

Not “The Last of Us”: The fungi that really SHOULD scare you

Dr. Shawn R. Lockhart, PhD D(ABMM) FAAM

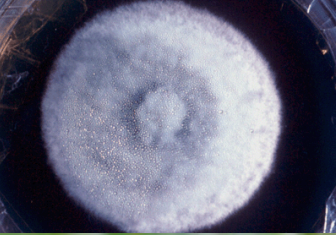
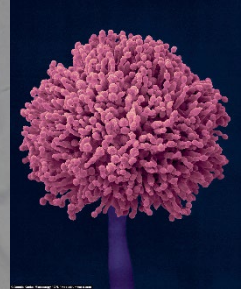
Mycotic Diseases Branch

Centers for Disease Control and Prevention

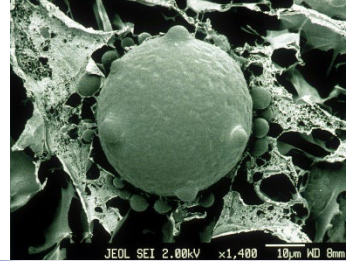
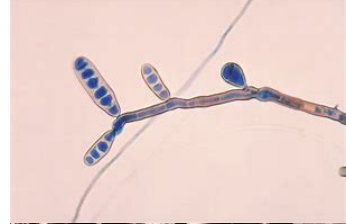
NYCASM

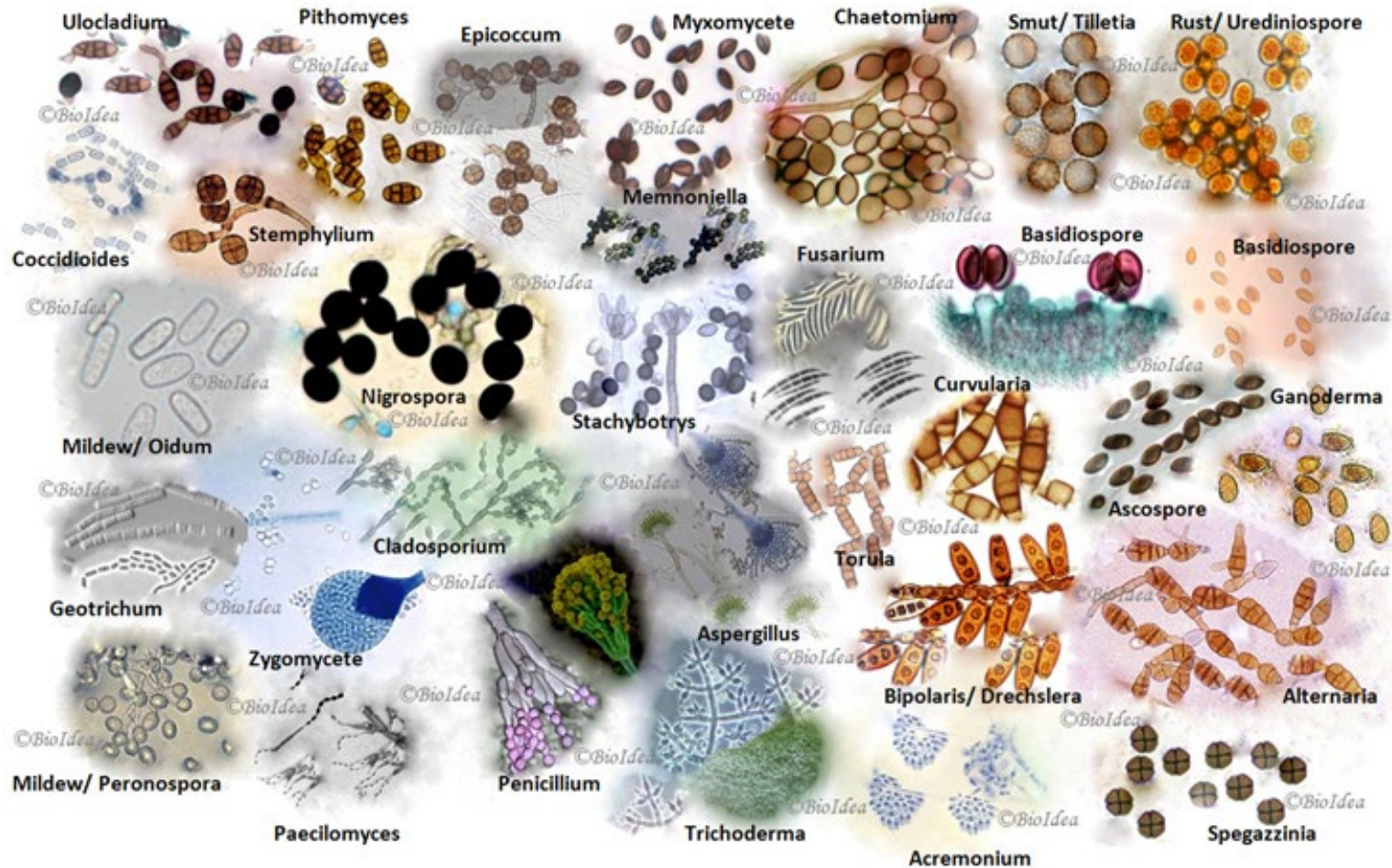
6/2/2023





2,500,000 species





600

species are
pathogenic to
mammals

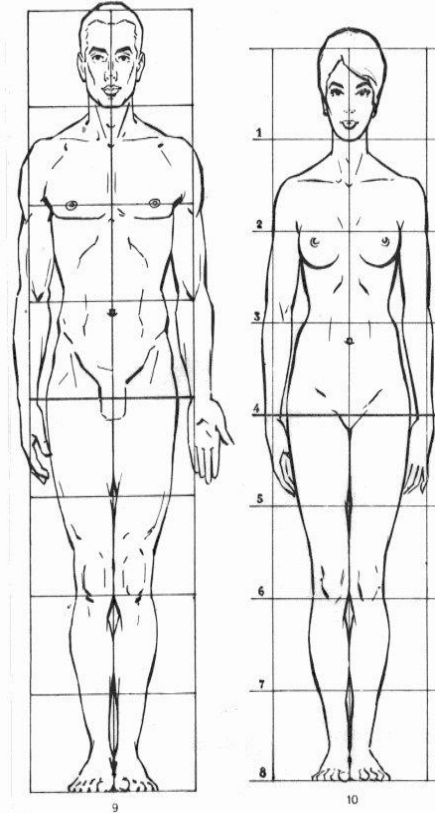




Fungi have an image problem



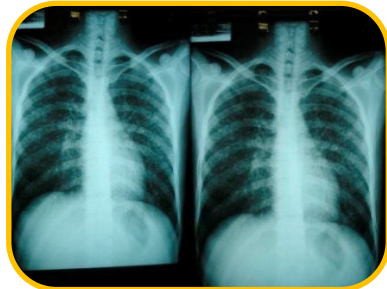
Spectrum of fungal diseases



Superficial



Subcutaneous



Invasive Fungal Disease

Typical patient with invasive fungal disease



When you think of emerging infections and outbreaks, you think of...

MRSA

Monkeypox

SARS-CoV2

Ebola

CRAB

Marburg

Cholera

... and not of fungus.



Cryphonectria parasitica



Pseudogymnoascus destructans



Batrachochytrium dendrobates



Batrachochytrium salamandrivorans



Magnaporthe oryzae



Puccinia graminis

Is this what's next?

*From a CDC fungal disease expert, here's what you need to know about **The Last of Us***

We may not need to worry about turning into zombies, but we do need to 'Think Fungal', the HBO show is right on that



Right fungus Wrong time

(Apologies to Dr. John)



Fusarium Keratitis among contact wearers



Outbreak of fungal keratitis 2005-2006

- Over 250 cases worldwide
- First cases in Hong Kong and Singapore, 2005



The image shows a screenshot of a news article from The New York Times. The page header includes a navigation menu with 'SECTIONS', 'HOME', and 'SEARCH', and the newspaper's name 'The New York Times'. The article is dated 'BUSINESS DAY' and is titled 'Lens Cleaner Is Recalled Worldwide' in a large, bold, italicized font. The author is identified as 'By BARNABY J. FEDER' and the date is 'MAY 16, 2006'. The main text of the article, which is a correction, states that Bausch & Lomb is halting worldwide sales of its ReNu With MoistureLoc cleaner for soft contact lenses due to a risk of blinding fungal infection.

SECTIONS HOME SEARCH The New York Times

BUSINESS DAY

Lens Cleaner Is Recalled Worldwide

By BARNABY J. FEDER MAY 16, 2006

Correction Appended

Bausch & Lomb said yesterday that it was halting worldwide sales of its ReNu With MoistureLoc cleaner for soft contact lenses because tests showed that its misuse could leave consumers at risk for a potentially blinding fungal infection.

Fusarium keratitis associated with contact lens solution



What was wrong with the lens solution??

