Surveillance of Invasive Mold Infections

March 24, 2017

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Disclosures

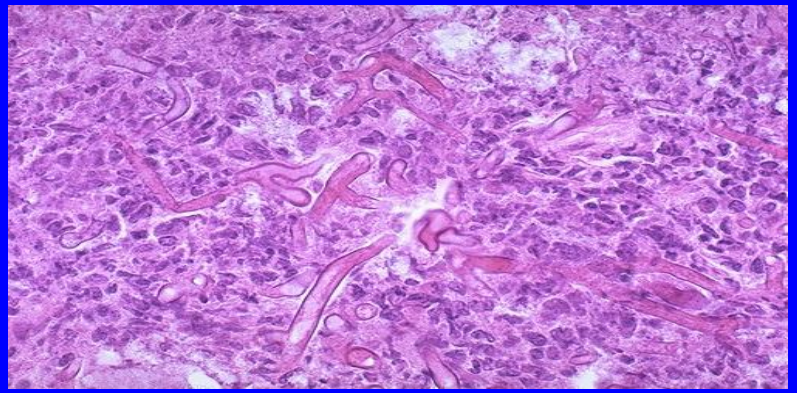
- None

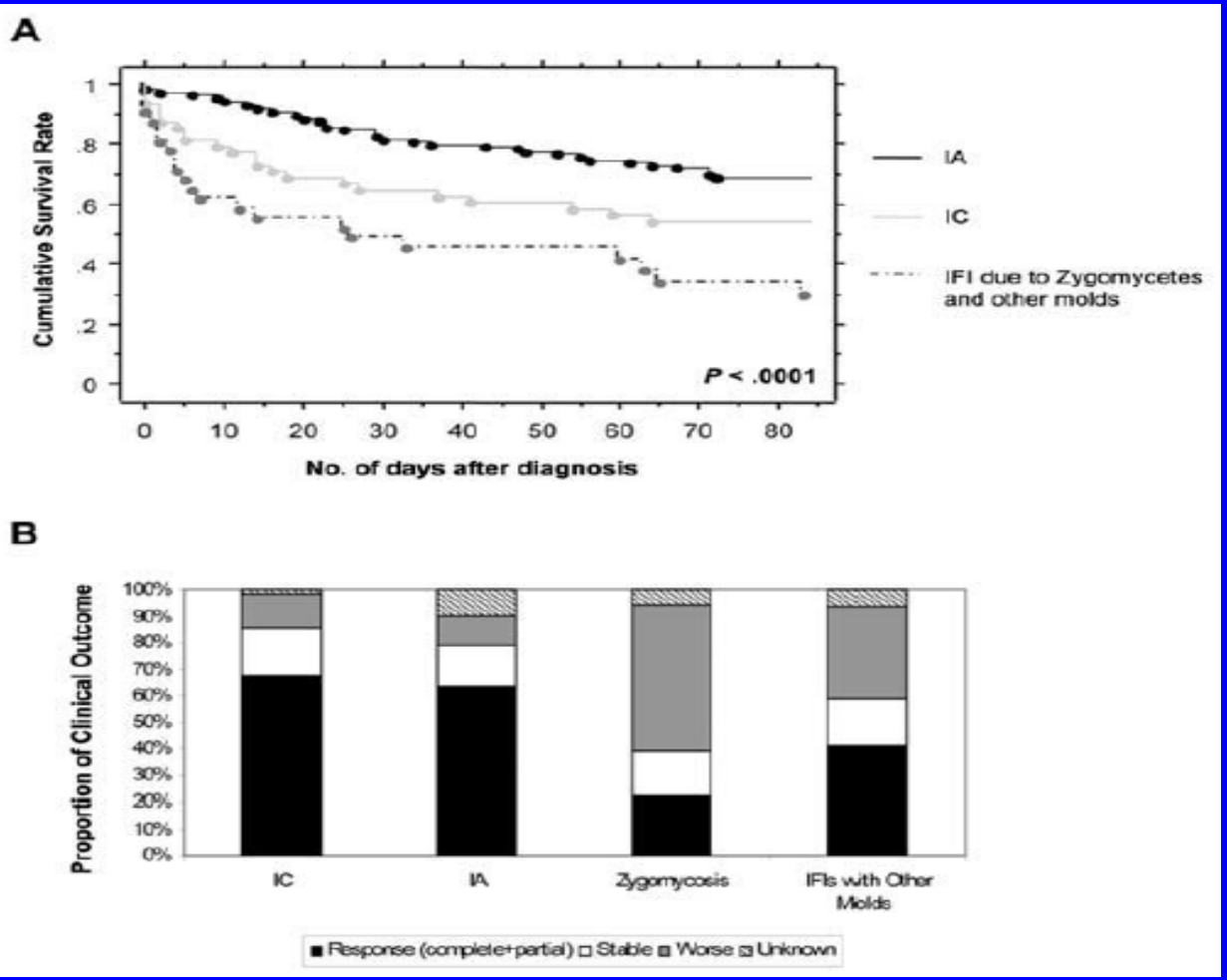
Objectives

- Importance of Molds
- Mold Surveillance systems
- EIP Pilot project

Importance of Invasive Molds

- Molds (v yeasts) = hyphal structures, grow by branching/ extension
- Spectrum of Disease
  - superficial (e.g. allergic bronchopulmonary aspergillosis)
  - invasive (e.g. cavitary lung mucormycoses)
- Major cause of morbidity and mortality, especially in immunocompromised hosts





PATH Alliance Registry, 2009

A. 12-wk survivial

*Overall mortality - 46.7%

Zygomycetes – 64.3%

Invasive Aspergillus – 35%

B. 12 wk post transplant, response to therapy for invasive fungal infections

Neofytos CID 2009

Epidemiology

- 12.4 infections per million persons/yr for *Aspergillus* spp
- Sporadic outbreaks
  - natural disasters (Mucorales)
  - combat injuries (Fusarium, Aspergillus, Mucorales)
  - nosocomial (Exserohilum)
