Occupational exposures and diseases

Raquel Sabino
Department of Infectious Diseases
Reference Unit for Parasitic and Fungal Infections
Summary

• Occupational exposure and sources of fungal exposure

• *Aspergillus* exposure

• Diseases associated with *Aspergillus* occupational /indoor exposures

• Case studies on *Aspergillus* occupational exposure
Occupational exposure vs. development of fungal disease

- **Oral**
  - Contaminated food

- **Inhalation**
  - Aerosols in the air

- **Dermal**
  - Physical contact with contaminated materials

**Exposure**

**Adverse Health Effects**

**Mild**
- Runy Nose
- Sneezing
- Coughing
- Congestion
- Sore Throat
- Itchy Eyes
- (…)

**Severe**
- Sinus Infection
- Asthma
- ABPA
- SAFS
- Rhinosinusitis
- Hypersensitivity pneumonitis
- Cancer
- Death
Occupational exposure vs. development of fungal disease

Exposure

- Oral
  - Contaminated food
- Inhalation
  - Aerosols in the air
- Dermal
  - Physical contact with contaminated materials

Fungal Species (including toxinogenic potential)
Fungal Load
Environment
Exposed Person worker

Adverse Health Effects

- Temperature, humidity…
- Presence of large amounts of dust and particles

Exposed Person worker

Health Effects

- Immune system
- Personal features (gender, genetic background, smoking, medication…)
- Previous respiratory condition
Exposure to Fungal conidia

Home
Workplace
During hospitalization (especially during construction or renovation work)
Occupational exposures to fungi

Most important fungi related with fungal exposure:

- Cladosporium
- Alternaria
- Stachybotris
- Penicillium
- Aspergillus
**Aspergillus conidia**

With dry wall spores, dessication-resistant

- Very light
- Produced in large amounts
- Easy to dissociate
- Very easy to disperse
- Long time in the air, associated to other particles
- Easily airborne and inhaled

---

**Why are Aspergillus so commonly found in occupational environments?**

- Ability to grow at a high range of temperatures
- High nutritional versatility
- Moisture environments
- Good growth on a high variety of construction materials (concrete, acrylic paints, wood based and cellulose based materials)
- Associated with decomposing organic mater
Major route of occupational disease is inhalation

<table>
<thead>
<tr>
<th>Particle size</th>
<th>Fate</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 - 30 µm</td>
<td>visual pollution</td>
</tr>
<tr>
<td>5.5 - 9 µm</td>
<td>settle in nose/throat</td>
</tr>
<tr>
<td>3.3 - 5.5 µm</td>
<td>lodge in main breathing passages</td>
</tr>
<tr>
<td>2 - 3.3 µm</td>
<td>lodge in small breathing passages</td>
</tr>
<tr>
<td>1 - 2 µm</td>
<td>lodge in bronchi</td>
</tr>
<tr>
<td>0.3 - 1 µm</td>
<td>penetrate to bronchioles and alveoli</td>
</tr>
<tr>
<td>0.1 - 0.3 µm</td>
<td>penetrate to bronchioles and alveoli</td>
</tr>
</tbody>
</table>
**Aspergillus conidia**
With dry wall spores, dessication-resistant

Very light

Produced in large amounts

Easy to dissociate

Very easy to disperse

Long time in the air, associated to other particles

Easily airborne and inhaled

**Why are Aspergillus so commonly found in occupational environments?**

- Ability to grow at a high range of temperatures
- High nutritional versatility
- Moisture environments
- Good growth on a high variety of construction materials (concrete, acrylic paints, wood based and cellulose based materials)
- Associated with decomposing organic mater
Prevalence of *Aspergillus* spp. in highly contaminated occupational environments

125 air samples
125 surface samples

A Murine Inhalation Model to Characterize Pulmonary Exposure to Dry Aspergillus fumigatus Conidia

Amanda D. Buskirk1, Brett J. Green1, Angela R. Lemons1, Ajay P. Nayak1, W. Travis Goldsmith2, Michael L. Kashon3, Stacey E. Anderson1, Justin M. Hettick1, Steven P. Templeton1, Dori R. Germolec4, Donald H. Beezhold1*

