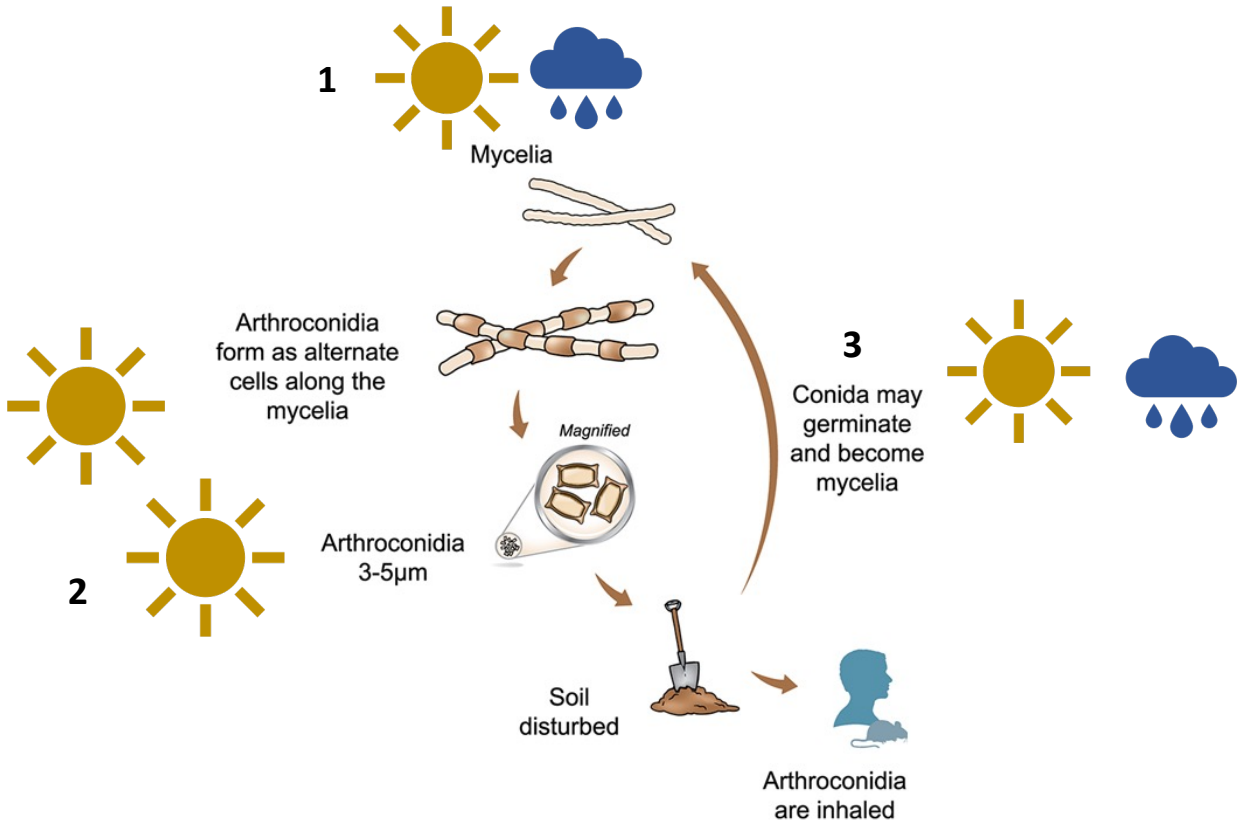
Host-associated form

Ecological niche

- **Soil?**

- **Rodents/rodent habitats?**

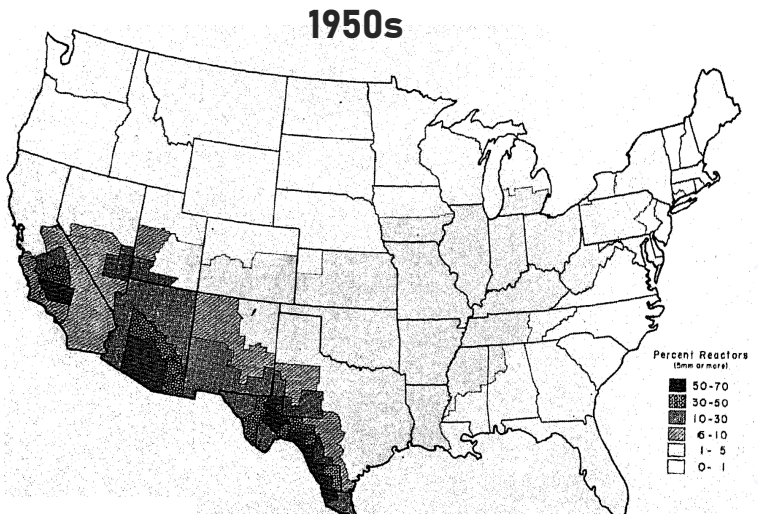
Interannual variation in precipitation (drought) and temperature correlated with seasonal anomalies

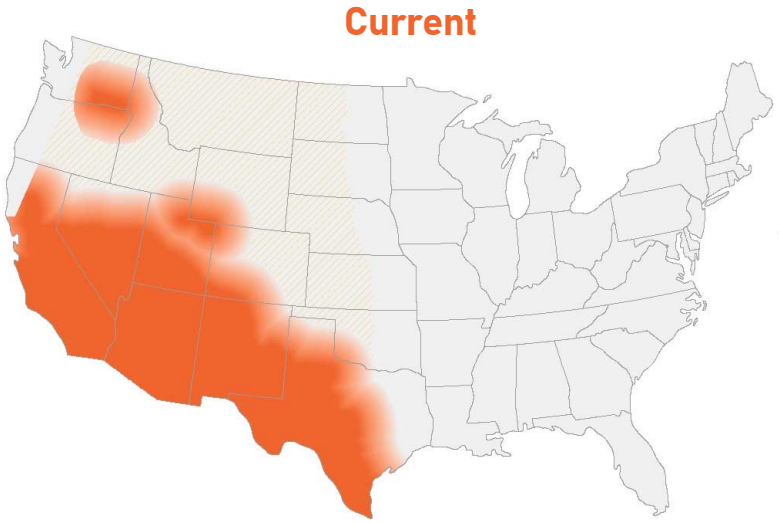


Combination of extreme climate events are leading to more people at risk for Valley Fever

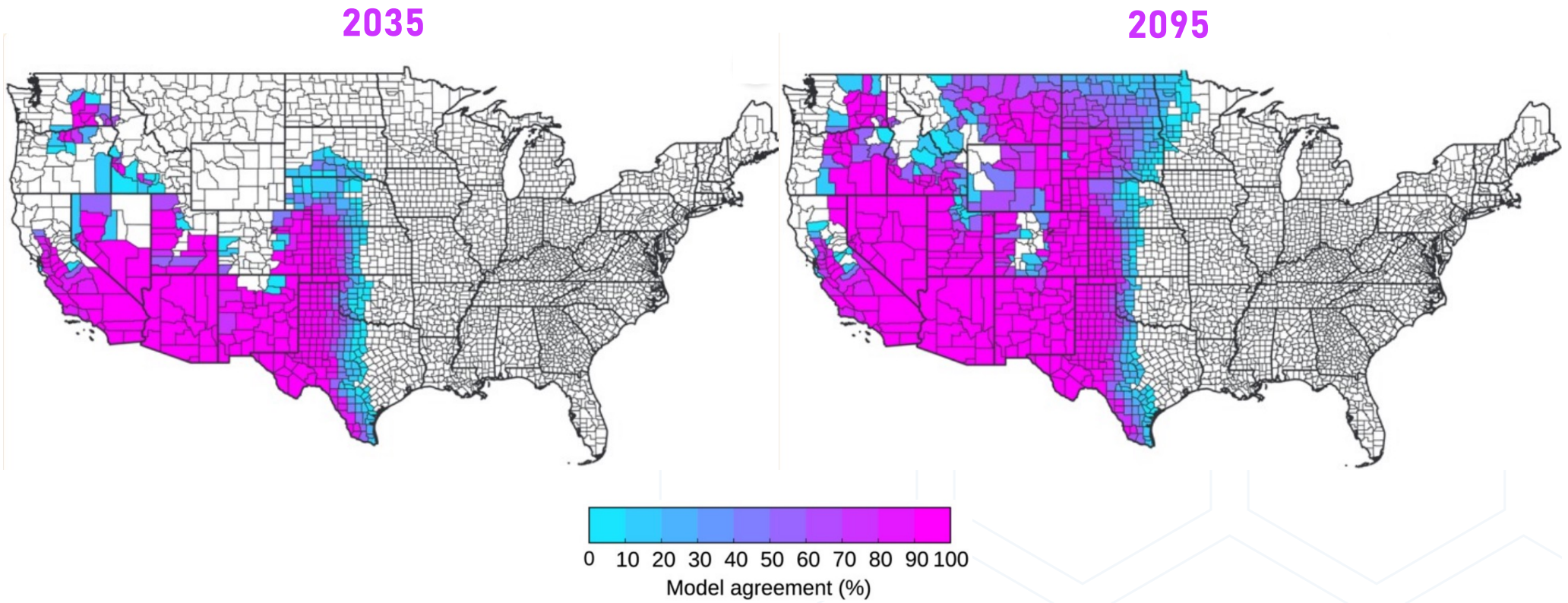
Coccidioides species primarily endemic to Southwestern United States

Areas of endemicity





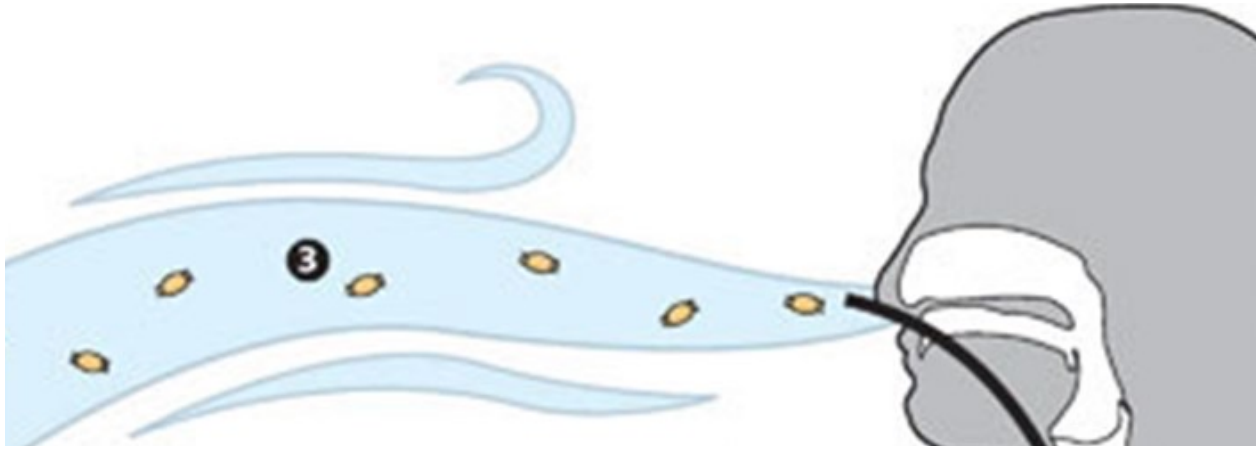
Climate modeling analyzing temperature and precipitation patterns predicts expansion of Valley Fever endemic range



GeoHealth, Volume: 3, Issue: 10, Pages: 308-327, First published: 30 August 2019, DOI: (10.1029/2019GH000209)

Coccidioides in the air?

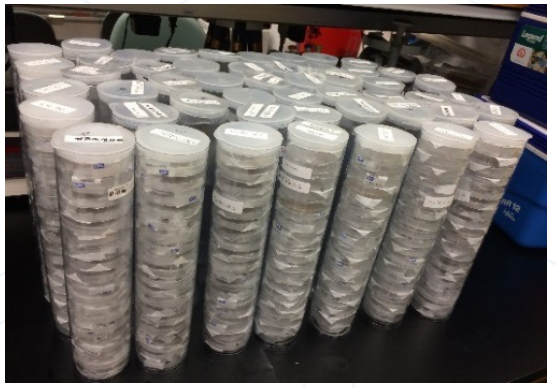
- Seasonal variation?
- Geographic distribution?
- Weather events?
- Climate change?
- Construction?



