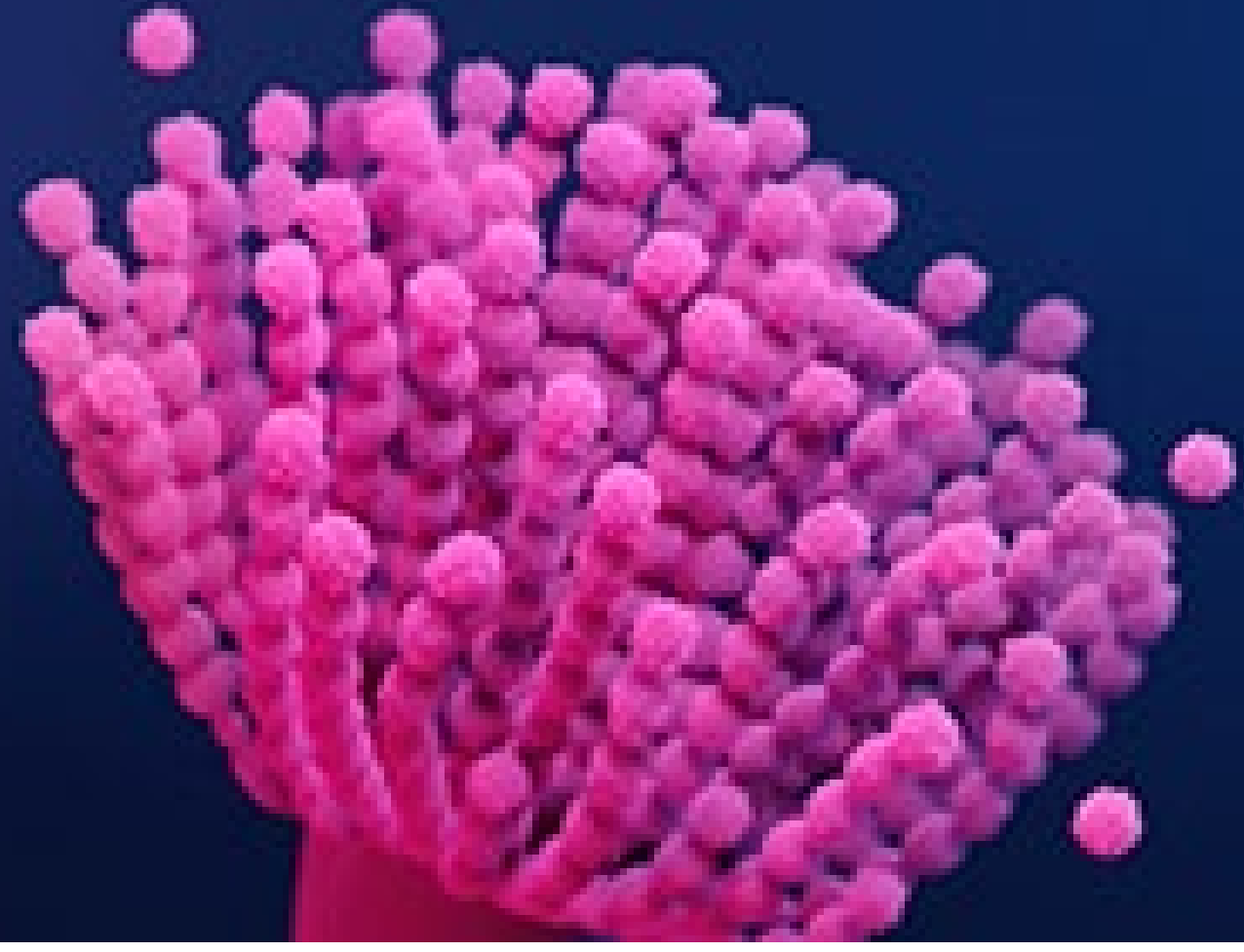
Centers for Disease Control and Prevention

Diagnostics, resistance testing, and surveillance capabilities in local and national levels: health care systems and agricultural systems



