Environmental Epidemiology and Prevention of Mould Infection

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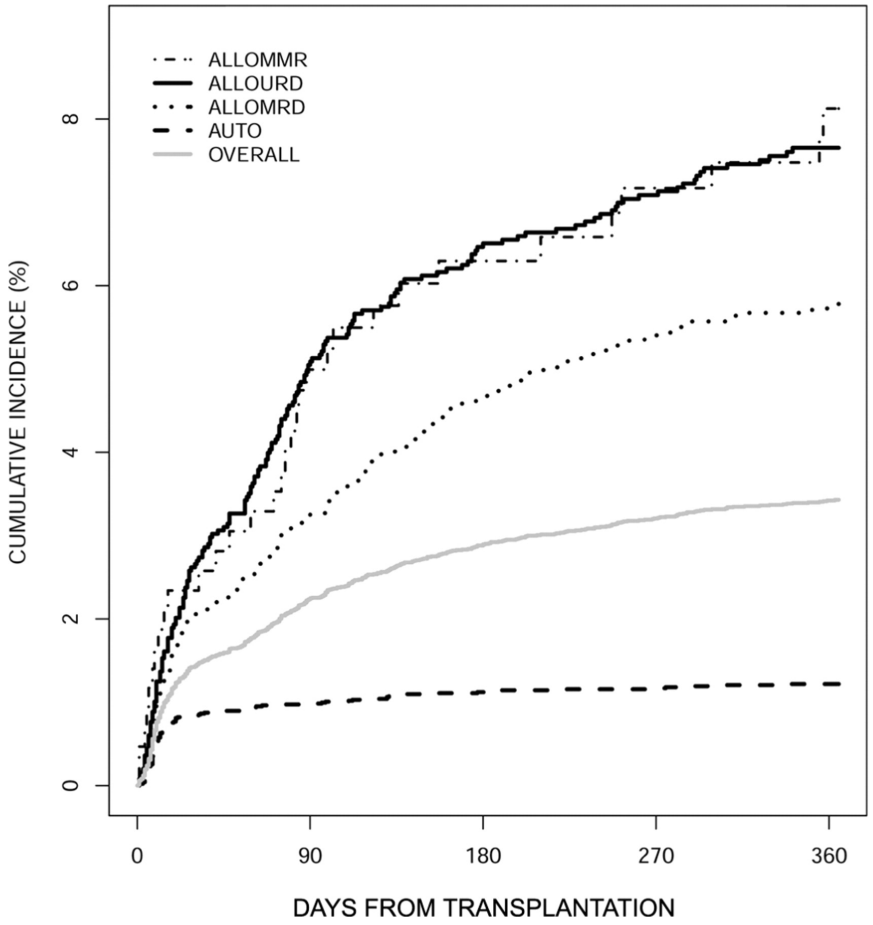
Disclosures:
Consultant to Durata
Spouse: Consultant to Astellas, Toyama, Merck, Durata

Cumulative incidence curves for IFI HSCT recipients in TRANSNET.



Allogeneic mismatched related
Allogeneic unrelated
Allogeneic matched related
Autologous

Dimitrios P. Kontoyiannis et al. Clin Infect Dis. 2010;50:1091-1100

IFI by Solid Organ Transplant Type
TRANSNET

IFI type	Kidney (n = 332)	Liver (n = 378)	Pancreas (n = 128)	Lung (n = 248)	Heart (n = 99)	Small bowel (n = 22)
Candidiasis	164 (49)	255 (68)	97 (76)	56 (23)	48 (49)	19 (85)
Aspergillosis	47 (14)	42 (11)	6 (5)	109 (44)	23 (23)	0 (0)
Zygomycosis	8 (2)	9 (2)	0 (0)	8 (3)	3 (3)	0 (0)
Other mold	10 (3.0)	9 (2.4)	4 (3.1)	49 (19.8)	7 (7.1)	0 (0.0)
Unspecified mold	7 (2.1)	8 (2.1)	0 (0.0)	7 (2.8)	2 (2.0)	0 (0.0)
Cryptococcosis	49 (15)	24 (6)	6 (5)	6 (2)	10 (10)	1 (5)
Endemic mycoses	33 (10)	17 (5)	8 (6)	3 (1)	3 (3)	0 (0)
Pneumocystosis	5 (1)	0 (0)	1 (1)	4 (2)	3 (3)	0 (0)
Other yeast	6 (1.8)	9 (2.4)	5 (3.9)	0 (0.0)	0 (0.0)	1 (5)
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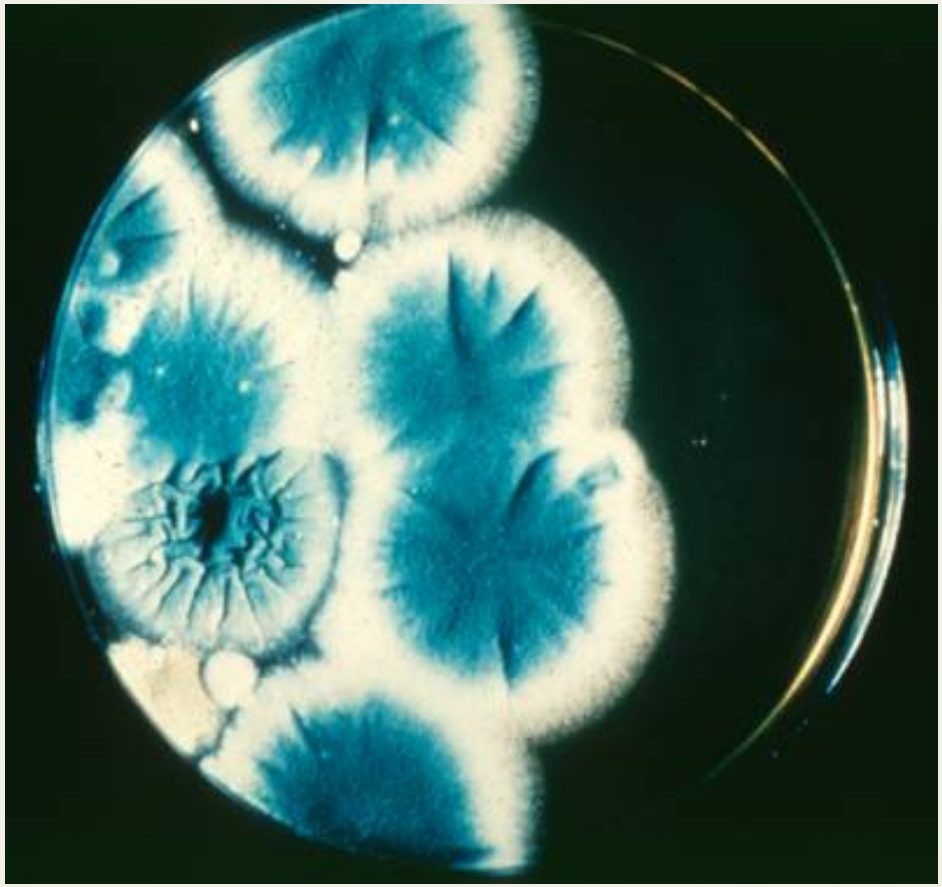
Peter G. Pappas et al. Clin Infect Dis. 2010;50:1101-1111