CocciWatch: *Coccidioides* environmental surveillance via air sampling, Arizona and California

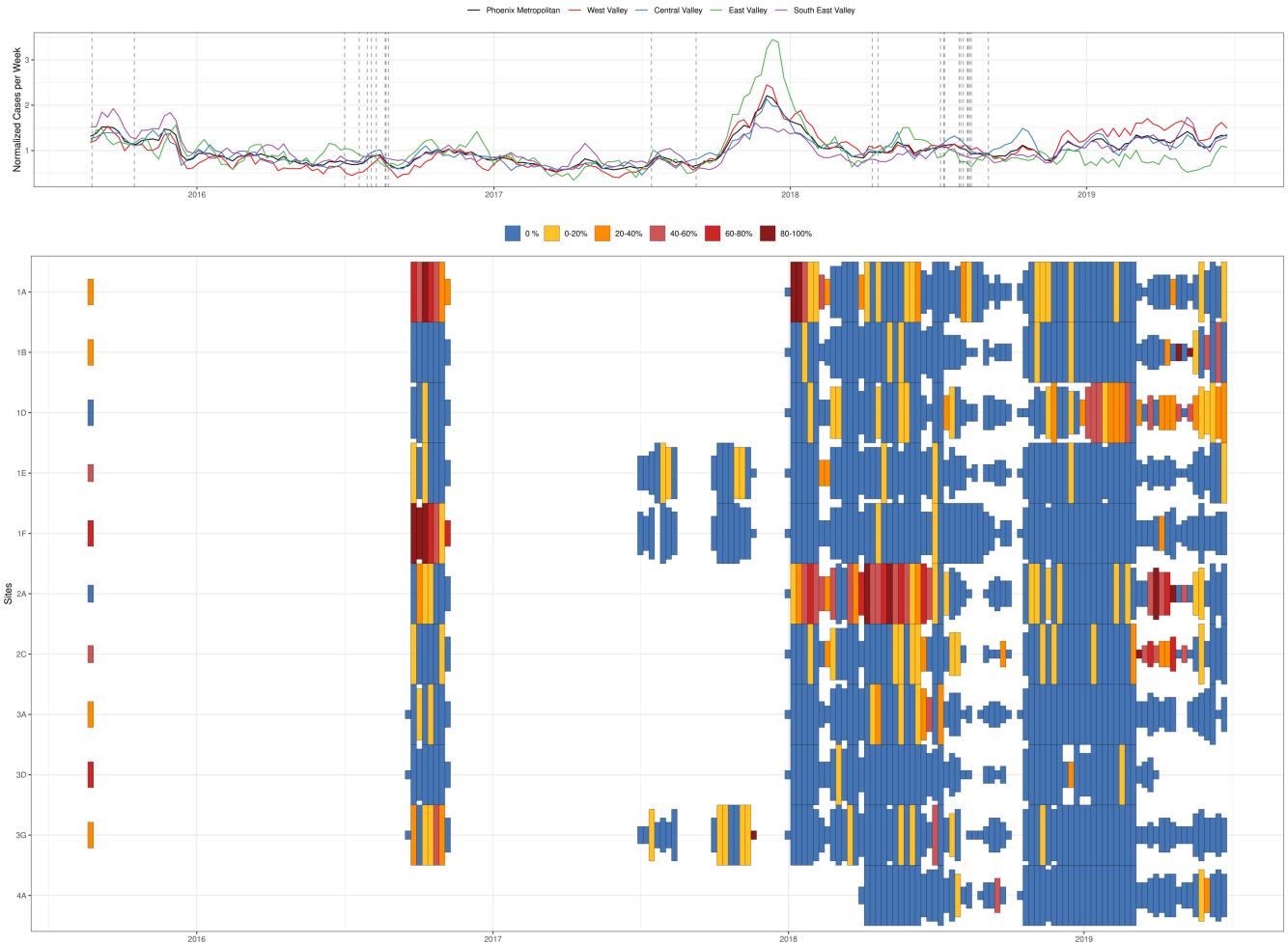
High-volume air sampler

Hydrophobic PTFE filter

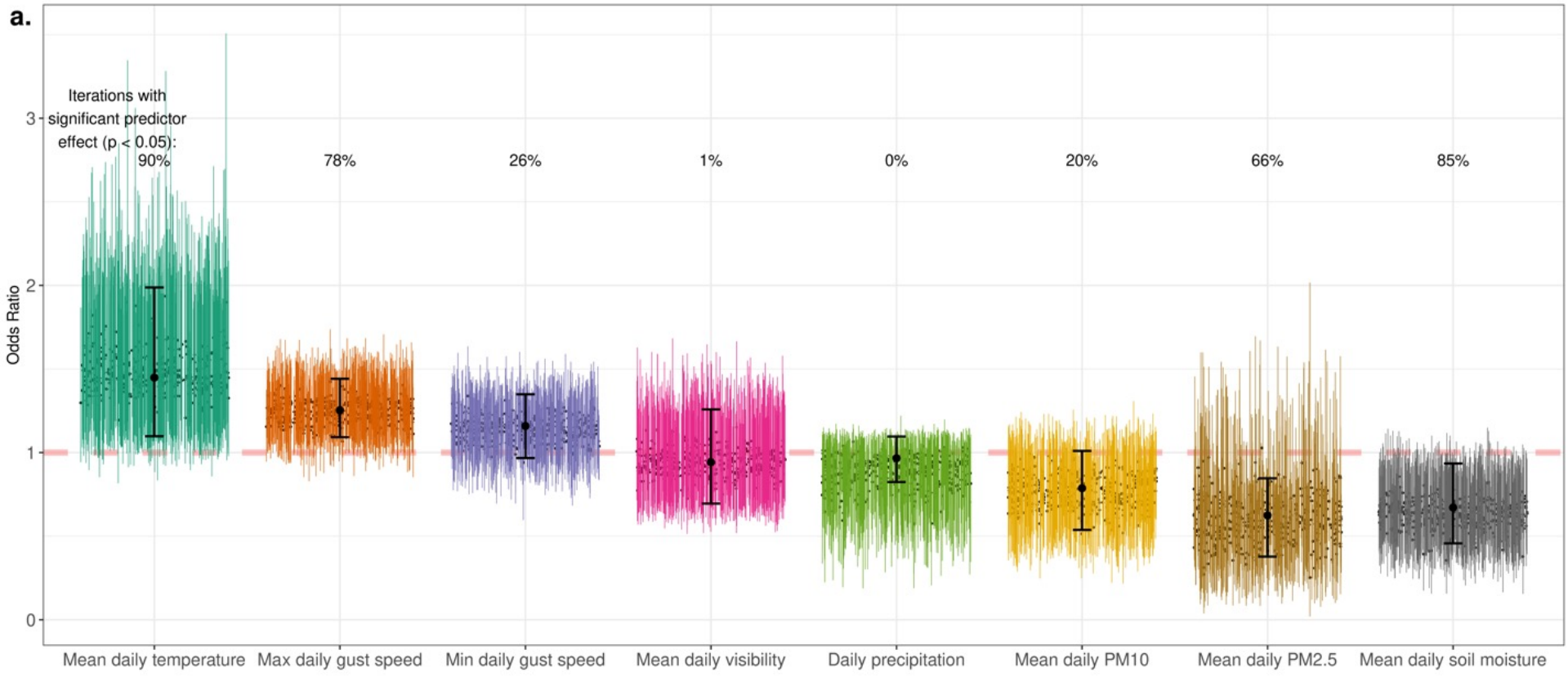


CocciWatch- Surveillance conclusions

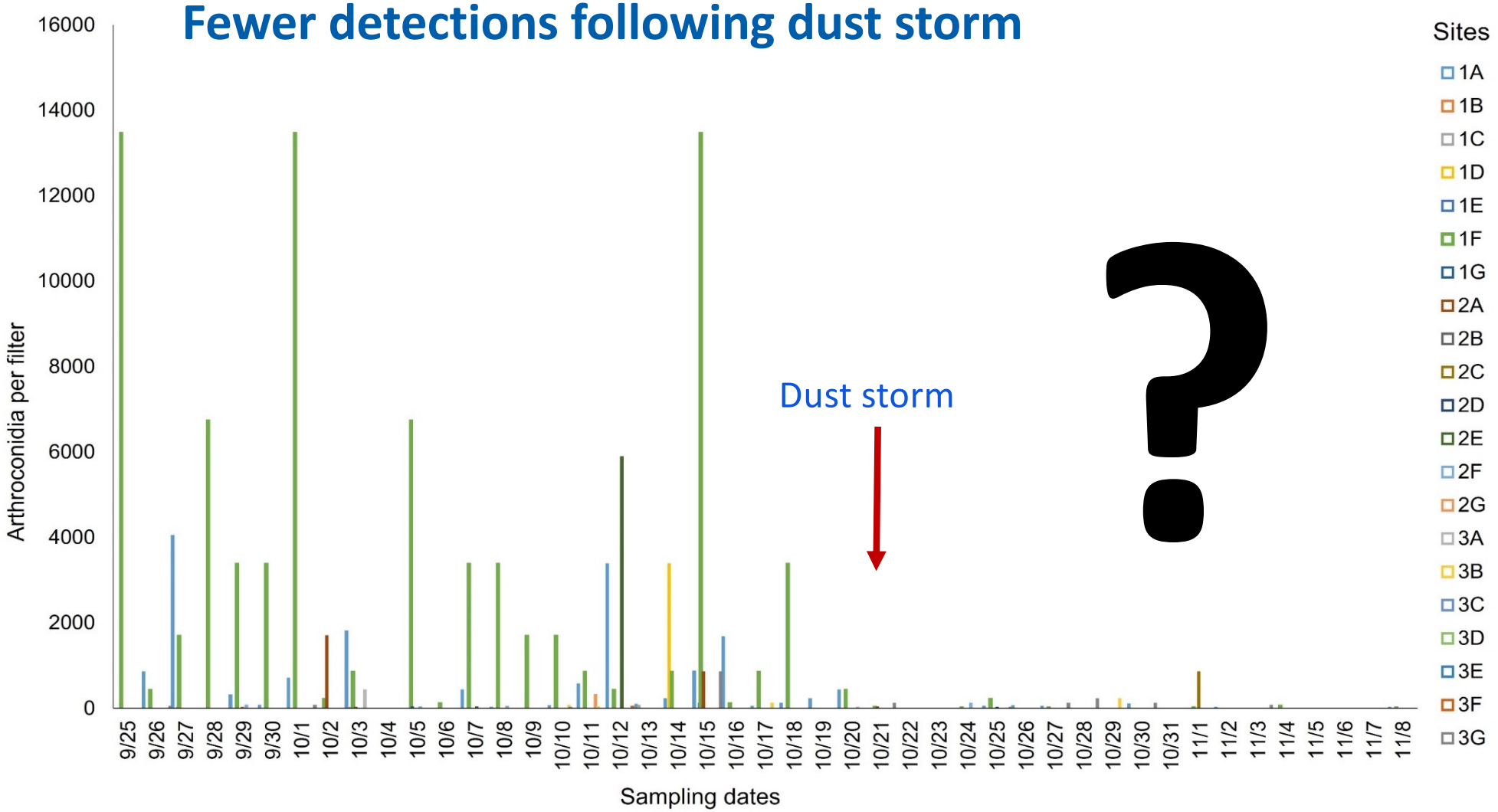
- **High variance in prevalence across space and time suggesting that risk is spatially and temporally variable.**
  - Supported by ecology- *Coccidioides* must be introduced into the soil and then aerosolized.
- **Local drivers influence site prevalence.**
  - Specific weather patterns?
  - Soil disturbance?
  - Land cover around sites?



Effect of daily environmental measures on filter prevalence across the study period



Fewer detections following dust storm



Wildfire smoke as a potential source of Valley Fever? Emerging field of pyroaerobiology

PERSPECTIVE | EPIDEMIOLOGY

Science

Wildfire smoke, a potential infectious agent

LEDA N. KOBZIAR AND GEORGE R. THOMPSON III

ECOSYSTEMS

Wildfires launch microbes into the air. How big of a health risk is that?

