Diagnosing Fungal Infections and Antimicrobial Resistance at our Current Diagnostic Capacity

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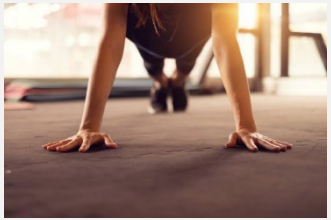
Bottom Line

- Diagnostic tests are limited for fungi
  - *Candida* easy to grow from blood, but only 50-70% of time
- Antimicrobial resistance testing is not widespread (still) and often not done
  - Need more genetic markers
- Challenging tests to develop and interpret (but not impossible)

Because of these factors, tests are often not ordered or considered

Meet Zoe



38 years old,
healthy
Lives in the
Netherlands

Presents to Doctor

- Headaches
- Sore Throat
- Joint Pain
- Cough
- Runny Nose
- Fever

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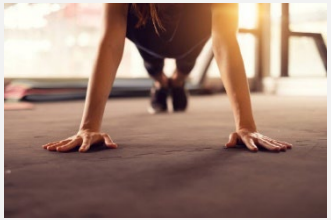

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Testing - Positive rapid influenza diagnostic

Treatment - Oseltamivir (Antiviral therapy)

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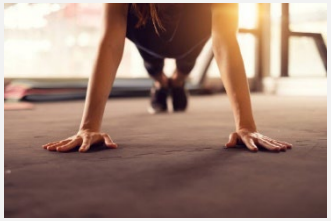

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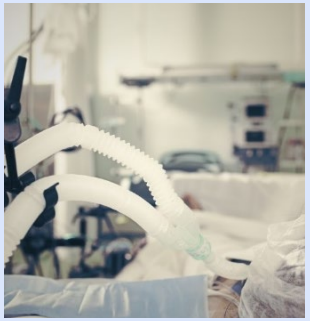

Day 5
Worse – admitted with pneumonia given antibacterials
Day 6
Respiratory failure, Severe sepsis, intubated

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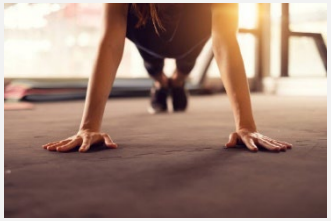

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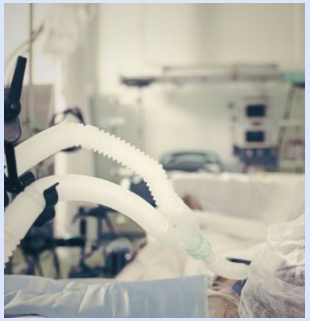

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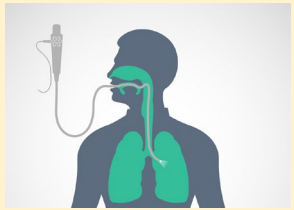

Day 7
Testing - CT scan, Blood tests,
BAL: Bronchoalveolar lavage

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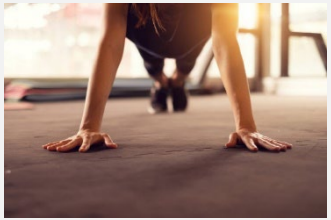

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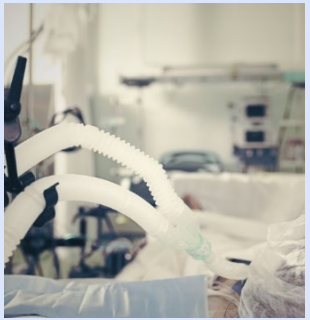

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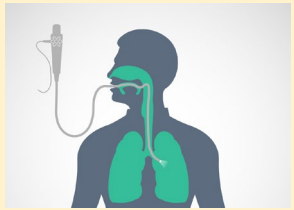
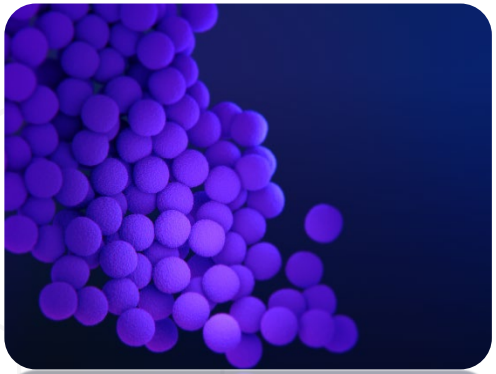