Invasive Aspergillosis



Aspergillus

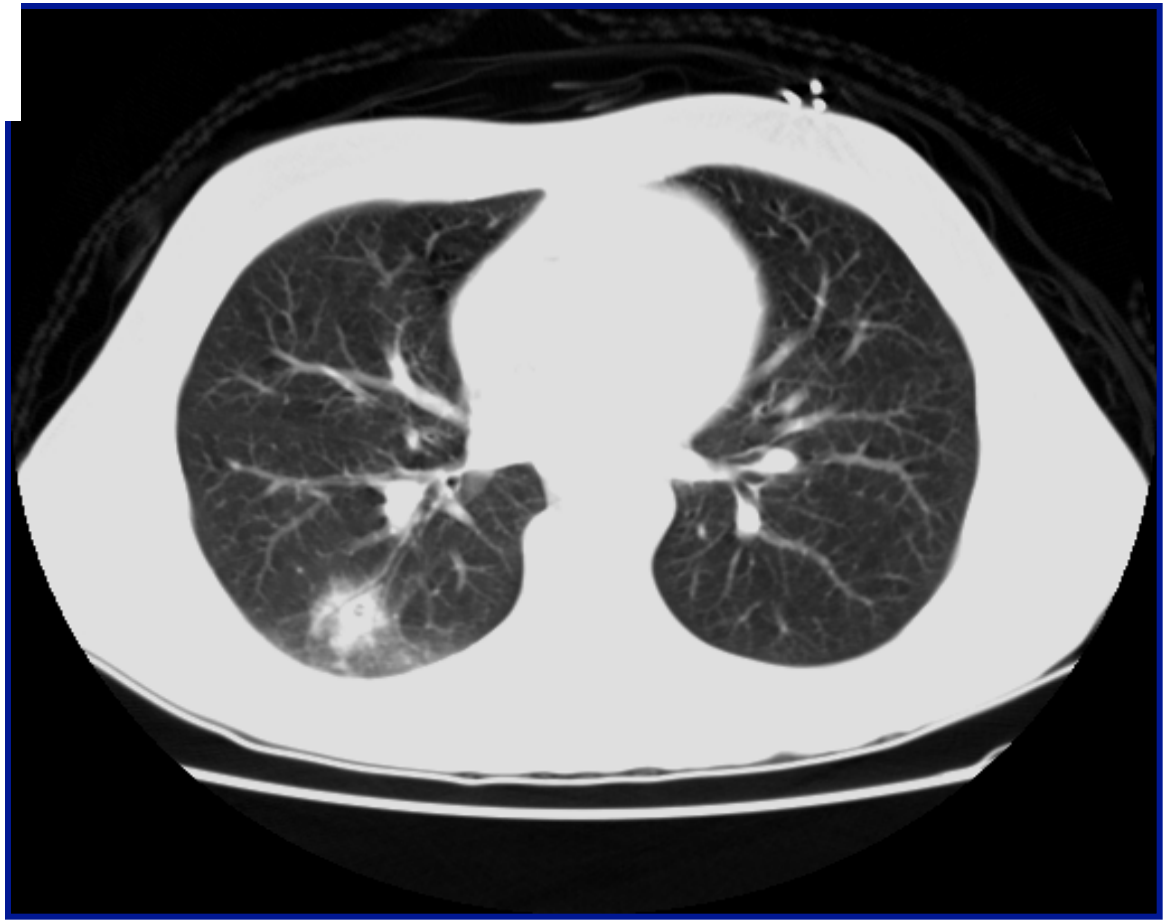
Ubiquitous mold:

- Soil, water, decaying vegetation

Sources

- Unfiltered air/ventilation systems
- Dust from renovation/ construction
- Environmental sources
- Food/plants
- Water supply

Halo Sign



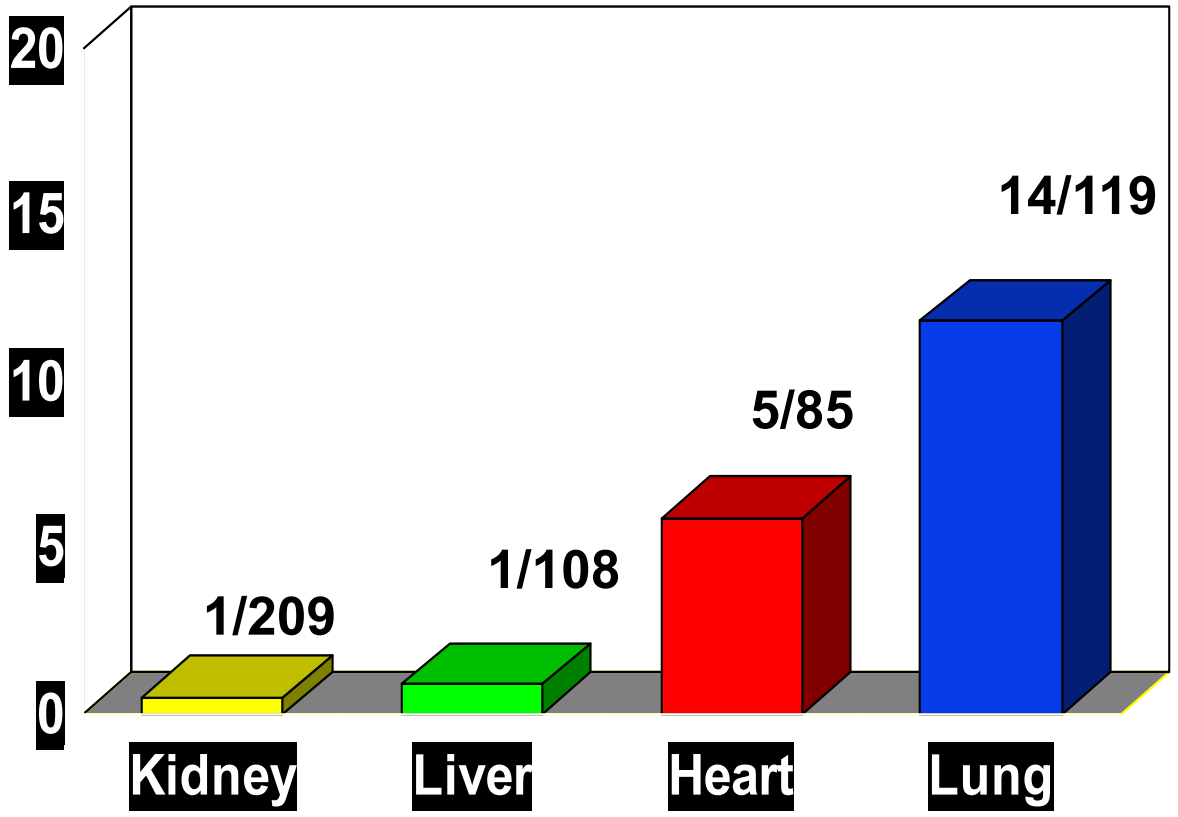
Aspergillus and Construction

- Association between aspergillosis outbreaks and construction
- Environmental controls associated with decreased risk
  - ✓ Maintain negative pressure
  - ✓ Install appropriate barriers
  - ✓ Control traffic in construction areas
  - ✓ Monitoring of airborne spore count

Arnow 1991; Wald 1997; Cornet 1999; Patterson 2000; Chang 2008; Berger 2011

Aspergillosis in Solid Organ Transplant

UTHSCSA Experience



Patterson JE, et al. *Transplant Infect Dis* 2000;2:22-8

Interventions: Aspergillosis in SOT

- Environmental
  - ➢ Immediate
    - Removal of carpet, plants
    - HEPA filtration
    - Construction barriers, precautions
  - ➢ Long term - New unit
    - Point of use HEPA filtration
    - Positive pressure rooms
    - 15 air changes/hour

Patterson JE et al. Transplant Infect Dis 2000:2:22-8

Interventions: Aspergillosis in SOT

- Prophylaxis (lung and heart txn)
  - Itraconazole 200 mg BID (capsule) X 3 months
  - Monitor levels
  - Itraconazole 200 mg q d (oral solution)
    - Enhanced bioavailability

Aspergillosis in Solid Organ Transplant

UTHSCSA

Rate	Before (%) 1991-92	After (%) 1993-98	p value
Aspergillus infection SOT	9.4 (8/85)	1.5 (7/452)	p<.05
Attrib. MR in SOT	8.2 (7/85)	1.8 (8/439)	p<.05
Infection/colonization in lung txn	42 (14/33)	22.5 (14/62)	p<.05
Early attrib. MR in lung txn	15 (5/33)	3.2 (2/62)	p<.05

Patterson JE et al Transplant Infect Dis 2000:2:22-8

Aspergillus and Construction

- Multi-barrier concept
  - Seal windows and doors adjacent to construction
  - Dust protection walls erected
  - Facility air positive pressure
  - Doors next to construction site closed
    - Shift entrance
  - Walkways protected from demolition
  - 3-staged external air filtration, including HEPA
  - Soil moistened to minimize dust generation
  - Airborne-particle sampling

