

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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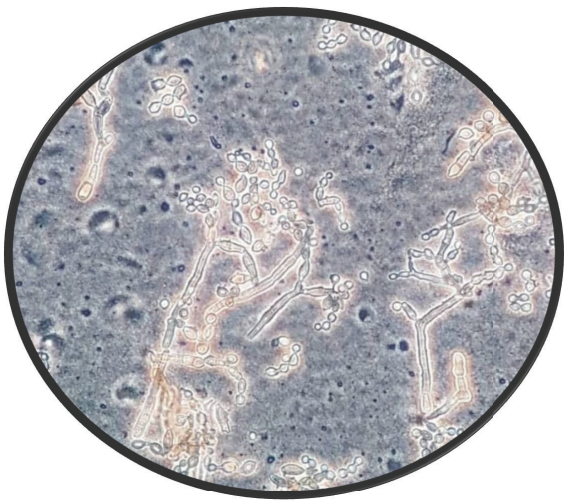


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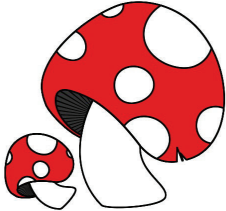
March 21, 2024

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



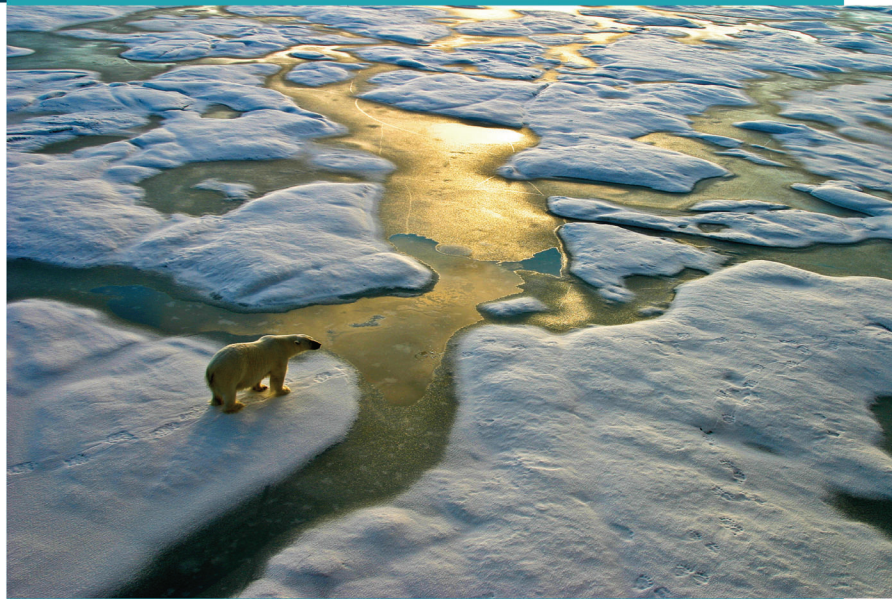


**Our Risk for
Infectious Diseases
is Increasing
because of
Climate Change**



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.



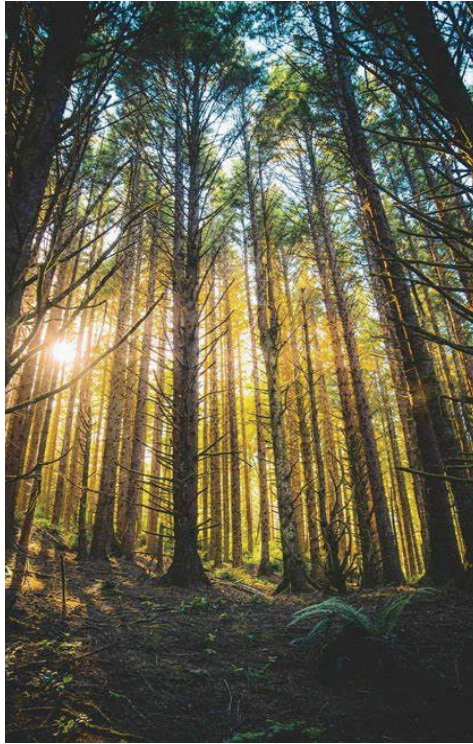
Vose, RS, DR Easterling, KE Kunkel, AN LeGrande, MF Wehner, 2017: Temperature changes in the United States. In: Climate Science Special Report: Fourth National Climate Assessment, Volume I. pp. 185-206, DOI: 10.7930/J0N29V45

Anticipated Trends

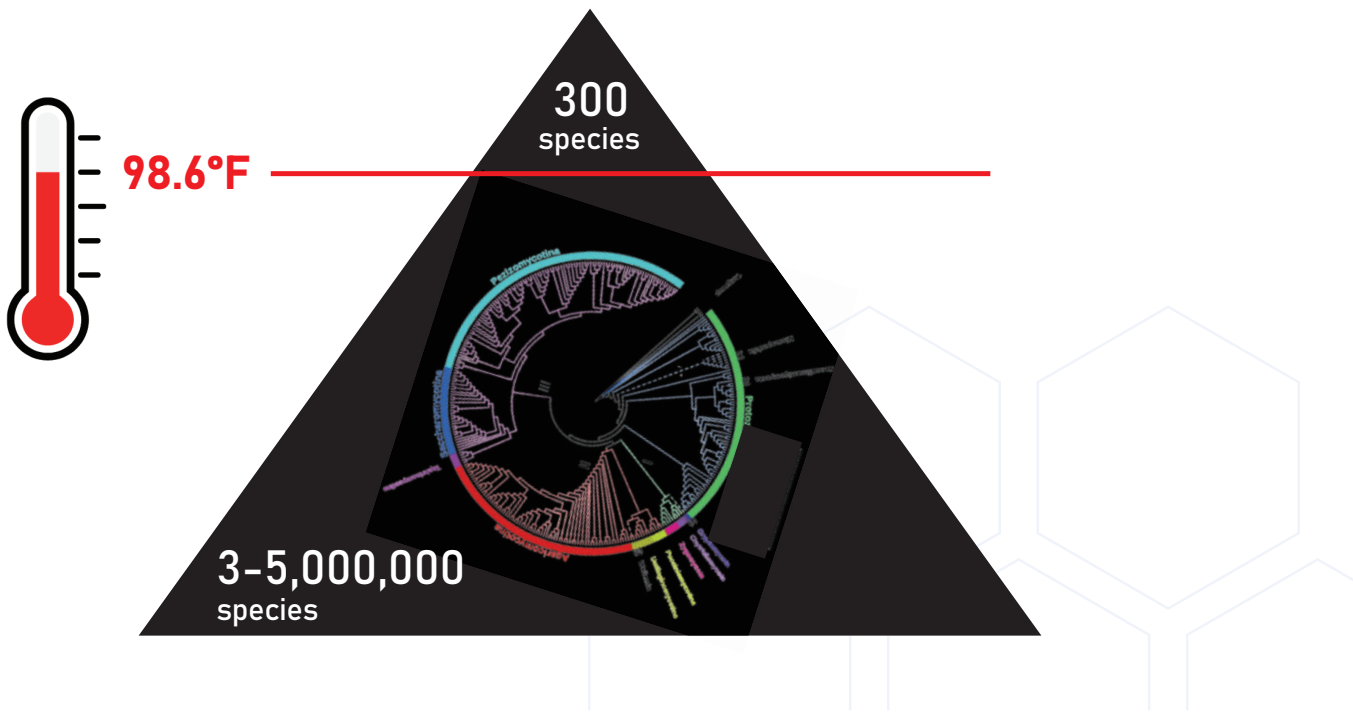
- ▶ Longer and warmer summers
- ▶ Shorter and milder winters
- ▶ Fewer frost days
- ▶ More intense heat waves;
less intense cold waves
- ▶ More extreme and
unpredictable weather events