Shawn Lockhart PhD, D(ABMM) FAAM

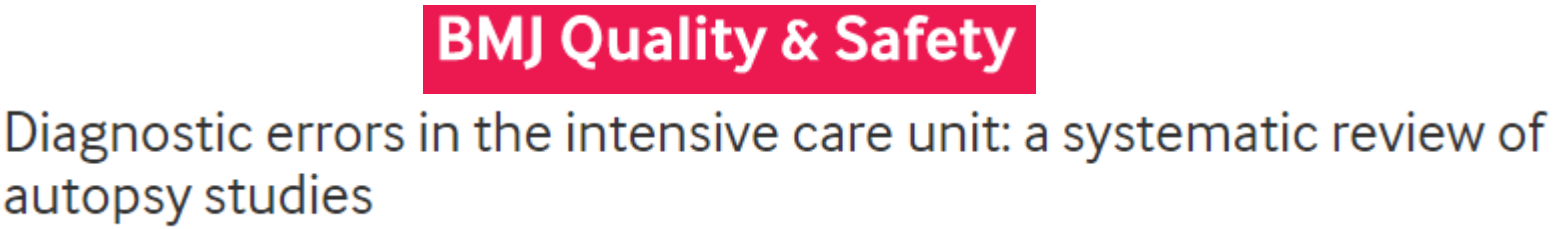
Senior Clinical Laboratory Advisor

Senior Advisor for AMR

Mycotic Diseases Branch

Centers for Disease Control and Prevention

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



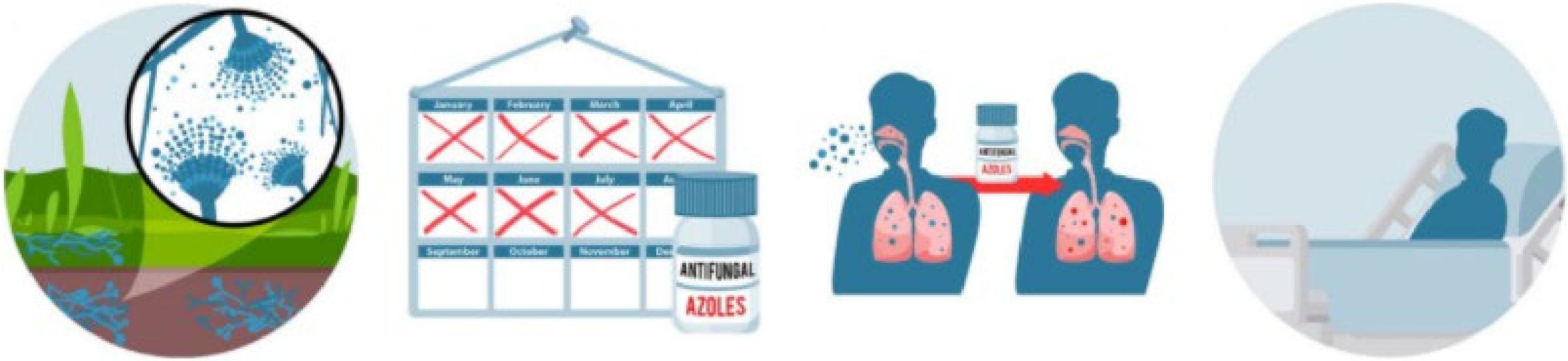
- **8%** of autopsied ICU deaths involved a **potentially lethal missed diagnosis**
- Most common: “pulmonary embolism, myocardial infarction, pneumonia, **and aspergillosis**”

Winters B. BMJ Qual & Safety. 2012.

Key needs:

- Better diagnostics for fungal infections in general and *Aspergillus* infections specifically
  - Point of care test
  - Affordable tests for resource-limited settings

Since mold-active azole use began in 1990s, resistance was periodically observed in patients on long-term therapy; rarely for patients with severe acute illness (they usually died or recovered)



- Many different mutations
- Rarely transmissible

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

Compared with Europe, where up to 20% of cases are resistant in some hospitals, small number of US cases detected to date

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

Search

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

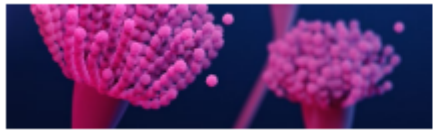
Multidrug-Resistant *Aspergillus fumigatus* Carrying Mutations Linked to Environmental Fungicide Exposure — Three States, 2010–2017