Berger Am J Infect Control 2011
Environmental Infection Control MMWR 2003

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Phaeohyphomycosis

Phaeohyphomycoses

- Etiologic agents
  - *Alternaria* spp., *Bipolaris* spp., *Curvalaria* spp., *Exserohilum* spp., *Exophila* spp.
- Mycotic infections caused by dematiaceous fungi (melanin in cell walls)
- Fontana Masson stain
- Tropical, subtropical and temperate climates

Phaeohyphomycoses in Organ Transplant

- 79% skin/soft tissue or joint
  - 7% MR
  - Predominantly *Exophiala* spp.
- 21% systemic invasive infections
  - 57% MR
  - Brain abscesses (AmB cured 2/5)
  - *Ochroconis* spp., *Dactylaria* spp.

Singh 1997

Phaeohyphomycoses in TRANSNET

Table 2. Site of infection by transplant type.

Site	Stem cell transplant n = 26 (%)	Solid organ transplant n = 30 (%)
Pulmonary	15 (57.7)	8 (26.7)
Disseminated	12 (46.2)	19 (63.3)
Cutaneous/SC	6 (23.1)	16 (53.3)
Sinus	6 (23.1)	3 (10)
Bloodstream	3 (11.5)	0
CNS	1 (3.85)	0

McCarty Med Mycol 2015

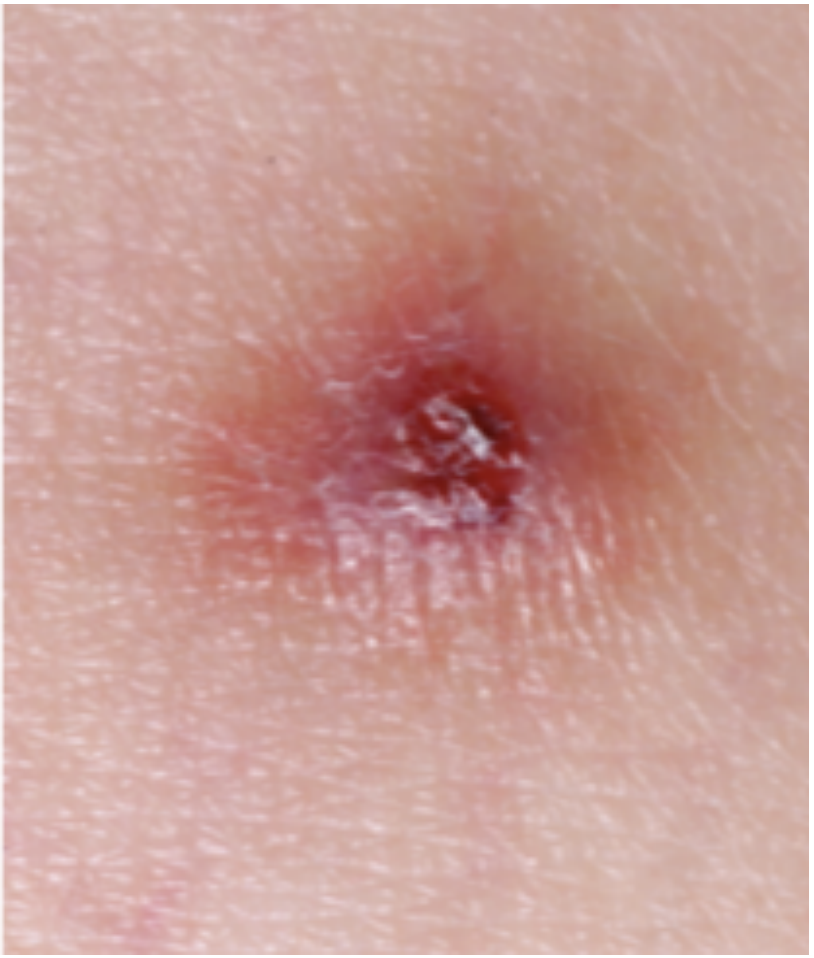
TRANSNET

Table 3. Organisms causing phaeohyphomycosis.

Organism Genus	Number (%) n = 56	Number of deaths (
Alternaria	18 (32.1)	6 (33.3)
Exophiala	6 (10.7)	0
Cladophialophora	5 (8.9)	1 (20)
Scopulariopsis	5 (8.9)	2 (40)
Curvularia	4 (7.1)	1 (25)
Phialemonium	4 (7.1)	1 (25)
Exserohilum	3 (5.4)	1 (33.3)
Sterile Black Mold	3 (5.4)	0
Microascus	2 (3.6)	0
Bipolaris	1 (1.8)	1 (100)
Chaetomium	1 (1.8)	1 (100)
Cladosporium	1 (1.8)	0
Ochroconis	1 (1.8)	0
Phaeoacremonium	1 (1.8)	0
Rhinocladiella	1 (1.8)	0