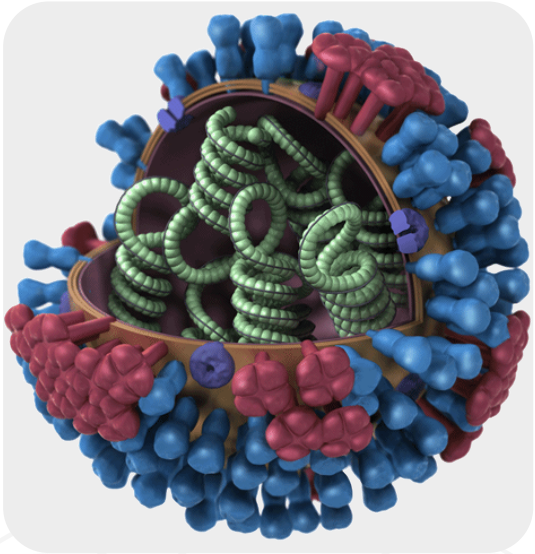
Day 7
Testing - CT scan, Blood tests, BAL: Bronchoalveolar lavage

Day 20
Expired

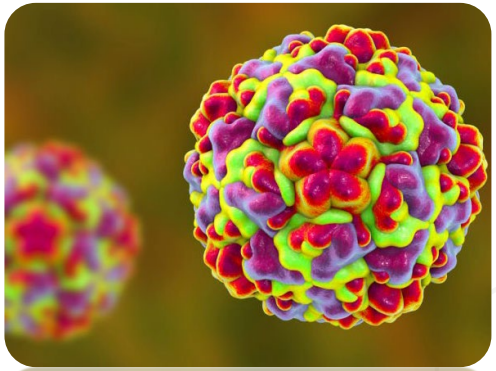
Possible infectious causes of Zoe's death: Influenza complication with bacterial or other viral infections



Bacteria

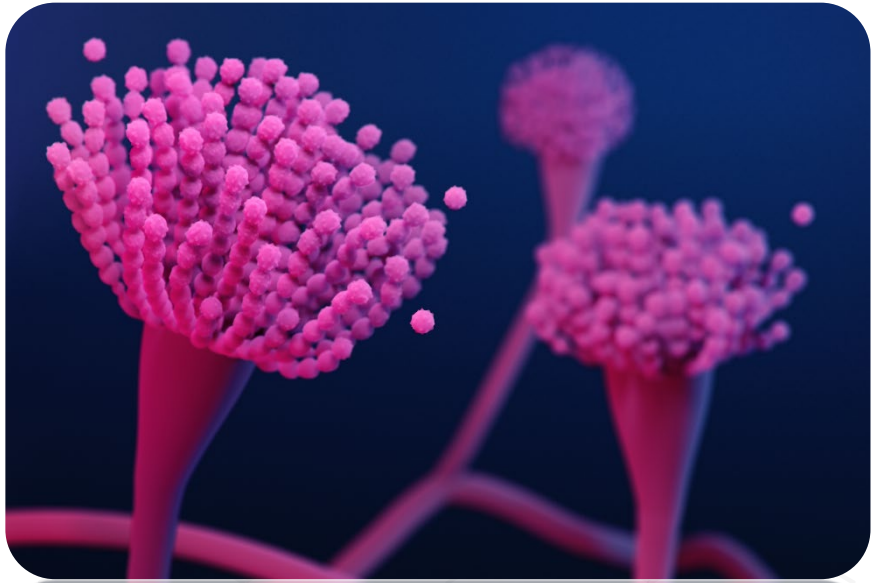


Influenza



Other viruses

Ultimate cause of death: Influenza complication with fungal infection



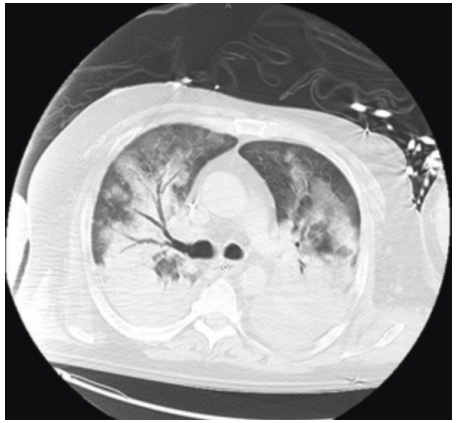
Ultimate cause:

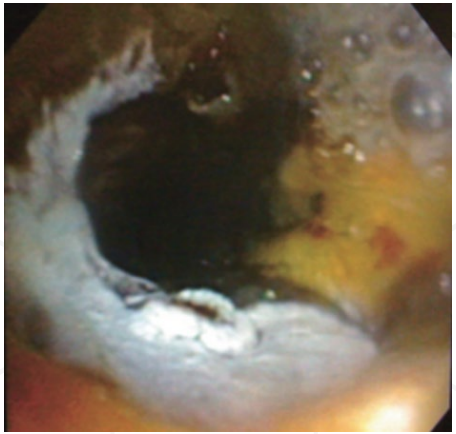
Fungus, ***Aspergillus fumigatus***

Influenza Associated Pulmonary Aspergillosis (IAPA)

- IAPA gained recognition during 2009 H1N1 pandemic influenza
  - Lack of classical risk factors of IA (leukemia, neutropenia, transplant (stem cell, solid organ)
  - ICU and intubated patients

- Subsequent studies have found high rates of IAPA (7.2 - 28.1%)

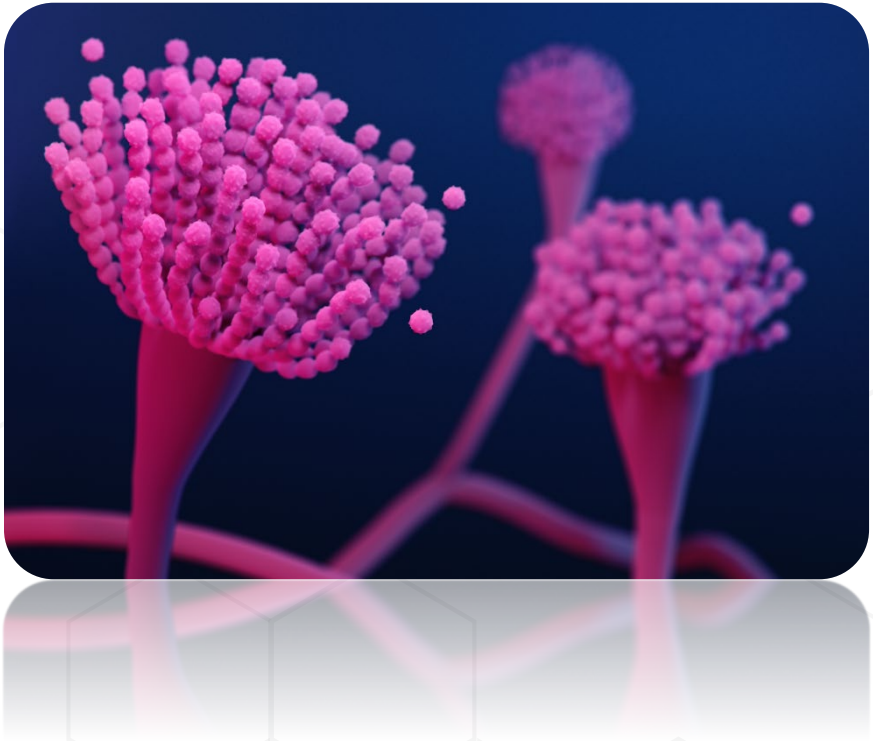