1 Allergy and Clinical Immunology Branch, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia, United States of America, 2 Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia, United States of America, 3 Biostatistics and Epidemiology Branch, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Morgantown, West Virginia, United States of America, 4 Toxicology Branch, National Toxicology Program Division, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, United States of America

Abstract

Most murine models of fungal exposure are based on the delivery of uncharactized extracts or liquid conidia suspensions using aspiration or intranasal approaches. Studies that model exposure to dry fungal aerosols using whole body inhalation have only recently been described. In this study, we aimed to characterize pulmonary immune responses following repeated inhalation of conidia utilizing an acoustical generator to deliver dry fungal aerosols to mice housed in a nose only exposure chamber. Immunocompetent female BALB/c mice were exposed to conidia derived from Aspergillus fumigatus wild-type (WT) or a melanin-deficient (Δalb1) strain. Conidia were aerosolized and delivered to mice at an estimated deposition dose of 1 × 107 twice a week for 4 weeks (8 total). Histopathological and immunological endpoints were assessed at 4, 24, 48, and 72 hours after the final exposure. Histopathological analysis showed that conidia derived from both strains induced lung inflammation, especially at 24 and 48 hour time points. Immunological endpoints evaluated in bronchoalveolar lavage fluid (BALF) and the mediastinal lymph nodes showed that exposure to WT conidia led to elevated numbers of macrophages, granulocytes, and lymphocytes. Importantly, CD8+ IL17+ (Tc17) cells were significantly higher in BALF and positively correlated with germination of A. fumigatus WT spores. Germination was associated with specific IgG to intracellular proteins while Δalb1 spores elicited antibodies to cell wall hydrophobins. These data suggest that inhalation exposures may provide a more representative analysis of immune responses following exposures to environmentally and occupationally prevalent fungal contaminants.
Diseases associated with occupational/indoor exposures to *Aspergillus*

1) Allergic and other hypersensivity responses
2) Mycotoxicosis
3) Irritant effects caused by mold exposure
4) Opportunistic infection
Diseases associated with occupational/indoor exposures to *Aspergillus*

1) Allergic and other hypersensitivity responses

2) Mycotoxicosis

3) Irritant effects caused by mold exposure

4) Opportunistic infection

- It is estimated 3 to 10% of the world's population is allergic to molds

- *Aspergillus* cause a large number of allergic diseases: allergic bronchopulmonary aspergillosis, rhinitis, allergic sinusitis and hypersensitivity pneumonitis.

RHINITIS AND ALLERGIC SINUSITIS
Nasal congestion, sneezing, and runny or itchy nose.
Nasal obstruction with polyps

SAFS - SEVERE ASTHMA WITH FUNGAL SENSITIZATION
Occurs in patients with asthma
Fungal-associated (severe) asthma

Fungi responsible: Many, some alone, some collectively. *Aspergillus fumigatus, Penicillium chrysogenum, Cladosporium herbarum, Alternaria alternata, Candida albicans, Trichophyton* spp. and probably others.

ABPA –ALLERGIC BRONCOPULMONAR ASPERGILLOSIS
Occurs mainly in patients with asthma or cystic fibrosis

Hypersensivity reaction due to colonization of the bronchi with *Aspergillus*

Bronchial inflammation, obstruction, mucus accumulation, respiratory failure
Two year follow-up of a garbage collector with allergic bronchopulmonary aspergillosis (ABPA).

Allmers HJ, Huber H, Raab H

Abstract

BACKGROUND: Separate collection of biodegradable garbage and recyclable waste is expected to become mandatory in some western countries. A growing number of persons engaged in garbage collection and separation might become endangered by high loads of bacteria and fungi. Case history and examination A 25 year old garbage collector involved in emptying so-called biological garbage complained of dyspnea, fever, and mucosal symptoms during work beginning in the summer of 1992. Chest X-ray showed streaky shadows near both hilus reaching into the upper regions. IgE- and IgG-antibodies (CAP, Pharmacia, Sweden) were strongly positive for Aspergillus fumigatus with 20.5 KU/L and 186%, respectively. Total IgE was also strongly elevated with 5430 KU/L.