McCarty Med Mycol 2015

Alternaria in SOT



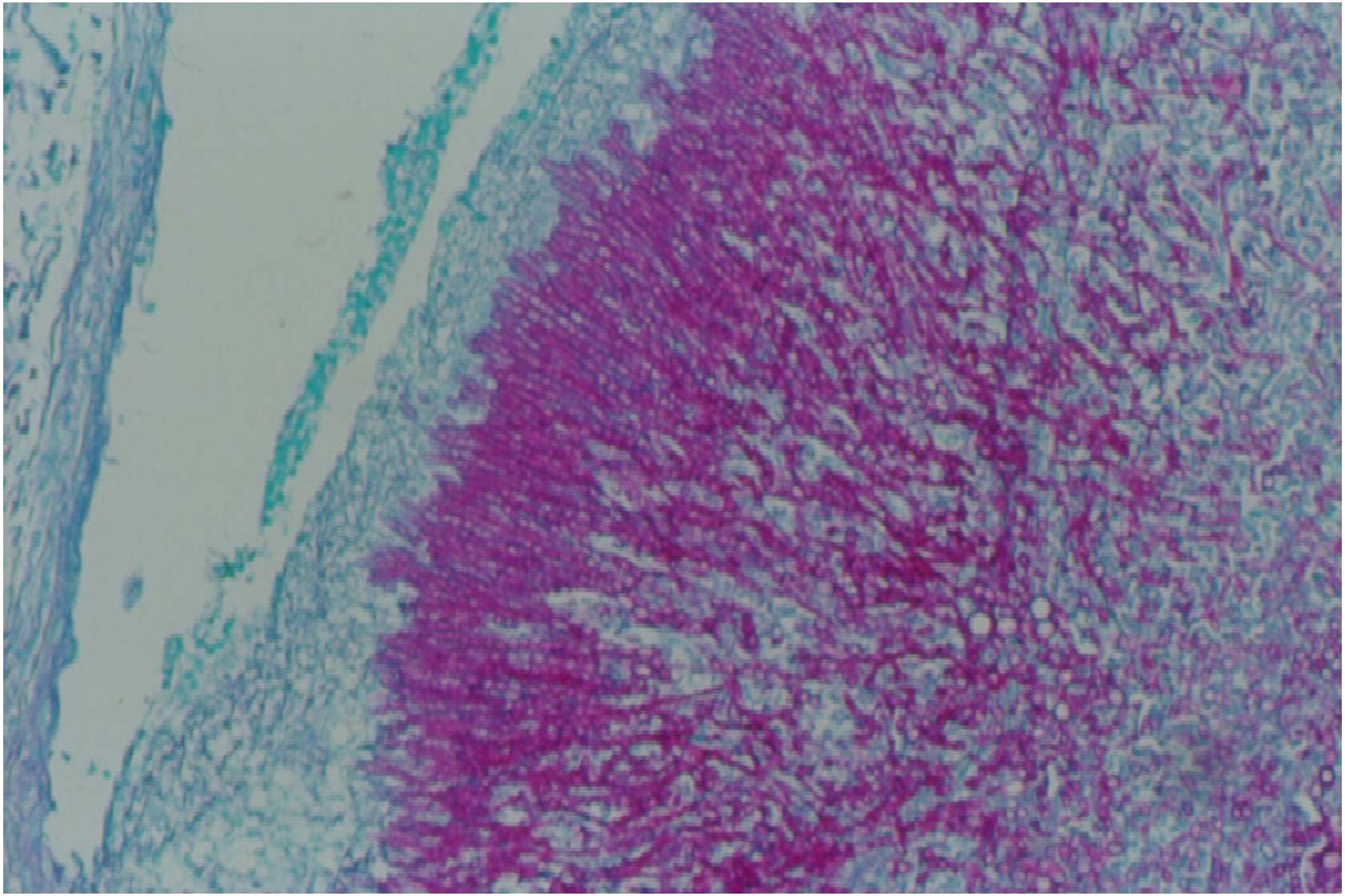
Boyce. Transplant Inf Dis 2010

Case

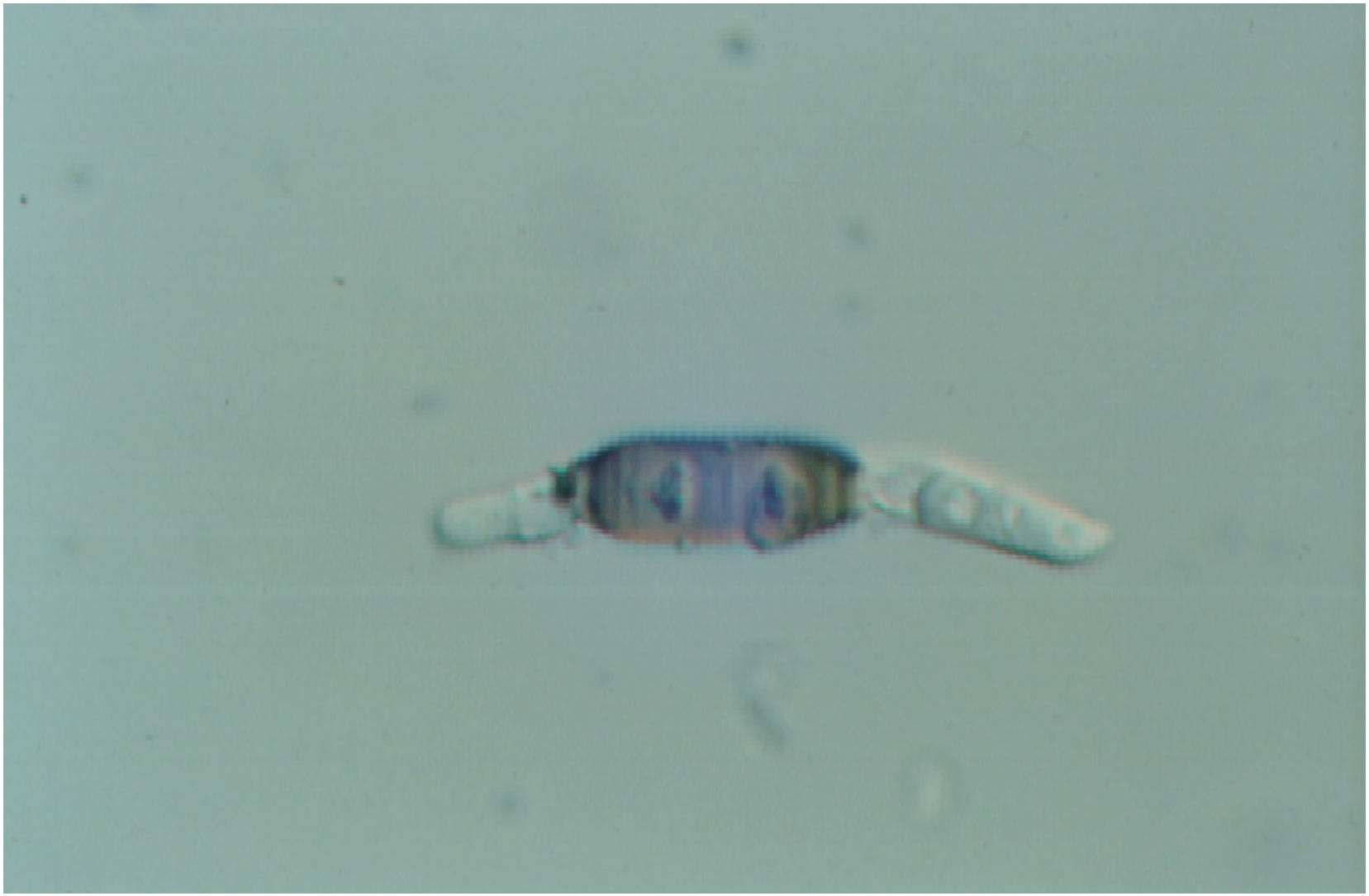
- 50 yo man with cardiogenic shock
- Heart transplant
  - ventilator pneumonia
  - *Ps. aeruginosa* sepsis
- Persistent sepsis, afebrile
- Focal neurologic findings, brain lesions
- Died
  - Autopsy performed

Case

- Autopsy
  - ➢ Disseminated fungal infection
    - Lungs, brain, kidneys, liver
    - "*Aspergillus*"
- Post-mortem and pre-mortem cultures
  - ➢ *Bipolaris* spp.



Bipolaris



Case

- 60 year old man end-stage liver disease
- Liver and kidney transplant
- Complications:
  - hematoma, renal insufficiency
  - persistent fever
  - brownish-black wound exudate
- Wound culture
  - *Exserohilum* spp.
- Evacuated hematoma
  - *Enterococcus* spp.

Case

- Recovered after
  - Wound irrigation and local debridement
  - Liposomal ampho
  - Evacuation of hematoma
  - Broad-spectrum antimicrobials
- Epidemiologic investigation done