- All sterility tests were negative
- Numerous unopened lots tested by multiple labs – no growth
- *Fusarium* growth from opened solutions obtained from patients' homes

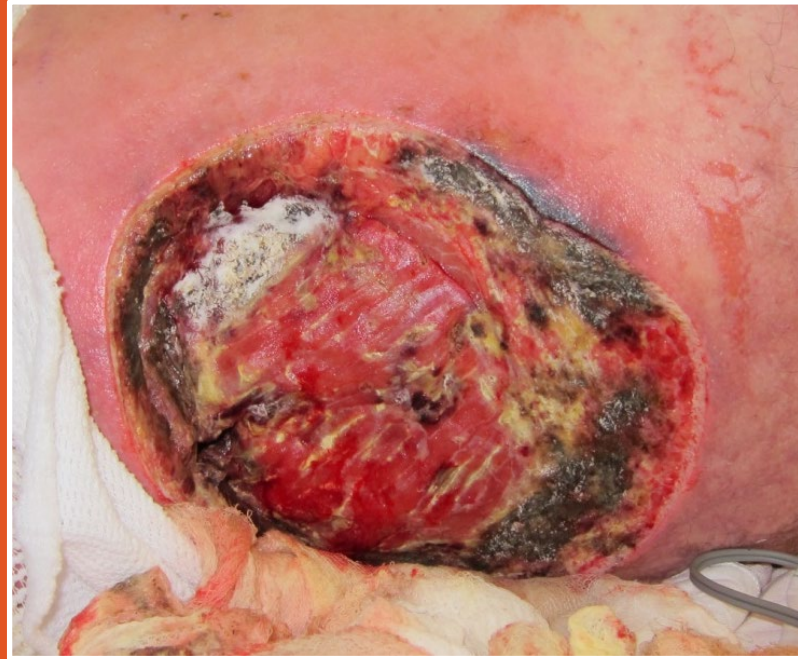
Lens Care Solution Is Faulted

By BARNABY J. FEDER AUG. 23, 2006



An outbreak of fungal infections linked to ReNu With MoistureLoc has raised some questions about the safety

Apophysomyces trapeziformis infections among
Joplin tornado victims



Tornado in Joplin, Missouri

- May 22, 2011
 - Category EF-5
 - Maximum wind speeds >200 mph
- Densely populated neighborhood, commercial district
- 1,000 persons injured, 160 deaths



Severe fungal soft tissue infections among Joplin tornado victims 13 cases – 5 deaths



Scalp wound with cutaneous
mucormycosis

*Apophysomyces
trapeziformis*



Saprophytic fungus in the
class Mucormycetes

Commonalities?

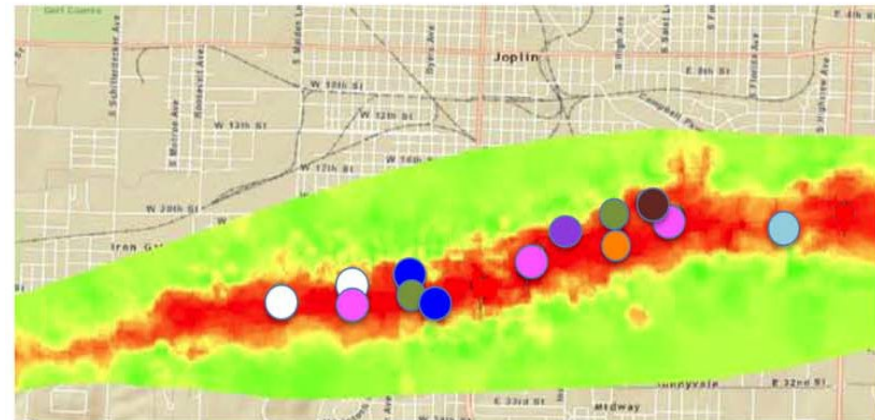
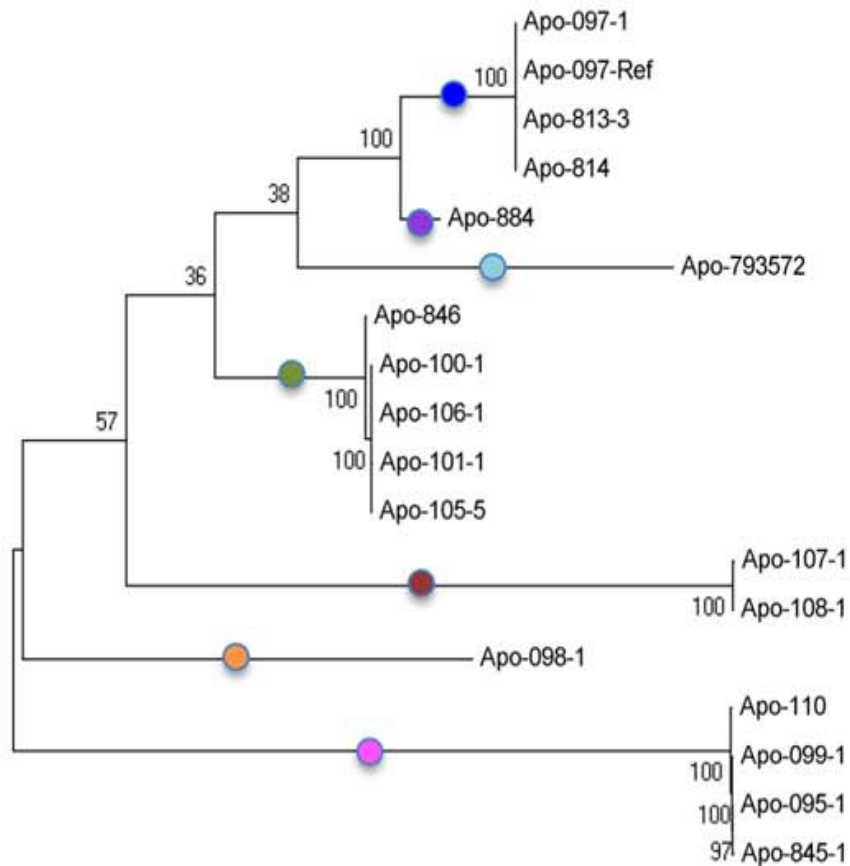
- Multiple puncture wounds and lacerations
 - Cases averaged 5 puncture wounds

- No common products
- No infections with other molds



Home of a case patient

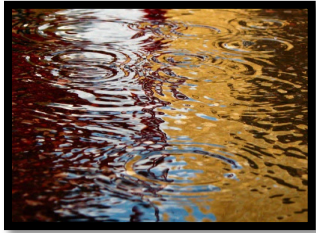
WGS revealed no “common source”



One Theory

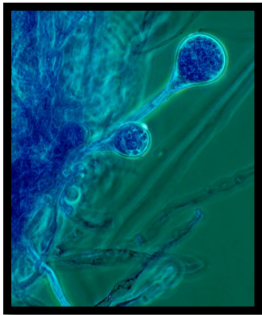


High rainfall in weeks prior to tornado



Pooling of water in natural reservoirs

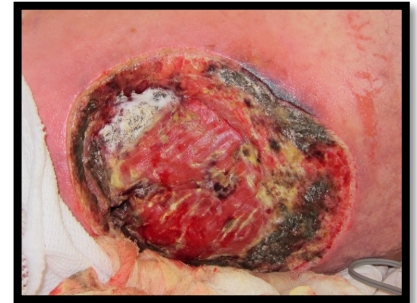
Pocket of spores



High winds of EF-5 tornado



A. trapeziformis infection



Fungal Meningitis following steroid injections



abc NEWS HOT TOPICS: Body in Towed Car • Magic Johnson Son • Mike Ric

Home U.S. World Politics Video Investigative Health Enter

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HOME > HEALTH

New Fungal Meningitis Cases and Spinal Infections Continue to Baffle Doctors

Shawn Lockhart looks at the meningitis-causing fungus *Exserohilum rostratum* at the mycotic lab at the Centers for Disease Control and Prevention in Atlanta. (Pouya Dianat/AP Photo)

The image shows a man in a white lab coat, identified as Shawn Lockhart, looking through a microscope. He is in a laboratory setting. In the background, a computer monitor displays a microscopic image of the same fungus shown in the left image. The ABC News logo and navigation menu are visible at the top of the page.

Fungal Meningitis following steroid injections

- Tennessee Department of Health (TNDOH) contacted CDC about a patient with culture-confirmed *Aspergillus* meningitis
 - Patient was immunocompetent (unusual for *Aspergillus* infection)
 - Received epidural steroid injection at Clinic A in TN on July 30, 2012



Initial Testing in Tennessee

- A couple patients grew *Exserohilum rostratum* from their CSF
- *Exserohilum rostratum* found in methylprednisolone acetate used for pain injections

