





Fungal Outbreaks

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Overview

- Four outbreak scenarios will be presented
- Take-home messages will be discussed
- Questions from the audience will be entertained

Starting points for fungal outbreak investigation

- Gather epidemiological data on the outbreak
- Establish a case definition
- Determine possible hypotheses
- Define course of action to test the hypotheses

Tools for outbreak investigation

- Human assets
- Clinical microbiology laboratory
 - Identification
 - Strain typing
- Case studies
- Sampling
 - Environmental
 - Air

Role Players in a Fungal Outbreak Investigation

- Hospital Staff involved with the patients
- Hospital Infection Control Officers
- Hospital Laboratory Personnel
- Public Health Laboratory Personnel
- Public Health Epidemiologists
- Statisticians
- Regulatory Agencies?

Outbreak #1

- In March of 2013 CDC was contacted by Arizona Department of Public Health about a cluster of Aspergillus in Hospital A
 - Baseline was 2 Aspergillus cases/month
 - September 2012-March 2013 4.7 Aspergillus cases/month

An outbreak investigation was initiated

 Cases were defined as proven, probable, or possible Aspergillus spp infection on or after the third day of hospitalization in Hospital A between September, 2012 and March, 2013

Initial Assessment

Five patients isolates were available

• 3 Aspergillus tubingensis, 2 Aspergillus fumigatus

 Construction had been going on next door to the hospital

Initial assessment

Incidence of positive *Aspergillus* spp cultures, Hospital A, January 2011– March 2013



Questions for Outbreak #1

 Should environmental testing for Aspergillus be performed in the hospital?

Should the isolates be typed?

What other testing might be useful?

Environmental testing was performed

Sample location	Description	Sample Type	Number of samples	Fungal Growth		
Endoscopy back ro	om					
	Endoscope closet	Surface	3	Aspergillus niger		
	Vent	Surface	2	Aspergillus niger		
	Vent	Surface 2		Aspergillus spp		
	Bronch 19 holder	Surface	1	Aspergillus niger		
Patient room 1204						
	Vent	Swab	1	Aspergillus niger		
Patient room 1212						
	On table near window	Air	1	Aspergillus niger		
	Window sill edge	Surface	1	Aspergillus niger		
Patient room 1223						
	Vent	Swab	1	Aspergillus niger		
	Window sill edge	Surface	1	Aspergillus niger		
Patient room 1233						
	Vent over bed	Swab	2	Aspergillus niger		
Patient room 1235						
	Window sill	Surface	2	Aspergillus niger		
Basement hallway						
	West side of facility	Air	1	Aspergillus spp		

Particle counts were taken

HVAC reduction of particle counts was inconsistent

Location	Time & Date	85-90% reduction	2 µm	85-90% reduction	5 µm	85-90% reduction			
2nd Floor – Non-ICU									
HVAC Supply	4/4/13	127-191	691	69-104	136	14-20			
HVAC Supply	4/18/13	38-58	229 23-34		45	5-7			
Room 1223									
	9:58am 4/18/13	No	49	No	9	No			
	12:17am 4/18/13	Yes	32	Yes	7	Yes			
Room 1235									
	12:22pm 4/18/13		281 No		8	Yes			
Room 1233									
	9:58am 4/18/13	Yes	14	Yes	2	Yes			
Other 2 nd Floor									
HVAC Supply	4/4/13	111-166	588	59-88	118	12-18			
HVAC Supply	4/18/13	34-51	191	19-29	33	3-5			
Near elevator/connector									
	10:13am 4/4/13	Yes	107	No	22	No			
	12:36pm 4/18/13	No	139	No	9	No			

Recommendations

- Hire an environmental consultant to assist with remediation during construction
- Increase cleaning practices while construction is ongoing
- Increase surveillance for Aspergillus infection, especially in high risk patients

OUTBREAK #2

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Case History

- A 57-year-old man with multiple comorbidities undergoes a coronary aortic bypass surgery (left int mamm)
- Complicated postsurgical period
- Cardiogenic shock requiring an intraaortic balloon pump. Open sternum 4 days
- Reintervention due to cardiac tamponade