Floor sweeper

Floor Sweeper with dust guard/HEPA

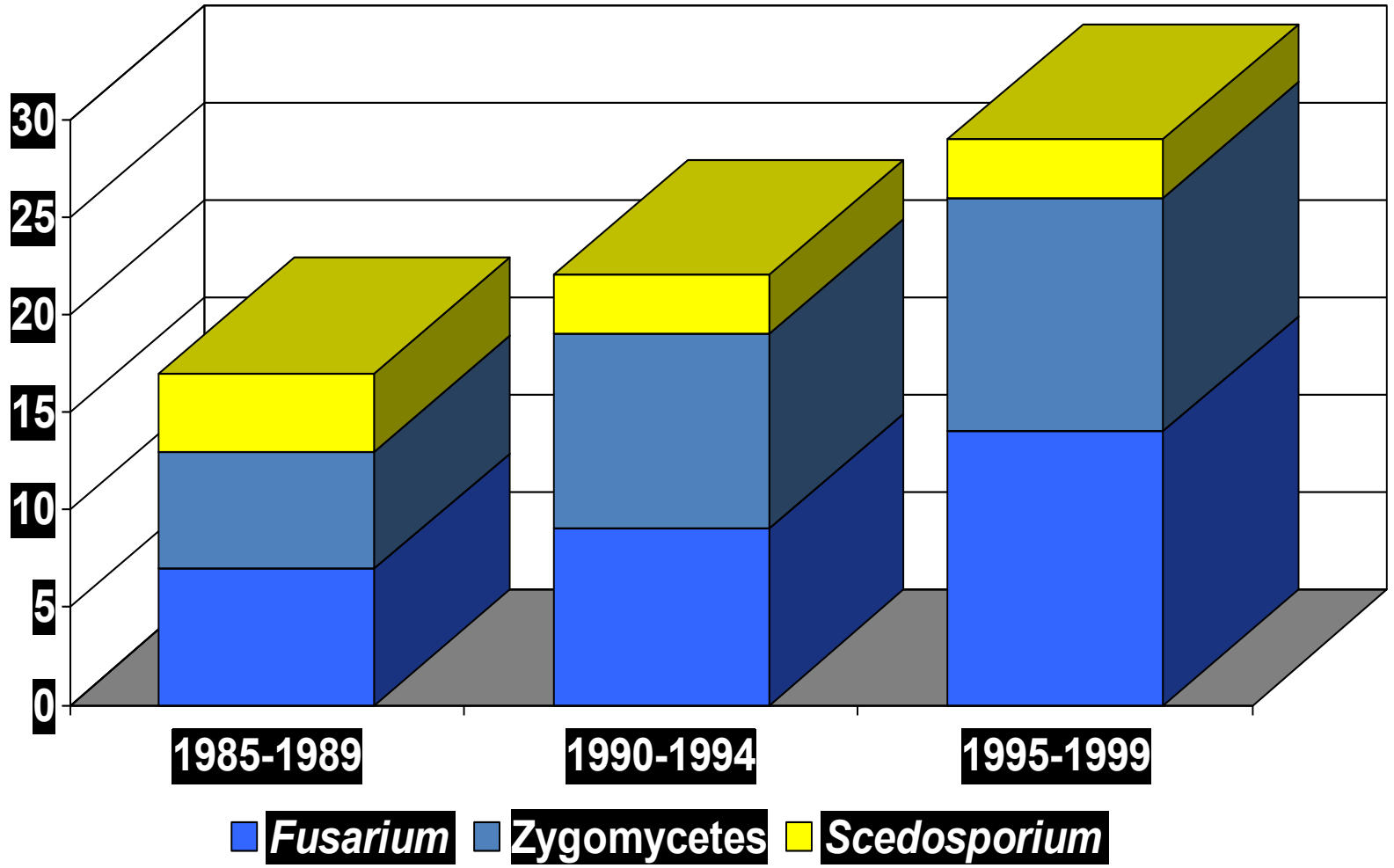
Invasive Fungal Dermatitis

- ELBW infants (≤ 1000 gm)
- Erosive, crusting skin lesions
- High rate of systemic fungal infections (69%)
- Etiologies
  - *C. albicans*
  - Other *Candida* spp.
  - *Aspergillus*
  - *Trichosporon beigelii*
  - *Curvularia* spp., *Bipolaris* spp.

Rowen, Pediatrics 1995

Invasive fungal dermatitis

Non-*Aspergillus* Moulds in Marrow Transplantation



