ECCMID

Vienna, Austria
10–13 April 2010

ESCMID Young Investigator Award 2010

Aspergillus and Aspergillosis: From the Environment to the Patient

Dr. Jesús Guinea
Clinical Microbiology and Infectious Diseases Department
Hospital Gregorio Marañón
Madrid (Spain)

Educational Background

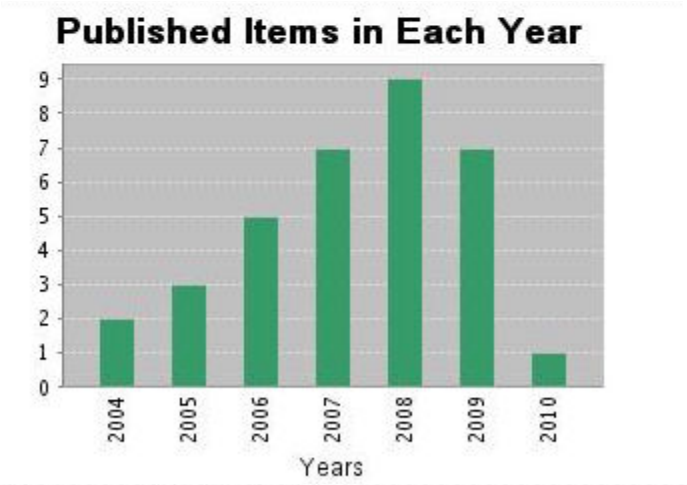
- BSc in Pharmacy (1996). University of Navarra
- Training period in Clinical Microbiology (1998). Gregorio Marañón Hospital (Madrid)
- Starting research in mycology (2002) and completed PhD (2005)

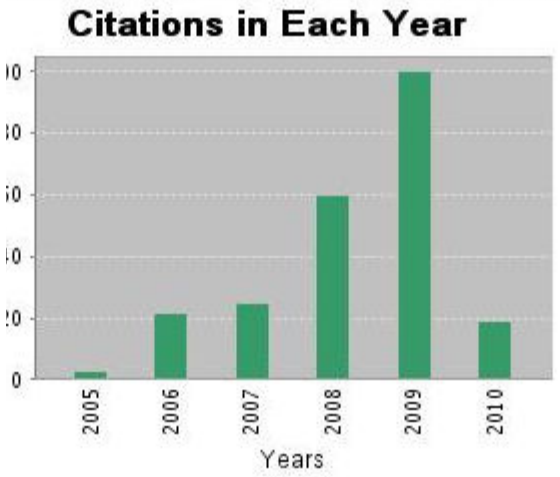
Principle Professional Influences

- **Dr. Emilio Bouza (Madrid, Spain)**
- **Dr. David W. Denning (Manchester, UK)**
- **Dr. Corné Klaassen (Nijmegen, the Netherlands)**
- **Dr. Darío García de Viedma (Madrid, Spain)**

Scientific Credentials

- 34 articles published in international journals
  - ✓ JCM / AAC: 9
  - ✓ Med Mycol: 6
  - ✓ CMI: 3
  - ✓ JAC / CID: 2
  - ✓ Other: 14
- Hirsch index: 9





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Main Research in Mycology

- Antifungal susceptibility testing
- Diagnosis of invasive fungal infections
- Molecular genotyping
- Environmental aspects of *Aspergillus*
- Epidemiology of invasive fungal infections

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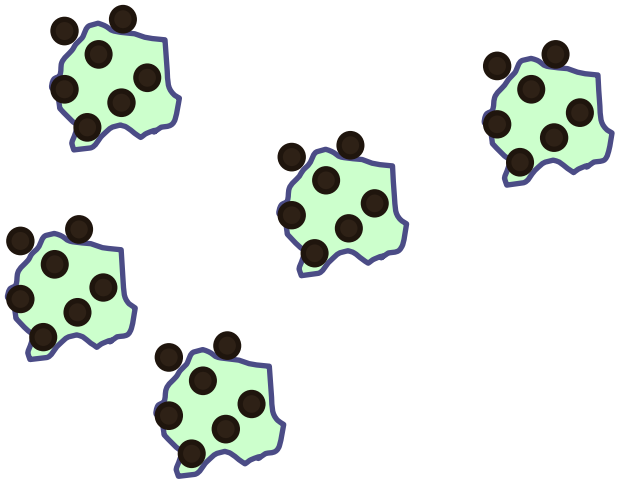
Aspergillus and Aspergillosis

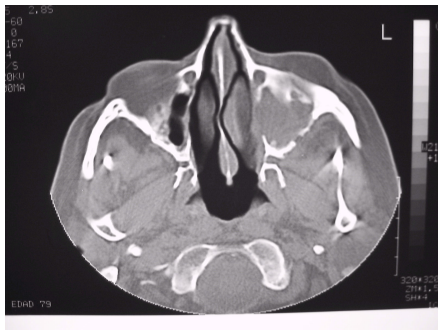
1. What are the normal loads of *Aspergillus* in the air?
2. What is the air-patient relationship?
3. Are there azole-resistant *Aspergillus fumigatus* isolates in the air of Madrid?
4. Are there new populations at risk of invasive aspergillosis?

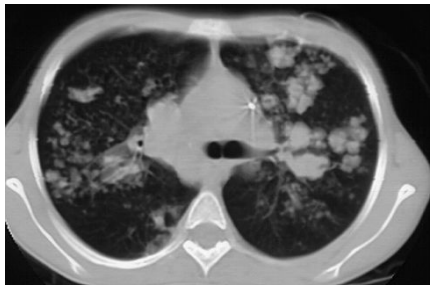
BIOAEROSOLS

OUTDOOR/HOSPITAL AIR

PATIENTS







What Are the Normal Levels of Molds and *Aspergillus* Conidia in the Air Under Normal and Special Conditions?