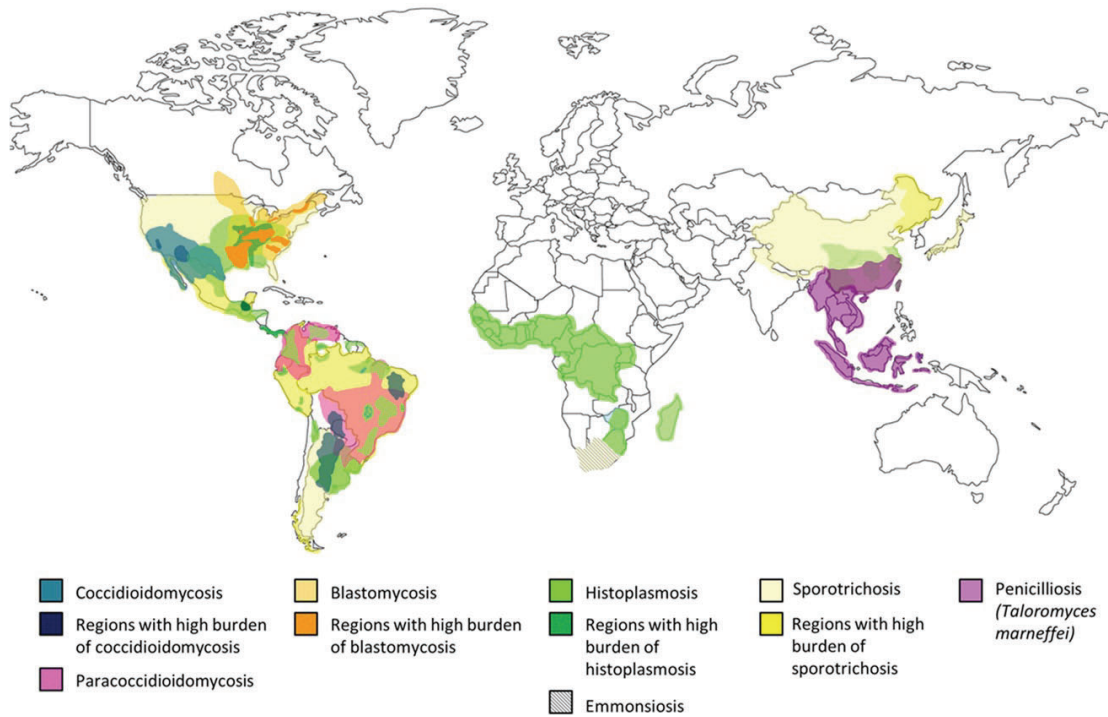
Disease-causing fungi are inextricably linked to our environment



Few fungi can grow at 98.6°F (37 °C)



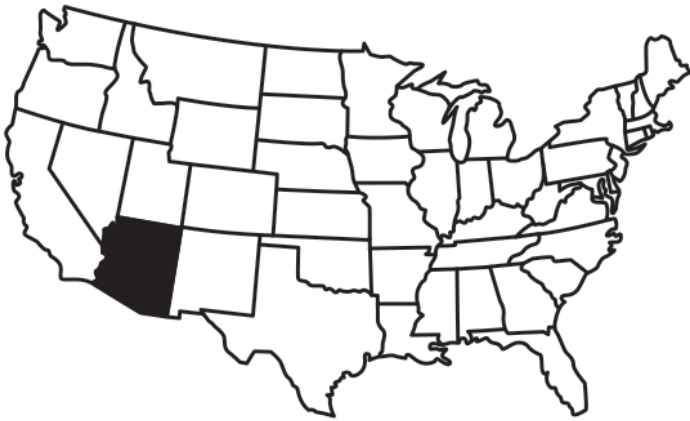
The Endemic Fungi (Geographic)



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



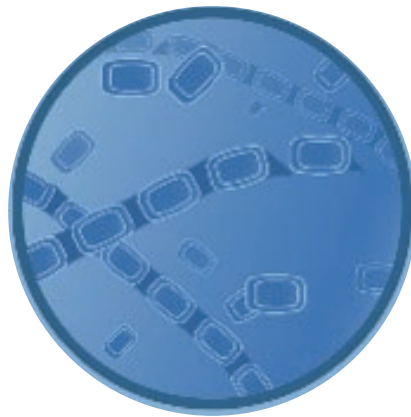
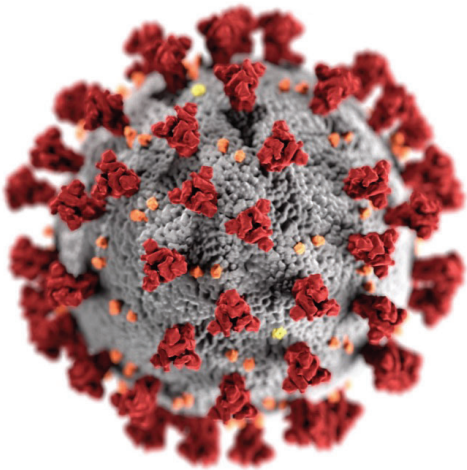
Increased pulse rate



Sweats



Fungal Diseases in the COVID Era: Hiding in Plain Sight

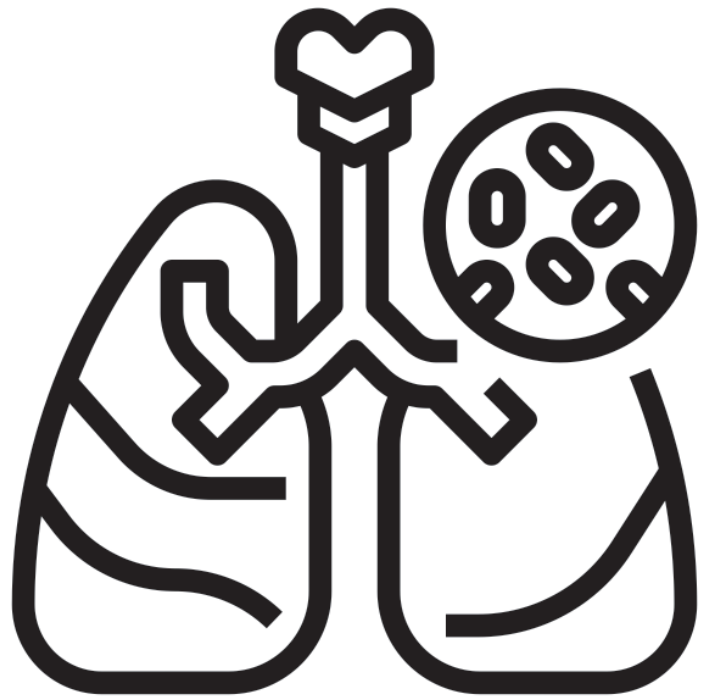


- Three negative SARS-CoV-2 tests
- Strict home isolation
- Tested negative for Valley fever



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

COUGH? FEVER? EXHAUSTED?

If you live in or have traveled to
the Southwest, ask your doctor
about Valley fever.

www.cdc.gov/fungal



Coccidioides immitis* and *Coccidioides posadasii



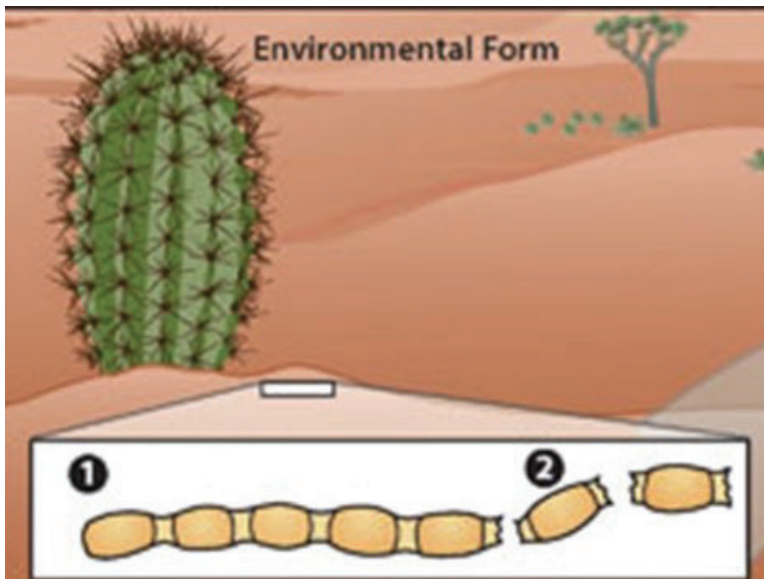


Dimorphic Fungi Two Forms “Valley Fever”