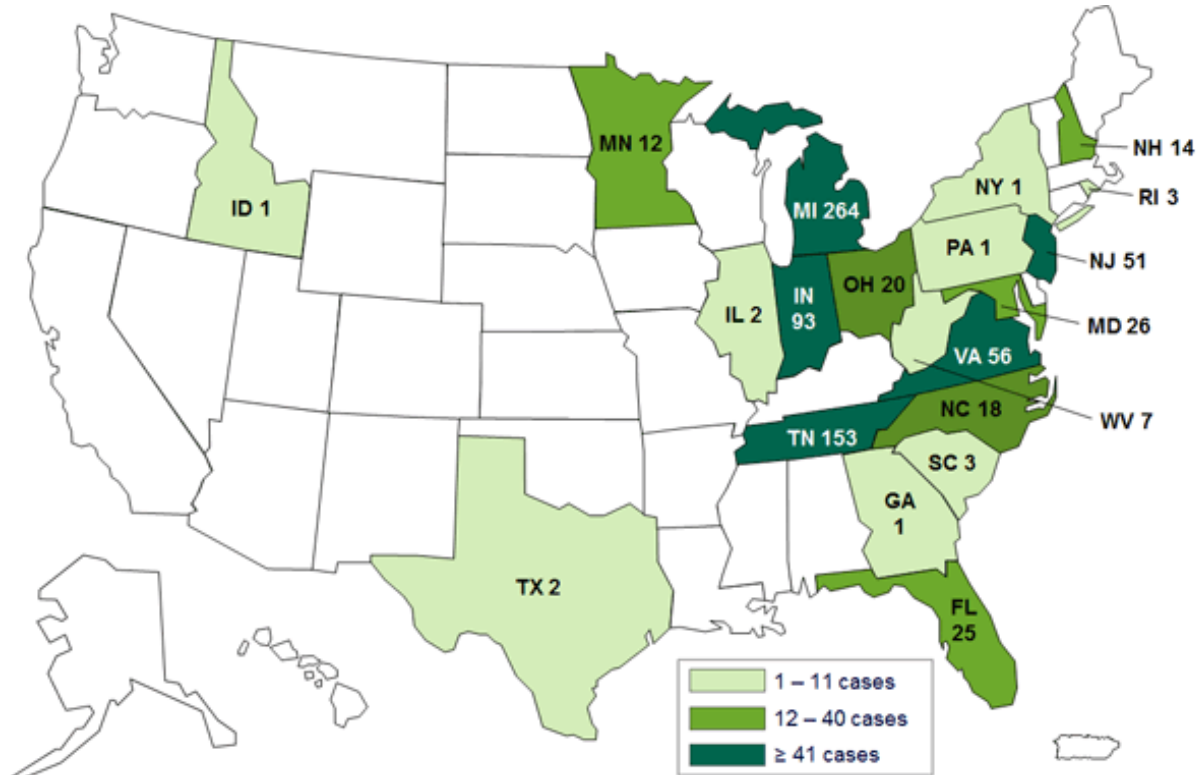


Exserohilum rostratum



Plant pathogen that causes leaf and root rot. Heat tolerant fungus that is an occasional pathogen of humans primarily causing non-invasive fungal sinusitis

Largest healthcare associated and deadliest fungal outbreak ever recorded



- Over 14,000 people exposed to tainted medication
- Equal number of vials recalled
- Case count:753
- States:20
- Deaths:65



Organisms recovered from unopened MPA

TABLE 5 Viable bacteria and fungi recovered from unopened MPA vials

Lot no.	Organisms
05212012@68	<i>Paecilomyces formosus</i> , <i>Exserohilum rostratum</i> ^a
06292012@26	<i>Exserohilum rostratum</i> , <i>Rhodotorula laryngis</i>
08102012@51	<i>Exserohilum rostratum</i> , <i>Cladosporium cladosporioides</i> , <i>Bacillus subtilis</i> , <i>Bacillus pumilus</i> , <i>Rhodotorula laryngis</i> , <i>Rhizopus stolonifer</i>

^a *E. rostratum* DNA was detected in one vial from this lot.

Severe irregularities in manufacturing practices



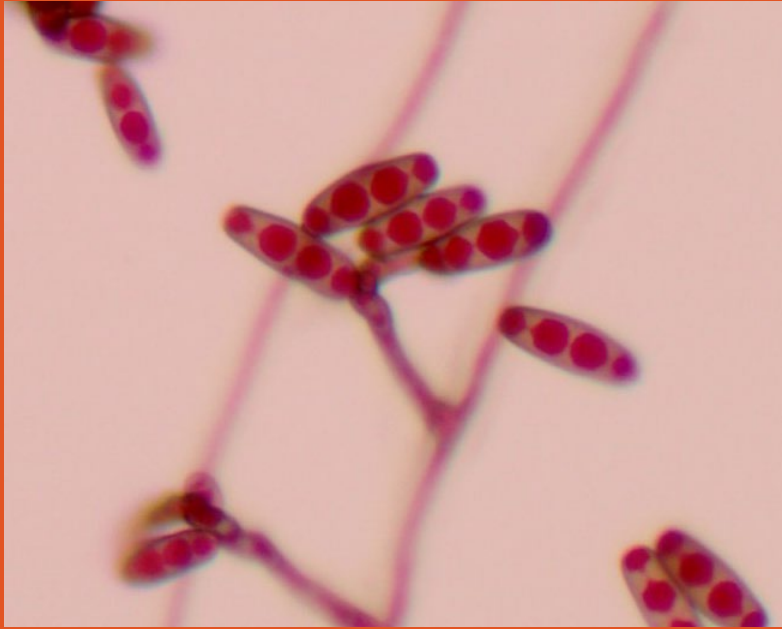
5 people convicted of federal charges in Framingham compounding pharmacy case

By [Travis Andersen](#) Globe Staff, December 13, 2018, 4:28 p.m.



19





Bipolaris surgical site infections

First notification...

- Texas Department of State Health Services called CDC
- Discuss 4 cases of *Bipolaris* surgical site infections (SSI) in cardiothoracic surgery (CT) patients at Hospital A
 - Thought to be related to construction
 - Hospital performed remediation in 2012

Bipolaris species



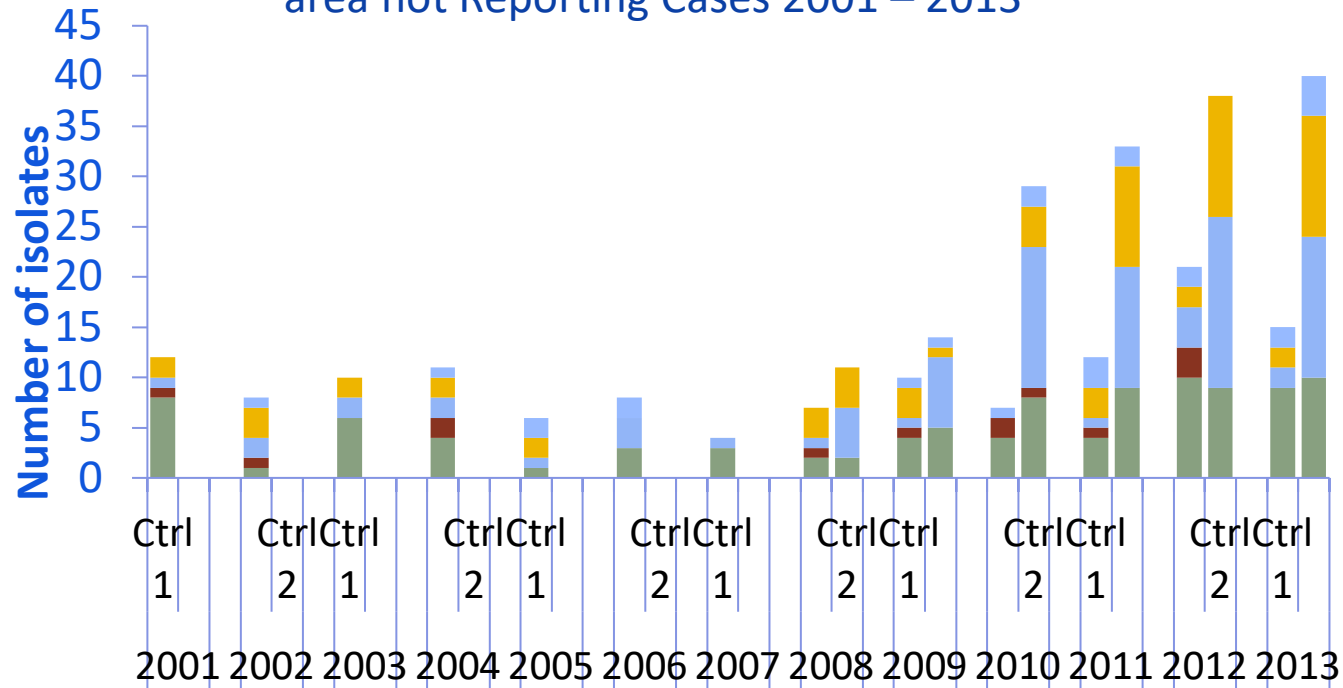
Plant pathogen common in soil. Heat tolerant fungus that is an occasional pathogen of humans primarily causing non-invasive fungal sinusitis

Within 1 year it jumped to...