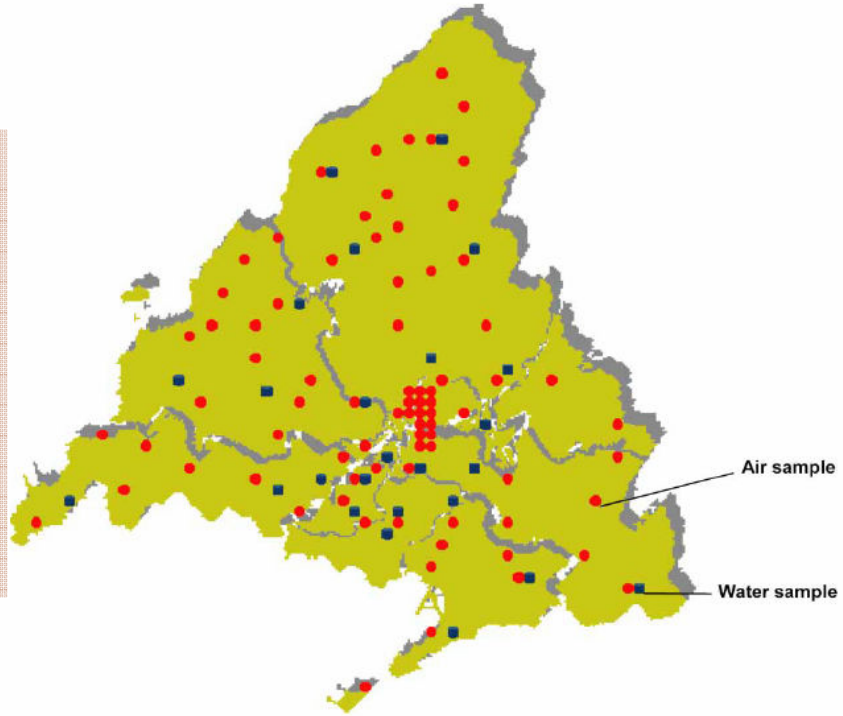
Aspergillus in the Air of Madrid

Outdoor environmental levels of *Aspergillus* spp. conidia over a wide geographical area

JESÚS GUINEA, TERESA PELÁEZ, LUIS ALCALÁ & EMILIO BOUZA

Clinical Microbiology and Infectious Diseases Department, Hospital General Universitario 'Gregorio Marañón'. Universidad Complutense, Madrid, Spain

Province of Madrid
Rural and urban environment
332 samples of air
148 samples of water
4 seasons



Guinea et al. Med Mycol 2006

Aspergillus in the Air of Madrid

	Filamentous fungi	*Aspergillus*	*Aspergillus fumigatus*
Range	**0-685**	**0-85**	**0-70**
Median	**35-105**	**0-5**	**0**

Differences between seasons (highest in autumn)