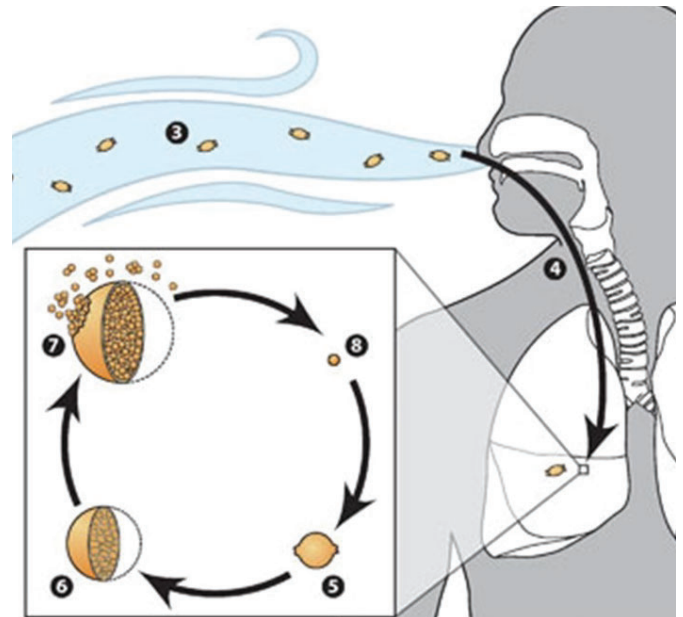
25°
Infectious

37°
Not infectious

Biology of *Coccidioides*



Environmental form



Host-associated form

Ecological niche

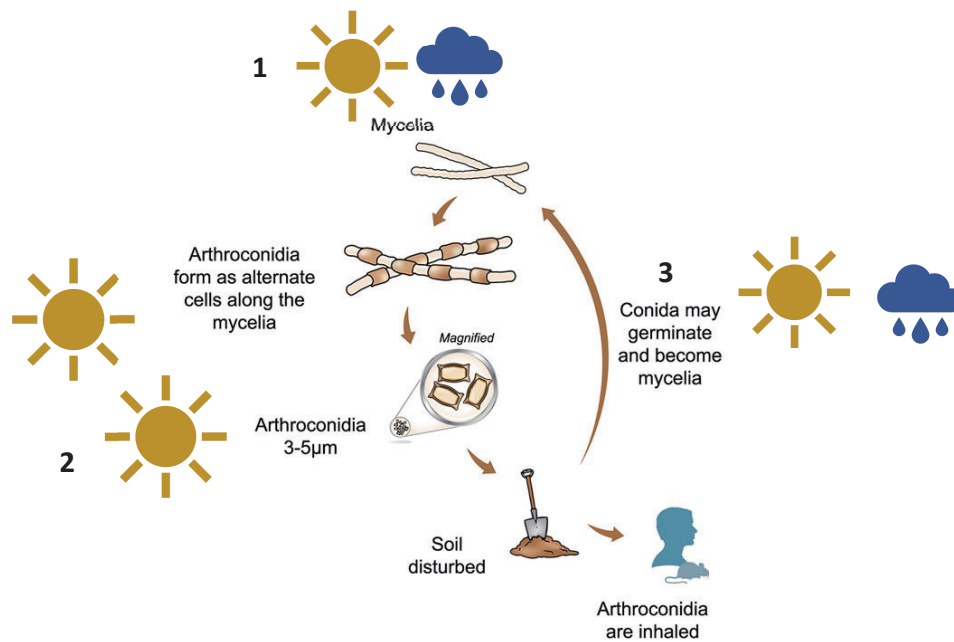
- Soil?



- Rodents/rodent habitats?



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

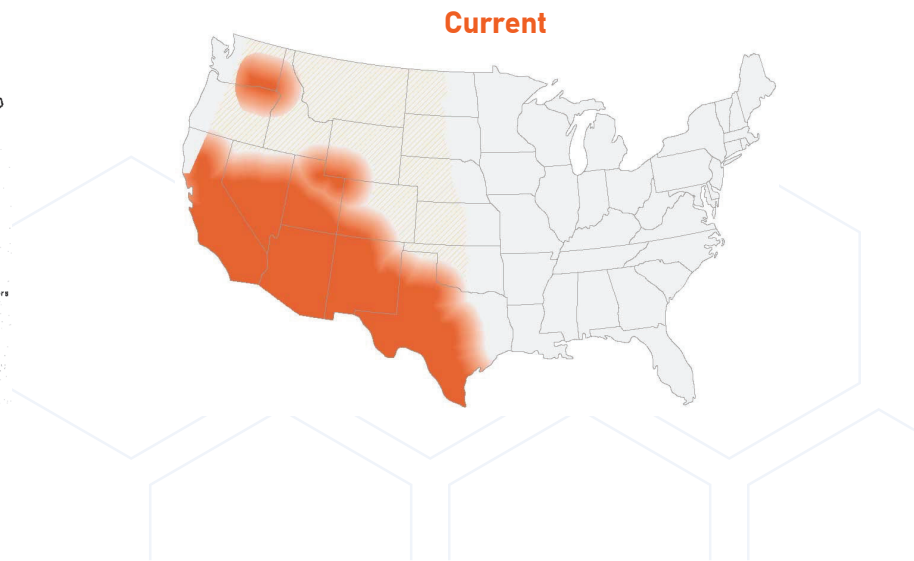
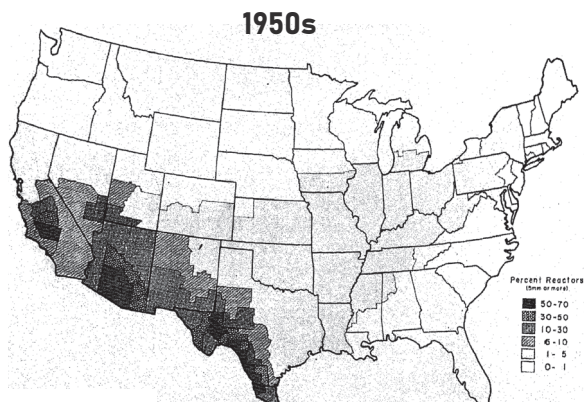


Combination of extreme climate events are leading to more people at risk for Valley Fever

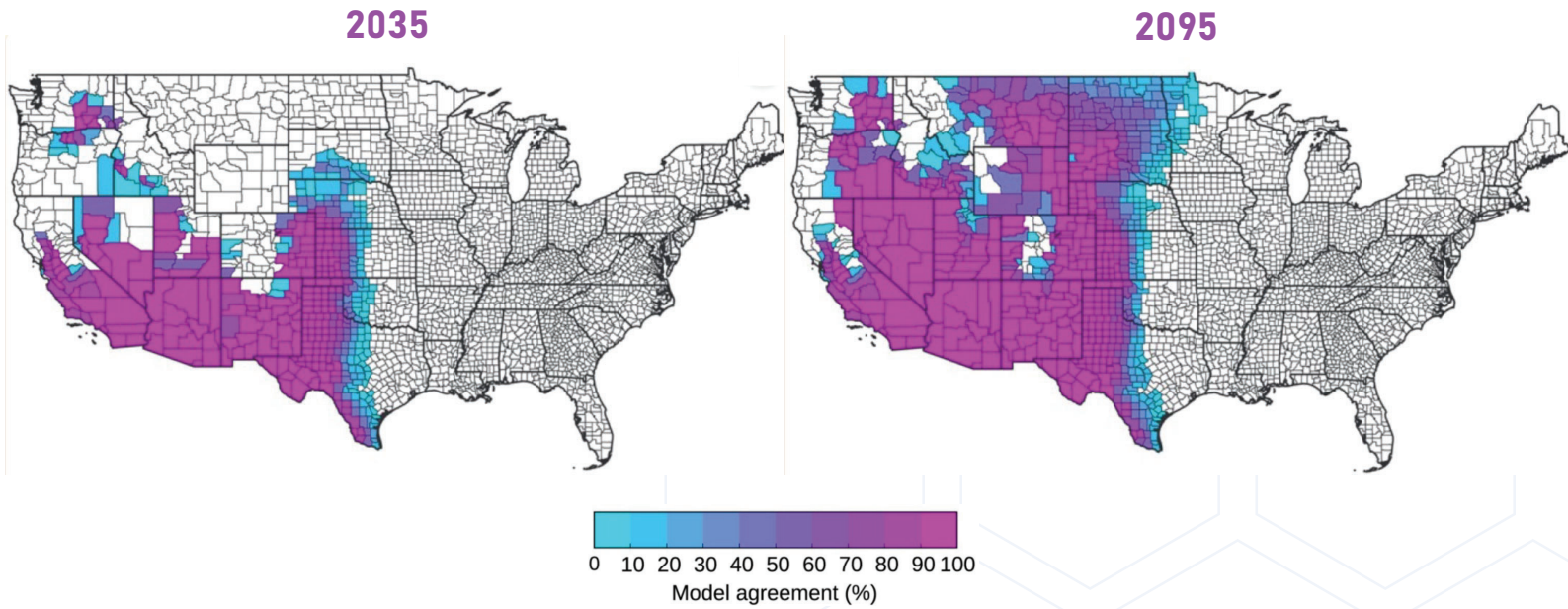


Coccidioides species primarily endemic to Southwestern United States

Areas of endemicity

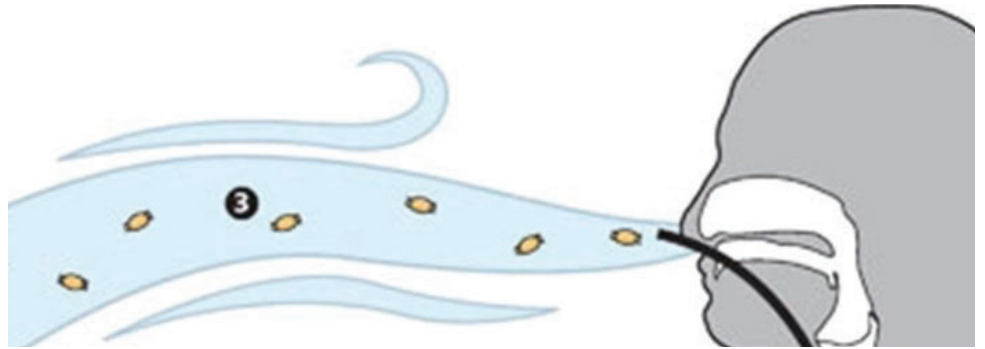


Climate modeling analyzing temperature and precipitation patterns predicts expansion of Valley Fever endemic range



Coccidioides in the air?