Marr KA et al. *Clin Infect Dis* 2002;34:909-17

Emergence of Zygomycetes in allogeneic HSCT recipients

Before introduction of voriconazole	Among patients receiving voriconazole
2 of 370 in 32 months (0.5%)[1]	4 of 124 in 10 months (3.2%)[1]
0 in 36 months[2]	4 of 45 in <12 months (8.9%)[2]
	6 of 139 in 60 months (4.3%)[3]

[1]Marty et al. *N Engl J Med* 2004; 350:950-2

[2]Siwek et al. *Clin Infect Dis* 2004; 39:584-7

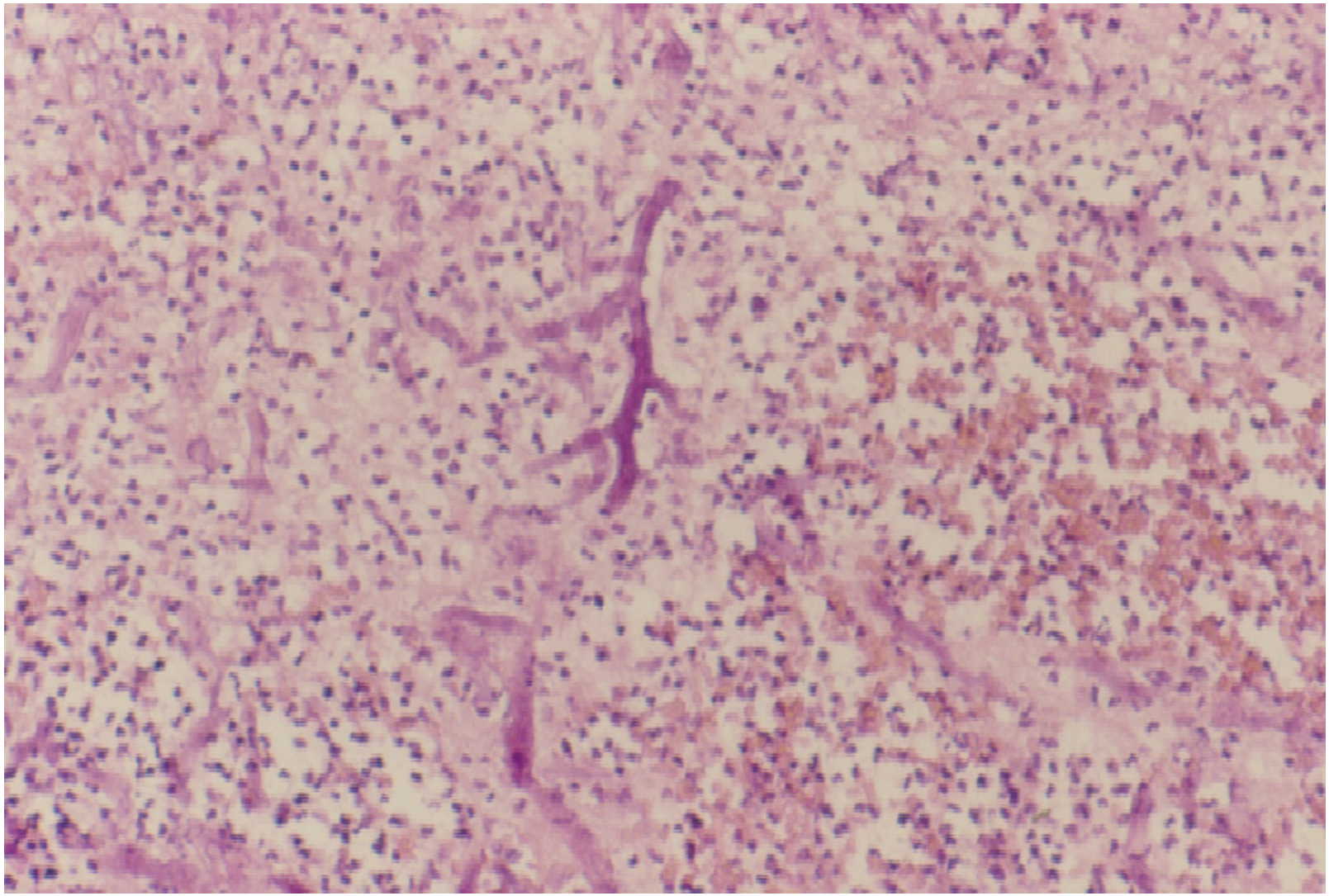
[3]Imhof et al. *Clin Infect Dis* 2004; 39:743-6