Weekly / September 28, 2018 / 67(38);1064–1067

ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES

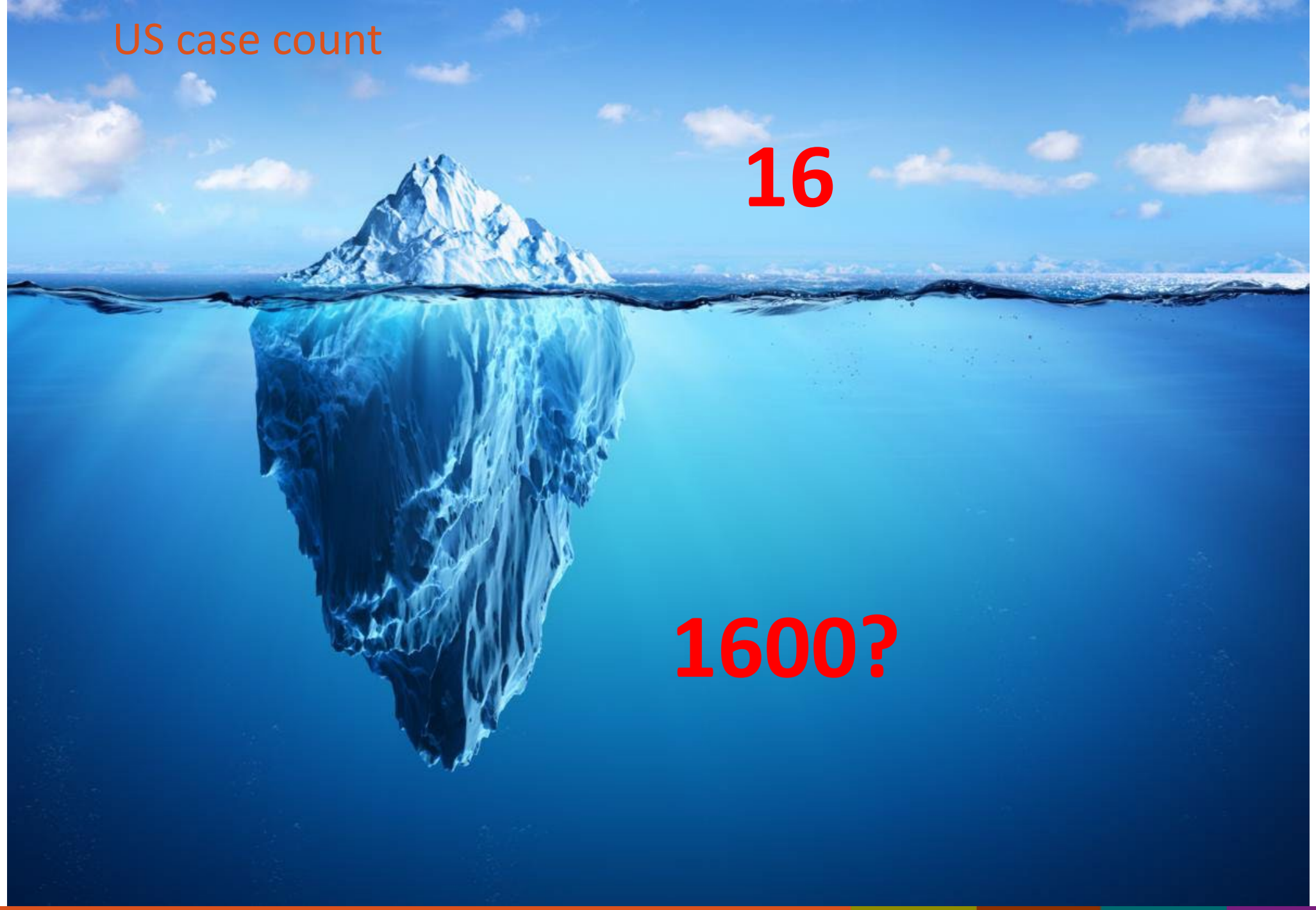
2019

Watch List



AZOLE-RESISTANT
ASPERGILLUS FUMIGATUS

Misconception: Few US cases identified = not a problem here?