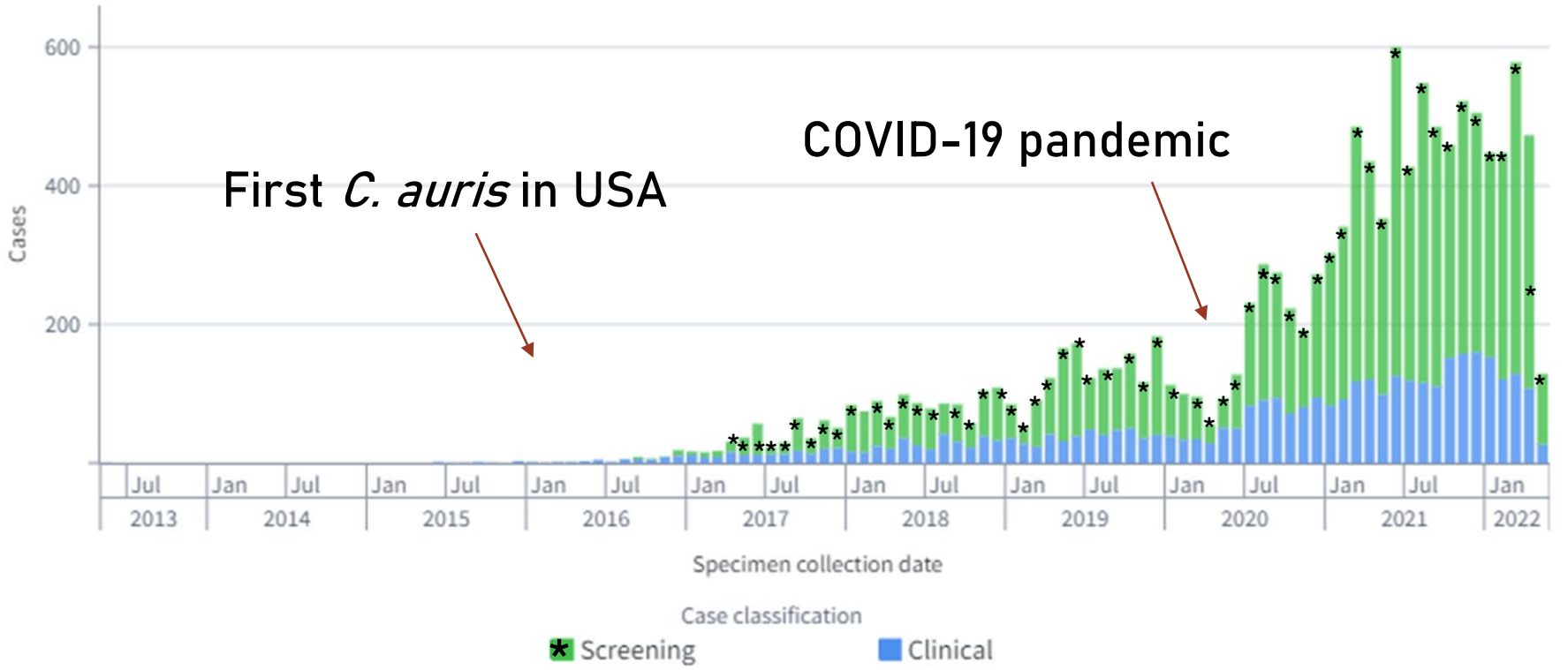
Adalja A et al. Influenza and Other Respiratory Viruses 2011;5: 225

COVID-19-associated Pulmonary Aspergillosis (CAPA)

- Increasing reports of CAPA, initially from Western Europe, but now many all over
- One of the most common COVID-19-associated fungal infections
- True rate of CAPA is unknown
  - Rates range from 0% to 33%



Candida auris large increases during COVID-19 (60%)



What tests are available for Aspergillosis?