Fire Fighters – Coccidioidomycosis

Digging a fire line disturbs soil that may contain cocci spores

Tailgate Training

Preventing Work-related Valley Fever in Wildland Firefighters

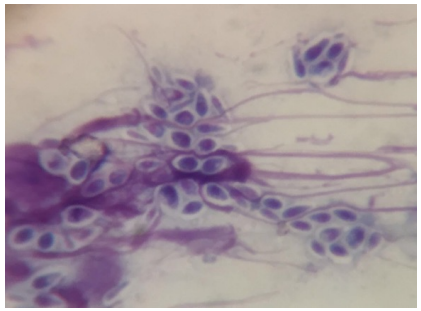
Sporotrichosis

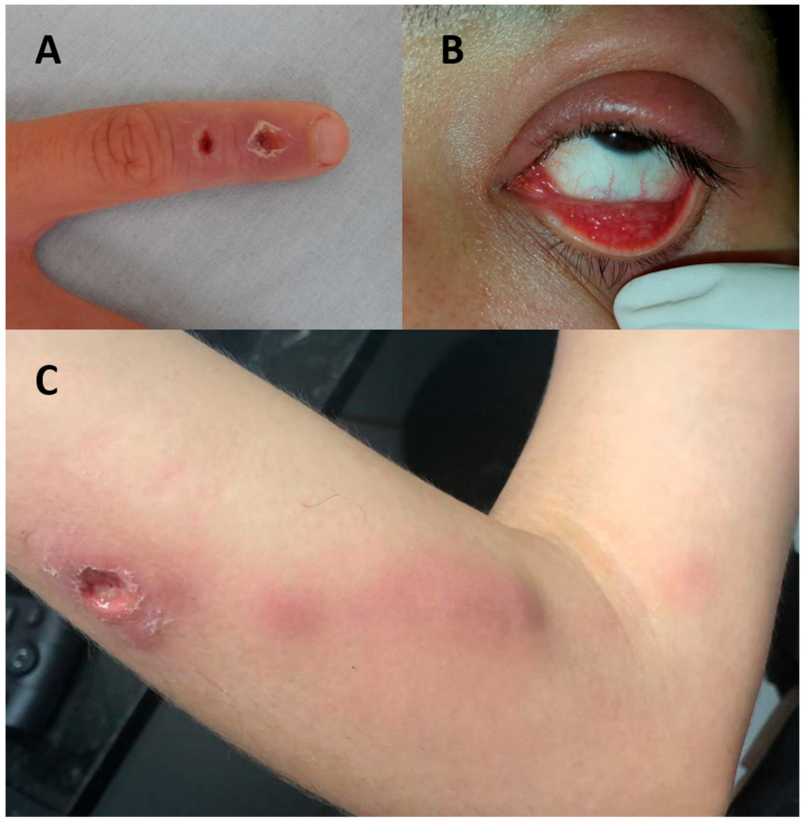
Sporothrix spp.

Sporotrichosis (Schenckii)

- Anecdotally called “Rose grower’s disease”
- Found on decaying plant matter and in peat and sphagnum moss
- Associated with animal scratches or bites

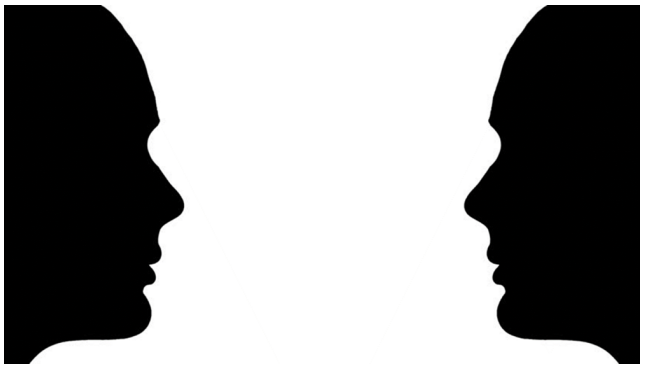
New Species Emerges: *Sporothrix brasiliensis*: Zoonotic Disease with Cats

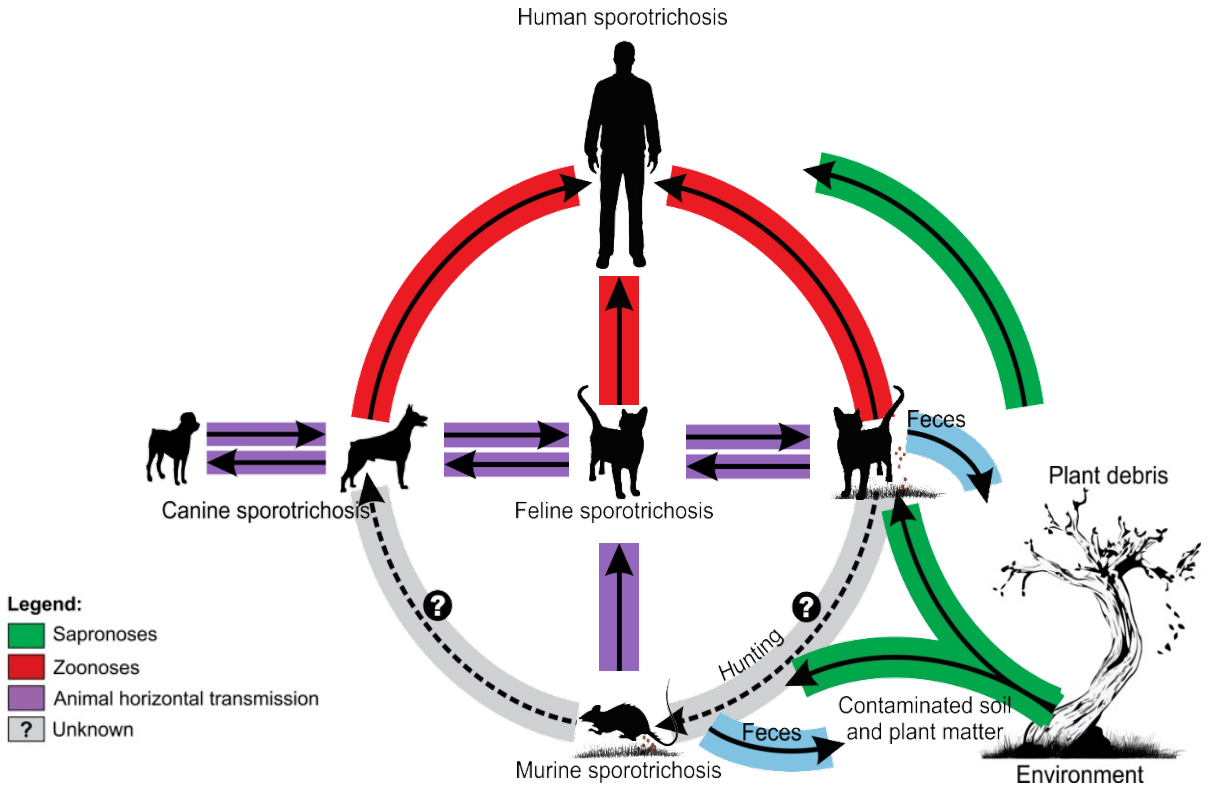




Rodrigues AM *et al*. 2016. **PLoS Pathogens**.

Dimorphic fungus:
Transmissible in Yeast and Mold Phase!

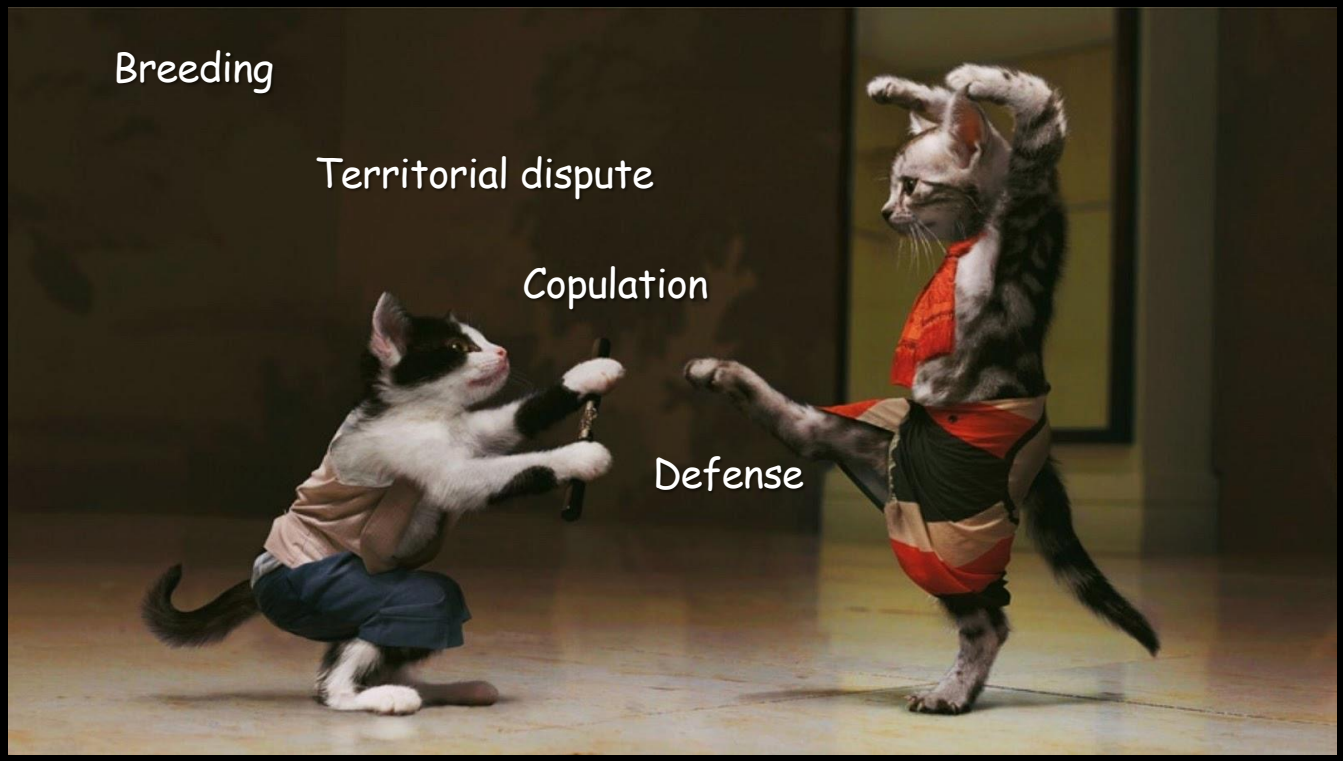




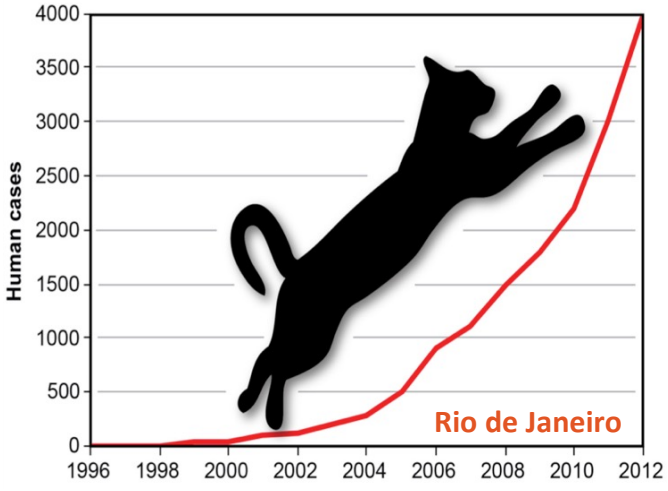
Rodrigues AM *et al*. 2016. **PLoS Pathogens**.