US case count
16
1600?

CAP proficiency for AFST

1. Test methods:	-
Broth macrodilution	18
Broth microdilution	9
Disk Diffusion	199
YeastOne colorimetric microdilution	38
Gradient diffusion strips (eg, Etest, MTS)	165
Vitek 2	8
Other	

~400 participants

Total number of commercial products for mold susceptibility testing in the US:

1) Gradient diffusion
2).
3).
4).

Mold-active antifungals

- Azoles
- Polyenes
- DHODH inhibitor, GPI-anchored protein inhibitor, tetrazoles

Key need:

- Increased capacity for antifungal susceptibility testing

Contents lists available at ScienceDirect

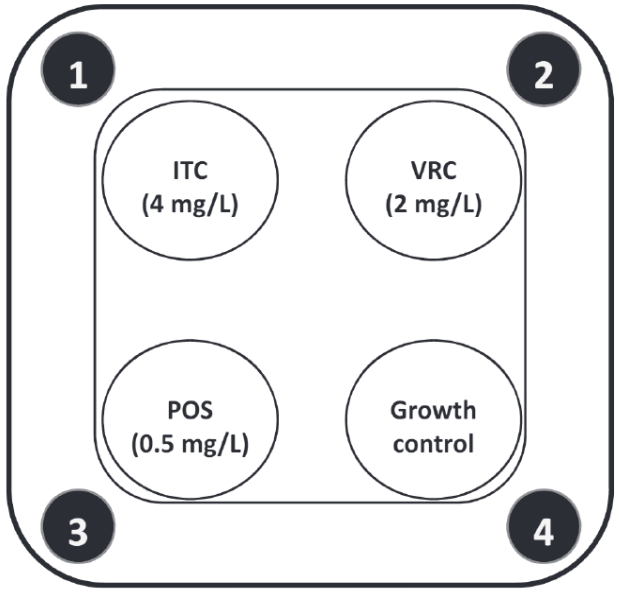
Clinical Microbiology and Infection

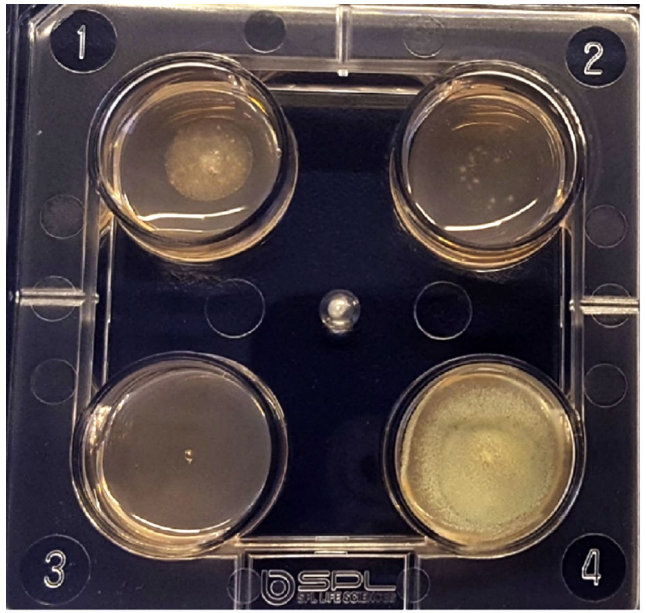
journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