Meteorological parameters

No water samples positive for *Aspergillus*

Guinea et al. Med Mycol 2006

Molds in the Hospital Air

Acremonium

Alternaria

Epicoccum

Rhinocladiella

Beauveria

Aspergillus

Cladosporium

Penicillium

Scedosporium

Zygomycetes

Fusarium

A. niger

A. flavus

A. fumigatus

A. versicolor

A. terreus

Richardson et al. J Hosp Infect 2000

Faure et al. J Hosp Infect 2002

Panagopoulou et al. J Hosp Infect 2002

Perdelli et al. Infect Cont Hosp Epidemiol 2006

Falvey et al. J Hosp Infect 2007

Satour et al. J Hosp Infect 2007

Fungal Load in the Hospital Air

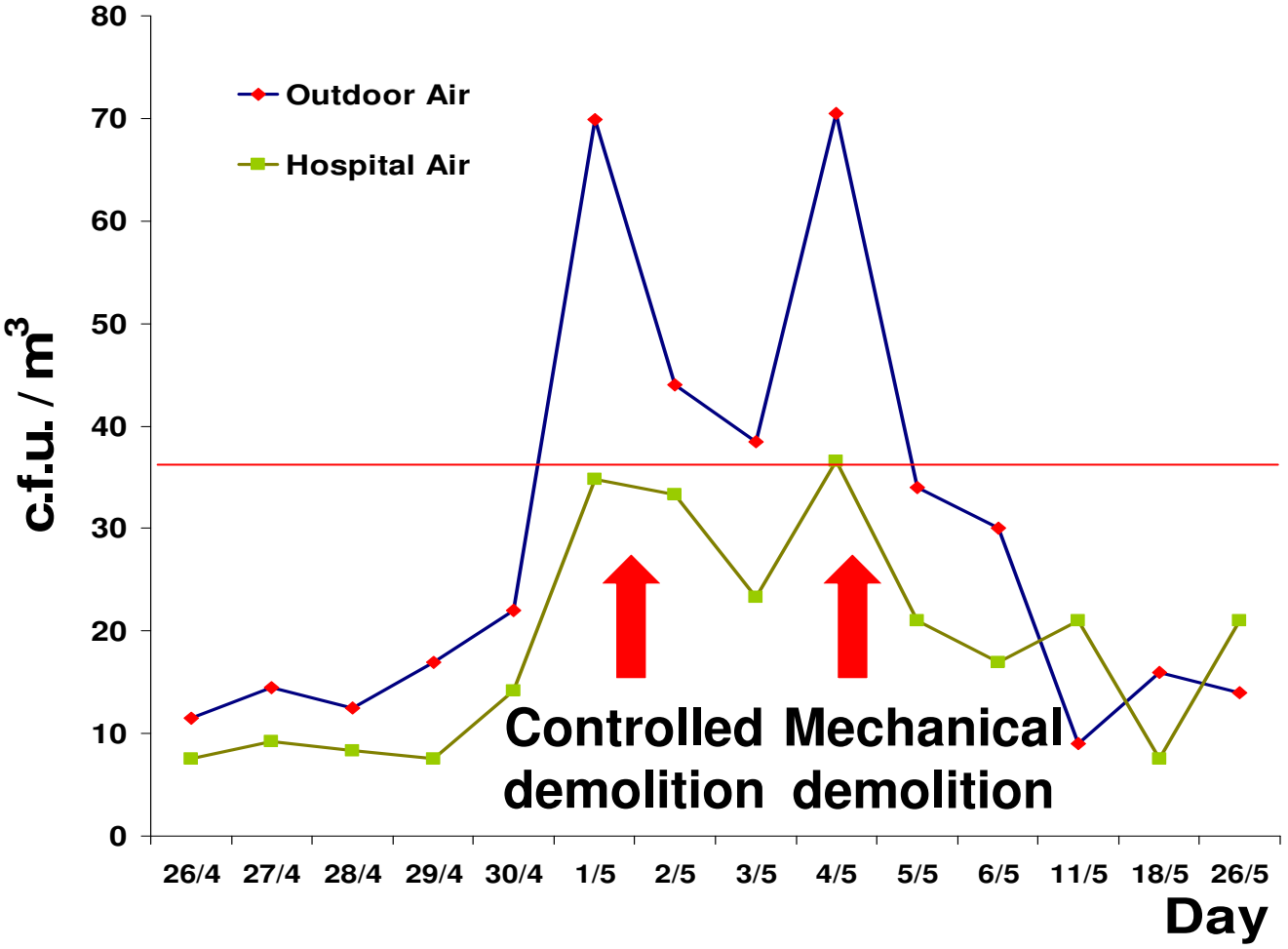
	Protected areas	Non-protected areas	Outdoor
Falvey 2007	1.4 (0-25)	21	50 (0-2540)
Perdelli 2006	5 (1-45)	10 (1-55)	57 (5-172)
Curtis 2005	41 (0-260)	53.2 (0-724)	257.8 (10-1340)
Bouza 2002	0	11.3 (0-35)	17.6 (5-40)
Panagop. 2002	No Data	1.3-22.6 (1.2-37)	No Data

Fungal Load in Air: Building Work


detecsa
CAVOSA


HOTEL

Fungal Load in Air: Building Work



Fungal Load in Air: Building Work

Demolition of a hospital building by controlled explosion: the impact on filamentous fungal load in internal and external air

E. Bouza, T. Peláez, J. Pérez-Molina, M. Marín, L. Alcalá, B. Padilla, P. Muñoz and the Aspergillus Study Team*

**Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario 'Gregorio Marañón', University of Madrid, Madrid, Spain*

Bouza et al. J Hosp Infect 2002

Normal Loads: Outdoor and Hospital

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 Vázquez [i], Rafael Zaragoza [j], Manuel Cuenca-Estrella [e,*] y Grupo de Estudio de Micología Médica de la SEIMC (GEMICOMED)

Outdoor air

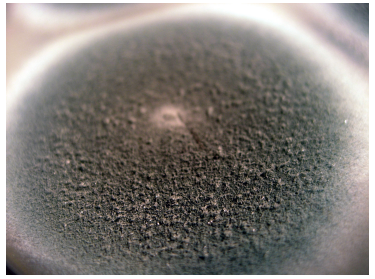
Range 0-105 c.f.u. / m^3

Unprotected hospital air

5-25 c.f.u. / m^3

HEPA filtered air

<0.1 c.f.u. / m^3



Ruiz-Camps et al. EIMC 2010

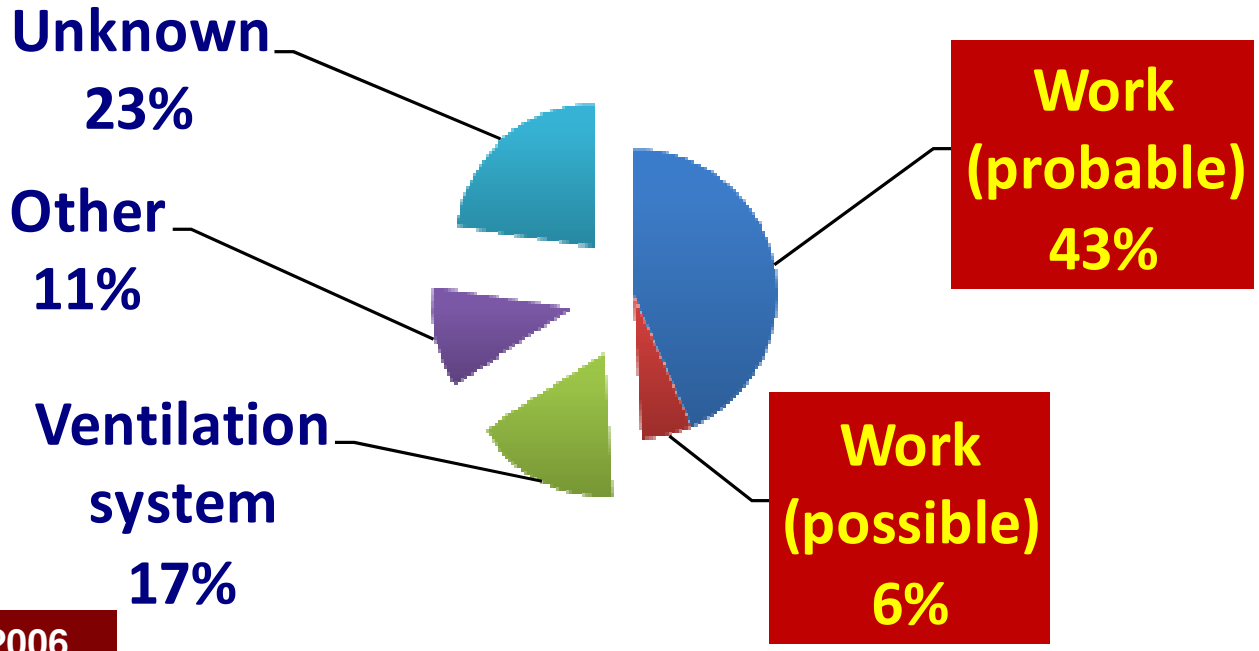
What Is the Air-Patient Relationship?