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



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

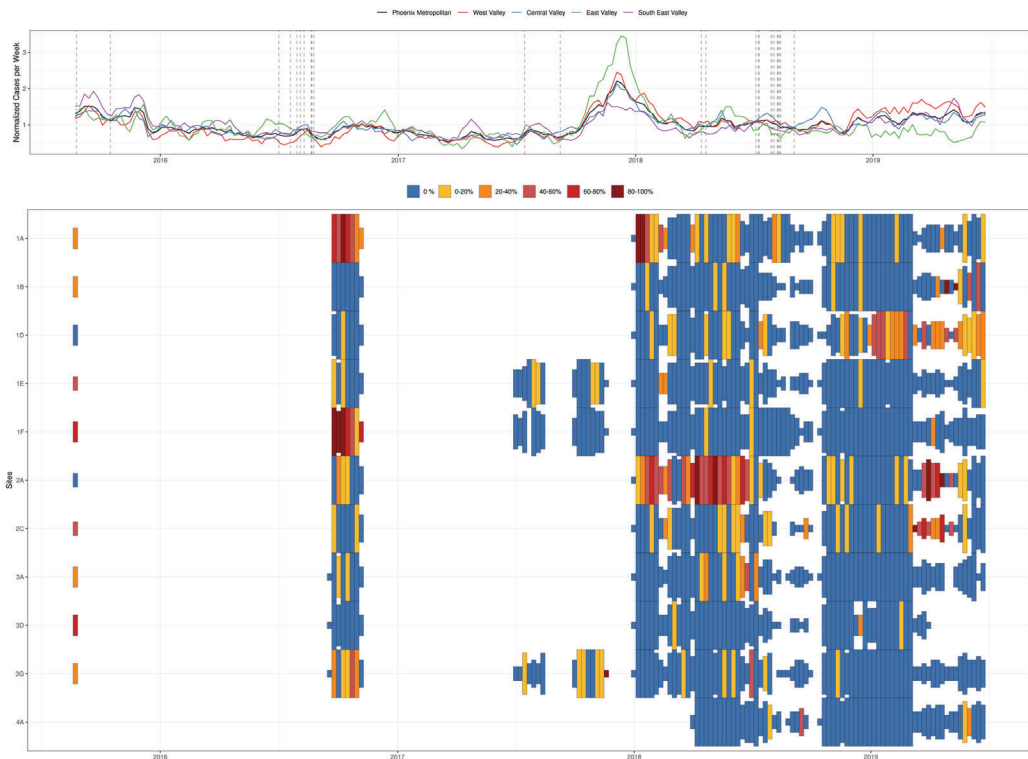
High-volume air sampler

Hydrophobic PTFE filter

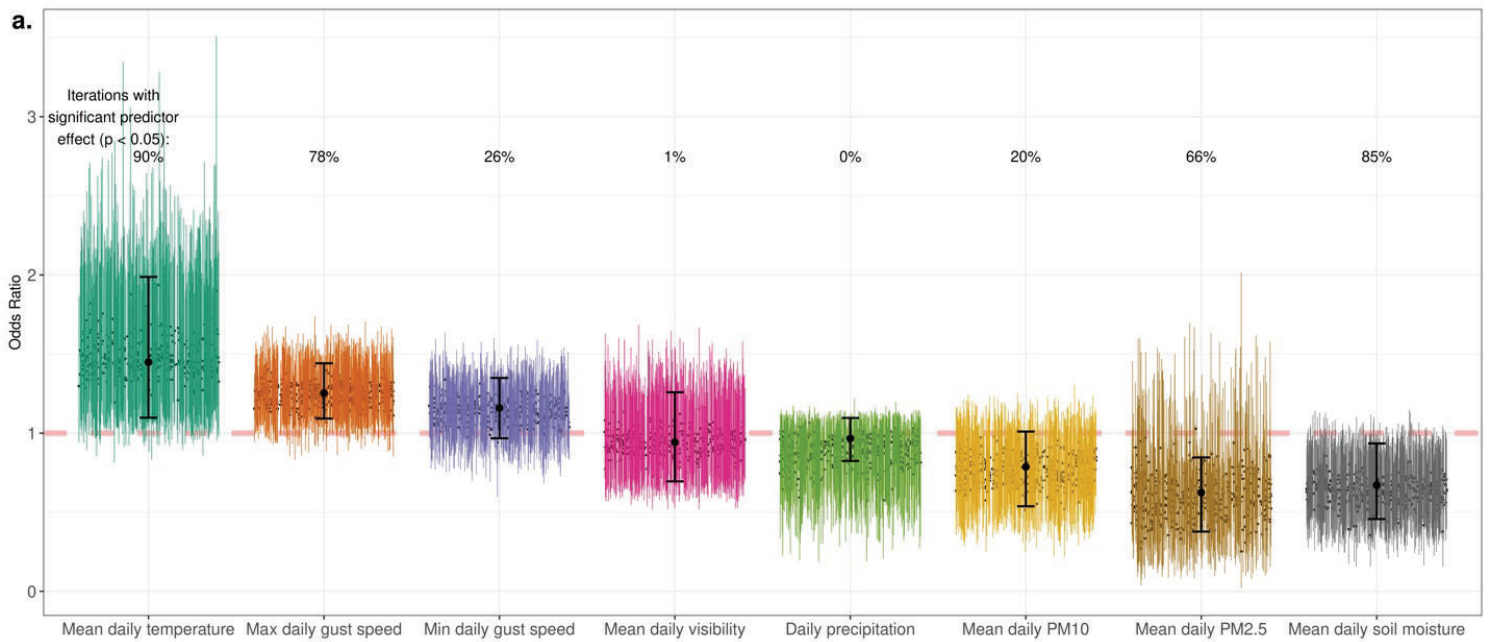


CocciWatch- Surveillance conclusions

- **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





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



Tailgate



Training

Preventing Work-related Valley Fever in Wildland Firefighters



Digging a fire line disturbs soil that may contain cocci spores



Sporotrichosis

Sporothrix spp.

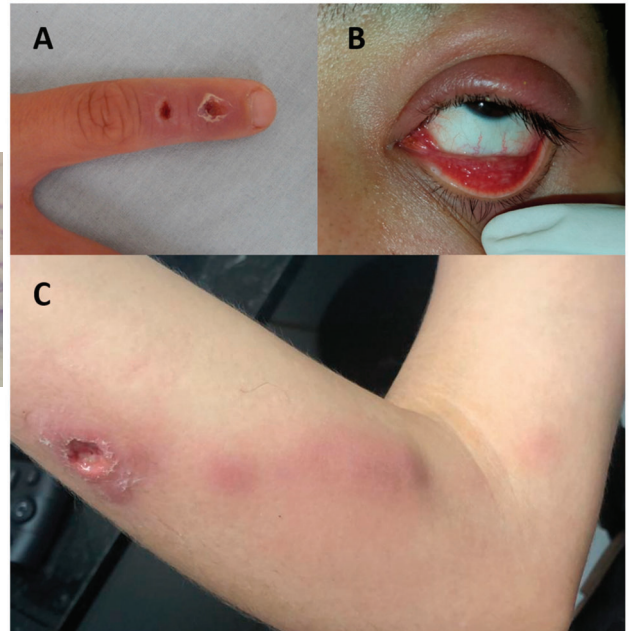
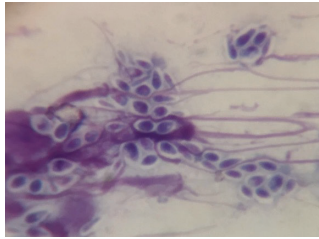


Sporotrichosis (Schenckii)