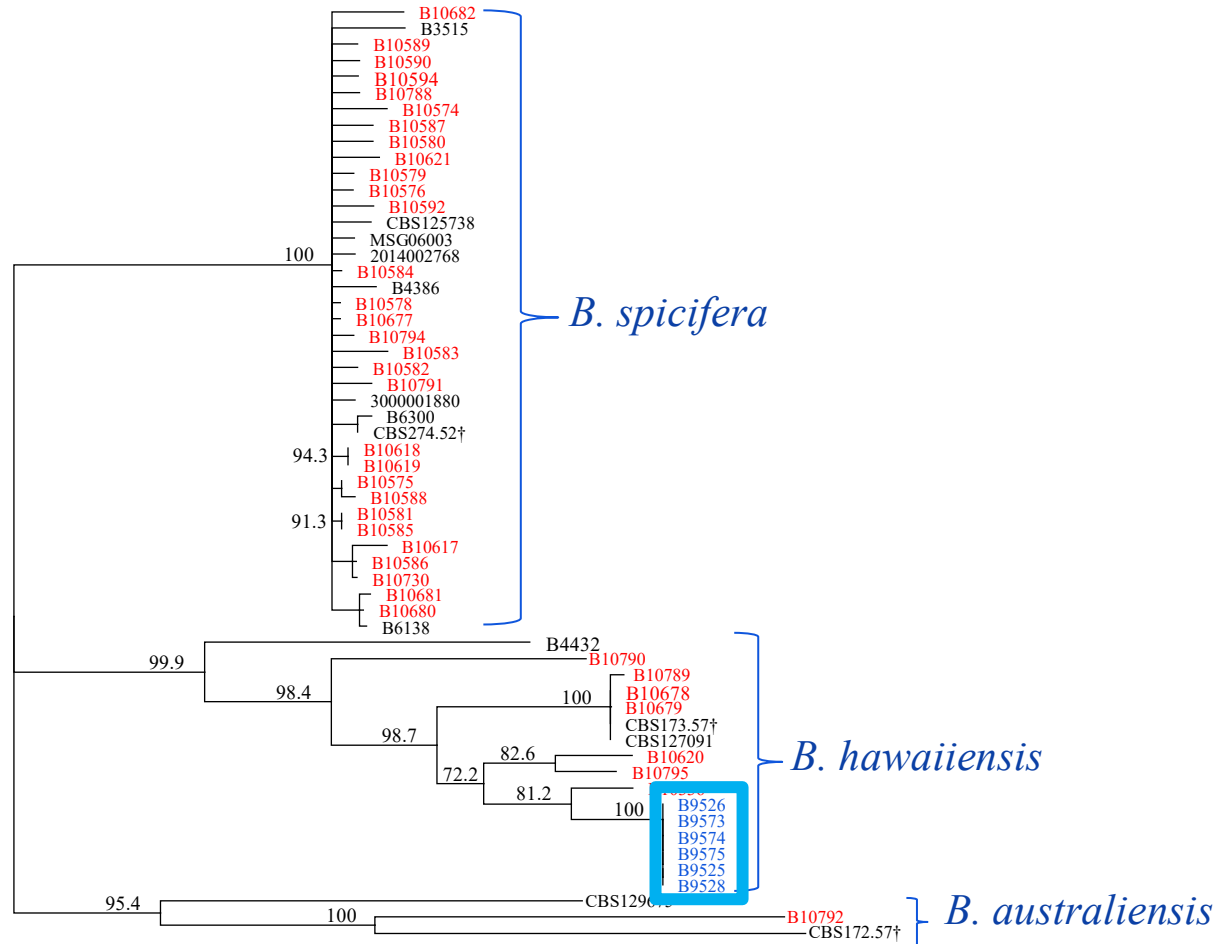
- 21 cases, 10 hospitals, 3 states
- All SSIs in cardiothoracic surgery patients
- No SSI with other molds in CT patients
- No *Bipolaris* infections seen in patients who underwent other types of surgery

Overall increase in *Bipolaris* cases in hospitals without case patients

All *Bipolaris* Isolates from Hospitals in the area not Reporting Cases 2001 – 2013



Phylogenetic tree of outbreak isolates based on MLST



What happened?

- Plant pathogen literature revealed that the southern US often had *Bipolaris* “blooms”
- Gel = growth media?

CAPA and CAM



RISE IN COVID CASES

COVID INDUCED BLACK FUNGUS



Blastomycosis in workers at a paper mill in Escanaba, Michigan



Cases linked to working at or visiting the paper mill since January, 2023

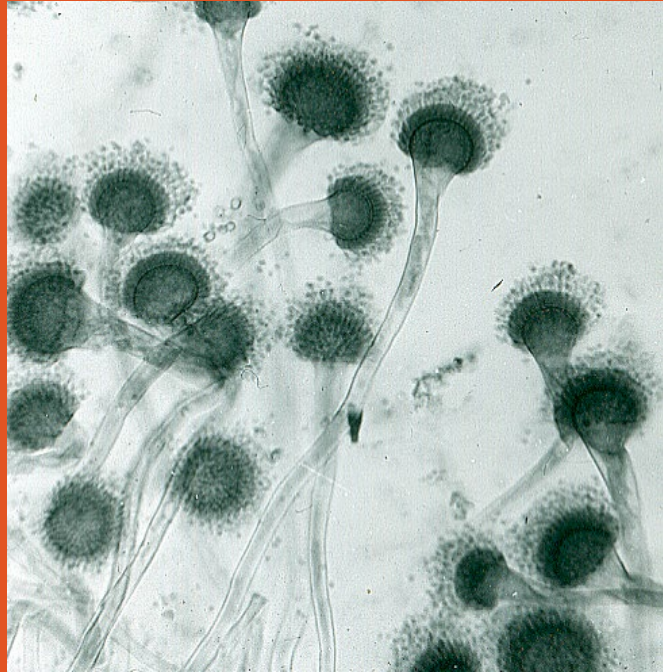
- One death, multiple hospitalizations
- No risk factors determined
- No source determined



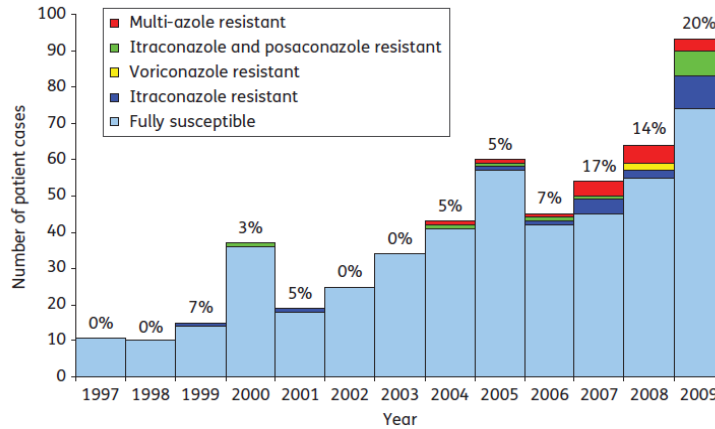
But that's not what keeps
me up at night...



Azole resistant *Aspergillus fumigatus*



Triazole resistance in *A. fumigatus* is rising



Prevalence of aspergillosis at a center in UK.