Sick cats may splash infectious yeast cells when shaking the head…

Cats act as a perfect source for the transmission of the disease

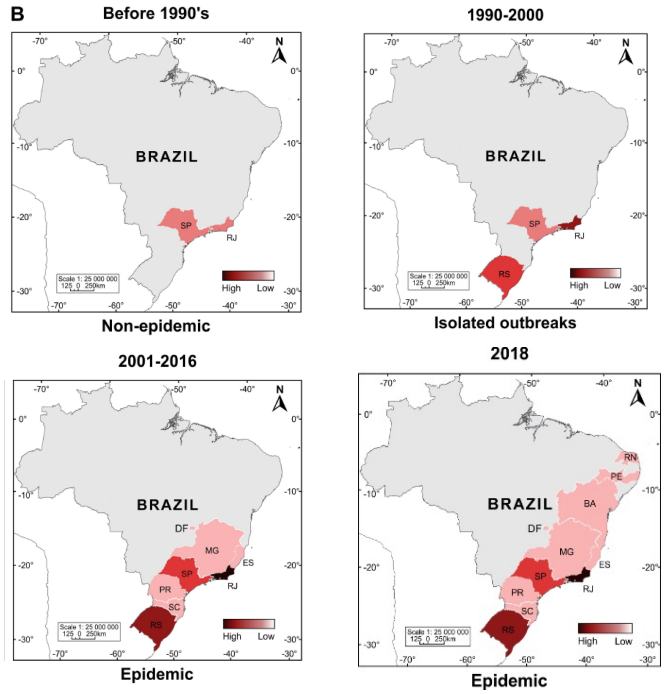


Rapidly Emerged in Brazil



Sporotrichosis cases diagnosed in FIOCRUZ-RJ between 1998 and 2012

human cases	4,000
feline cases	3,800
canine cases	120

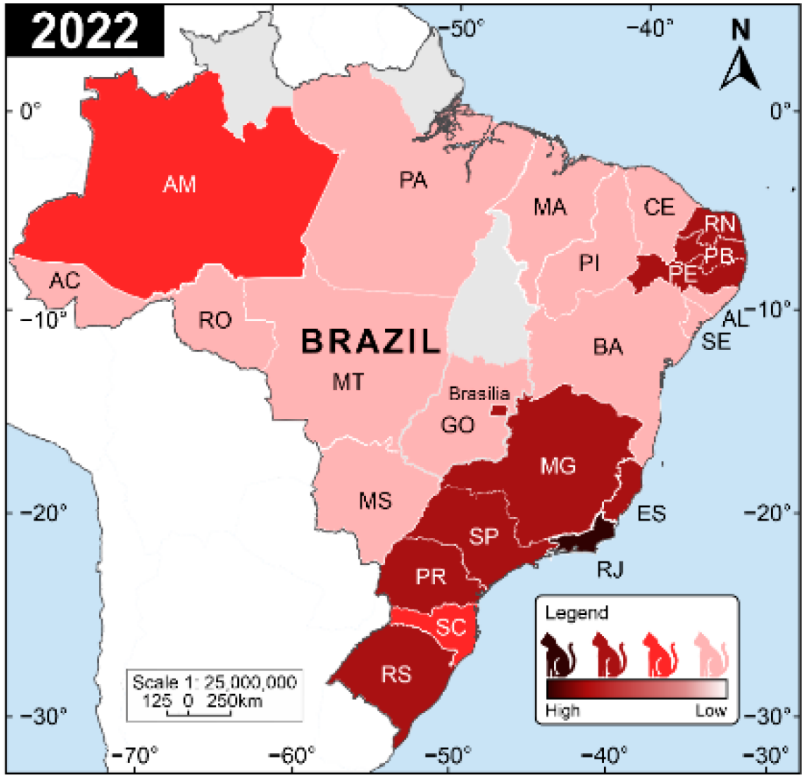


And recently reported from Argentina

Queiroz-Telles, Fahal, Falci, Carceres, Chiler, & Pasqualotto. **Lancet Infec Dis** 2017

Gremião et al. (2017), **PLoS Pathog.** 13(1): e1006077.

Cat-transmitted sporotrichosis is spreading rapidly in Brazil



Messias Rodrigues et al. 2022. J. Fungi

Where is this species located?

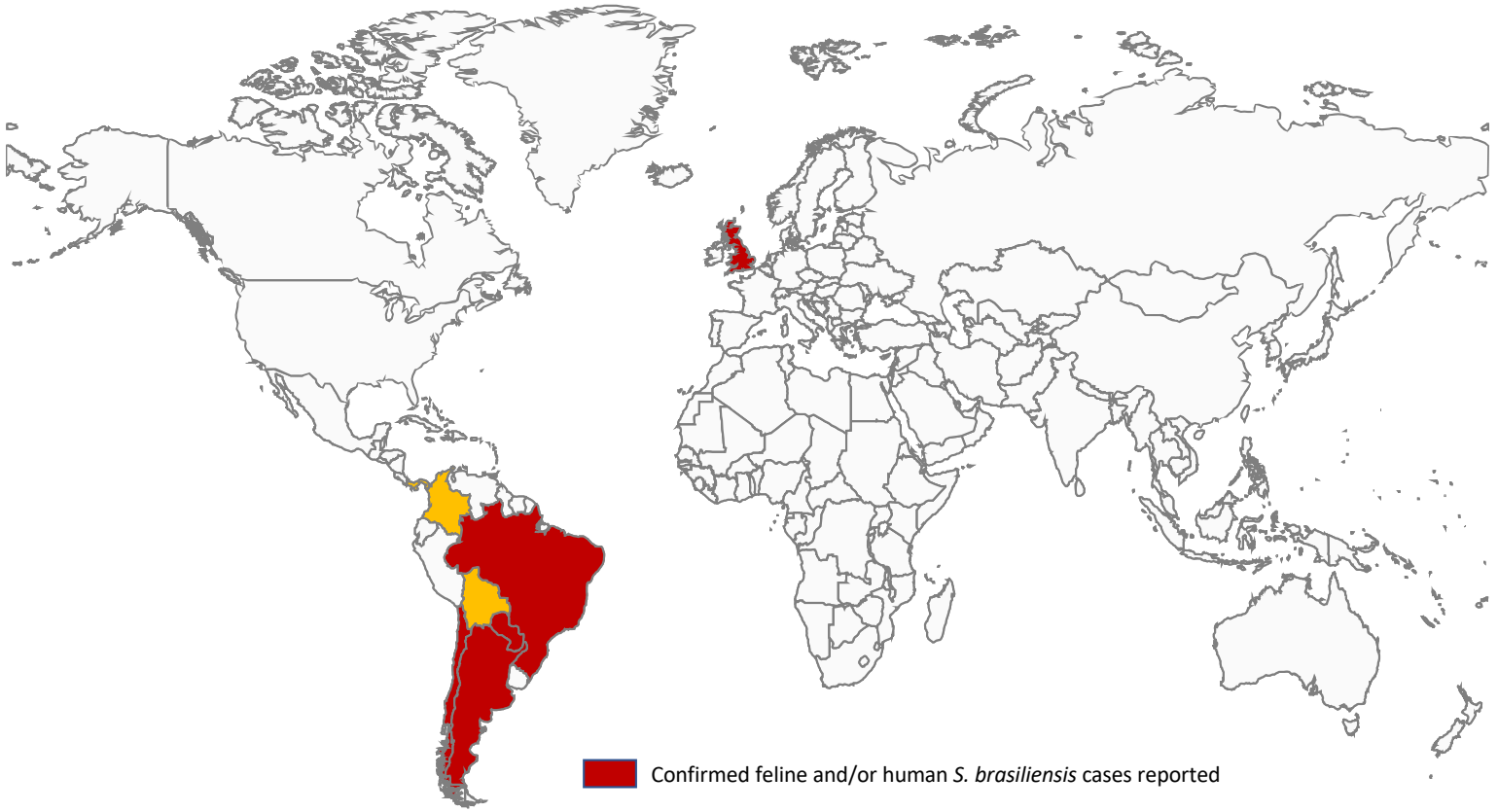
Brazilian epidemic in cats is caused by a single species, the fungus ***Sporothrix brasiliensis***. Until recently , this species was geographically restricted to Brazil.

Reports now in neighboring countries

Colombia, Paraguay, Bolivia and Argentina

Anderson et al Emerging Microbes & Infections , 2014

Cases are increasingly reported beyond Brazil



Revista Argentina de Microbiología
Volume 52, Issue 4, October–December 2020, Pages 350-351

Letter to the Editor

Sporothrix brasiliensis: A growing hazard in the Northern area of Buenos Aires Province?

Sporothrix brasiliensis: ¿una amenaza creciente en la región norte de la provincia de Buenos Aires?

Alejandro Etchecopaz [a], Miguel Scarpa [b], Javier Mas [c], María L. Cuestas [d]

Rev. Del Nacional (Itaugua). 2017; 9(2): 67-76 DEL NACIONAL

Caso Clínico

Esporotricosis trasmitida por gato doméstico. Reporte de un caso familiar

Sporotrichosis transmitted by domestic cat. A family case report

Jesús Manuel García Duarte[1], Víctor Raúl Wattiez Acosta[1], Patricia María Laura Fornerón Viera[1], Arnaldo Aldama Caballero[1], Graciela Asunción Gorostiaga Matiauda[1], Victoria Beatriz Rivelli de Oddone[1], José Guillermo Pereira Brunelli[2]

[1]Ministerio de Salud Pública y Bienestar Social, Hospital Nacional, Servicio de Dermatología. Itauguá, Paraguay.

[2]Ministerio de Salud Pública y Bienestar Social, Programa Nacional de Control de la Lepra, Dirección General de Vigilancia Sanitaria, Centro de Especialidades Dermatológicas. San Lorenzo, Paraguay

Open Access Case Report

Sporotrichosis Outbreak Due to *Sporothrix brasiliensis* in Domestic Cats in Magallanes, Chile: A One-Health-Approach Study

by Pamela Thomson [1,*], Carlos González [2,3], Olivia Blank [4], Valentina Ramírez [4], Camila del Río [1], Sebastián Santibáñez [1] and Pamela Pena [4]

[1] Laboratorio de Microbiología Clínica y Microbioma, Escuela de Medicina Veterinaria, Facultad de Ciencias de la Vida, Universidad Andrés Bello, Santiago 8370134, Chile
[2] Laboratorio de Anatomía e Histopatología, Escuela de Medicina Veterinaria, Facultad de Ciencias de la Vida, Universidad Andrés Bello, Santiago 8370134, Chile
[3] Laboratorio de Histopatología, CITOVET, Ñuñoa, Santiago 7750538, Chile
[4] Clínica Veterinaria Timaukel, Punta Arenas 6210648, Chile
* Author to whom correspondence should be addressed.

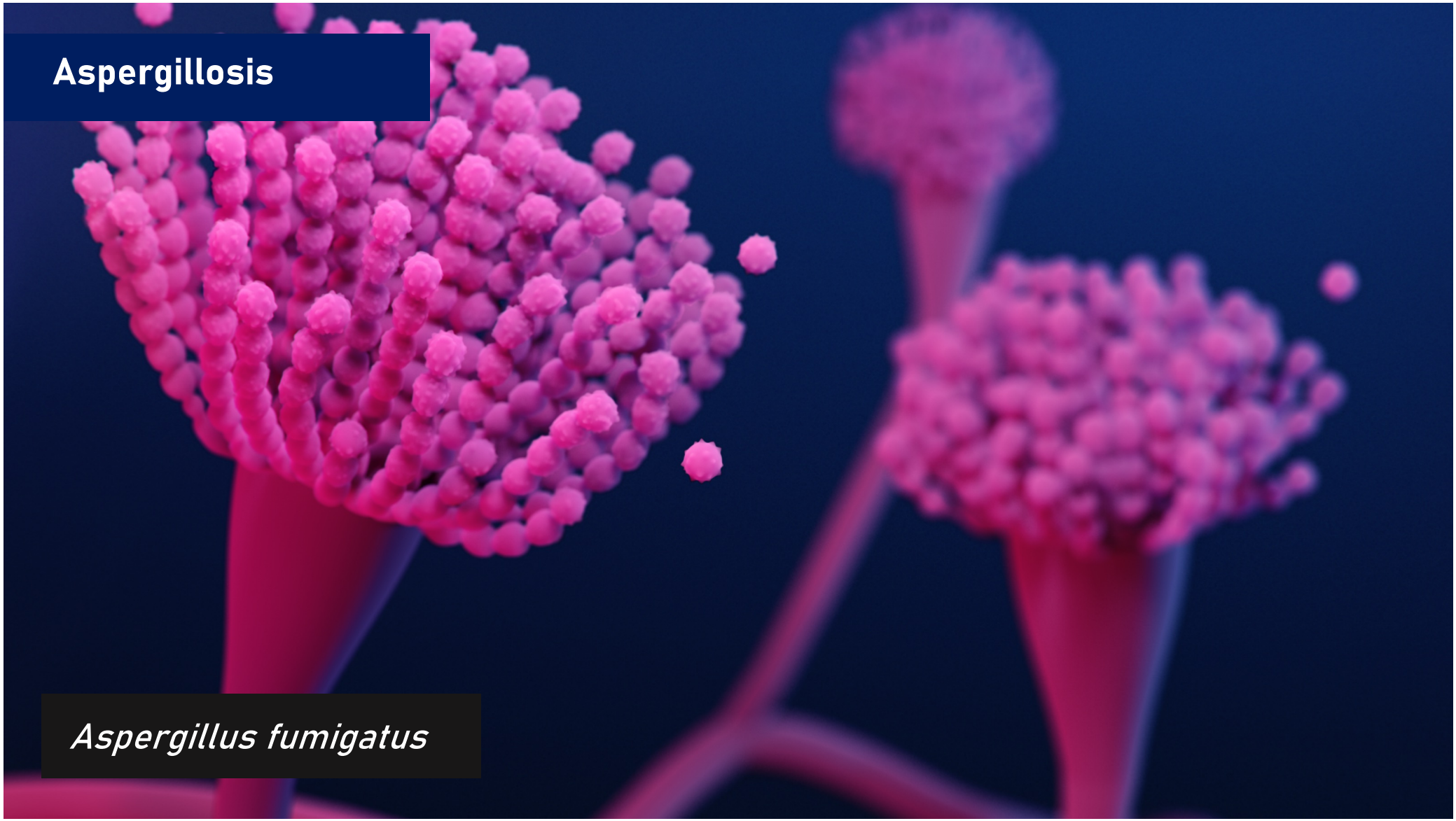
J. Fungi **2023**, *9*(2), 226; https://doi.org/10.3390/jof9020226