- Increasing use of anti-fungal prophylaxis in high risk patients = increase in mold infections over recent decades
  - HSCT patients, invasive mold infections may be more common than candida (43% v 28%)

Rees, CID 1998
Kontoyiannis CID 2010
Neofytos CID 2009
Pfaller CID 2006

Antifungal Resistance – an Emerging problem

- Low-prevalence (3.2%), but global problem
- Associated with poorer clinical outcomes
- Associated with antifungal (-azole) use?
- Environmental mechanisms?
  - chronic colonization in cystic fibrosis or allergic bronchopulmonary aspergillosis
  - Widespread use of azoles for agricultural purposes

Van der Linden Emerg ID 2015
Verweij CID 2016

Verweij CID 2016

Surveillance Systems in Place

- Current State - Limited
  - Single center studies
  - Large Database/Hospital discharge diagnoses
  - Population based – Berkeley/CDC – 3 N. California Co
  - Host-specific
    - solid-organ (TRANSNET)
    - stem cell transplant networks (PATH Alliance, TRANSNET)
  - Limited Diagnostic ability
    - >50% speciation lacking

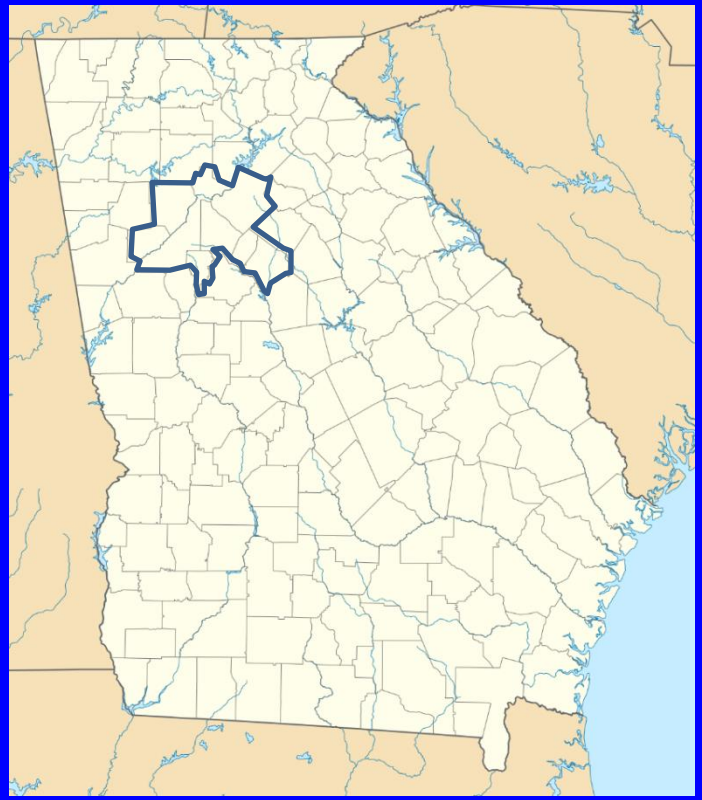
Rees, CID 1998
Kontoyiannis CID 2010
Neofytos CID 2009
Pfaller CID 2006