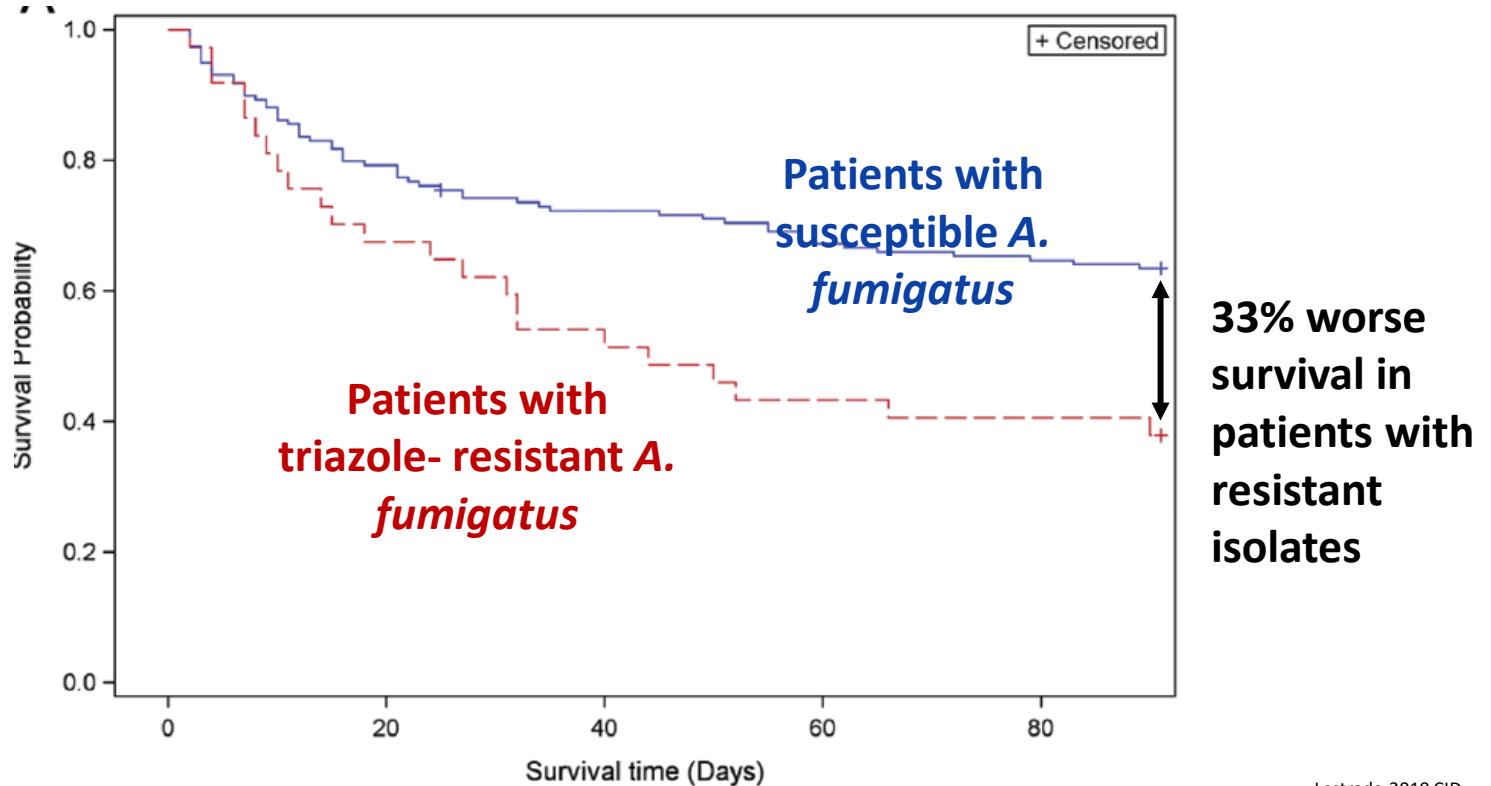
—Bueid et al. 2010



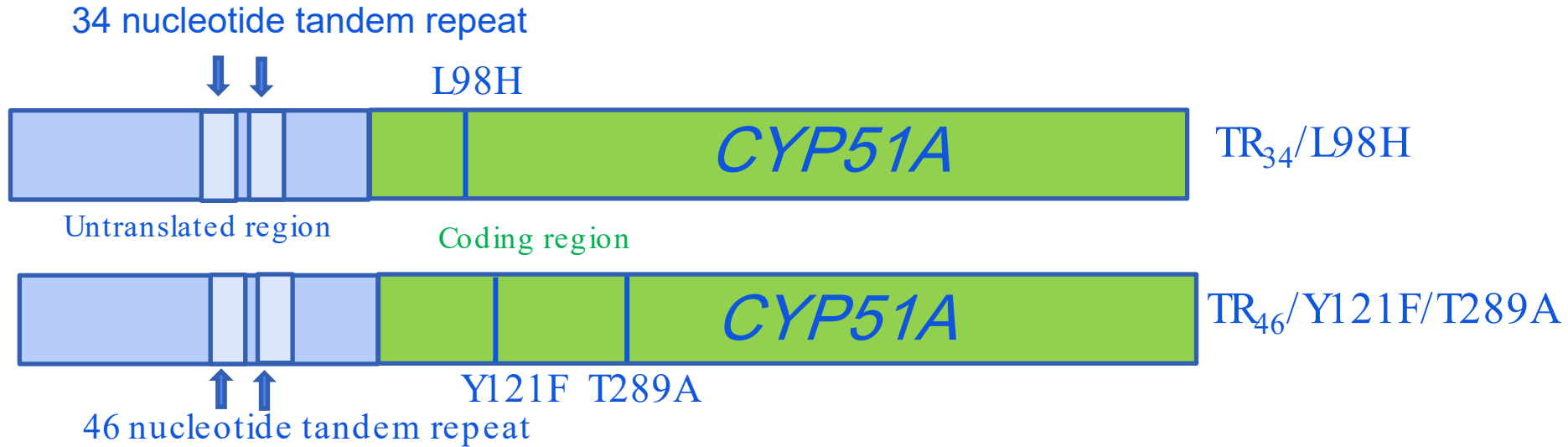
Prevalence of Triazole Resistance at a center in UK and the Netherlands.

—Verweij et al. 2009

Emerging triazole resistance is deadly



Primary mechanism of resistance



TR₃₄ and TR₄₆

How *Aspergillus* becomes resistant

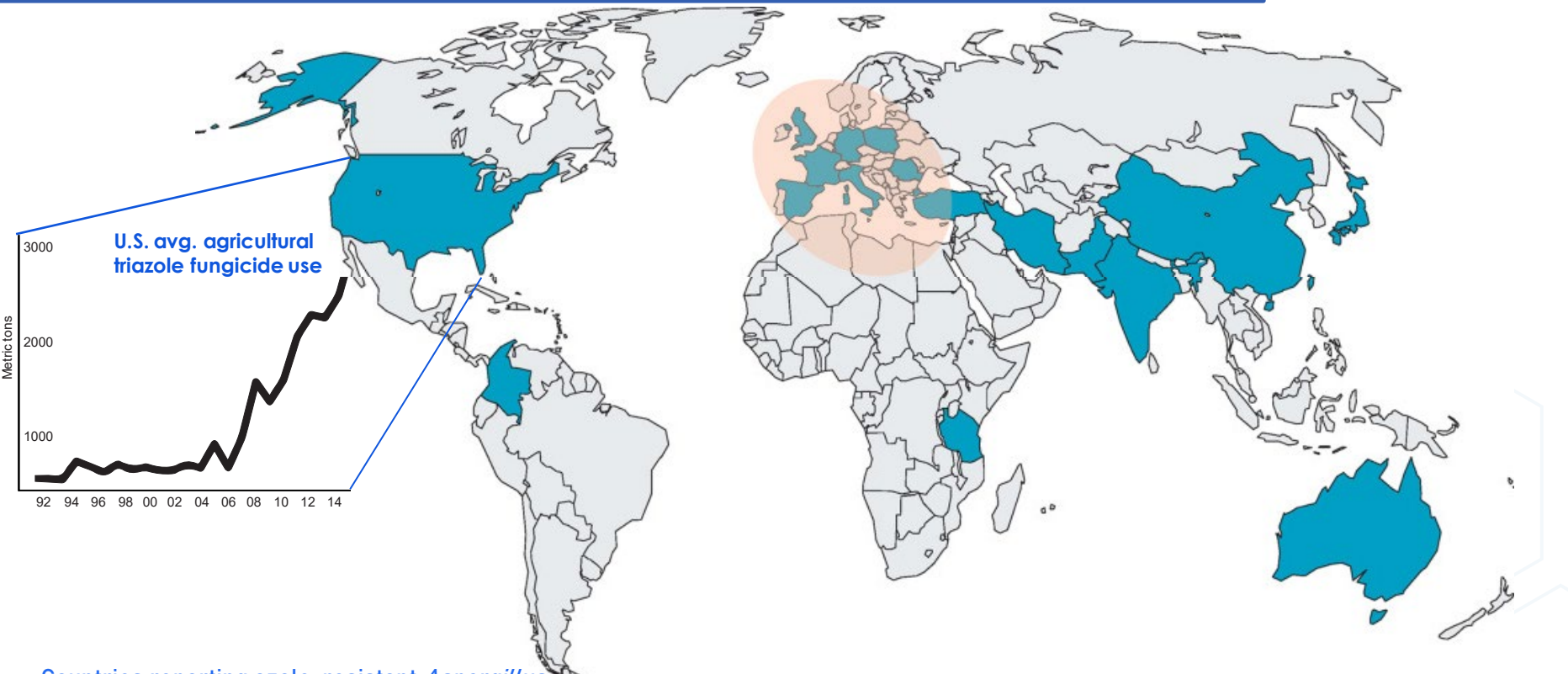
In a Patient



In the Environment

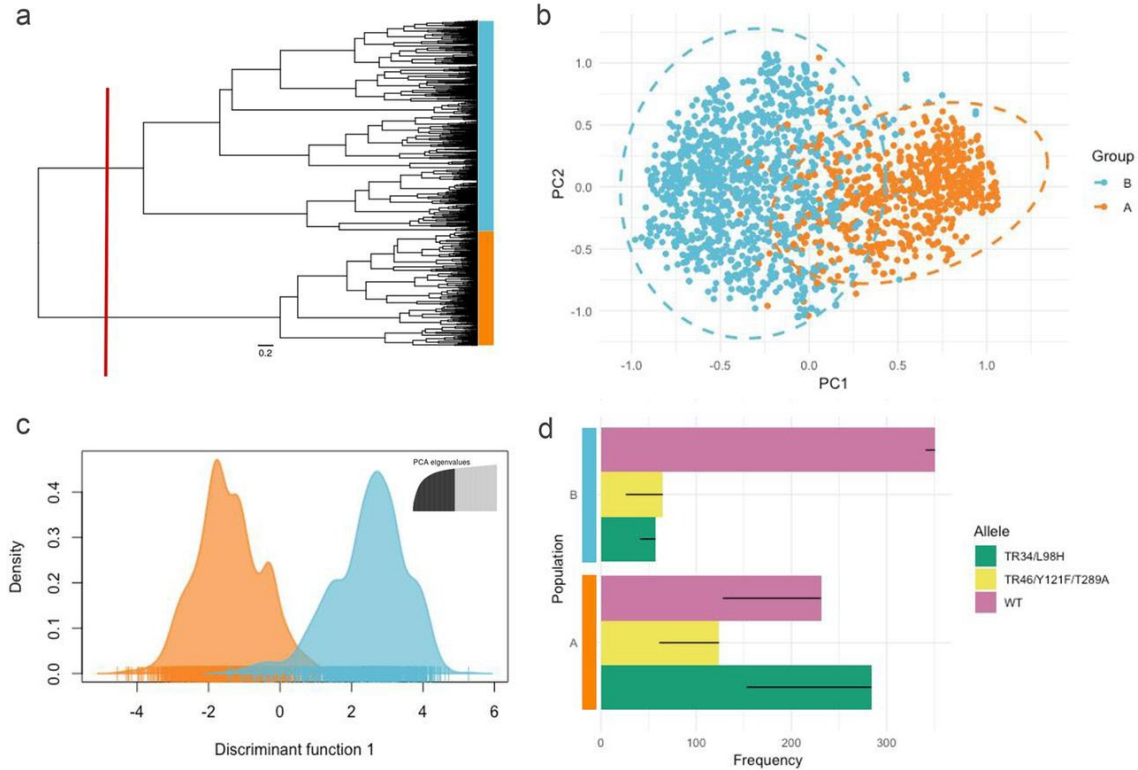


Azole-resistant *A. fumigatus* linked to fungicide use is a global One Health AMR threat



Countries reporting azole-resistant *Aspergillus fumigatus* with TR₃₄/L98H or TR₄₆/Y121F/T289A modifications as of 2017