A One Health approach in needed for controlling cat-transmitted sporotrichosis

- Veterinarians
- Clinicians
- Microbiologists
- Epidemiologists
- Border health

One Health and Fungal Diseases | Fungal Diseases | CDC

Aspergillosis

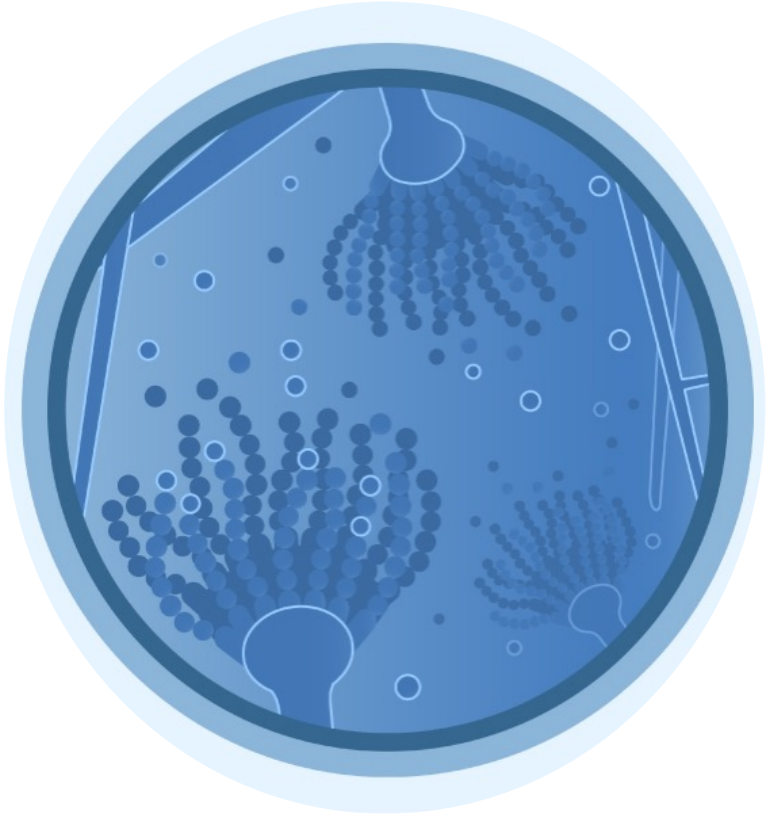


Aspergillus fumigatus

Background on Aspergillosis

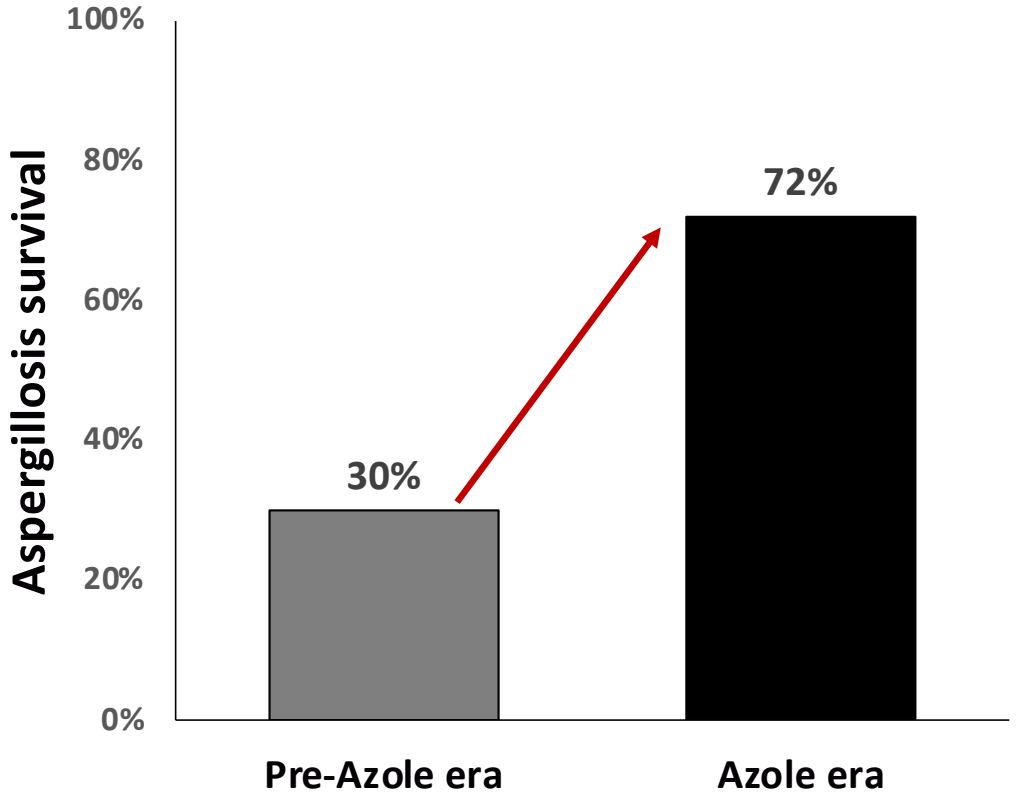
- **Rare** fungal infection via lung

- Affects **severely immunocompromised** people (e.g., stem cell transplant, hematologic malignancy)



Trizole antifungals are critical for treating aspergillosis and saving lives

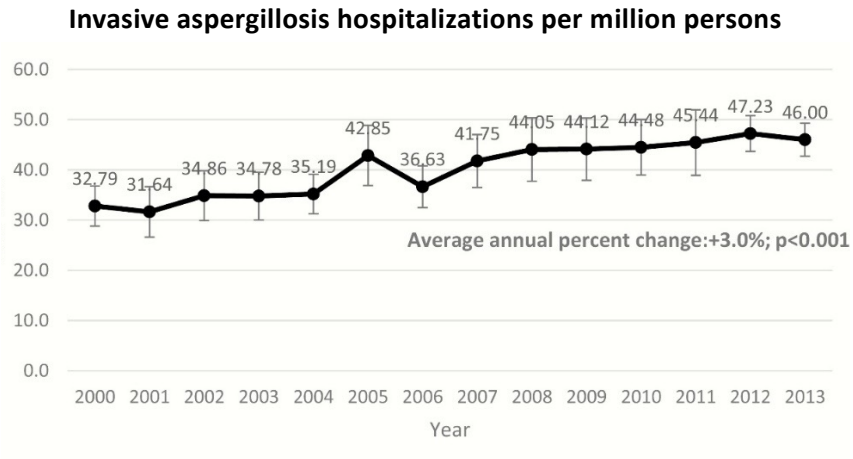
Introduction of mold-active triazole medications in 1990s dramatically improved survival



Verweij et al 2015 CID

BUT actually, infections may not be so rare: Burden of invasive aspergillosis is substantial and undercounted

- Until recently, **no public health surveillance**
- Best estimates come from **administrative data**:
  - ~15,000 hospitalizations/year
  - ~800 deaths/year
- But these are likely **massive underestimates**
  - Underdiagnosis
  - Undercoding



Benedict K, et al. Clin Infect Dis. 2019
Rayens E, et al. Clin Infect Dis. 2021
Vallabhaneni, et al. Open Forum Infectious Diseases 2017.

Aspergillosis is one of the most common missed diagnoses in the ICU, based on autopsy studies

BMJ Quality & Safety

Diagnostic errors in the intensive care unit: a systematic review of autopsy studies

- **8%** of autopsied ICU deaths involved a **potentially lethal missed diagnosis**
- Most common: “pulmonary embolism, myocardial infarction, pneumonia, **and aspergillosis**”

Winters B. BMJ Qual & Safety. 2012.

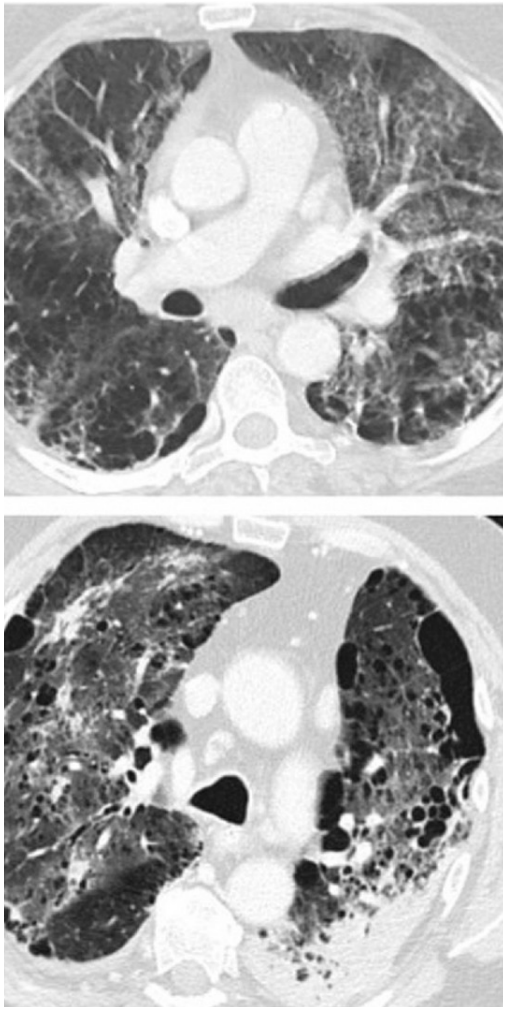
Increasingly identified in non-immunocompromised populations, including those with influenza and COVID-19