Assays with FDA and CE label or USA CLIA approval

Antibody detection systems

- Immunodiffusion

IMMY

Antigen detection systems

- Ag EIA and Ag LFA

IMMY BIO-RAD

ERA 中娜生物 DNK VirClia® monotest

- (1–3)-β-D-glucanLFA

FUJIFILM Value from Innovation Fungitell® (1→3)-β-D-Glucan Assay

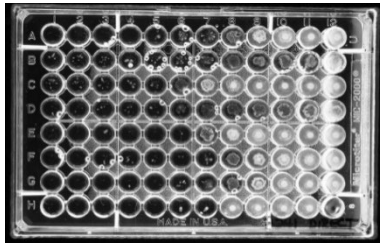
DNA detection systems

- None approved by FDA on clinical specimens

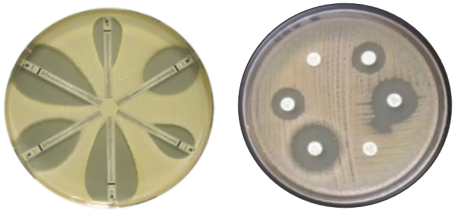
Products commercially available only in Europe

Name/Brand	Methodology	Characteristics
AsperGenius/ Pathonostics	Multiplex real-time PCR	3 species of *Aspergillus* and 4 genes of resistance to azoles
MycoReal Aspergillus / Ingenetix	Multiplex real-time PCR	*A.fumigatus*, *A.terreus*, *A.flavus*, *A.niger* and *A.nidulans*
SeptiFast Test / Roche	Real-time PCR	*Candida* and *Aspergillus*
Affigene / Cepheid	Multiplex real-time PCR	3 species of *Aspergillus*

Methods for antifungal susceptibility testing (AFST)



Broth microdilution



Agar diffusion

Automized

↑ Concordance

↑ Cost/Ease

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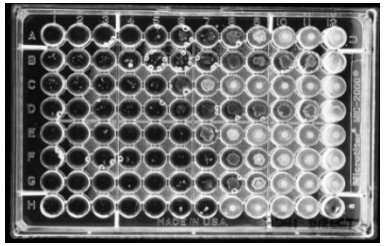

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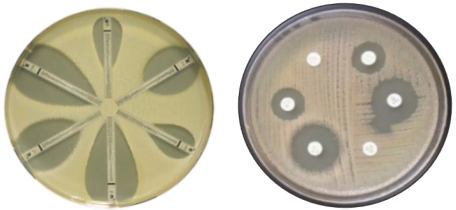

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FDA approved

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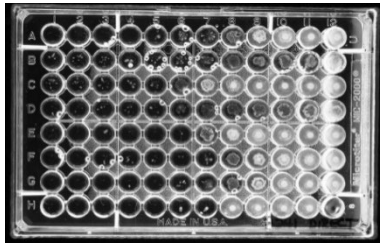

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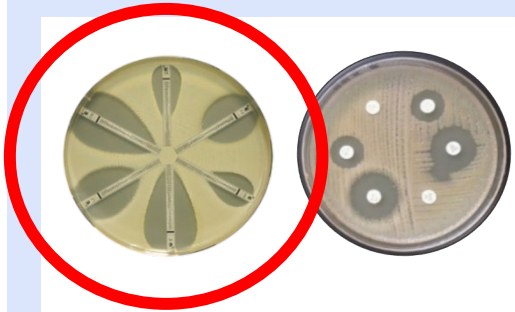

Agar diffusion

Automized

Only one commercially available for mold

Participation in CAP AFST proficiency

- >400 participants in last CAP AFST proficiency
  - 49% use VITEK 2
  - 44% use YeastOne (*Candida* broth micro)
  - 8% use gradient diffusion
  - 4% use broth microdilution

No commercially available proficiency testing for mold AFST!

Antifungal Susceptibility Testing

- Better automated system for fungi, including molds
- Rapid tests
- Incentivized testing

Within the next decade we will go from 3 to as many as 6 or 7 systemically active classes of antifungals.

We need to provide AFST to make sure our patients are getting the best choice.

What's Needed:

- Elevating the importance of address fungal diseases and putting them on par with bacterial disease development. This means, additional investment and development of new:
  - POC fungal diagnostics for patient care;
  - POC Susceptibility tests for resistance to antifungals;
  - Antifungal treatment options; and
  - Antifungal prevention options (e.g. vaccines and decolonizing agents).

- Funding sustainability (short term supplement funding will expire in the next couple years)
  - Of critical AR fungal surveillance programs that turn data into prevention:
  - For health departments and healthcare facilities. We will need a more robust workforce, increased laboratory expertise, and infection prevention control capacity that can address fungal threats.

Thank You

@CDC_AR

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