Outcome

- Some days later: Postsurgical mediastinitis
 - Cultures Aspergillus fumigatus and A. flavus







ospital General Universitario Gregorio Marañón



Postsurgical aspergillosis

NO UNDERLYING IMMUNOSUPPRESION NECESSARY

- Tissue damage or prosthetic material (188/500 MHS)
- Early manifestations
 - 14 d vs 45 d in HT
- Always exclude **air** contamination
- Outbreaks
 - Common participation of *nonfumigatus* species (mainly *A. flavus*)



Pacemaker



Eye surgery

Pasqualotto AC CMI 2006; RP Vonberg, JHI 2006; S. J. Vandecasteele, CID 2002₁₆

Environmental Air Monitoring

- Surveillance of air spores by volumetric air sampling (Merck MAS sampler)
- Air
 - Operating rooms: negative
 - ICU: 200 CFU/m3 Aspergillus
 - Genotypically identical
 - Microsatellite assay based on short tandem repeats (STRAf) (Guinea J, Klaassen C)



Air – Patient Relationship



Air – Patient Relationship



Aspergillus IN THE HOSPITAL AIR

Documento de consenso

Recomendaciones sobre la prevención de la infección fúngica invasora por hongos filamentosos de la Sociedad Española de Microbiología Clínica y Enfermedades Infecciosas (SEIMC)

Isabel Ruiz-Camps^a, Jose María Aguado^b, Benito Almirante^a, Emilio Bouza^c, Carmen Ferrer Barbera^a, Oscar Len^a, Lorena López-Cerero^d, Juan Luis Rodríguez-Tudela^e, Miguel Ruiz^f, Amparo Solé^g, Carlos Vallejo^h, Lourdes Vázquezⁱ, Rafael Zaragoza^j, Manuel Cuenca-Estrella^{e,*} y Grupo de Estudio de Micología Médica de la SEIMC (GEMICOMED)

Guidelines for the prevention of invasive mould diseases caused by filamentous fungi by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

I. Ruiz-Camps¹, J. M. Aguado², B. Almirante¹, E. Bouza³, C. F. Ferrer-Barbera¹, O. Len¹, L. Lopez-Cerero⁴,

J. L. Rodríguez-Tudela⁵, M. Ruiz⁶, A. Solé⁷, C. Vallejo⁸, L. Vazquez⁹, R. Zaragoza¹⁰ and M. Cuenca-Estrella⁵ GEMICOMED (Medical Mycology Study Group of SEIMC)

Aspergillus IN THE HOSPITAL AIR

Outdoor air Range 0-105 c.f.u. / m³ Unprotected hospital air 5-25 c.f.u. / m³

HEPA filtered air

<0.1 c.f.u. / m³

Ruiz-Camps et al. CMI 2011

Ruiz-Camps et al. EIMC 2010

Outbreak of Invasive Aspergillosis After Major Heart Surgery Caused by Spores in the Air of the Intensive Care Unit



T. Peláez,^{12,3} P. Muñoz,^{12,3} J. Guinea,^{12,3} M. Valerio,^{1,2} M. Giannella,^{1,2} C. H. W. Klaassen,⁴ and E. Bouza^{1,2,3}

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Clinical Infectious Diseases 2012;54(3):e24-e31

Air – Patient Relationship

• 10 patients with proven IA (n=2), probable IA (n=4), and

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colonized (n=4) by A. fumigatus
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- Not severely immunocompromised (two with COPD)
- Environmental control in the air of the unit
- Clinical (n=108) and environmental (n=59) isolates
- Molecular genotyping (STRAf)



Patient	Age, Years (Sex)	Surgery Date	IA Diagnosis Date (Days After Surgery)	Underlying Condition	Procedure	Clinical Manifestation	Treatment	Clinical Outcome
1	57 (male)	3 December 2006	9 December 2006 (6)	Diabetes mellitus, postsurgical ventricular dysfunction	Cardiac bypass surgery, additional surgery due to hemorrhage	Mediastinitis	CAS and surgical drainage	Death
2	52 (male)	7 May 2007	23 May 2007 (16)	FK and MMF, corticosteroids, hypogammaglobulinemia, prolonged MV, CAVHF	Heart transplantation	IPA	CAS and VOR	Death
3	56 (female)	11 September 2007	15 September 2007 (4)	FK and MMF, corticosteroids, breast cancer, multiorgan failure	Emergency heart transplantation after CABG and ventricular assistance	IPA	CAS	Death
4	82 (female)	10 October 2007	13 October 2007 (3)	COPD, chronic renal failure, myeloma, corticosteroids, CAVHF	Valve replacement and bypass	IPA	CAS and VOR	Death
5	82 (female)	11 January 2008	18 February 2008 (38)	Asthma, corticosteroids, CAVHF	Valve replacement	IPA	No treatment	Death
6	84 (female)	11 January 2008	24 March 2008 (72)	Diabetes mellitus, prolonged MV, additional surgery, hypogammaglobulinemia	Valve replacement	IPA	CAS and VOR	Death
7	57 (female)	25 February 2008	15 April 2008 (49)	FK and MMF, corticosteroids, COPD, hypogammaglobulinemia, CMV disease, CAVHF	Heart transplantation, additional surgery	Mediastinitis and IPA	CAS and VOR	Survival