Bronchial challenge testing with commercially available Aspergillus fumigatus extract resulted in an immediate-type asthmatic reaction.

Two years later he was still symptomatic and antibodies persisted at lower levels.

CONCLUSIONS: Our diagnosis was allergic bronchopulmonary aspergillosis (ABPA) including asthmatic responses as well as hypersensitivity pneumonitis (extrinsic allergic alveolitis) due to exposure to finely powdered fungi. A growing number of persons engaged in garbage collection and handling are exposed and at risk to develop sensitization to fungi due to exposure to dust of biodegradable waste. Further studies are necessary to show if separate collection of biodegradable waste increases the health risks due to exposure to bacteria and fungi in comparison to waste collection without separation.
Allergic bronchopulmonary aspergillosis due to Aspergillus oryzae.

Aoyama K, Takizawa H, Suzuki M, Miyashita S, Ichinohe M, Yasuoka Y.

Abstract
A 19-year-old female student with allergic bronchopulmonary aspergillosis (ABPA) due to Aspergillus oryzae is reported. This organism was used for fermentation starter to make soybean paste in her father's workshop adjacent to the home where she lived. ABPA might be considered an occupational disease in certain situations.

PMID: 2433938
HYPERSENSITIVITY PNEUMONITIS

- Inflammation of the alveoli within the lung caused by hypersensitivity to inhaled organic dusts with a large variety of antigens.

- Sufferers are commonly exposed to the dust by their occupation or hobbies.

- Hypersensitivity pneumonitis associated with *Aspergillus*:

  - Tobacco worker's lung
  - Compost lung
  - Farmer's lung
  - Malt worker's lung

*Aspergillus* spp. associated to up to 80% of the cases

A. *fumigatus* associated to 80% of the cases
Esparto grass lung

Stipa tenacissima

Familiar presentation of occupational hypersensitivity pneumonitis caused by aspergillus-contaminated esparto dust

A. Moreno-Anollo, C. Dominguez-Noche, A. Carmen Gil-Adrados, and RM. Cosmes

Allergy Unit, Hospital Virgen del Puerto, Plasencia (Caceres), Spain. Centro de Salud, Castillo de Bypadla (Toledo), Spain.

Hypersensitivity pneumonitis in workers exposed to esparto grass (Stipa tenacissima) fibers

Miguel Hinojosa, MD, Juan Frey, MD, Belen De La Hoz, MD, Raimundo Alcazar, MD, and Antonio Sueiro, MD, Madrid and Jaen, Spain.
80 workers analyzed
47 (58.8%) workers in poultry
33 (41.2%) in swine farms

Incidence of diagnosed asthma was 8.8%

5% occupational asthma

High prevalence of respiratory symptoms in professionals without asthma
- wheezing associated with dyspnea (24%)
- dyspnea after strenuous activities (12%)
- sneezing, runny nose, or nasal stuffiness (19%)

TABLE 1. Quantitative Results Obtained From Aspergillus Isolation From the Air, Surfaces and Coverage of the Floor in the Analyzed Settings
Diseases associated with occupational exposures/indoor to *Aspergillus*

1) Allergic and other hypersensitivity responses

2) Mycotoxicosis

3) Irritant effects caused by mold exposure

4) Opportunistic infection
Most important mycotoxins produced by *Aspergillus*

<table>
<thead>
<tr>
<th>Mycotoxin</th>
<th>Aspergillus Species</th>
<th>Target organ</th>
<th>Acute toxicity</th>
<th>Chronic Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxins (AFB1)</td>
<td><em>A. flavus</em> <em>A. parasiticus</em></td>
<td>Liver</td>
<td>Gastrointestinal disturbance, jaundice, photosensitivity, hepatosplenomegaly, ascites, coma, death</td>
<td>Chronic liver injury, cirrhosis, ascites, liver carcinoma</td>
</tr>
<tr>
<td>Ochratoxins (OTA)</td>
<td><em>A. ochraceus</em> <em>A. alliaceus</em> <em>A. auricomus</em> <em>A. carbonarius</em> <em>A. melleus</em> <em>A. niger</em> (...)</td>
<td>Kidney</td>
<td>Acute renal failure</td>
<td>Chronic renal injury in Balkan endemic nephropathy</td>
</tr>
<tr>
<td>Sterigmatocystin</td>
<td><em>A. versicolor</em></td>
<td>Liver</td>
<td>hepatosplenomegaly</td>
<td>liver carcinoma</td>
</tr>
</tbody>
</table>