Air–Patient Relationship

- **INDIRECT (epidemiology)**
  1. Nosocomial outbreaks during building works
  2. Reduction of cases with air treatment with HEPA filtration
- **DIRECT**
  1. High levels - Higher risk
  2. Genotyping Clinical - Air isolates

Nosocomial Outbreaks: Indirect

- Outbreak database (www.outbreakdatabase.com)
- 53 outbreaks from 1966 to 2005
- 458 patients ► 65.3% hematological
- Most IPA



Vonberg et al. J Hosp Infect 2006

HEPA-Filtered Air: Indirect

- Tertiary hospital (Lyon)
- 3 units. One was relocated
- Impact on the incidence of IFI

	Re-located unit	Control units
Before	9 (13.2%)	Similar
After	1 (1.6%)	Similar

Benet et al. CID 2007

High Levels – Higher Risk: Genotyping

Case report

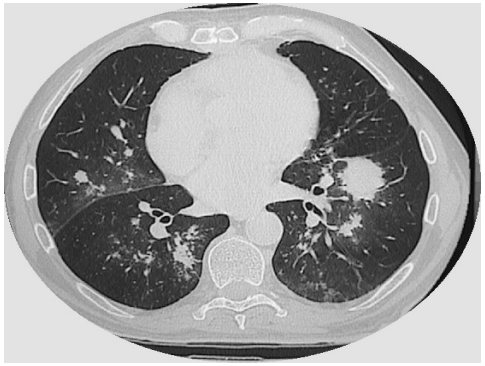
P. Muñoz
J. Guinea
T. Peláez
C. Durán
J.L. Blanco
E. Bouza

Nosocomial invasive aspergillosis in a heart transplant patient acquired during a break in the HEPA air filtration system

Muñoz P, Guinea J et al. Transplant Infect Dis 2004

High Levels – Higher Risk: Genotyping

- 59 years. Heart transplant recipient
- Low risk of IA
- **340-385** c.f.u./m^3
- Follow-up and IPA diagnosis
- Similar genotypes in air and respiratory samples
- **Incubation period: 20-25 days.**