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

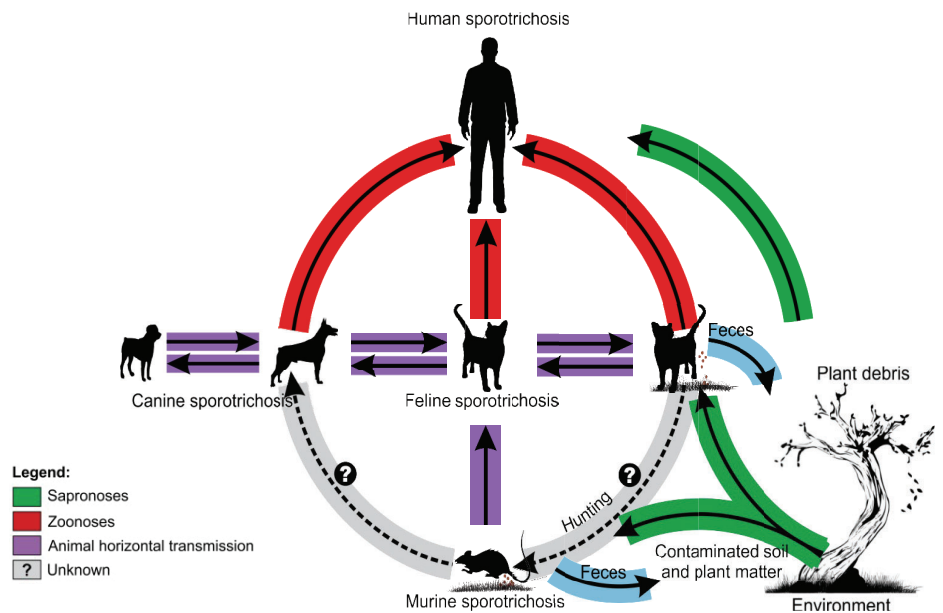
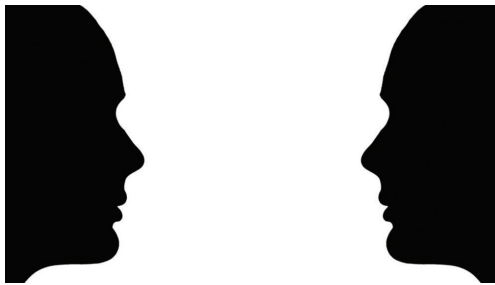


New Species Emerges: *Sporothrix brasiliensis*: Zoonotic Disease with Cats



Rodrigues AM et al. 2016. PLoS Pathogens.

Dimorphic fungus: Transmissible in Yeast and Mold Phase!

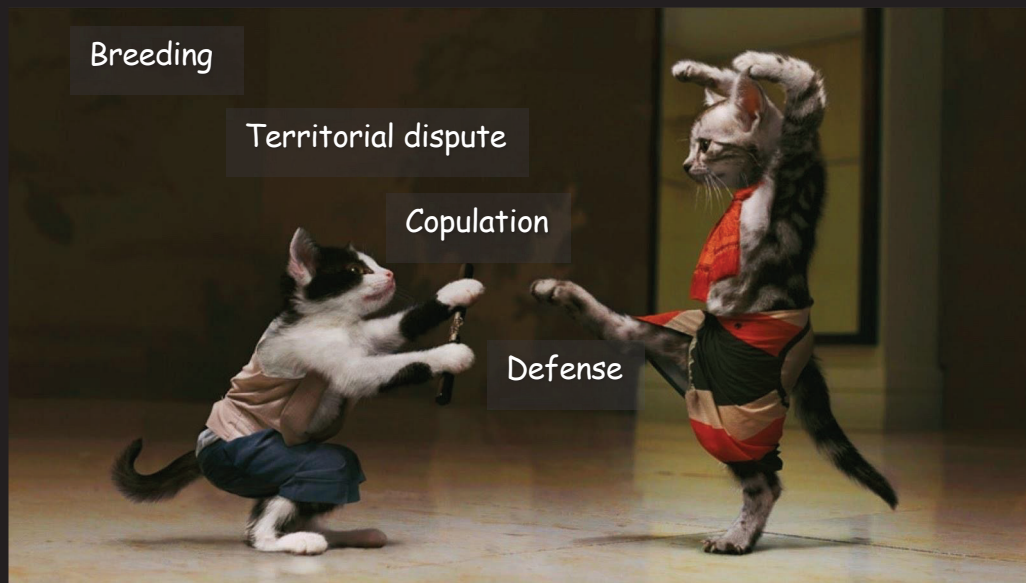


Rodrigues AM et al. 2016. PLoS Pathogens.

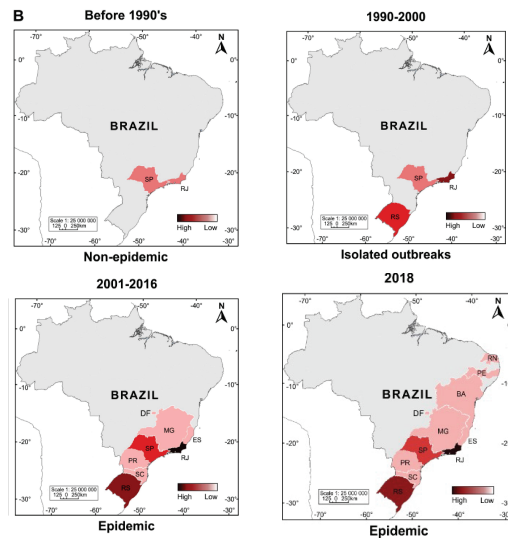
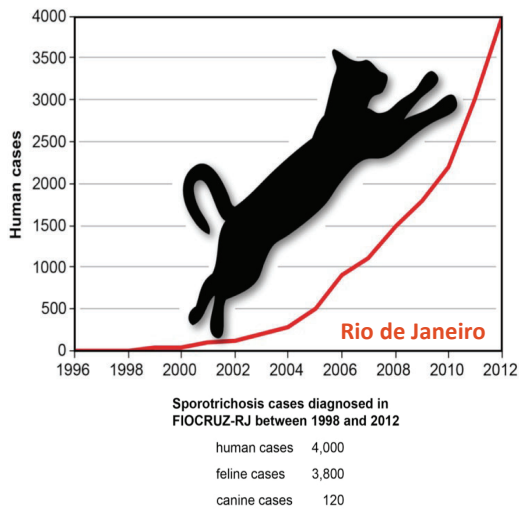
Sick cats may splash infectious yeast cells when shaking the head...



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

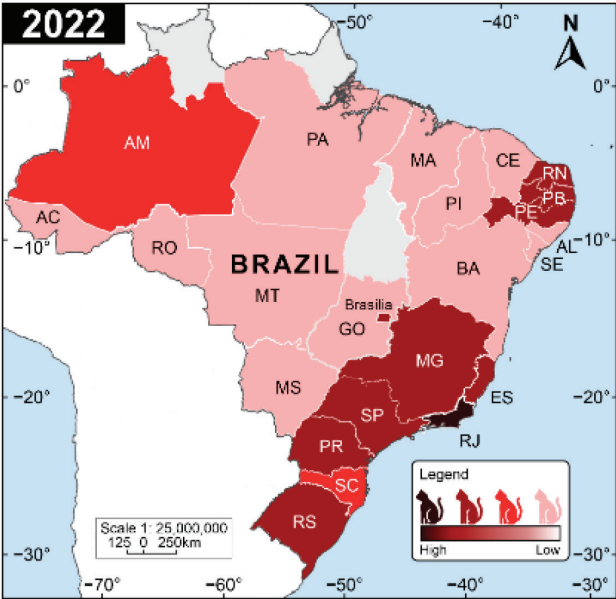


Rapidly Emerged in Brazil



And recently reported from Argentina

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.

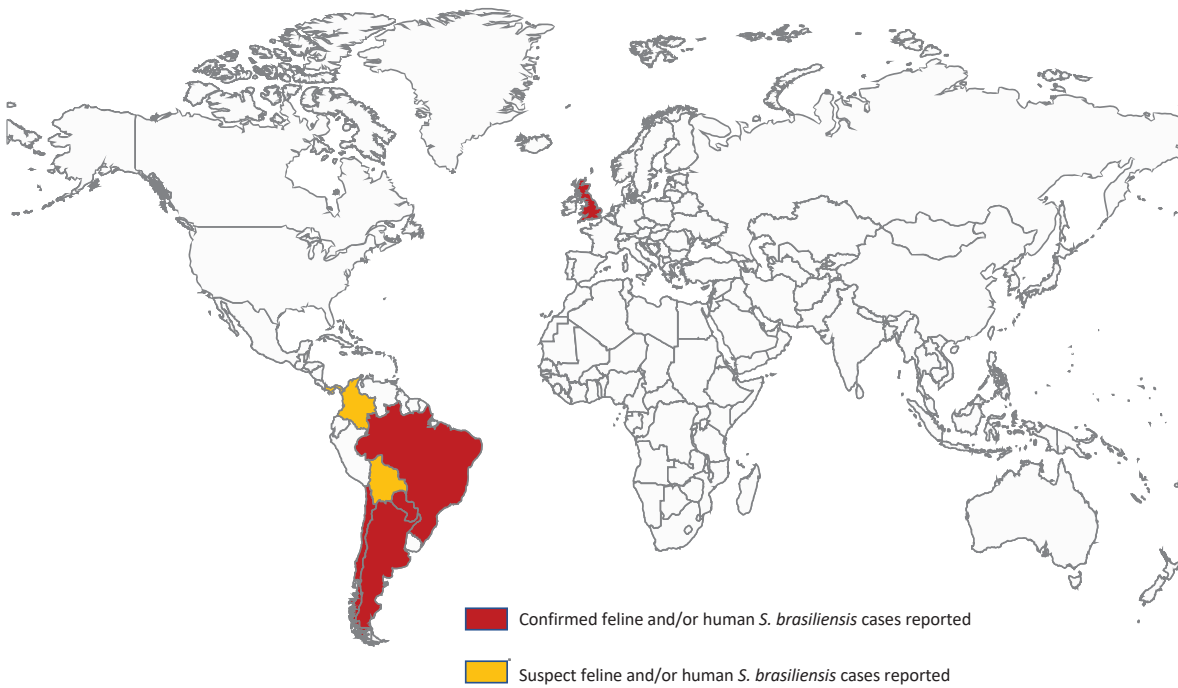
Reports now in neighboring countries

Colombia, Paraguay, Bolivia and Argentina




Anderson et al *Emerging Microbes & Infections*, 2014

Cases are increasingly reported beyond Brazil










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 Echeverría¹, Miguel Scarpa², Javier Mas³, María L. Cuevas⁴ 