THE LANCET
Respiratory Medicine

Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study

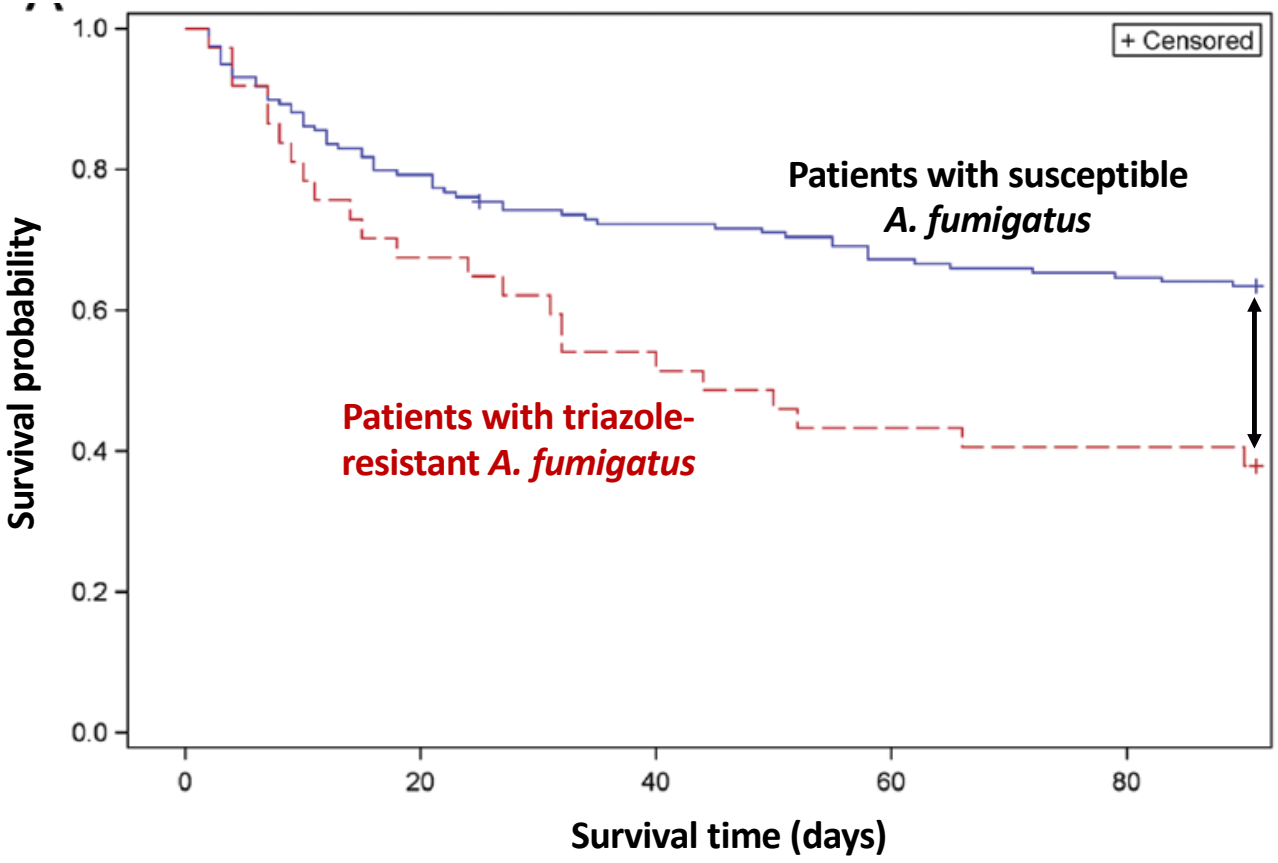
EMERGING INFECTIOUS DISEASES®

COVID-19–Associated Pulmonary Aspergillosis, March–August 2020



Koehler P, et al. Mycoses. 2020

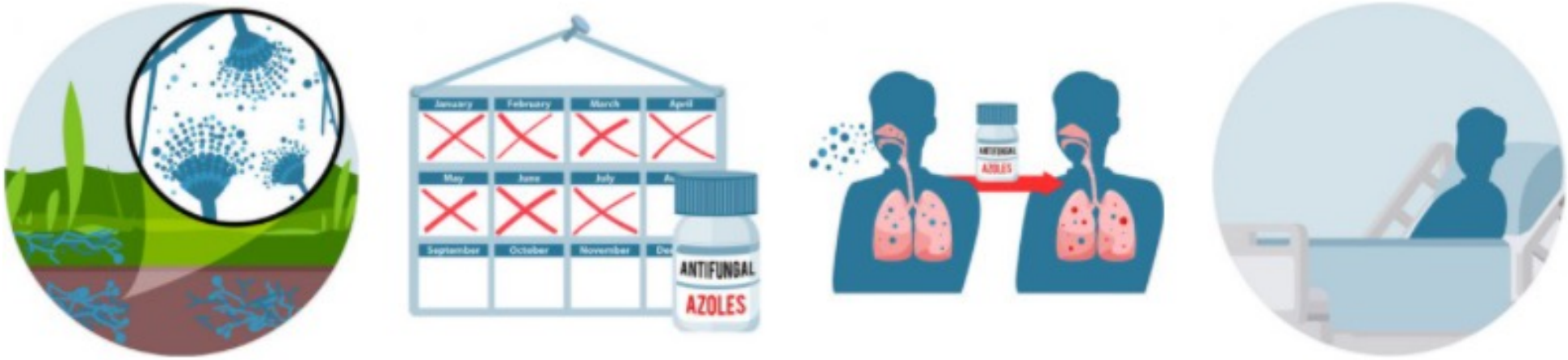
Emerging triazole resistance kills patients and sends us back to the pre-azole era



33% worse survival in patients with resistant isolates

Lestrade 2019 CID

Since clinical use of mold-active azole use began in 1990s, resistance was periodically observed in patients on long-term therapy

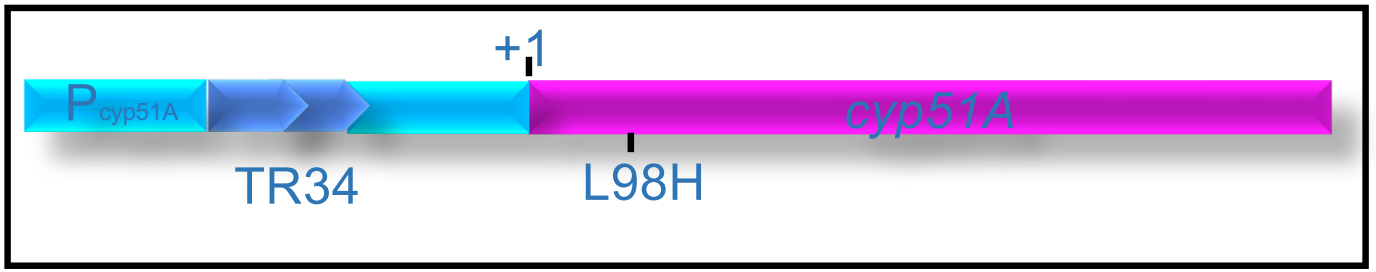


- Many different mutations lead to azole resistance

https://www.cdc.gov/fungal/diseases/aspergillosis/azole-resistant-aspergillus.html

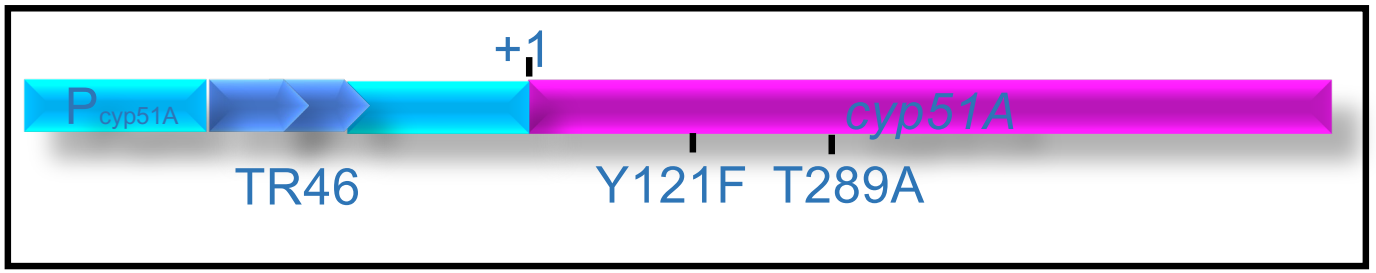
A concerning puzzle: two genotypes emerge in late 1990s/early 2000s, primarily in patients without triazole treatment (not the long term therapy patients)

“TR34”



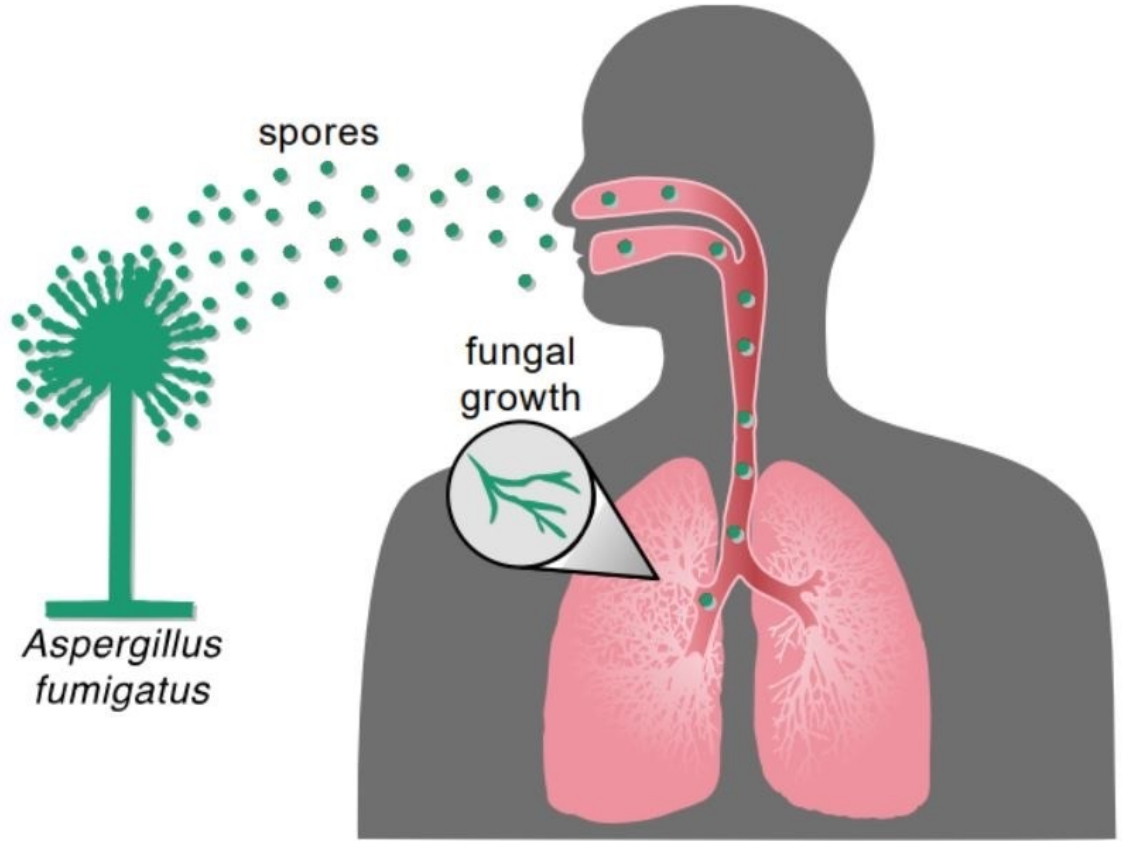
Causes Pan-Azole Resistance: Itraconazole, Voriconazole, Posaconazole

“TR46”



Causes Resistance to Preferred Drug: Voriconazole

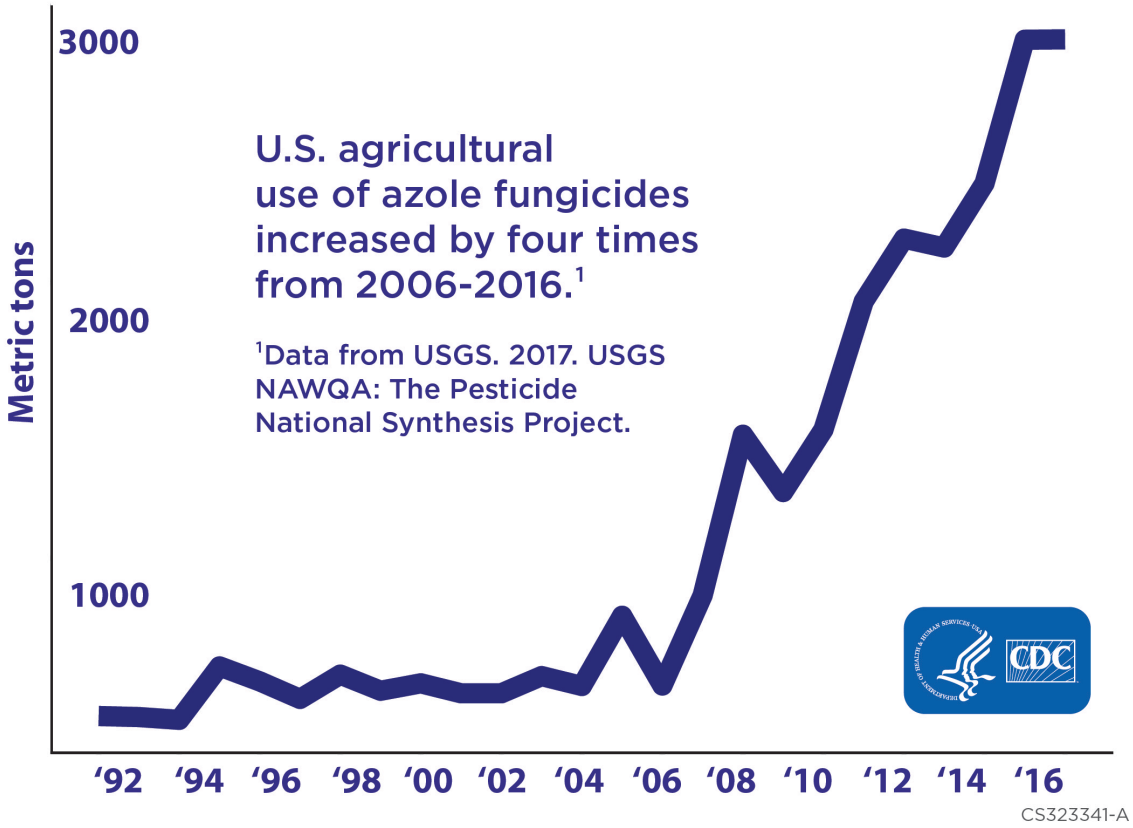
Patients inhale *A. fumigatus* that is already azole resistant



Steenwyk JL, et al. bioRxiv. 2020
Van der Linden JWM, et al. Emerg Infect Dis. 2011

Agricultural fungicides are driving drug-resistant *Aspergillus fumigatus* infections

What does environmental triazole fungicide use look like in the United States?