Muñoz P, Guinea J et al. Transplant Infect Dis 2004

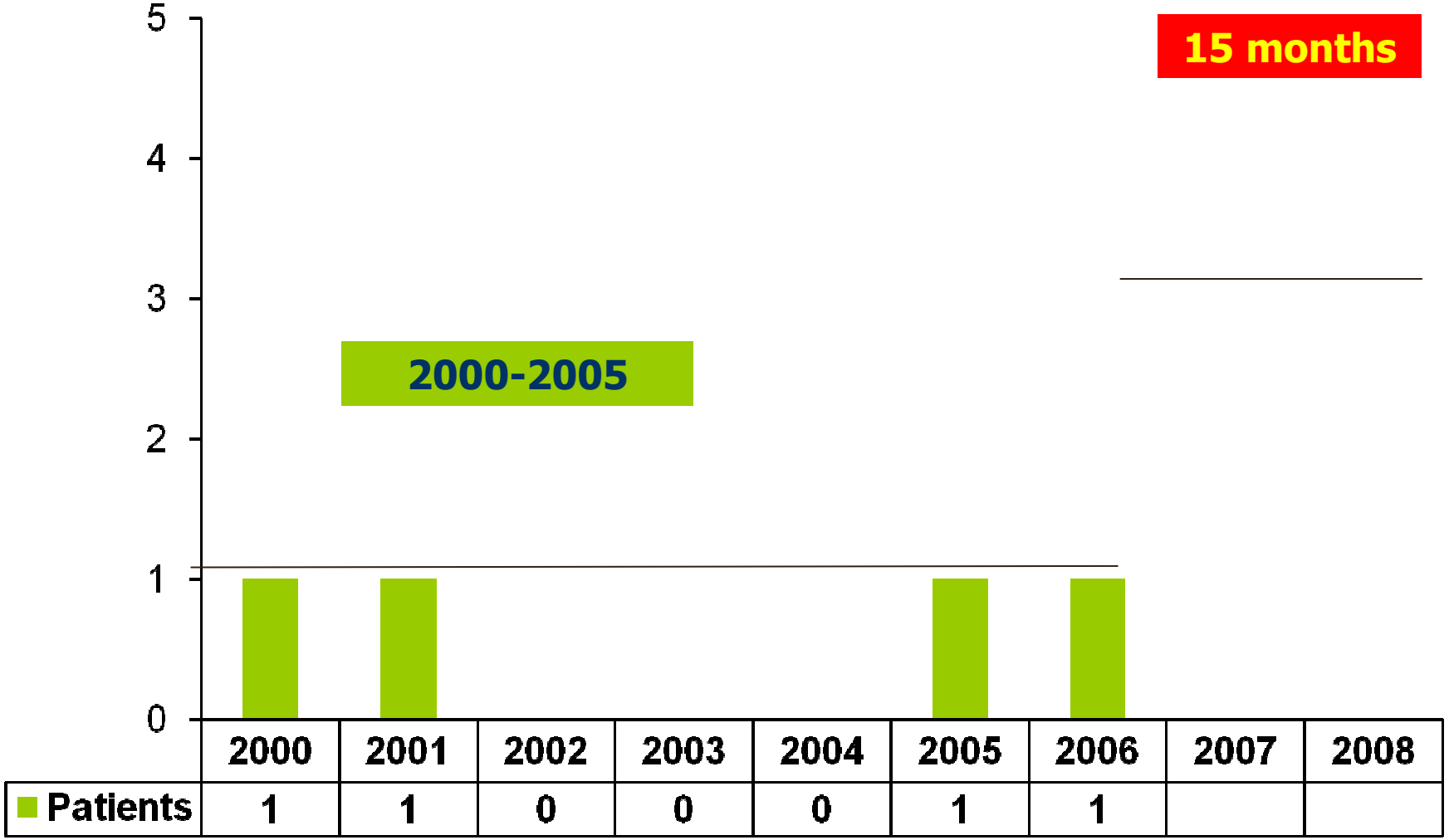
High Levels – Higher Risk: Direct

Outbreak of Invasive Aspergillosis in an Intensive Care Unit (ICU) for Major Heart Surgery (MHS). The Case for Abnormally High Levels of Airborne *Aspergillus* Conidia: Presence of Similar Genotypes in Air and Clinical Samples

Peláez T, Guinea J, Klaassen C, Meis J, Muñoz P, García de Viedma D, Flores R, Gama B, Recio S and Bouza E

Peláez et al. ECCMID 2009 (O-244)