Airborne concentrations of mycotoxins found in different occupational settings

Detection of AFB1 in the serum of poultry and swine workers

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Range level of AFB1 (ng/ml)</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swine workers</td>
<td>34</td>
<td>Positive to AFB1: 18, 53%</td>
<td>1.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative to AFB1: 16, 53%</td>
<td></td>
</tr>
<tr>
<td>Poultry workers</td>
<td>11</td>
<td>Positive to AFB1: 6, 55%</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative to AFB1: 7</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>30</td>
<td>Positive to AFB1: 0</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative to AFB1: 30</td>
<td></td>
</tr>
</tbody>
</table>

Occupational exposure to AFB1 by inhalation

Diseases associated with occupational/indoor exposures to *Aspergillus*

1) Allergic and other hypersensitivity responses

2) Mycotoxicosis

3) Irritant effects caused by mold exposure

4) Opportunistic infection
Molds produce a number of potentially irritating substances that can be divided into microbial volatile organic compounds (MVOCs) and particulates (e.g., spores, hyphae fragments, and their components like glucans, chitins ...).

<table>
<thead>
<tr>
<th>TABLE 1 Commonly Detected MVOCs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohols</strong></td>
</tr>
<tr>
<td>1-Butanol</td>
</tr>
<tr>
<td>2-Butanol</td>
</tr>
<tr>
<td>2-Methyl-1-butanol</td>
</tr>
<tr>
<td>2-Methyl-1-propanol</td>
</tr>
<tr>
<td>3-Methyl-1-butanol</td>
</tr>
<tr>
<td>3-Methyl-2-butanol</td>
</tr>
<tr>
<td>3-Octanol</td>
</tr>
<tr>
<td>1-Octen-3-ol</td>
</tr>
<tr>
<td>2-Octen-1-ol</td>
</tr>
<tr>
<td>2-Pentanol</td>
</tr>
<tr>
<td><strong>Ethers</strong></td>
</tr>
<tr>
<td>3-Methylfuran</td>
</tr>
<tr>
<td>2-Pentylfuran</td>
</tr>
<tr>
<td><strong>Esters</strong></td>
</tr>
<tr>
<td>Isooctyl acetate</td>
</tr>
<tr>
<td>Ethyl isobutyrate</td>
</tr>
<tr>
<td>Ethyl-2-methylbutyrate</td>
</tr>
<tr>
<td><strong>Ketones</strong></td>
</tr>
<tr>
<td>2-Heptanone</td>
</tr>
<tr>
<td>2-Hexanone</td>
</tr>
<tr>
<td>3-Octanone</td>
</tr>
<tr>
<td><strong>Terpenoids</strong></td>
</tr>
<tr>
<td>Geosmin</td>
</tr>
<tr>
<td>2-Methylisoborneol</td>
</tr>
<tr>
<td><strong>Sulfur and nitrogen compounds</strong></td>
</tr>
<tr>
<td>Dimethyl disulfide</td>
</tr>
<tr>
<td>2-Isopropyl-3-methoxy pyrazine</td>
</tr>
</tbody>
</table>

Nasal congestion
Airway hyperreactivity
Upper and lower respiratory symptoms
Eye irritations
Headache
Fatigue/tiredness
Joint pains
Skin symptoms
Flu-like symptoms
Nausea
Gastro-intestinal symptoms

Contradictory studies showing (or not) this possible relationship
Diseases associated with occupational/indoor exposures to *Aspergillus*