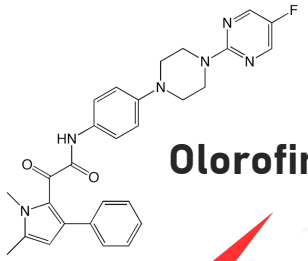


Toda M, et al. Enviro Health Persp. 2021

Promising clinical antifungal effective against azole-resistant aspergillosis shares mechanism of action with recently authorized agricultural fungicide

Development pipelines

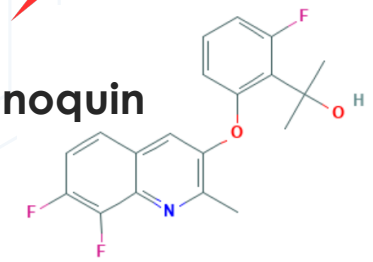
Clinical



Olorofim

Environmental

Ipflufenoquin



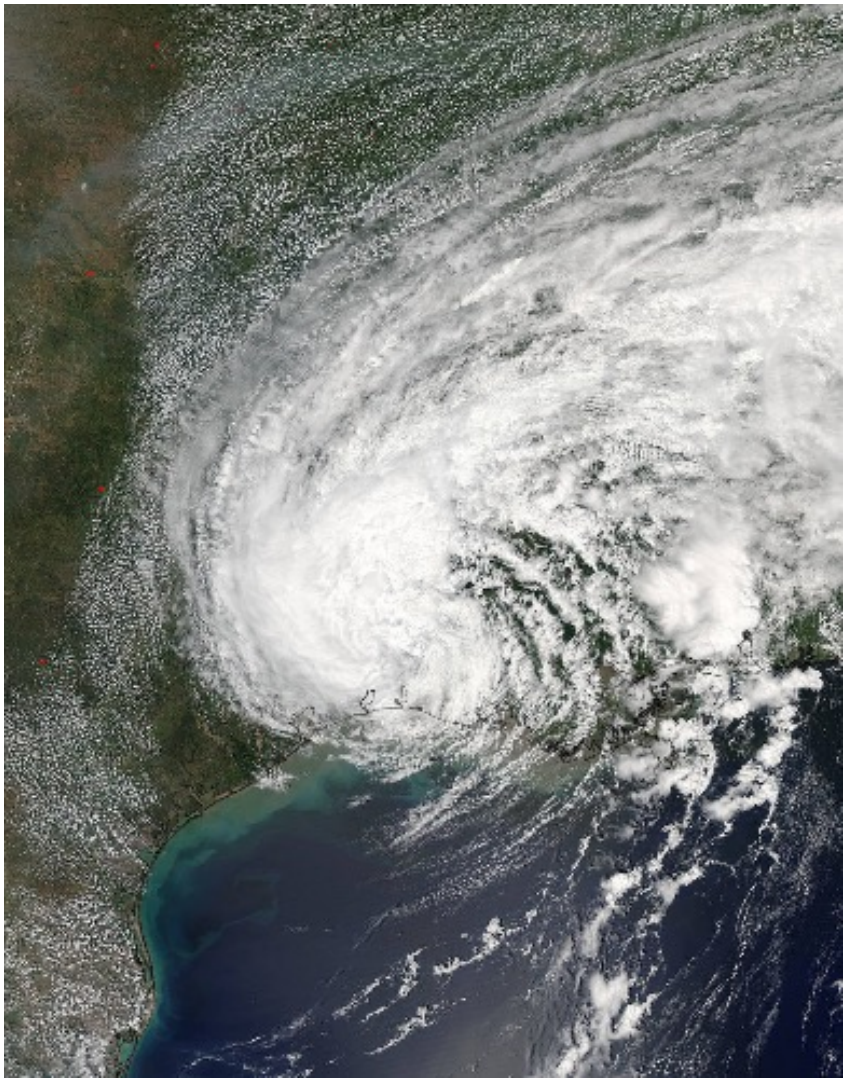

Hurricanes and
Flooding

Hurricane Katrina - New Orleans, October 2005

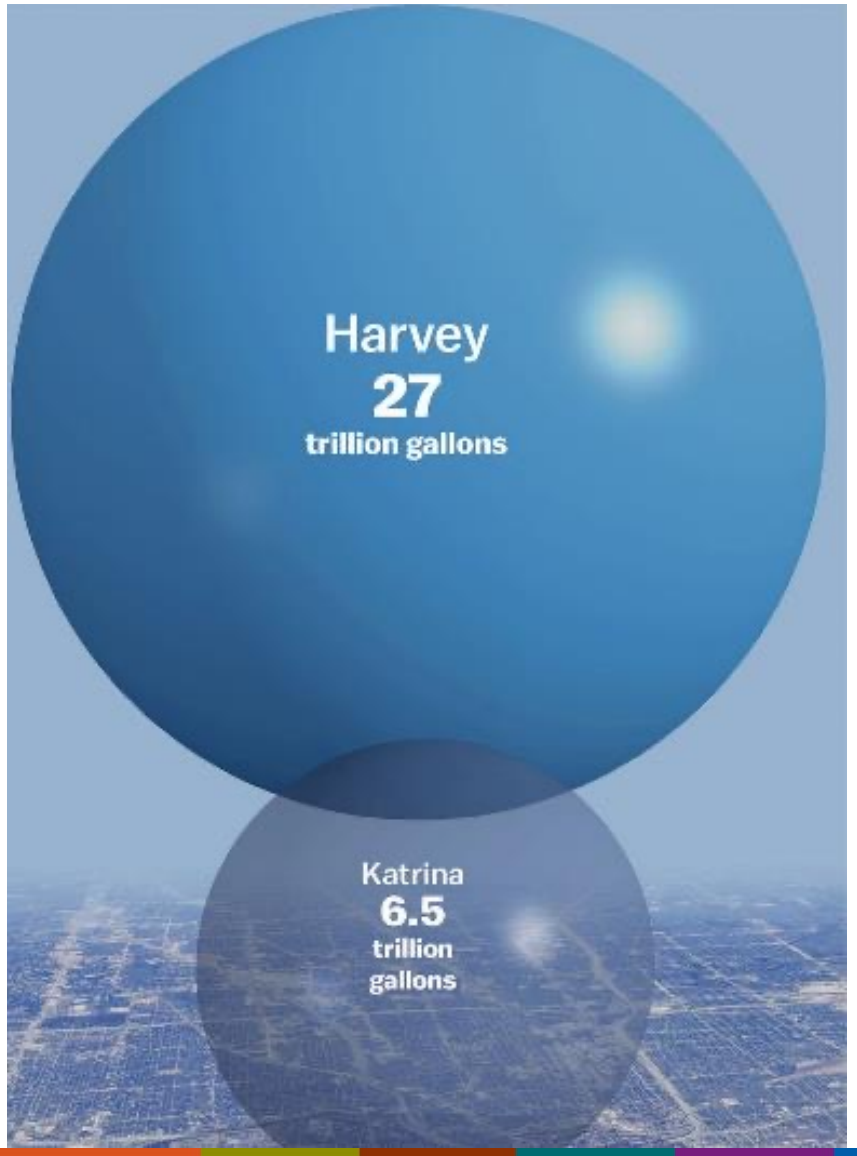
- 68% of homes had roof damage with water
- 46% (~100, 000 homes) had visible mold damage

- Immunocompromised population returning to clean homes
- NO INVASIVE DISEASE (small number studied)

Morbidity and Mortality Weekly Report 2006;55:41-4



NASA/NOAA GOES Project



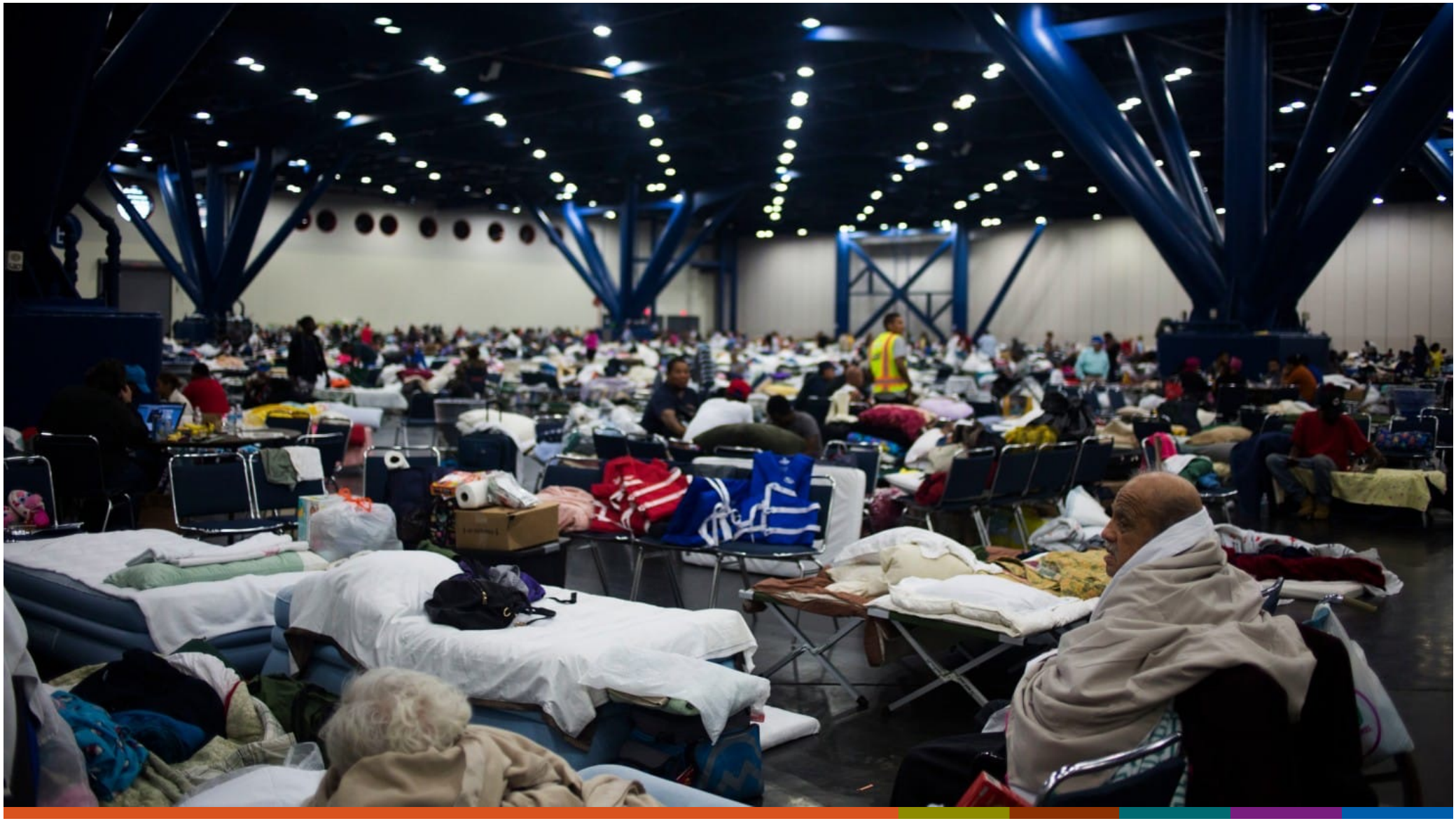
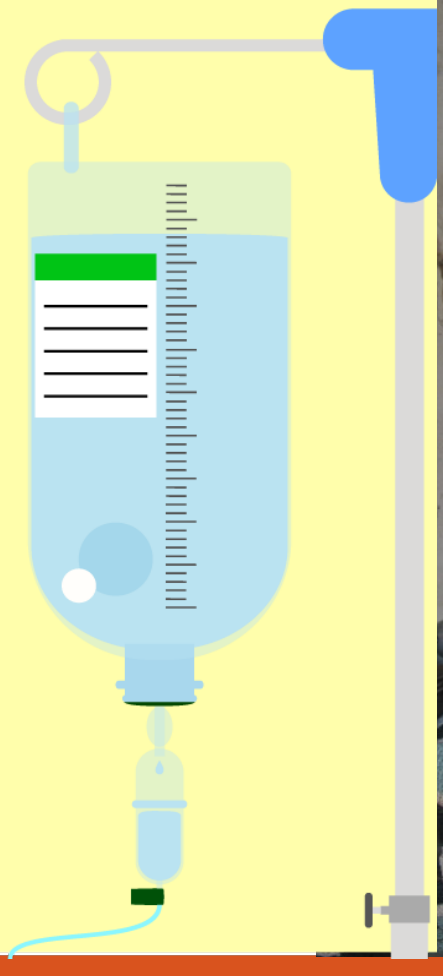