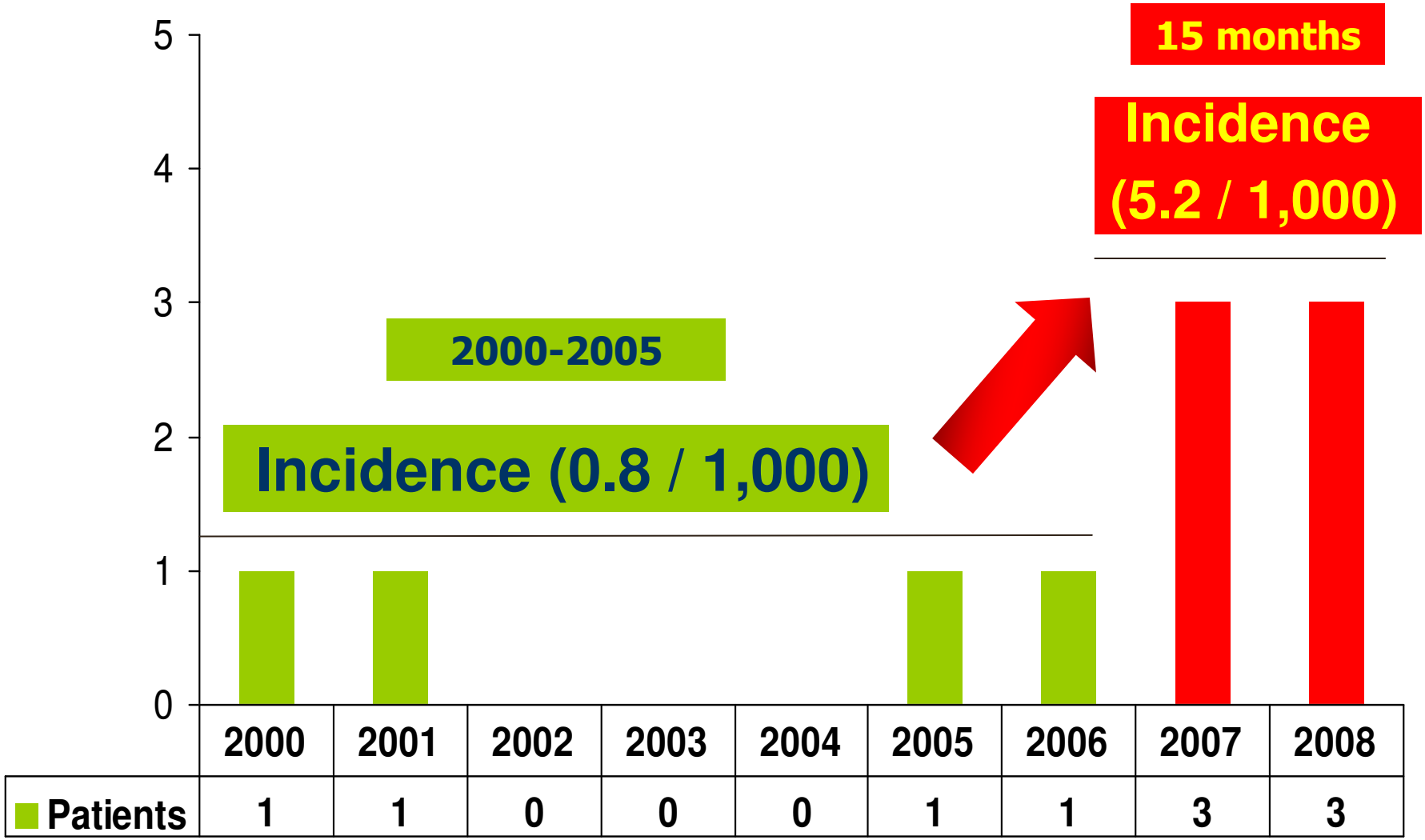
High Levels – Higher Risk: Direct



	2000	2001	2002	2003	2004	2005	2006	2007	2008
Patients	1	1	0	0	0	1	1		

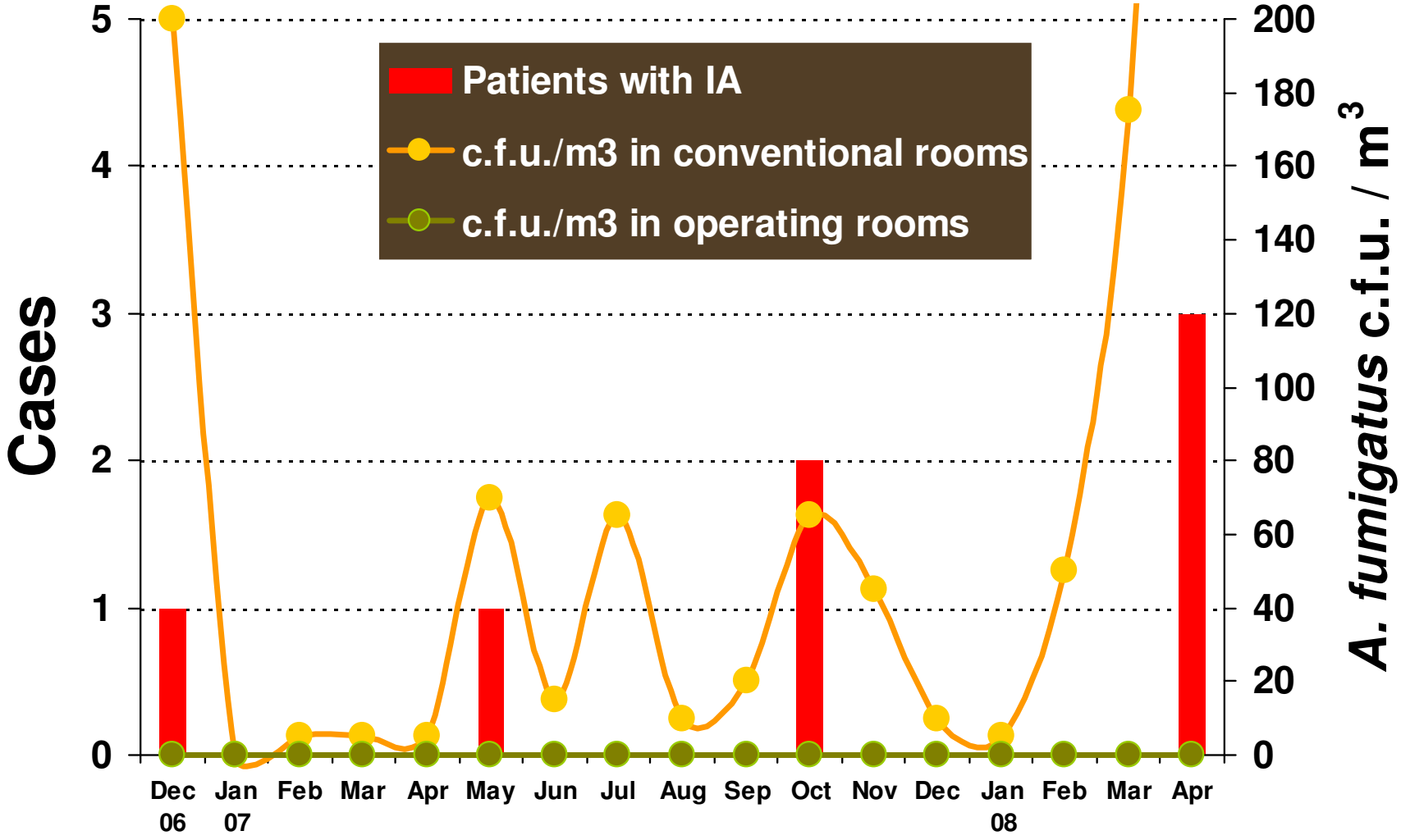
Peláez T, Guinea J et al. ECCMID 2009 (O-

High Levels – Higher Risk: Direct



Peláez T, Guinea J et al. ECCMID 2009 (O-

High Levels – Higher Risk: Direct



Peláez T, Guinea J et al. ECCMID 2009 (O-

High Levels – Higher Risk: Genotyping

223 *A. fumigatus* clinical and environmental isolates. Molecular genotyping (STR*Af*)

Patient	Diagnosis	Related genotypes air-patient
1	Mediastinitis	+
2	IPA	-
3	IPA	Not genotyped
4	IPA	+
5	IPA	-
6	IPA	-
7	Mediastinitis	+

Are There Azole-Resistant *Aspergillus* Isolates in the Air of Madrid?