Rev. Del Nacional (Buenos Aires) 2017;9(2):87-91 **DEL NACIONAL**
 Caso Clínico
Esporotricosis transmitida por gato doméstico. Reporte de un caso familiar
Sporotrichosis transmitted by domestic cat. A family case report
 Jesús Manuel García Duarte¹, Víctor Raúl Wasth Acosta², Patricia María Laura Formentón Viera³, Anabela Helena Caldeira⁴, Gabriela Rosendo González Herrera⁴, Victoria Beatriz Novelli de Odoño⁴, José Guillermo Penabaz Bruna⁴

¹Ministerio de Salud Pública y Bienestar Social, Hospital Nacional, Servicio de Dermatología, Itauguá, Paraguay.
²Ministerio 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 Thomson¹  Carlos González^{2,3}  Olivia Blank⁴  Valentina Ramírez⁴,  Camila del Río¹,  Sebastián Santibáñez¹ and  Pamela Pena⁴

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, CITIOVET, Ñaúfoa, Santiago 7750538, Chile.
⁴ Clínica Veterinaria Temaukel, Punta Arenas 6210048, Chile.
^{*} Author to whom correspondence should be addressed.

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

- Veterinarians
- Clinicians
- Microbiologists
- Epidemiologists
- Border health



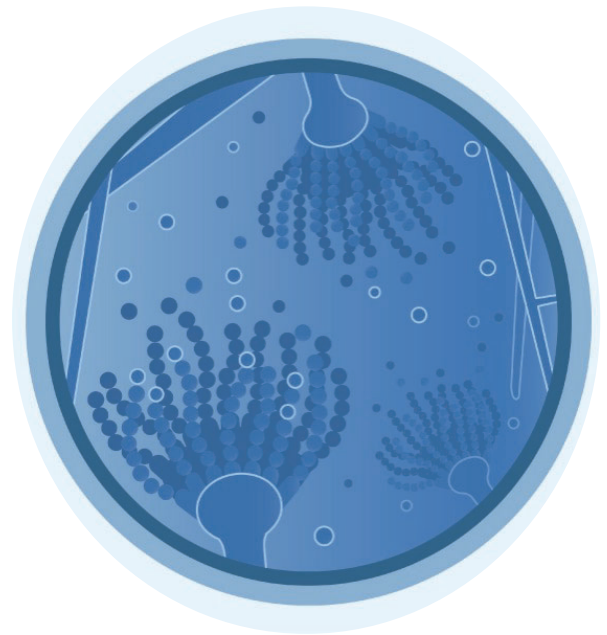
A microscopic image of Aspergillus fumigatus. The image shows several spherical, multi-celled spores (conidia) arranged in a dense, rounded cluster. The spores are light pinkish-purple. The background is dark blue. There are also some individual spores scattered around the main cluster. The overall appearance is that of a typical Aspergillus conidial head.

Aspergillosis

Aspergillus fumigatus

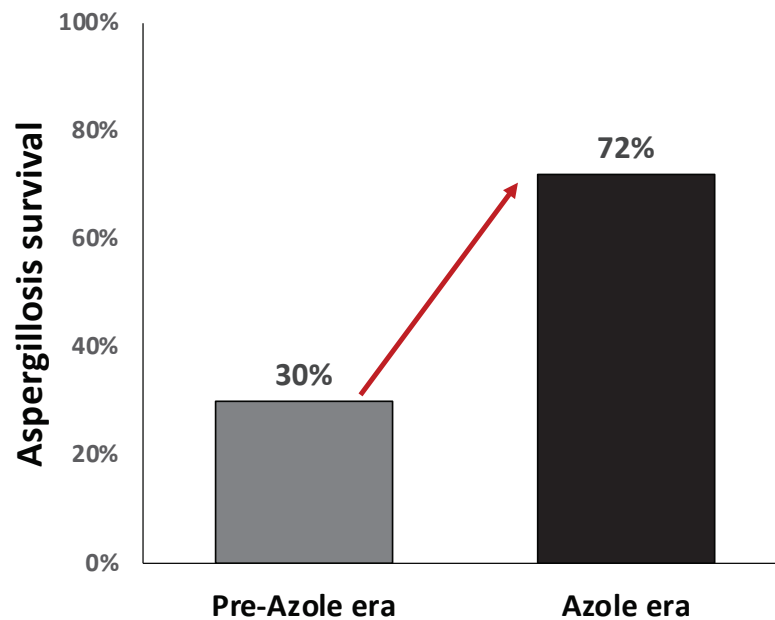
Background on Aspergillosis

- **Rare** fungal infection via lung
- Affects **severely immunocompromised** people (e.g., stem cell transplant, hematologic malignancy)



Triazole antifungals are critical for treating aspergillosis and saving lives

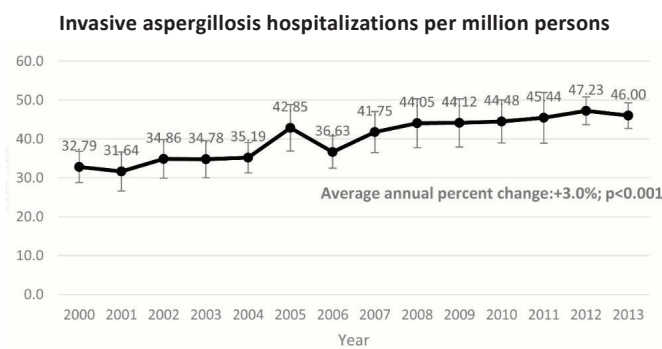
Introduction of mold-active triazole medications in 1990s dramatically improved survival



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**”

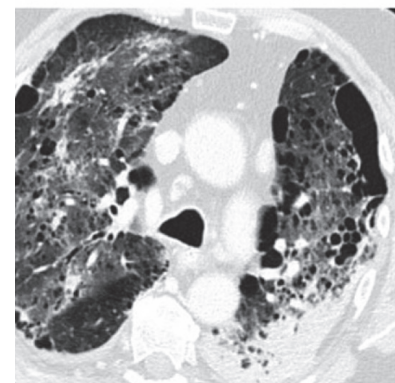
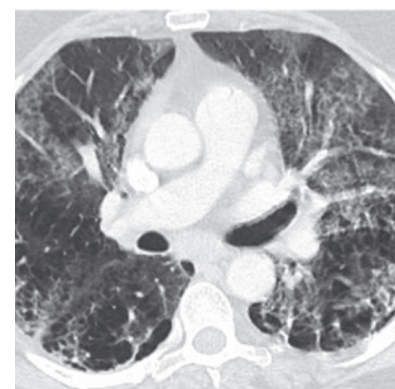
Increasingly identified in non-immunocompromised populations, including those with influenza and COVID-19