Non-random distribution of Azole^R *A. fumigatus*



Little surveillance for cases in the US

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

Search

EMERGING INFECTIOUS DISEASES®

EID Journal > Volume 28 > Number 9—September 2022 > Main Article

Volume 28, Number 9—September 2022

Research Letter

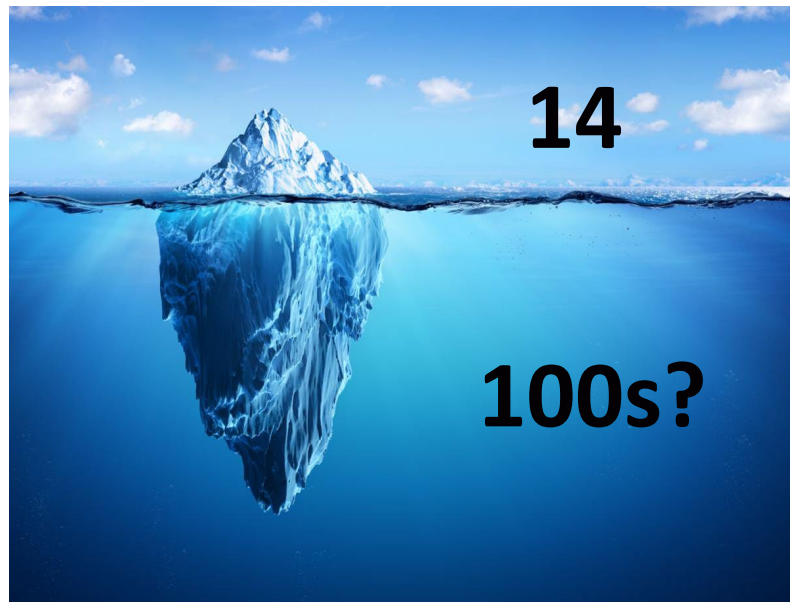
Fatal Fungicide-Associated Triazole-Resistant *Aspergillus fumigatus* Infection, Pennsylvania, USA

Kennedy Bradley¹, Audrey Le-Mahajan¹, Beth Morris, Tiina Peritz, Tom Chiller, Kaitlin Forsberg, Natalie S. Nunnally, Shawn R. Lockhart, Jeremy A.W. Gold², and Jane M. Gould²

On This Page

CDC's 2019 Watch List

- Infrequently found in the United States or not well understood
- CDC and public health experts are closely monitoring



Emergence of *Trichophyton indotineae*



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



Morbidity and Mortality Weekly Report (*MMWR*)

Notes from the Field: First Reported U.S. Cases of Tinea Caused by *Trichophyton indotineae* — New York City, December 2021–March 2023

Weekly / May 12, 2023 / 72(19);536–537

[Print](#)

Avrom S. Caplan, MD¹; Sudha Chaturvedi, PhD²; YanChun Zhu, MS²; Gabrielle C. Todd, PhD²; Lu Yin, MD¹; Adriana Lopez, MD¹; Lisa Travis, MD¹; Dallas J. Smith, PharmD^{3,4}; Tom Chiller, MD³; Shawn R. Lockhart, PhD³; Karen A. Alroy, DVM⁵; William G. Greendyke, MD⁵; Jeremy A. W. Gold, MD³ ([VIEW AUTHOR AFFILIATIONS](#))

Typical dermatophytosis



Concise Communication

Terbinafine-resistant strain of *Trichophyton interdigitale* strain isolated from a tinea pedis patient

Junichiro Hiruma, Hiroyuki Kitagawa, Hiromitsu Noguchi, Rui Kano ✉, Masataro Hiruma, Hiroshi Kamata, Kazutoshi Harada

First published: 15 February 2019 | <https://doi.org/10.1111/1346-8138.14809> | Citations: 28

Case Reports | J Dermatol. 2020 May;47(5):e192-e193. doi: 10.1111/1346-8138.15300.

Epub 2020 Mar 10.

Caution and warning: Arrival of terbinafine-resistant *Trichophyton interdigitale* of the Indian genotype, isolated from extensive dermatophytosis, in Japan

Utako Kimura ^{1,2}, Masataro Hiruma ², Rui Kano ³, Tadahiko Matsumoto ^{2,4}, Hiromitsu Noguchi ^{2,4}, Kenji Takamori ¹, Yasushi Suga ¹



Journal de Mycologie Médicale
Volume 29, Issue 4, December 2019, Pages 352-355



Case report

A new mutation in the SQLE gene of *Trichophyton mentagrophytes* associated to terbinafine resistance in a couple with disseminated tinea corporis

A. Hsieh ^a, S. Quenan ^a, A. Riat ^b, L. Toutous-Trellu ^a, L. Fontao ^{a, b} ✉

Emergence of Terbinafine Resistant *Trichophyton mentagrophytes* in Iran, Harboring Mutations in the Squalene Epoxidase (SQLE) Gene

Simin Taghipour, Forough Shamsizadeh, [...], and

Mahdi Abastabar

> *Fungal Genet Biol.* 2019 Dec;133:103266. doi: 10.1016/j.fgb.2019.103266. Epub 2019 Sep 3.

A unique multidrug-resistant clonal *Trichophyton mentagrophytes*/*Trichophyton interdigitale* complex causing an ongoing alarming dermatophytosis outbreak in India: Genomic insights and resistance profile

Ashutosh Singh ¹, Aradhana Masih ¹, Juan Monroy-Nieto ², Pradeep Kumar Singh ¹, Jolene Bowers ², Jason Travis ², Ananta Khurana ³, David M Engelthaler ², Jacques F Meis ⁴, Anuradha Chowdhary ⁵

Infection (2020) 48:889–897

<https://doi.org/10.1007/s15010-020-01498-1>

ORIGINAL PAPER



Intrinsic resistance to terbinafine among human and animal isolates of *Trichophyton mentagrophytes* related to amino acid substitution in the squalene epoxidase

Dominik Łagowski ¹ ✉ · Sebastian Gnat ¹ ✉ · Aneta Nowakiewicz ¹ ✉ · Marcelina Osieńska ¹ ✉ · Mariusz Dyląg ² ✉

Molecular Epidemiology and Antifungal Susceptibility of *Trichophyton* Isolates in Greece: Emergence of Terbinafine-Resistant *Trichophyton mentagrophytes* Type VIII Locally and Globally

by Maria Siopi ¹ ✉ ✉, Ioanna Efsthathiou ¹ ✉, Konstantinos Theodoropoulos ² ✉ ✉, Spyros Pournaras ¹ ✉ and Joseph Meletiadis ^{1,*} ✉ ✉



> [Mycopathologia](#). 2020 Dec;185(6):947-958. doi: 10.1007/s11046-020-00455-8. Epub 2020 May 24.

Trichophyton indotineae sp. nov.: A New Highly Terbinafine-Resistant Anthropophilic Dermatophyte Species

Rui Kano ¹, Utako Kimura ², Maki Kakurai ³, Junichiro Hiruma ⁴, Hiroshi Kamata ⁵, Yasushi Suga ², Kazutoshi Harada ⁴

Affiliations [+](#) expand

PMID: 32449054 DOI: [10.1007/s11046-020-00455-8](#)


Steroid-modified Dermatophytosis

- Concerns regarding steroid-modified tinea with improper drug usage
- Common to obtain over-the-counter medications
- Atypical presentation



Trichophyton indotineae surveillance

- As for most fungal infections there is no surveillance for dermatophytosis
- Very few labs identify dermatophytes to species almost none perform AFST
- First signs will be severe infections and patients failing therapy



STARRING

Candida auris



Urgent Threats

These germs are public health threats that require urgent and aggressive action:



CARBAPENEM-RESISTANT
ACINETOBACTER



CANDIDA AURIS



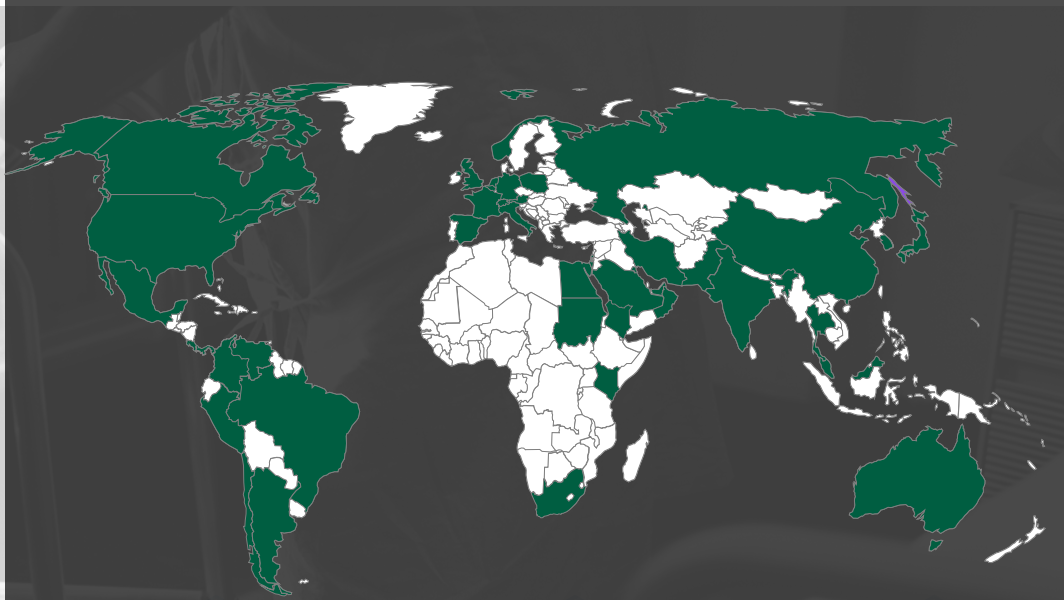
CLOSTRIDIoidES DIFFICILE



CARBAPENEM-RESISTANT
ENTEROBACTERIACEAE



DRUG-RESISTANT
NEISSERIA GONORRHOEAE

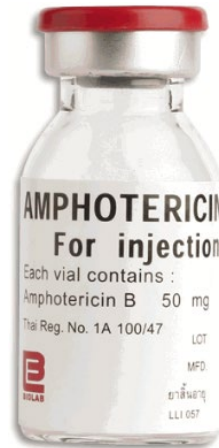


- Emerged suddenly
- Reported in >40 countries
- Highly transmissible healthcare-associated infection
- Highly resistant to antifungal drugs
- Increasing rates of pan-resistance