Case

- 60 yo man in SICU s/p IABP
- Persistent erythema/edema L groin after removal of IABP
- Cultures + *Serratia marcesens*
- Poor response to therapy
- Debridement X 2

Patterson. Yale J Biol Med 1988

Zygomycosis (*Rhizopus oryzae)*



Rhizopus delmar outbreak

- 5 cases, 11 months
- All fatal
- Childrens' hospital
- Skin sites
- Association w hospital linens
  - Culture positive
- Avoid environmental contamination

Duffy J. Pediatr Inf Dis J 2014

Rhizopus spp. Outbreaks

- Contaminated environment
  - –Adhesive bandages
  - –Hospital linen
- Skin entry, devices
  - –Immunocompetent
  - –Immunocompromised

Fusarosis and Hospital Water

- *Fusarium* infections in an oncology center
  - ➢Investigation
    - *Fusarium* isolated from 57% cultures
      - –Sink drains, faucet aerators, shower heads, water tank
    - Molecular typing
      - –Some patient isolates matched environmental isolates

Anaissie. Clin Infect Dis 2001;33:1871-8

Aspergillus and Hospital Water

- *Aspergillus* detected in water supply
  - ➢Water-related surfaces (7%)
  - ➢Water samples (24%)
    - Water tank lines, shower drains, shower heads, toilet bowls
  - ➢Higher concentrations in air from bathrooms
- Genetic similarity of one environmental isolate with a patient isolate

Anaissie. Clin Infect Dis 2002;34:780-9

Healthcare-associated Mould Infections

Hosts:

Immunocompetent & Immunocompromised

Etiologies:

- *Aspergillus* spp.
- Phaeohyphomycoses
  - *Exserohilum, Bipolaris,* others
- *Mucorales* spp.
- *Fusarium* spp.
- *Scedosporium apiosperma*

Preventive Measures

- Protective environment in hospital for high risk patients BMT, severely granulocytopenic
- Minimize fungal spore counts
  - Point-of-use HEPA filtration
  - High rates of room air exchanges (> 12 AC/hr)
  - Directed airflow
  - Positive room air pressure relative to corridor
  - Well-sealed rooms
- Prevention of exposure to construction
- Remove plants, flowers, carpet from rooms
- Use of copper-8-quinolinolate

CDC guidelines for prevention of pneumonia, 2003; MMWR 2000

Preventive Measures

Prevention of exposure to construction

- Seal off transplant unit from construction site
- Clean newly constructed areas before patients enter
- Minimize aerosols
  - ➢ HEPA-filtered vacuums
  - ➢ Premoistened cloth wipes and mop heads
- Leave room only for essential procedures
- Pt use N95 mask when leaving room during periods of construction
  - – And/or avoid areas of construction
- Environmental cultures - not routine

CDC guidelines for prevention of pneumonia, 2003

Dust Control - Contractor Issues

Dust Control - Contractor Issues

Dust Control - Maintenance Issues

Environmental Controls

- Performance measures
  - Infection control risk assessment (ICRA)
  - Interprofessional team
    - Infection control, Engineering, Clinicians
  - Negative pressure in work zones
  - Positive pressure high risk areas
  - Provide construction crews entrances and services
  - Clean work zones daily
  - Frequent inspections for compliance
  - Include requirements in contract

Environmental Infection Control
MMWR 2003

Surveillance

- Active surveillance for invasive mould infections in immunocompromised pts
- Review microbiology data
- Periodic review of histopathologic and postmortem data
- If case(s) found
  - Epidemiologic investigation
  - Environmental inspection
  - Air sampling (not settle plates)

Environmental Infection Control
MMWR 2003

Preventive Measures

- Outside hospital
  - Chemoprophylaxis
  - ➢ Avoid exposure
    - Dusty environments
    - Construction
    - Chicken coops, caves
  - ➢ Prophylaxis
  - ➢ Avoid foods containing mould (blue cheese, pepper)

CDC guidelines for prevention of pneumonia, 2003; MMWR 2000

Approach to Fungal Infections

Prevention

- Prospective surveillance
- Prophylaxis
- Pre-emptive therapy

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MAY 2000
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FUNGUS FIGHTERS

BATTLING NOSOCOMIAL INFECTION RATE