THE LANCET
Respiratory Medicine

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

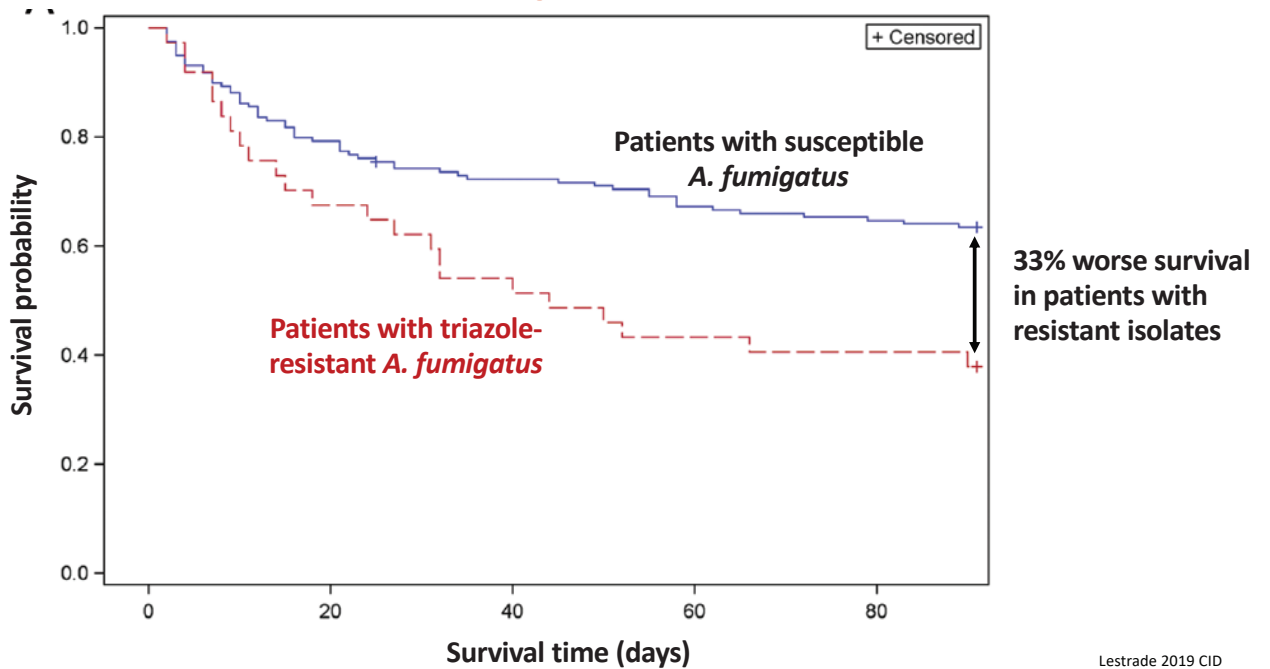
EMERGING INFECTIOUS DISEASES®

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

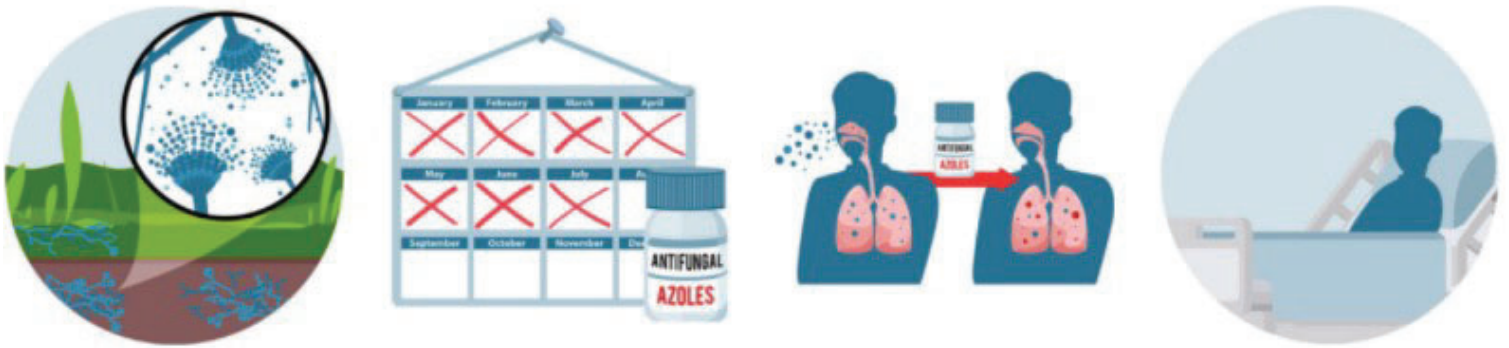


Koehler P, et al. Mycoses. 2020

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

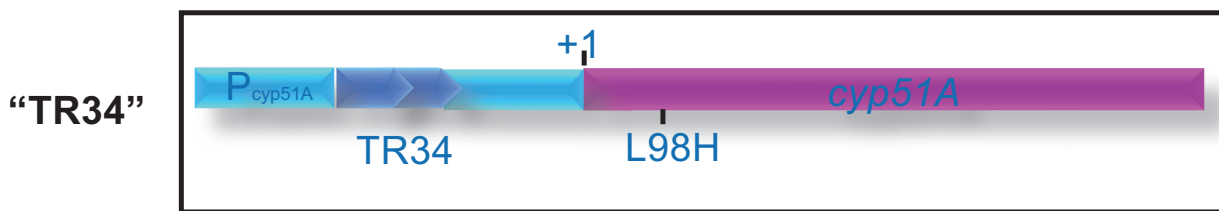


Since clinical use of mold-active azole use began in 1990s, resistance was periodically observed in patients on long-term therapy

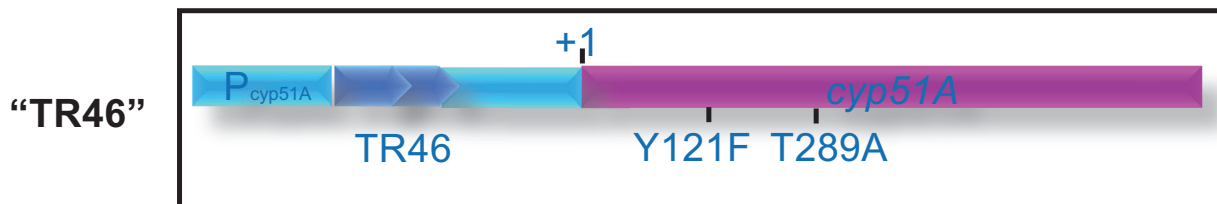


- Many different mutations lead to azole resistance

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

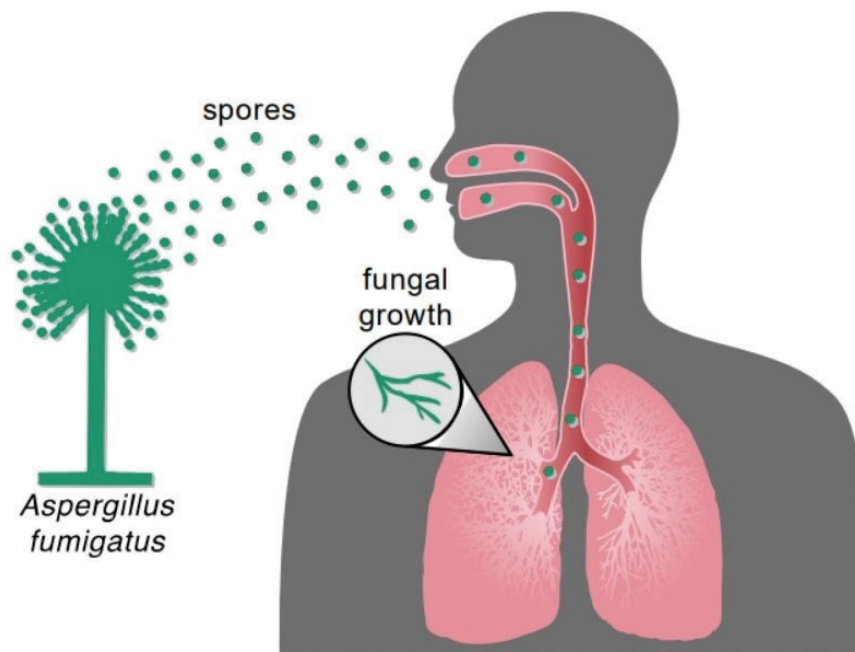


Causes Pan-Azole Resistance: Itraconazole, Voriconazole, Posaconazole



Causes Resistance to Preferred Drug: Voriconazole

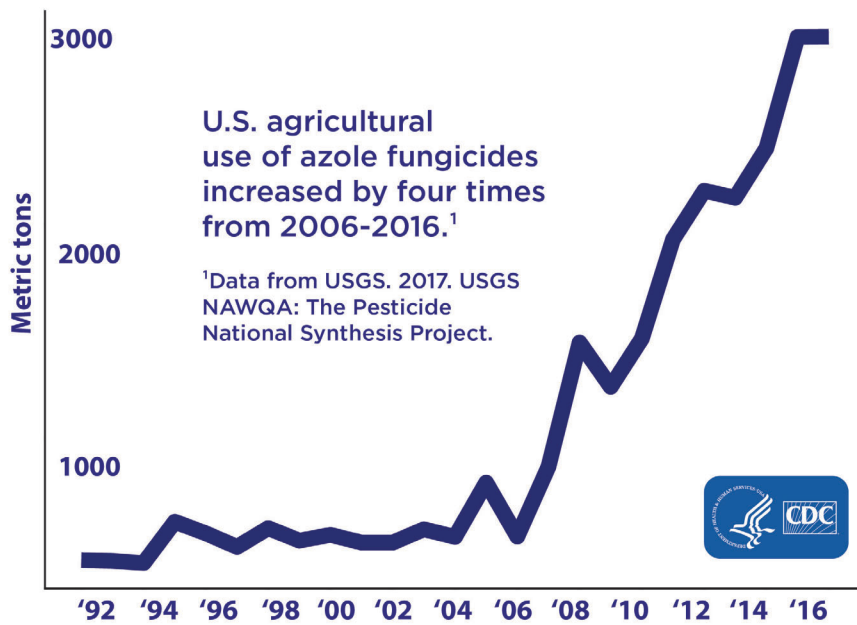
Patients inhale *A. fumigatus* that is already azole resistant