Photo by NIOSH

Photo by NIOSH

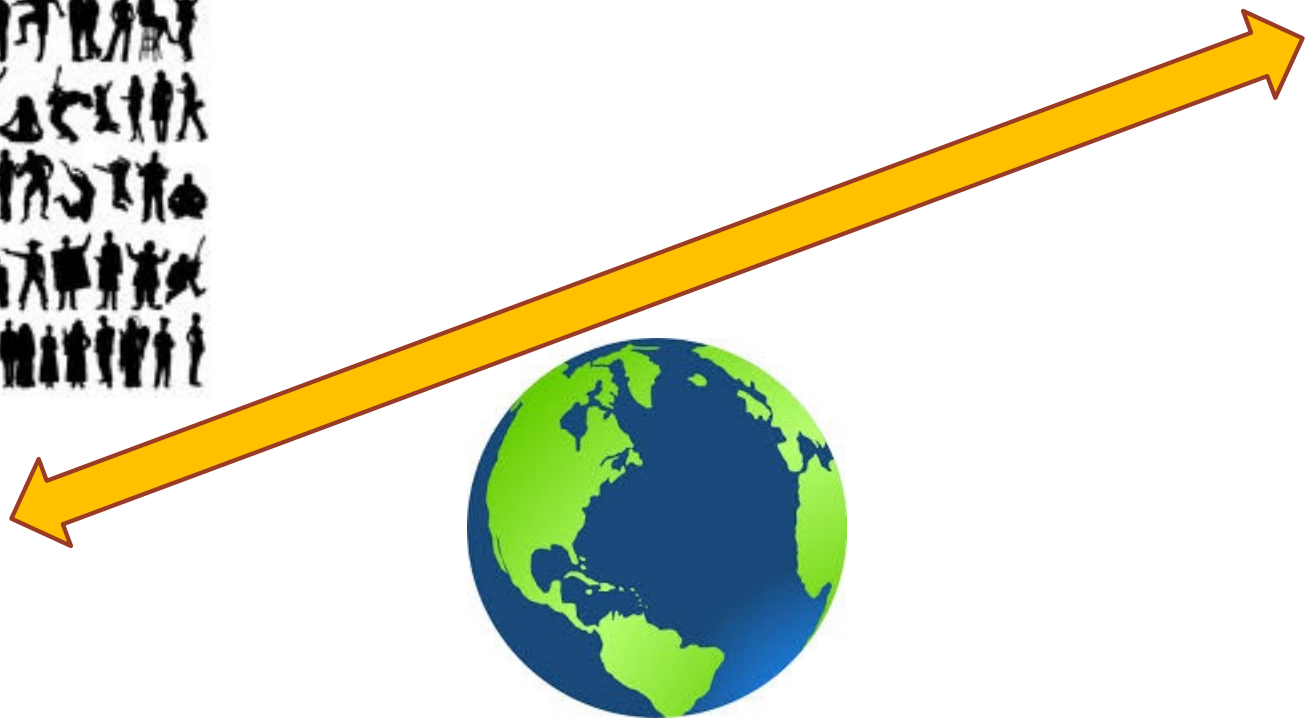
Immunocompromised (high risk) patients

- Inhalation
- Lung and sinuses
- High mortality rate

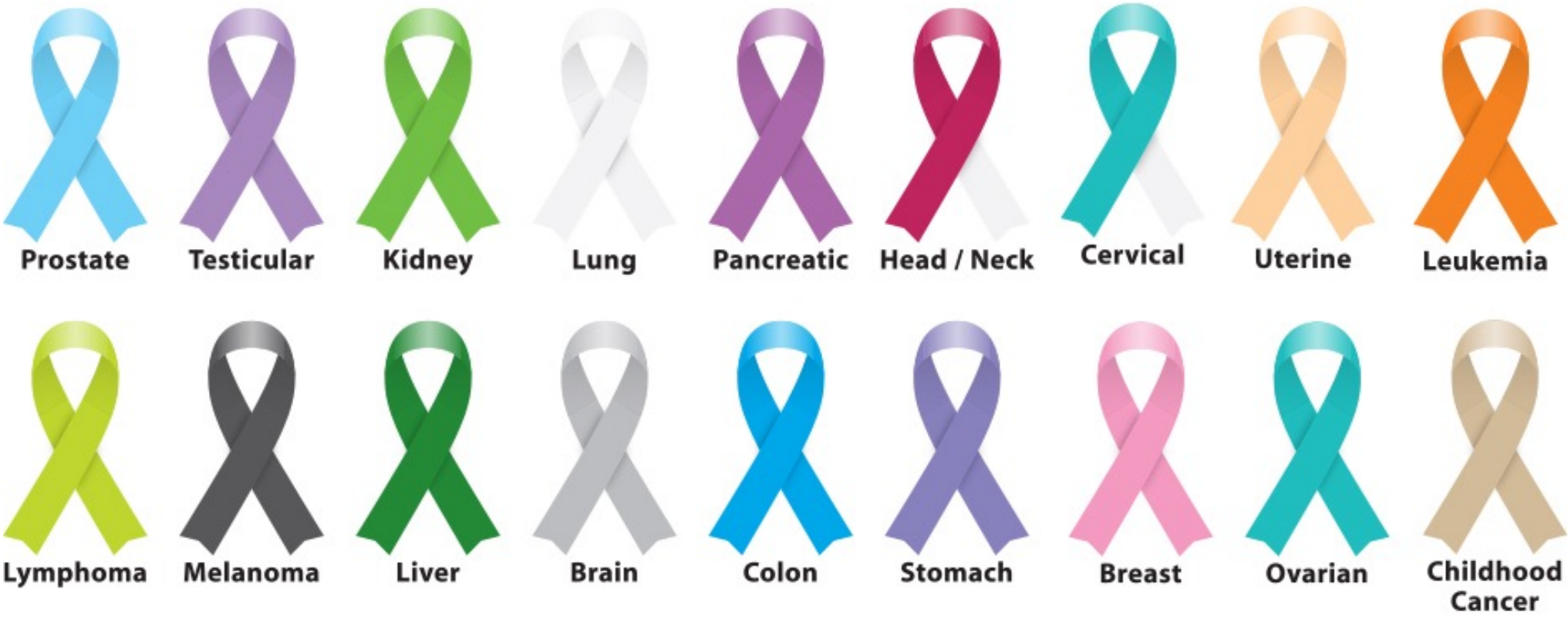


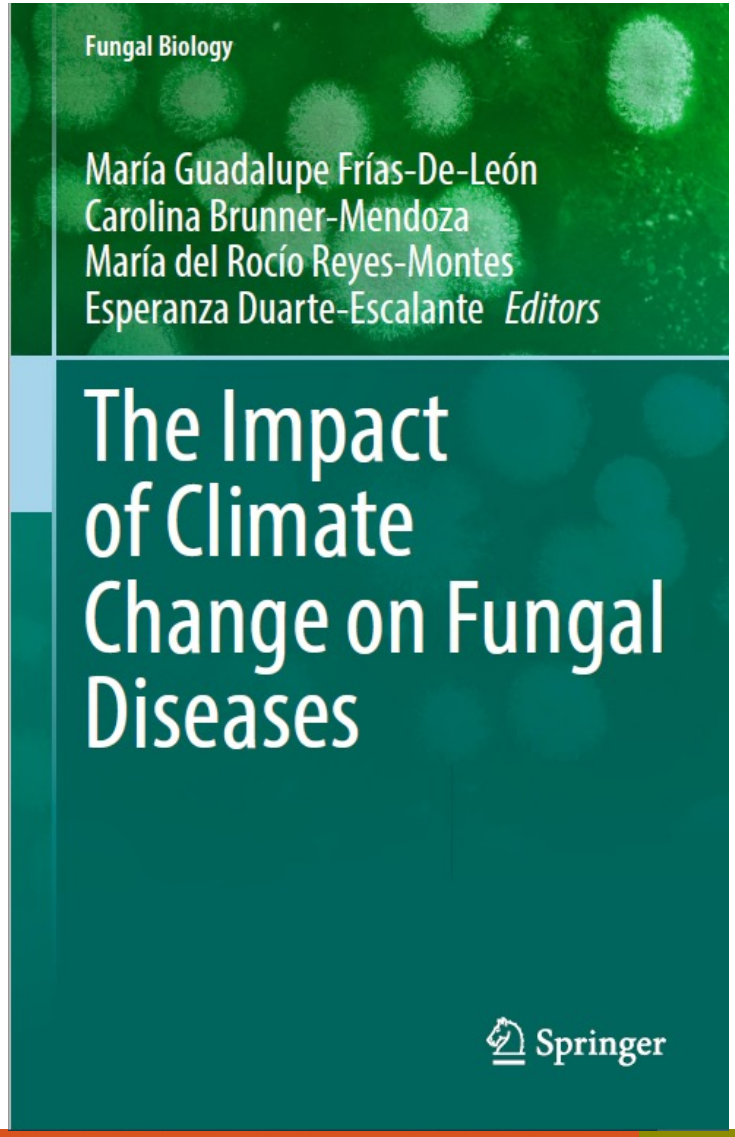
Final Thoughts

Environmental changes?



More population at risk




Fungal Biology
María Guadalupe Frías-De-León
Carolina Brunner-Mendoza
María del Rocío Reyes-Montes
Esperanza Duarte-Escalante Editors
The Impact of Climate Change on Fungal Diseases
Springer

Thanks

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TTY: 1-888-232-6348 www.cdc.gov

www.webbertraining.com/schedulep1.php

April 2, 2024	**COVID-19's CHALLENGES TO INFECTION CONTROL DOGMA** Speaker: **Prof. Michael Klompas**, Harvard University
April 11, 2024	*(FREE Teleclass)* **LESSONS LEARNED FROM A FAILED IMPLEMENTATION** Speaker: **Luize Fábrega Juskevicius** , University of São Paulo, Brazil
April 17, 2024	*(Australasian Teleclass)* **SOCIAL SCIENCE AND INFECTION PREVENTION AND CONTROL** Speaker: **Prof. Holly Seale**, University of New South Wales School of Population Health, Australia
April 25, 2024	**FLEXIBLE ENDOSCOPE REPROCESSING: FOCUS ON CORRECTING KEY WEAKNESSES** Speaker: **Prof. Michelle Alfa**, AlfaMed Consulting, Canada
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