Aspergillus: Resistance to Azoles

Antifungal Susceptibility of 596 *Aspergillus fumigatus* Strains Isolated from Outdoor Air, Hospital Air, and Clinical Samples: Analysis by Site of Isolation

J. Guinea, T. Peláez, L. Alcalá,* M. J. Ruiz-Serrano, and E. Bouza

Clinical Microbiology and Infectious Diseases Department, Hospital General Universitario "Gregorio Marañón," University of Madrid, Spain

- 175 outdoor isolates (2002-2003)
- 135 hospital air isolates (1994-2003)
- 286 clinical isolates (1999-2003)
- Itraconazole, voriconazole, and posaconazole

Guinea J et al. Antimicrob Agents Chemother 2005

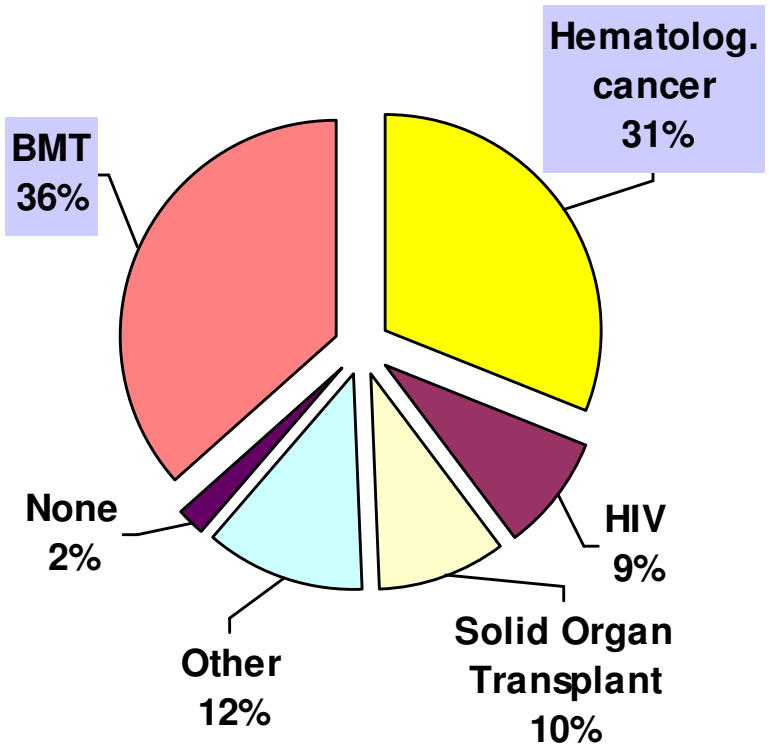
Aspergillus: Resistance to Azoles

- All strains showed a MIC ≤ 2 µg/ml
- No differences in susceptibility of isolates:
  - by site of isolation
  - from infected vs. colonized patients

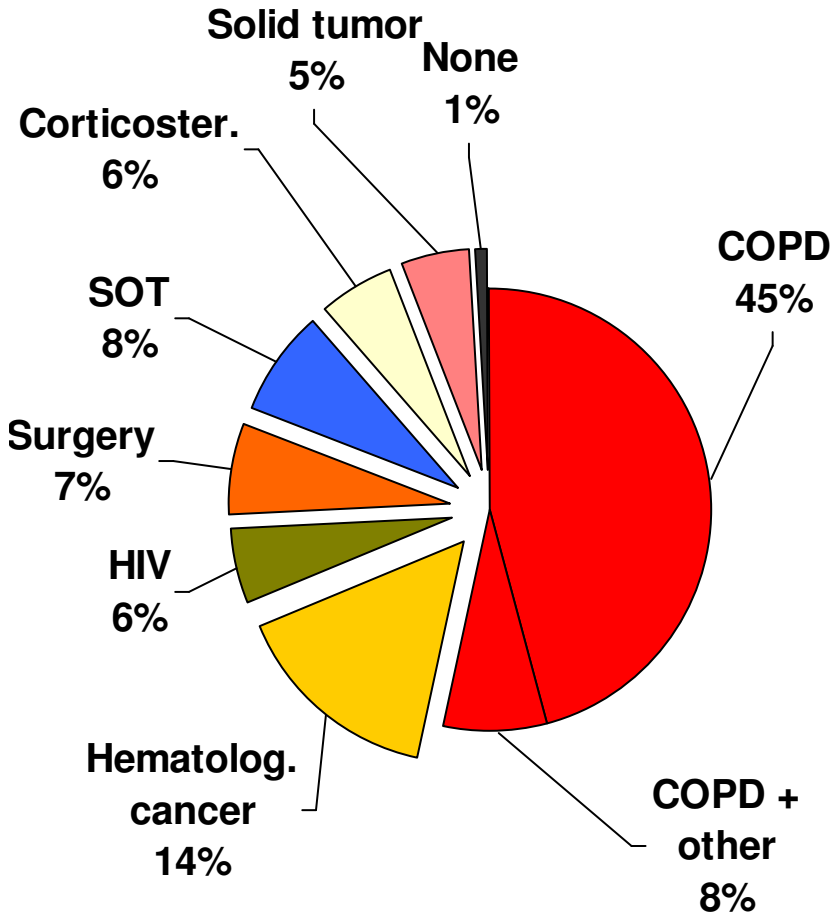
Guinea J et al. Antimicrob Agents Chemother 2005

Are we really finding invasive aspergillosis outside the hematological setting?