Goals for Invasive Mold Surveillance

- Determine population-based mold incidence rates
- Estimate mortality
- Monitor trends of mold species causing infections (emerging threats, outbreaks)
- Evaluate potential resistance patterns
- Examine the types of hosts (risk factors for disease) impacted by invasive mold

Catchment Area

- GA EIP - 8 counties
  - 28 hospitals
  - 4 million residents (2015)
- Pilot Project
  - Emory Hospital System
  - Grady Hospital
  - Atlanta Veterans Affairs



Partners

- Hospital microbiology, pathology personnel
- Georgia EIP
  - Hospital Acquired Infections
    - Candidemia Surveillance → Invasive Mold Surveillance ☺
- CDC Mycotic Diseases Branch
  - Epidemiology and Laboratory teams
- CDC Infectious Diseases Pathology Branch

Case Definition

"A diagnostic specimen (culture isolate, or fresh or fixed tissue) identified as a mold, including but not limited to: *Aspergillus*, Mucormycete molds, Phaeohyphomycete molds (pigmented molds), *Scedosporium*, and *Fusarium*, causing infection in a patient living in the catchment area."

A new case will be triggered by a positive culture or tissue histopathology for an invasive mold species
-excluding endemic fungi (dimorphic)
-excluding nails, allergic aspergillosis
-incident case if specimen collected is >60 days from first sample

CDC Diagnostics

Mycotic Disease Branch Laboratory

- Tissues
  - First forwarded to IDPB for evaluation
  - PCR: rDNA ITS 4/5, β-tubulin, IGS
  - Amplicon sequencing
- Cultures
  - Subculture for reference archive
  - PCR: rDNA ITS 4/5, β-tubulin, IGS
  - Amplicon sequencing
  - Antifungal susceptibility testing
    - Azoles
    - Echinocandins
    - Amphotericin B

Infectious Diseases Path Branch Lab

- Tissues
  - Stains (H & E, GMS)
  - Immunohistochemistry
  - Confirm presence of mold
  - Identify genus when possible
  - Return to MDB for sequencing

Case Report Form (CRF)

- Demographic information
- Co-morbidities, immunosuppressant medications
- Clinical Syndrome
- Co-infections – bacterial, viral (e.g. CMV)
- Radiographic information
- Laboratory information
  - Indirect tests for mold – galactomannan, B-D glucan
- Use of antifungals before/after diagnosis

MOLD INFECTION 2016 CASE REPORT FORM

atient name: _____ Medical Record No.: _____
(Last, First, MI)

ddress: _____ Hospital: _____
(Number, Street, Apt. No.)