Clinical Infectious Diseases 2012;54(3):e24-e31

Air – Patient Relationship

JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2011, p. 3498–3503 0095-1137/11/\$12.00 doi:10.1128/JCM.01159-11 Copyright © 2011, American Society for Microbiology. All Rights Reserved. Vol. 49, No. 10

Molecular Epidemiology of *Aspergillus fumigatus*: an In-Depth Genotypic Analysis of Isolates Involved in an Outbreak of Invasive Aspergillosis[∇]

Jesús Guinea,^{1,2,3,4}* Darío García de Viedma,^{1,2,3} Teresa Peláez,^{1,2,3,4} Pilar Escribano,^{1,2,3} Patricia Muñoz,^{1,2,3,4} Jacques F. Meis,⁵ Corné H. W. Klaassen,⁵ and Emilio Bouza^{1,2,3,4}

MAJOR ARTICLE

Outbreak of Invasive Aspergillosis After Major Heart Surgery Caused by Spores in the Air of the Intensive Care Unit

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Aspergillus IN THE HOSPITAL AIR



Nosocomial or Communityacquired?

59 years. Heart transplant. No risk facto

Discharged day +22.

- Readmitted day +29.
- **340-385** c.f.u./m³ on day + 7





- Similar genotypes in air and respiratory samples
- Incubation period: 18-25 days

Muñoz P et al. Transplant Infect Dis 2004

Australian Dust Storm Associated with Extensive Aspergillus sydowii Fungal "Bloom" in Coastal Waters

Gustaaf Hallegraeff,^a Frank Coman,^b Claire Davies,^b* Aiko Hayashi,^a David McLeod,^c Anita Slotwinski,^b Lucy Whittock,^a Anthony J. Richardson^{b,d,a}

- Abundant fungal spores
 (150,000/m3) and hyphae
 in coastal waters between
 Brisbane (27°S) and Sydney
 (34°S)
- A. sydowii (coral fan disease in the Caribbean)
- NO human or animal diseases reported





In this case

- Only one unit involved
- Although all the patients had been operated on, infection was acquired in the ICU not in the OR
- Outbreak control required major renovation of the air conditioning system of the ICU
- Molecular identity between environmental and clinical samples



Questions for Outbreak #2

- Cultures or particle counting?
- Air cultures: systematical or only when an outbreak is detected?
- Just inform CFUs of molds or each species?
- Risk cut-off?

Outbreak #3

- July, 2012
- 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

Outbreak #3

- November 22, 2013
- Texas Department of State Health Services again called CDC
 - Discuss 2 additional cases of *Bipolaris* SSI in CT surgery patients at Hospital A
 - Hospital B now reports 4 cases
 - Hospital B knew of an additional case at Hospital C in neighboring Arkansas

Initial assessment

- Patients with *Bipolaris* were exclusively SSI in CT post-op patients
 - This became the case definition

No SSI with other molds in CT patients

 No Bipolaris infections seen in patients who underwent other types of surgery

Epidemic Curve

- Bipolaris cases between 2008 and 2013 meeting the case definition of a SSI in a CT post-op patient
 - 21 case-patients with culture-confirmed Bipolaris
 - 10 different hospitals
 - 3 states

Hypotheses

Common medical device/product

- Topical agents used in chest
- Compounding pharmacy products

Related to change in surgical practices

• SSIs are increasing in general and *Bipolaris* is being isolated because of general increase in SSIs.

Uncovering baseline rates of this infection

• It was there all along and we're just now finding it

Environmental

- Fungal bloom of *Bipolaris* in the Southern US over recent years due to environmental changes
- Construction activities at these hospitals

Questions for Outbreak #3

 Should environmental testing be performed in the hospitals?