Resistance in *Candida auris*



85%
Azoles



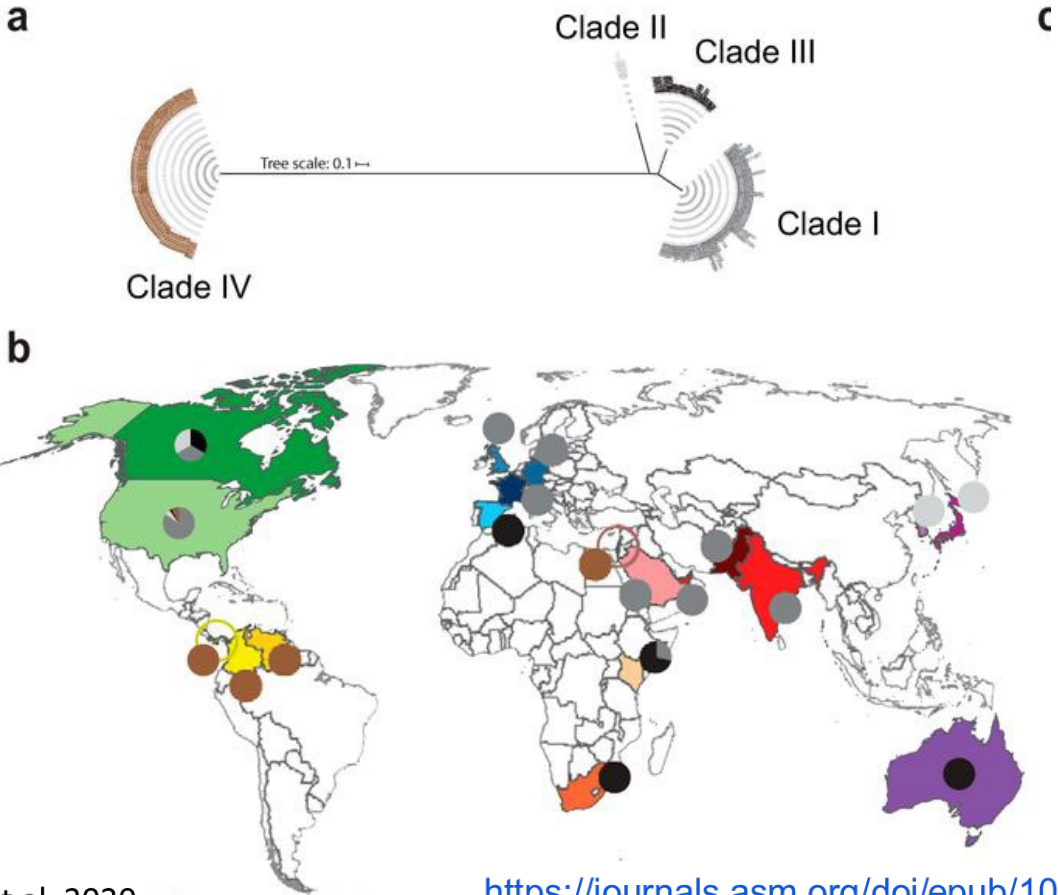
31%
Polyenes



4%
Echinocandins

~30% are multidrug resistant

Phylogenetic analysis of 304 isolates from 19 countries



C. auris cases reported per year – 2016 to 2021

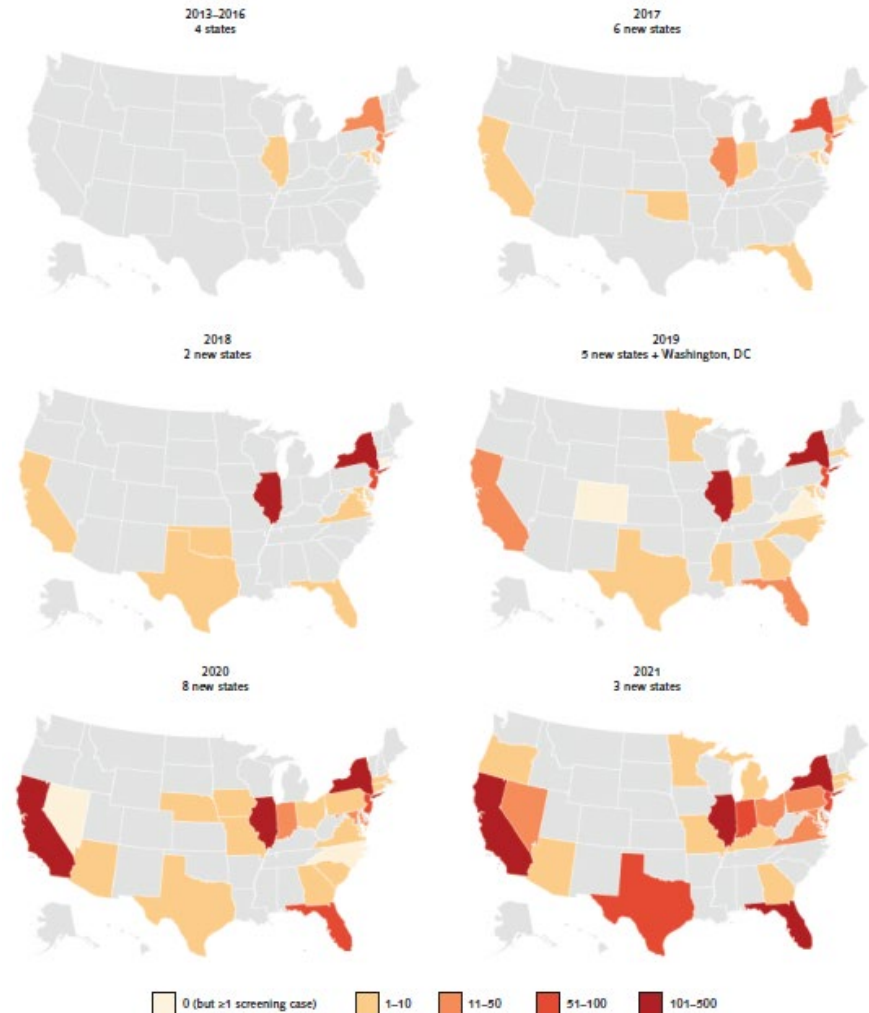
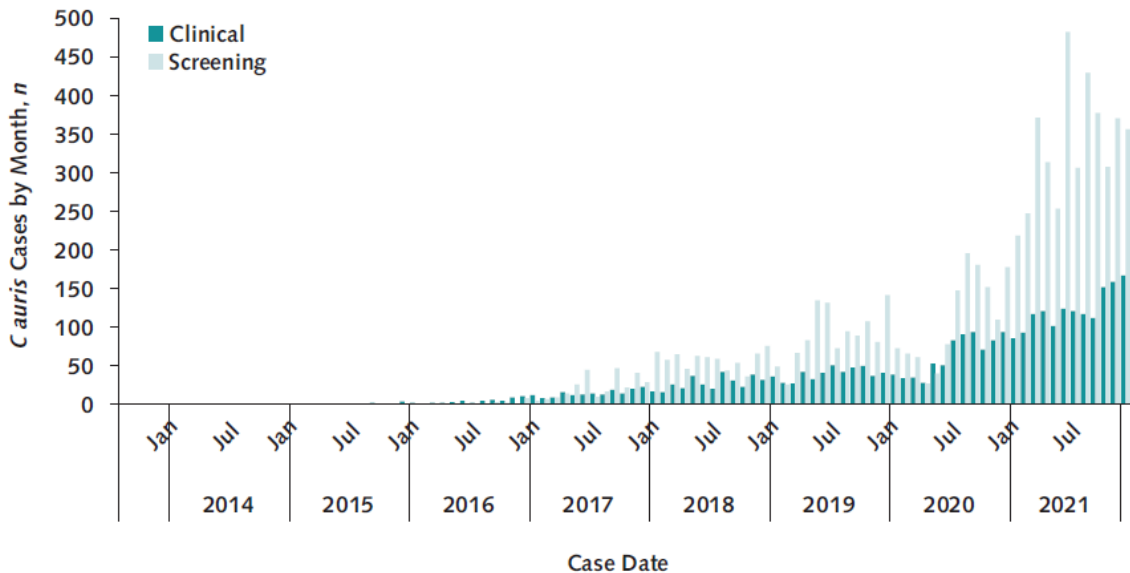


Figure 1. Number of clinical and screening *C auris* cases reported to the Centers for Disease Control and Prevention during 2013 to 2021.