_____ _____ Acc No. (Positive specimen): _____
(City, State) (Zip Code)

heck if not a case: ☐ Out of catchment area ☐ Duplicate e

. **State:** ☐☐ **2. County:** _____ **3. Census trac**

. **Date of birth:** ☐☐/☐☐/☐☐☐☐ (mm/dd

. **Sex at birth:** ☐ Male ☐ Female ☐ Other (specify)____

. **Ethnic Origin:** ☐ Hispanic or Latino ☐ Not Hispanic or Lati

0. **Race (check all that apply):** ☐ White ☐ Black or Afr
☐ Asian ☐ Native Haw

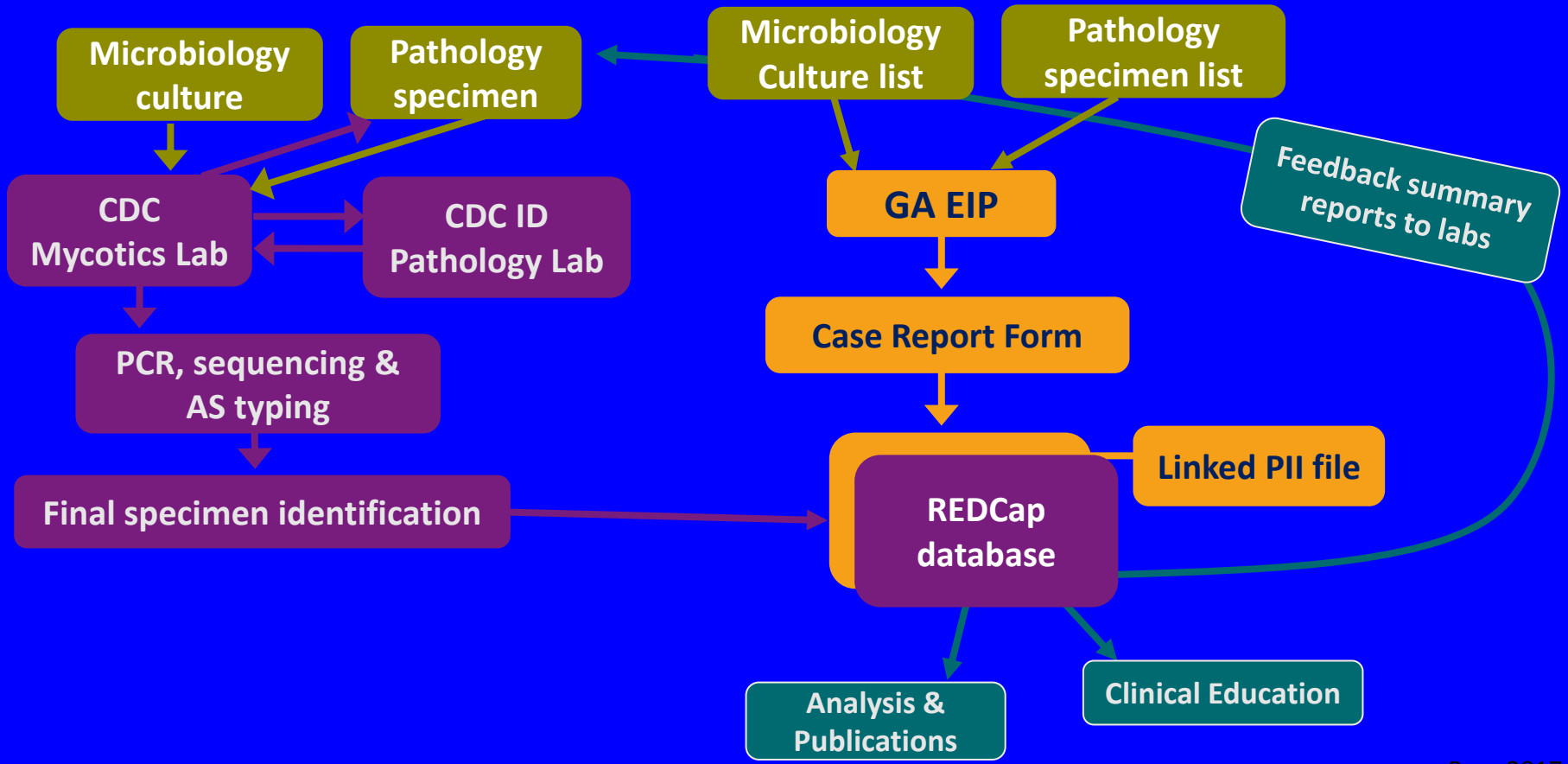
1. Incident Specimen
pecimen ID: _____
DC DASH #: _____

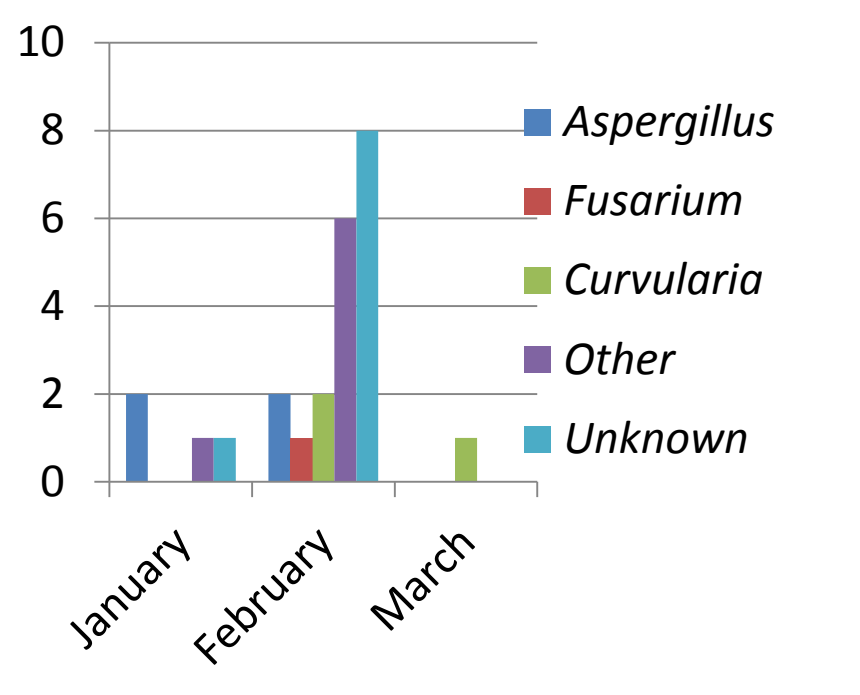
pecimen type:
☐ Culture
☐ Histopathology