Should the Bipolaris isolates be typed?

Environmental testing was not performed

- Multi-hospital outbreak, each hospital with its own conditions
- Isolates could be gathered from other sources such as sinus infections, wounds and nails

The isolates were typed

- Typing would allow us to rule in or out the possibility of a contaminated product
- No typing system existed for Bipolaris
- A multilocus sequence typing system was created



Hypotheses

- Common medical device/product
 - No common product among all patients
- Related to change in surgical practices
 - No increase in SSIs in any hospitals 2008-2013
- Uncovering baseline rates of this infection
 - An increase in *Bipolaris* was also seen in non-surgical infections
- Environmental
 - Only hypothesis that could not be ruled out

Overall increase in *Bipolaris* **isolates**

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



Sinus Eye Respiratory Skin/wound/nail Other

Recommendations

- Increase vigilance for infection; have a low threshold for suspicion
- Restrict movement in and out of operating rooms during procedures
- Increase infection control practices
- House patients with open chests in positive pressure rooms

OUTBREAK #4

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Outbreak # 4

3 MHS patients from the same unit develop fungemia caused by a «strange» yeast between 15-30 April





S. cerevisiae



hoporqp siteongpid

• Outbreak?

Case definition



Review of the 3 cases

Age/Sex	Underlying condition	Nutrition	IV Cat	Sb	Days	ABS	Other cultures	Disease	ττο	Died
76/M	Diabetes, MHS, ICU complications	TPN and E	yes	yes	9	Ceftriaxone, Metronidazole	Catheter	PVE	Flu	Yes
72/M	MHS, ICU complications	TPN and E	yes	yes	7	Vancomicin, Meropenem, Metronidazole	Hub	Fungemia	No	Yes
74/M	Rheumatoid arthritis. MHS, ICU complications	TPN and E	yes	yes	8	Vancomicin, rifampin Meropenem, ciprofloxacin, Metronidazole	-	Fungemia	Flu	Yes

Attitude

1. Cultured Ultralevura® capsules (*Saccharomyces boulardii*) from the unit

2. 5. cerevisae clinical samples and capsule samples sent to a Reference laboratory

- 3. Probiotics banned in the unit
- 4. Case control study (3 vs 41)
- 5. Rectal and pharyngeal swab to all patients of the unit
- 6. Literature review

Capsules culture

5. boulardii = 5. cerevisiae



Registered as *S. cerevisae* CBS 5926



Molecular study

Identical



Dr. Manuel Cuenca Estrella

Other results

Colonization study: negative

Case control study: Ultralevura 3/3 cases (media 8 d) and 2/41 controls

Outcome: no further case

MAJOR ARTICLE

Saccharomyces cerevisiae Fungemia: An Emerging Infectious Disease

Patricia Muñoz,¹ Emilio Bouza,¹ Manuel Cuenca-Estrella,³ Jose María Eiros,¹ Maria Jesús Pérez,² Mar Sánchez-Somolinos,¹ Cristina Rincón,² Javier Hortal,² and Teresa Peláez¹

Departments of 'Clinical Microbiology and Infectious Diseases and ²Heart Surgery, Hospital General Universitario "Gregorio Marañón," Universidad Complutense, and ³Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain Review of the literature

- (zsitoidorg & EE) zszbs 06 -
 - Fungemia (49; 82%)
 - Endocarditis or periaortic abscess (5)
 - Disseminated disease (4)
 - Liver abscess, esophageal ulcer (1 each)

- Also

- Empyema, pneumonia, vaginitis, peritonitis, UTI, celullitis, FUO, septic shock
- Crohn (S 50%, E 90%), asthma, ulcerative colitis, diarrhea





Ultralevura[®] in the ICU Capsules are opened and solved Administered through the NG tube Viable yeast recovered at 1 meter 2 hours later Persist in the hands of HCWs even after washing

Questions for Outbreak #4

- Careful with probiotics in critical patients
- Viable microorganisms stay in the surfaces for a long time and may contaminate the IV catheters

Recommendations

 High concentration of air spores should be considered another risk factor for IA.

 More collaborative studies are needed, since there are still many aspects to clarify.

Multidisciplinary efforts are needed to control a fungal outbreak.

Acknowledgements

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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.

National Center for Emerging and Zoonotic Infectious Diseases Division of Foodborne, waterborne and Environmental Diseases