Invasive Aspergillosis: Epidemiology



Patterson T et al. Med (Balt) 2000



Guinea J et al. ICAAC 2008 (M-717)

Invasive Aspergillosis: COPD

ORIGINAL ARTICLE 10.1111/j.1469-0691.2009.03015.x

Pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: incidence, risk factors, and outcome

J. Guinea[1,2], M. Torres-Narbona[1], P. Gijón[1], P. Muñoz[1,2], F. Pozo[2,3], T. Peláez[1,2], J. de Miguel[4] and E. Bouza[1,2]

1) Clinical Microbiology and Infectious Diseases Department, Hospital General Universitario Gregorio Marañón, Universidad Complutense, 2) CIBER de Enfermedades Respiratorias (CIBERES CD06/06/0058), Palma de Mallorca, 3) Pneumology Department and Clinical Epidemiology Unit, Hospital Universitario Doce de Octubre and 4) Pneumology Department. Hospital General Universitario Gregorio Marañón. Universidad Complutense. Madrid. Spain

Retrospective

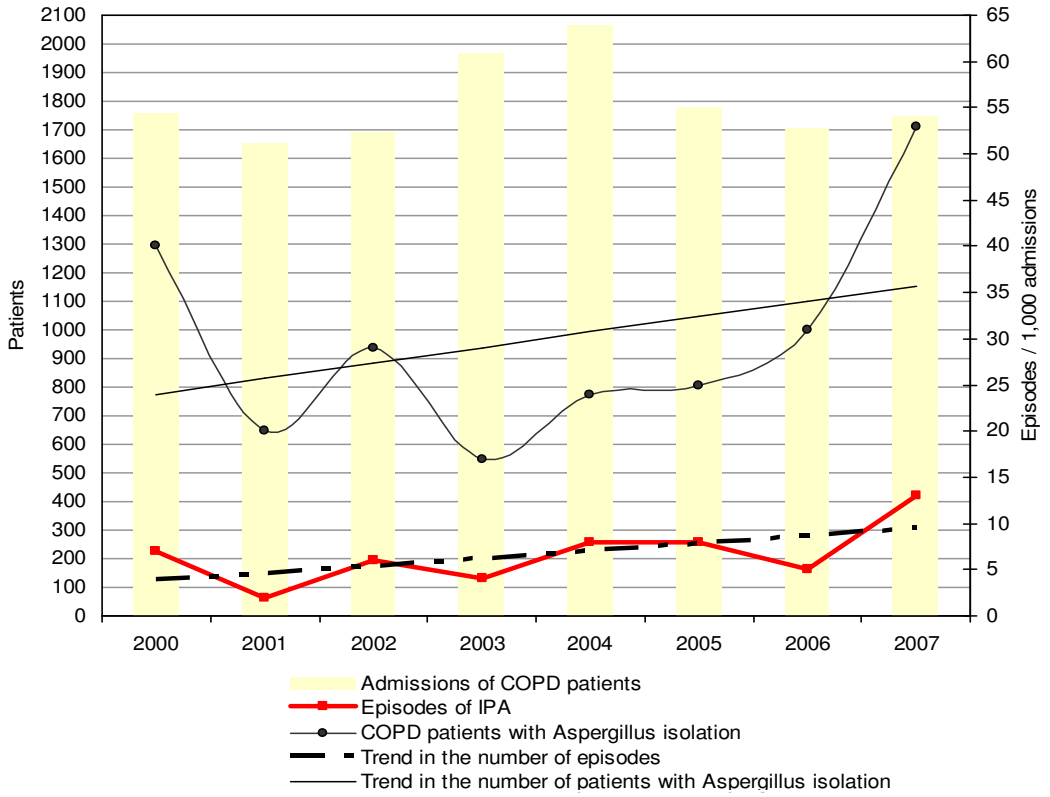
2000 – 2007

Patients with COPD and *Aspergillus* in lung

53 cases of probable IPA

Guinea J et al. CMI 2010

Invasive Aspergillosis: COPD



Patients in non-protected areas and no prophylaxis!!

Guinea J et al. CMI 2010

Invasive Aspergillosis: Surgery

Post-surgical invasive aspergillosis: An uncommon and under-appreciated entity☆

Julia Jensen [a], Jesús Guinea [a,b,*], Marta Torres-Narbona [a], Patricia Muñoz [a,b], Teresa Peláez [a,b], Emilio Bouza [a,b]

7 cases of post-surgical IA (1999 to 2006):

3 proven and 4 probable.

2 cases / 10,000 surgical interventions

10% of all cases of IA in our hospital

Jensen J, Guinea J et al. J Infect 2010

Invasive Aspergillosis: Surgery

Year	*Aspergillus* in operating rooms	*Aspergillus* in ward admissions
2000	-	Non-protected
2000	ND	Non-protected
2000	-	95 c.f.u. / m^3
2002	-	Non-protected
2003	ND	Non-protected
2003	-	Non-protected
2006	-	200 c.f.u. / m^3

MEDIASTINITIS AFTER HEART SURGERY

Jensen J, Guinea J et al. J Infect 2010

Our Future Research Lines in *Aspergillus* and Aspergillosis

Future Research Lines

1. **Better understanding of epidemiology**
   - **Molecular identification of *Aspergillus***
2. **Improvement of diagnosis**
   - **PCR and GM on respiratory samples**
3. **Improvement of antifungal treatment**
   - **Detection of azole resistance (*cyp51A*)**
   - **Monitoring serum azole levels (HPLC)**

Acknowledgements

All my family

All my friends

Dra. Patricia Muñoz

Dra. Teresa Peláez

Dra. Marta Torres Narbona

Dra. Pilar Escribano

Sandra Recio

Mercedes Marín

Luis Alcalá

Rocío Fernández

To all my colleagues of the Department of Clinical Microbiology, Hospital "Gregorio Marañón"