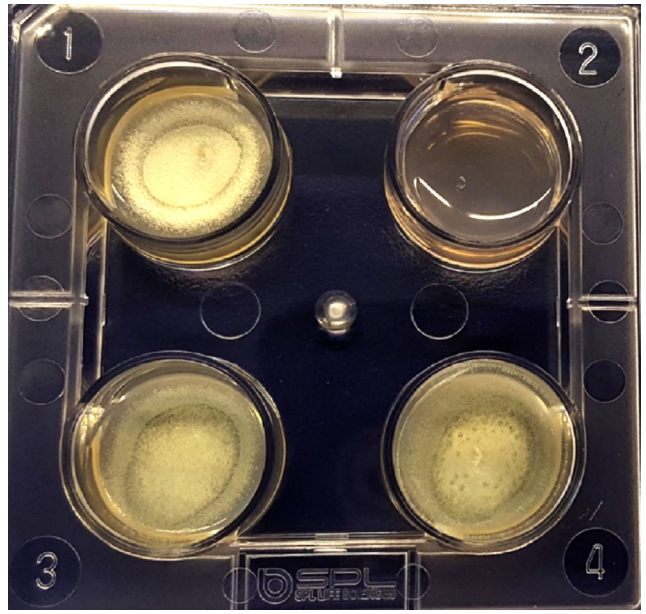
How to: EUCAST recommendations on the screening procedure E.Def 10.1 for the detection of azole resistance in *Aspergillus fumigatus* isolates using four-well azole-containing agar plates

J. Guinea [1,2], P.E. Verweij [3,†], J. Meletiadis [4,5], J.W. Mouton [3,5], F. Barchiesi [6], M.C. Arendrup [7,8,9,*] on behalf of Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)[‡]





Negative control



TR_{34}/L98H

Key need:

- Surveillance for antifungal resistance in molds; better grasp of the extent of the problem

J Antimicrob Chemother 2017; **72**: 2443–2446
doi:10.1093/jac/dkx168 Advance Access publication 1 June 2017

Journal of Antimicrobial Chemotherapy

Isolation of azole-resistant *Aspergillus fumigatus* from the environment in the south-eastern USA

Steven F. Hurst[1], Elizabeth L. Berkow[1], Katherine L. Stevenson[2], Anastasia P. Litvintseva[1] and Shawn R. Lockhart[1]*

OXFORD

G3 Genes | Genomes | Genetics

G3, 2022, **12(2)**, jkab427
https://doi.org/10.1093/g3journal/jkab427
Advance Access Publication Date: 13 December 2021
Fungal Genetics and Genomics

Evidence for the agricultural origin of resistance to multiple antimicrobials in *Aspergillus fumigatus*, a fungal pathogen of humans

S. Earl Kang,[1,†] Leilani G. Sumabat,[2,‡] Tina Melie,[2,§] Brandon Mangum,[1,2] Michelle Momany ,[1,*] and Marin T. Brewer[2,*]

Key need:

- Environmental surveillance, in close collaboration with agricultural groups

New finding: azole-resistant strains, including from humans, are resistant to other fungicide classes

New Results

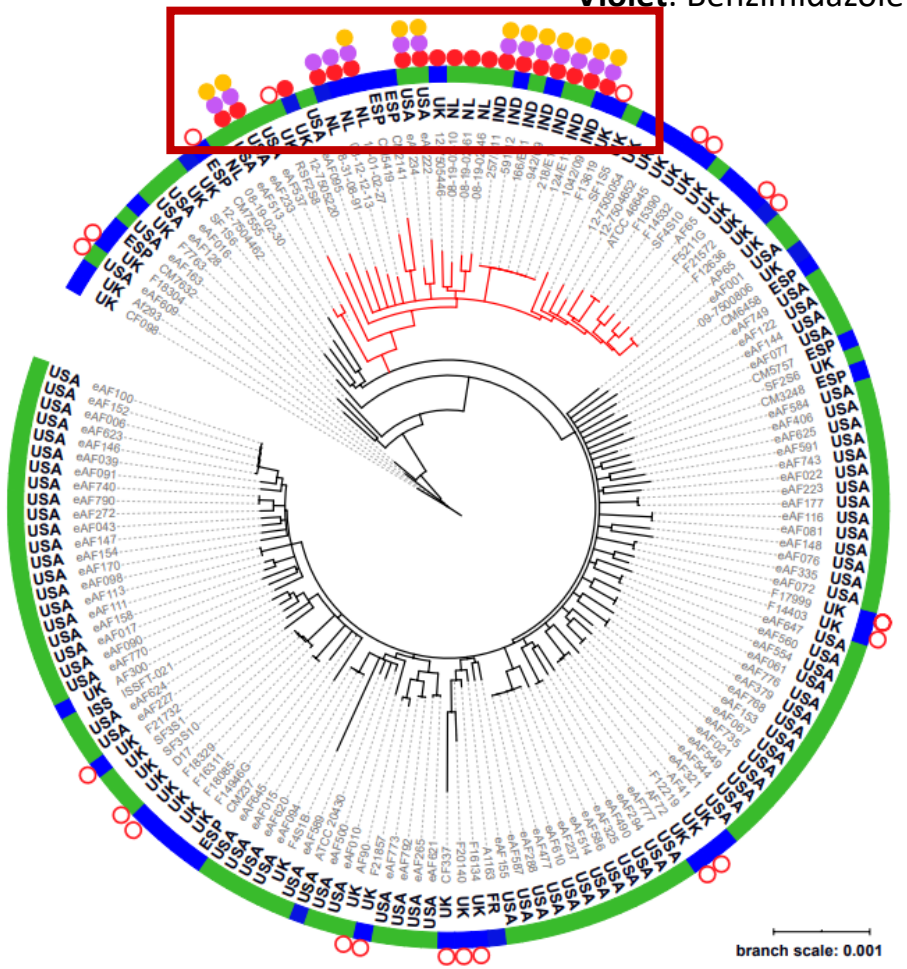
Evidence for the agricultural origin of antimicrobial resistance in a fungal pathogen of humans