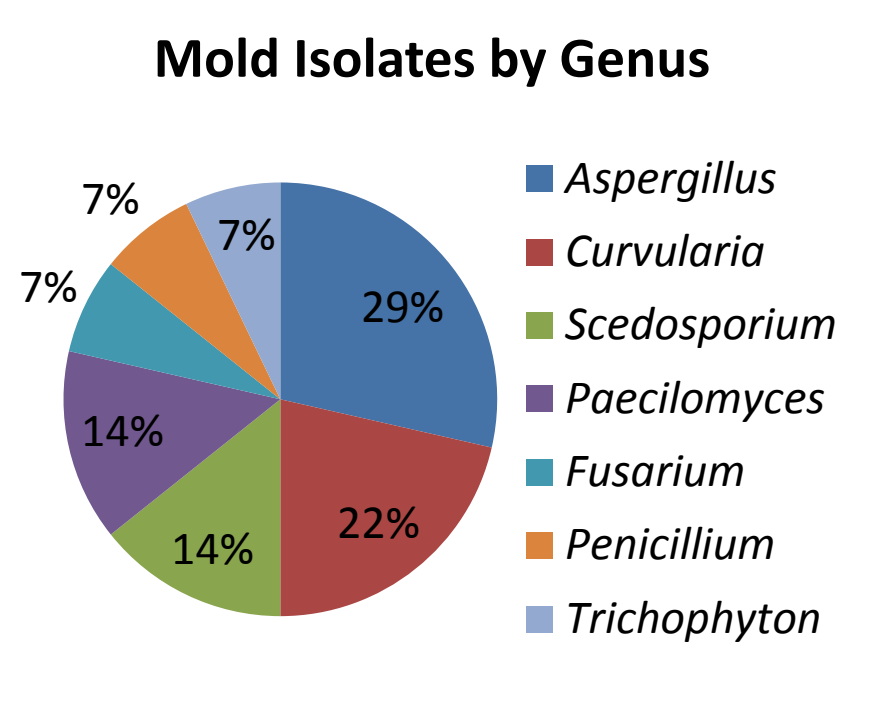
13. Mold Identification (check all that apply to this specimen)
☐ ***Aspergillus***
- ☐ *A. fumigatus*
- ☐ *A. niger*
- ☐ *A. flavus*
- ☐ *A. terreus*

14. Antifungal susceptibilities ☐ None performed or no results available	**MIC (e.g. 0.5, 2)**	
Amphotericin B (Ambisome, Abelcet)		☐ Unk
Anidulafungin (Eraxis)		☐ Unk
Caspofungin (Cancidas)		☐ Unk
Fluconazole (Diflucan)		☐ Unk

Work Flow


Microbiology culture
Pathology specimen
Microbiology Culture list
Pathology specimen list
CDC Mycotics Lab
CDC ID Pathology Lab
GA EIP
Feedback summary reports to labs
PCR, sequencing & AS typing
Case Report Form
Final specimen identification
Linked PII file
REDCap database
Analysis & Publications
Clinical Education


10
8
6
4
2
0
January
February
March
Aspergillus
Fusarium
Curvularia
Other
Unknown


Mold Isolates by Genus
29%
22%
14%
14%
7%
7%
7%
Aspergillus
Curvularia
Scedosporium
Paecilomyces
Fusarium
Penicillium
Trichophyton

Challenges

- Engaging and enlisting pathologists to submit tissue samples
- Diagnostic
  - Reliance on indirect methods is common (73%)
  - Probable (88%) > Proven
- Clinical data collection from medical records

Strengths

- Population based surveillance
- Collection of both microbiological and pathological specimens
  - Maximize the number of “proven” diagnoses
- Robust clinical data collection
- Use of electronic case reporting platform (REDCap)
- Molecular diagnostics for identification
- Antifungal resistance testing
- Provide feedback to local pathologists, microbiology lab

Acknowledgments

- Team Mold
  - Karyln Beer (CDC PI)
  - Sharon Tsay (CDC EIS)
  - Taylor Chambers (GA EIP)
  - Stepy Thomas (GA EIP)
  - Sasha Harb (GA EIP)
  - Suzanne Segler (GA EIP)
  - Monica Farley (GA EIP PI)
- GA EIP
- CDC Mycotic Diseases Branch
- CDC Infectious Disease Pathology Branch
- REDCap Team @ CDC
- Jeannette Guarner
- Microbiology staff & Pathologists at Emory UH, Atlanta VAMC, and Grady Hospital