NEWS

HEALTH & MEDICINE

A deadly fungus behind hospital outbreaks was found in nature for the first time

The discovery could spur search expeditions for the yeast in more places



***Candida auris* Discovery through Community Wastewater Surveillance during Healthcare Outbreak, Nevada, USA, 2022**



Alessandro Rossi, Jorge Chavez, Thomas Iverson, John Hergert,
Kelly Oakeson, Nathan LaCross, Chidinma Njoku, Andrew Gorzalski, Daniel Gerrity



PERSPECTIVE



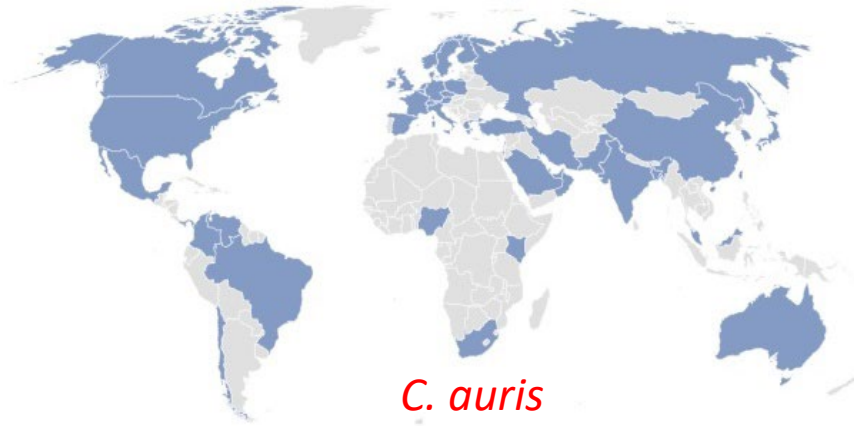
Role of Microbiota in the Skin Colonization of *Candida auris*

Brooke Tharp,^a Rachel Zheng,^a Garrett Bryak,^a  Anastasia P. Litvintseva,^b Mary K. Hayden,^c Anuradha Chowdhary,^{d,e}
 Shankar Thangamani^{a,f}

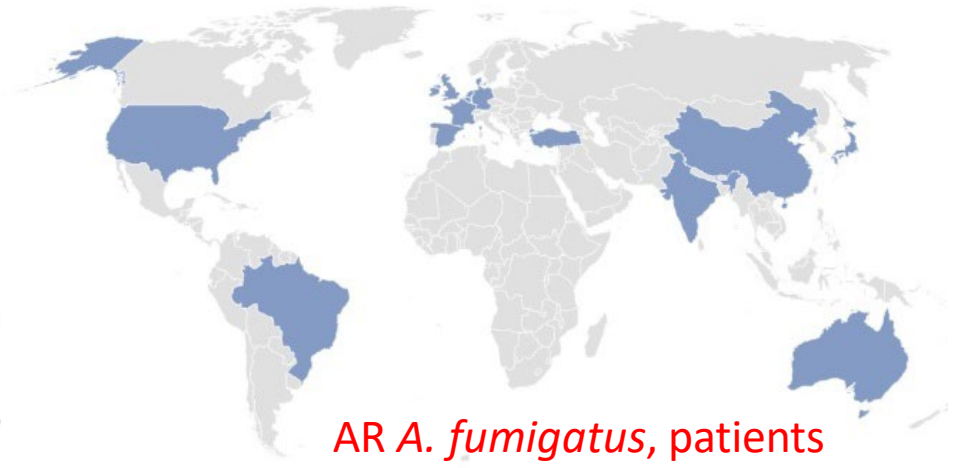
Two most basal clades only found in ears so far



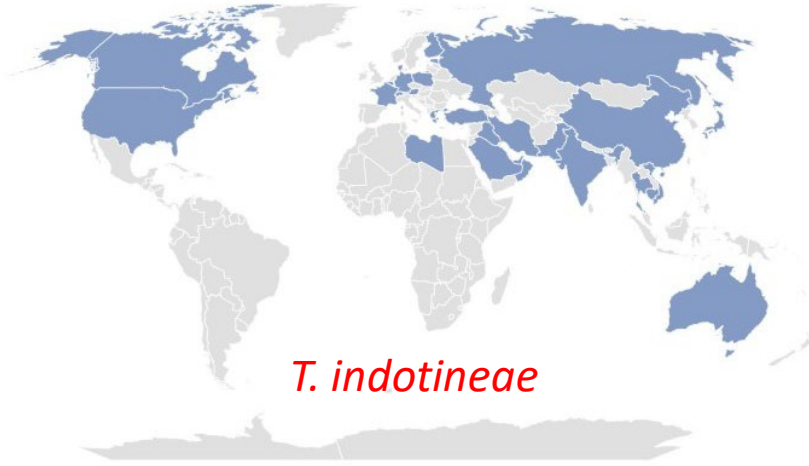
What ties azole-resistant *A. fumigatus*, *T. indotineae*, and *C. auris* together and makes them unique?



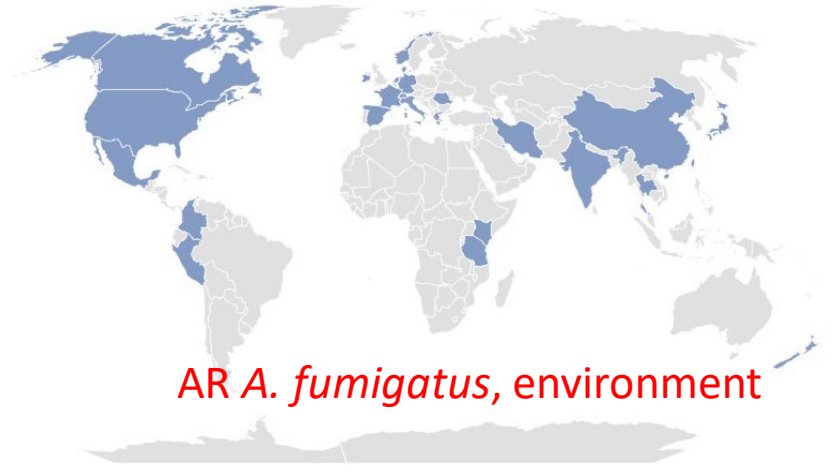
C. auris



AR *A. fumigatus*, patients

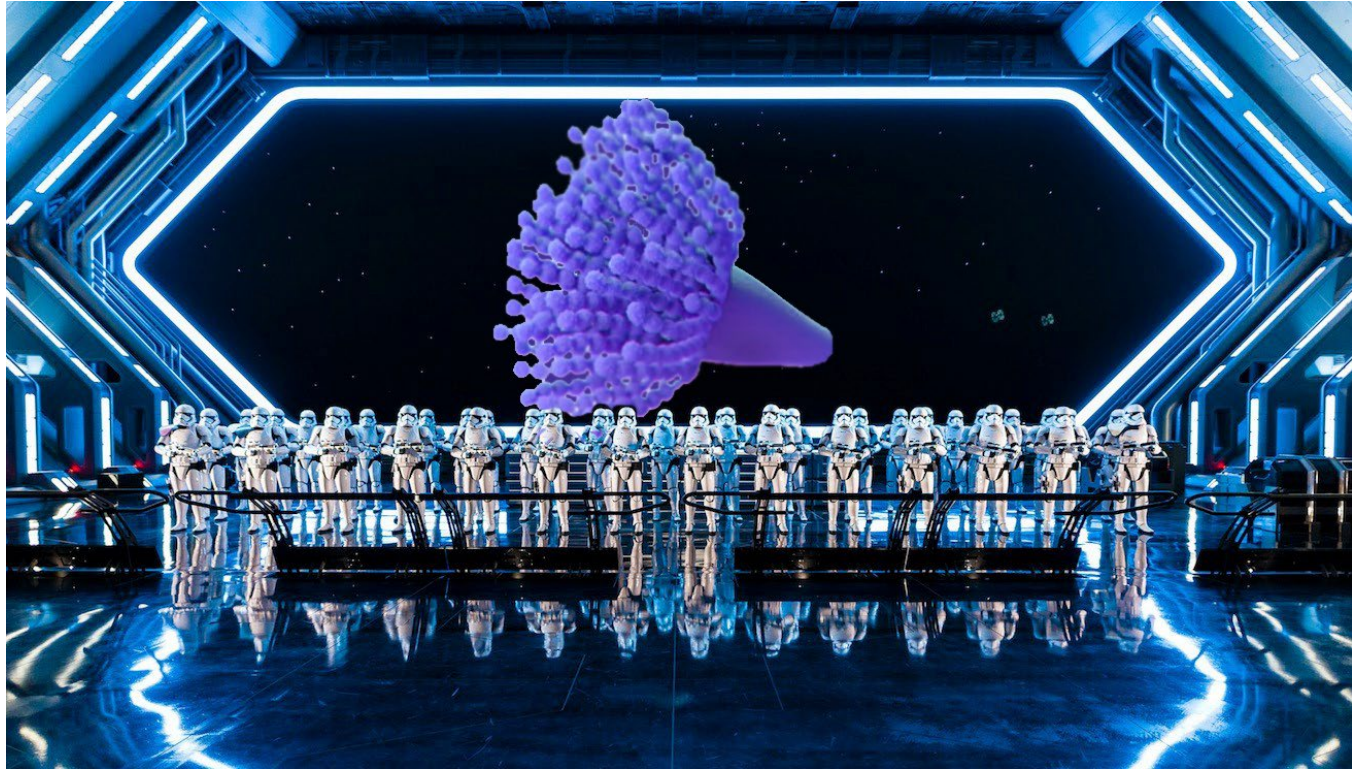


T. indotineae



AR *A. fumigatus*, environment

The Rise of the Resistance



Thank you! Questions?



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

Contact me at:
gyi2@cdc.gov

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.