S. Earl Kang, Leilani G. Sumabat, Tina Melie, Brandon Mangum, Michelle Momany, Marin T. Brewer

doi: https://doi.org/10.1101/2020.05.24.113787

- **Strobilurins commonly used in combination with triazole fungicides**
- **Not used in human medicine**
- **Clear evidence that patients are inhaling fungicide-resistant *A. fumigatus***

Red: Pan-azole resistant
Orange: Strobilurin resistant
Violet: Benzimidazole resistant



Old finding: azole-resistant strains, including from humans, are resistant to other fungicide classes

JCM
Journals.ASM.org

Frequency of Decreased Susceptibility and Resistance to Echinocandins among Fluconazole-Resistant Bloodstream Isolates of *Candida glabrata*

M. A. Pfaller,[a]* M. Castanheira,[a]* S. R. Lockhart,[b] A. M. Ahlquist,[b] S. A. Messer,[a]* and R. N. Jones[a,c]

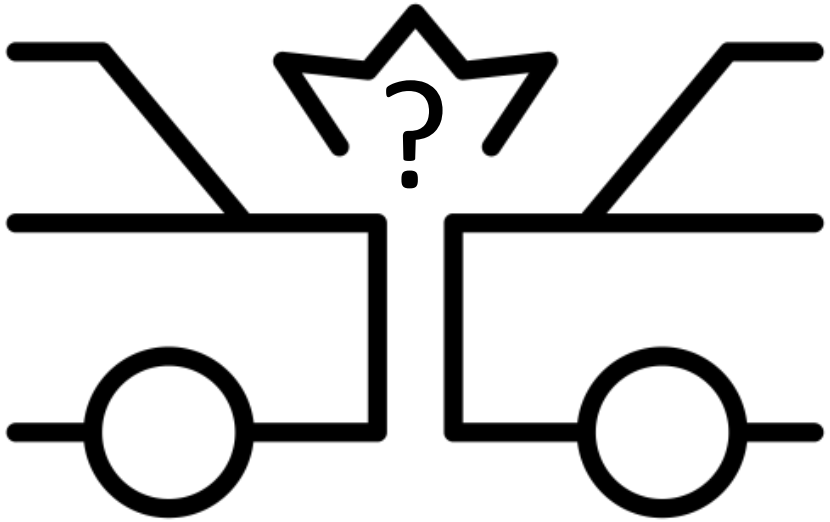
JMI Laboratories, North Liberty, Iowa, USA[a]; Mycotic Disease Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA[b]; and Tufts University School of Medicine, Boston, Massachusetts, USA[c]

Key need:

- Communication/crosstalk between mycologists of plants and humans

Hypothetical heading to Reality?

Olorofim



Ipfluquinone

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