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



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



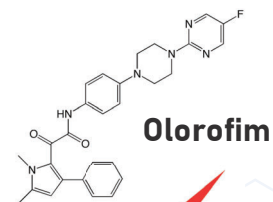
CS323341-A

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



Environmental

Ipflufenoquin





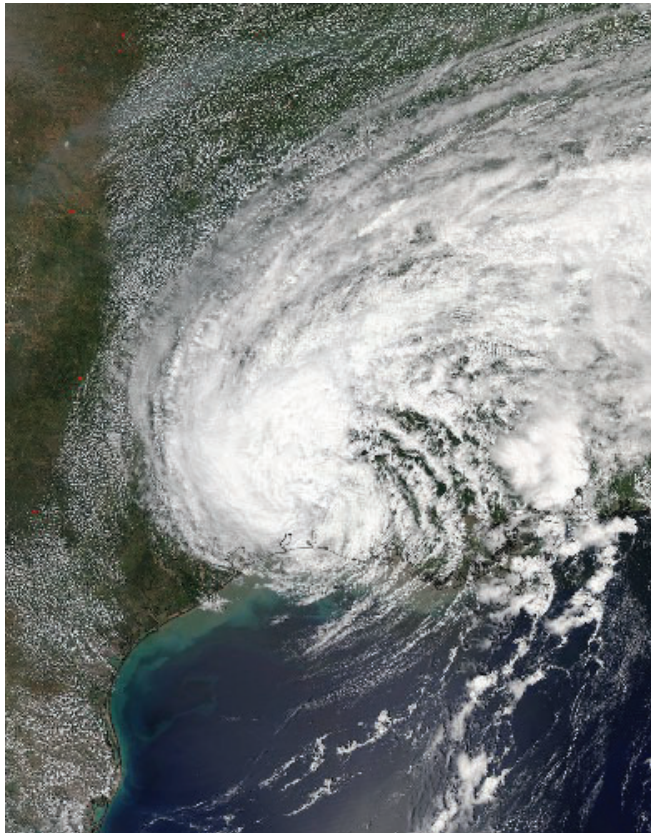
Hurricanes and Flooding

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

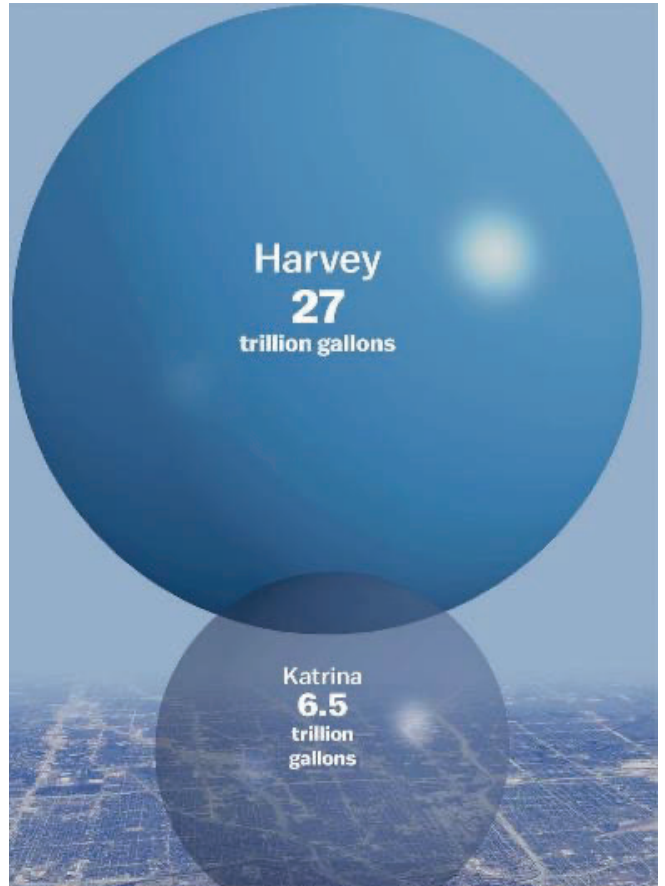






Photo by NIOSH





Photo by NIOSH



Immunocompromised (high risk) patients



- Inhalation
- Lung and sinuses
- High mortality rate

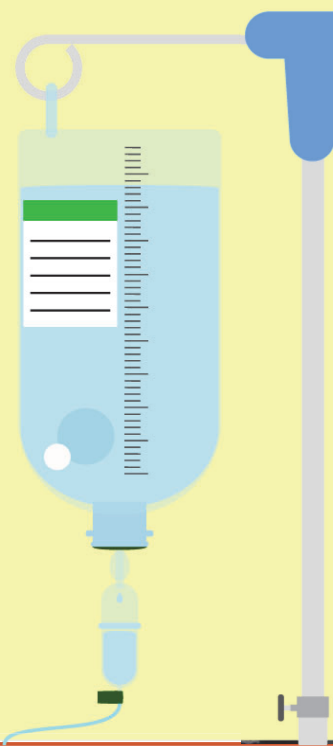
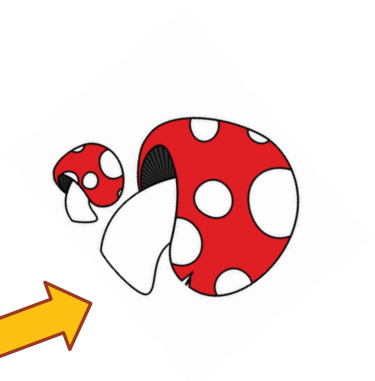
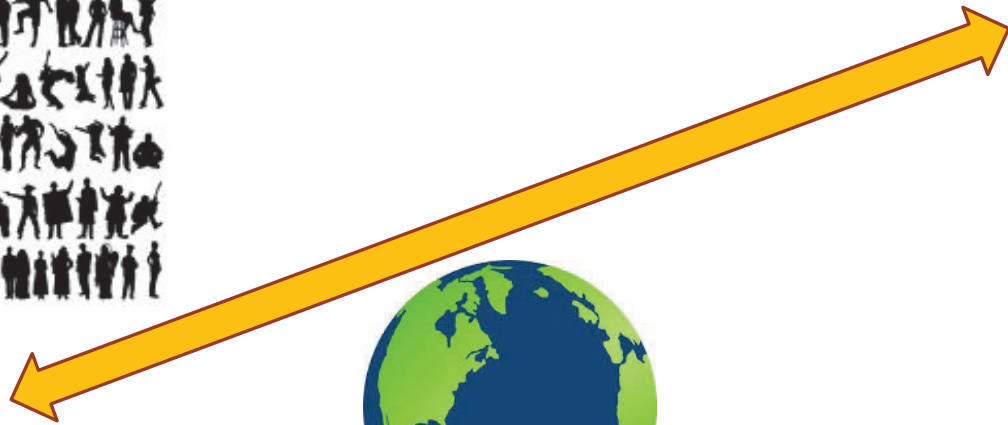


Photo by NIOSH

Final Thoughts

Environmental changes?







More population at risk



Prostate



Testicular



Kidney



Lung



Pancreatic



Head / Neck



Cervical



Uterine



Leukemia



Lymphoma



Melanoma



Liver



Brain



Colon



Stomach



Breast



Ovarian



Childhood
Cancer



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

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



**THINK FUNGUS.
SAVE LIVES.**

Some fungal infections can look like other illnesses. Early diagnosis and proper treatment are essential.

www.cdc.gov/fungal

DEPARTMENT OF HEALTH & HUMAN SERVICES
CDC

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



www.webbertraining.com/schedulep1.php

April 2, 2024

COVID-19's CHALLENGES TO INFECTION CONTROL DOGMA

Speaker: **Prof. Michael Klompas**, Harvard University

(FREE Teleclass)

April 11, 2024

LESSONS LEARNED FROM A FAILED IMPLEMENTATION

Speaker: **Luize Fábrega Juskevicius**, University of São Paulo, Brazil

(Australasian Teleclass)

April 17, 2024

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

(FREE Teleclass)

May 3, 2024

SPECIAL LECTURE FOR 5 MAY

Speaker: **Prof. Didier Pittet**, University of Geneva Hospitals, Switzerland

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