1) Allergic and other hypersensitivity responses

2) Mycotoxicosis

3) Irritant effects caused by mold exposure

4) Opportunistic infection
Nosocomial vs. Community-acquired aspergillosis

Occupational and indoor exposure

**Nosocomial**
- Due to a break in or contamination of hospital water system
- Due to a break in HEPA filtration system
- Due to construction or demolition work in the hospital or near by
- Other sources of *Aspergillus* found in hospital environment: Foods, Plants, Fabrics, Mattresses and pillows, Computers

**Community acquired**
- Due to the air quality/ *Aspergillus* burden in the patients’ houses
- Due to occupational or leisure activities developed leading to direct exposure to high amount of conidia

Adapted from: Praz-Christinaz et al. (2007). *Transplant Infect Dis*; 9: 175-181
Occupational risk assessment of aspergillosis after renal transplantation.

Prad Christoforou BM, Lazzar Blanchard C, Brelot MC, Drouot B.

Author information

Abstract
Returning to work after transplantation is a much-discussed topic today, especially as a measure to avoid permanent work disability. Many transplant patients regain their ability to work 2-6 months after transplantation. However, returning to work should not endanger their health. This means that occupational risks such as occupational exposure to Aspergillus spores must be evaluated. We evaluated the community-acquired aspergillosis risk and in particular the occupational aspergillosis risk, using the example of a 38-year-old construction worker immunosuppressed after renal transplantation. On one hand the risk is linked to the exposure to microorganisms that the individual is likely to be subjected to, and on the other hand to the factors that modify his state of susceptibility or resistance to these infectious agents. The necessity of immunosuppressive therapy after transplantation elevates the aspergillosis risk, especially 1-6 months after transplantation. There are many professions in which exposure to Aspergillus spores can occur. The risk of acquiring aspergillosis at work exists, but is not quantifiable today. Nevertheless, the risk should be minimized during the period of vulnerability by preventive measures such as restriction of certain activities, changing work methods and reorganizing the work day to adapt to the risk, and wearing personal protective equipment, as well as attention to information about aspergillosis risk and about the likelihood of exposure in the patient's professional and leisure activities.

PMID: 17511225 DOI: 10.1111/j.1365-2662.2007.00223.x
<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Late infections associated with chronic GVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fungi</td>
<td>Mostly invasive <em>Aspergillus</em> spp.</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>Mainly seen as PTLD</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Increasing incidence of late infections</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis jirovecii</td>
<td></td>
</tr>
</tbody>
</table>

Time after HSCT (months): 0 1 2 3 4 5 6 7 8 9 10 11 12 >12
House inspection: Avoiding moldy and dusty houses

Indoor exposure

Avoiding gardening and composting

Usage of protective equipment
4) Opportunistic infection (**ONLY in the immunocompromised host?**)
Acute invasive pulmonary aspergillosis, shortly after occupational exposure to polluted muddy water, in a previously healthy subject

Vikas Pilaniya¹, Kamal Gera¹, Rajesh Gothi², Ashok Shah¹

ABSTRACT

Invasive pulmonary aspergillosis (IPA) predominantly occurs in severely neutropenic immunocompromised subjects. The occurrence of acute IPA after brief but massive exposure to *Aspergillus* conidia in previously healthy subjects has been documented, although only six such cases have been reported. The diagnosis was delayed in all six of the affected patients, five of whom died. We report the case of a 50-year-old HIV-negative male, a water pipeline maintenance worker, who presented with acute-onset dyspnea and fever one day after working for 2 h in a deep pit containing polluted, muddy water. Over a one-month period, his general condition deteriorated markedly, despite antibiotic therapy. Imaging showed bilateral diffuse nodules with cavitation, some of which were surrounded by ground-glass opacity suggestive of a halo sign (a hallmark of IPA). Cultures of sputum/bronchial aspirate samples and serology were positive for *Aspergillus fumigatus*. After being started on itraconazole, the patient improved. We conclude that massive exposure to *Aspergillus* conidia can lead to acute IPA in immunocompetent subjects.

Keywords: Environmental exposure; Azoles; Water pollution; Immunocompetence; Invasive pulmonary aspergillosis.
Nosocomial vs. Community-acquired aspergillosis

**Occupational and indoor exposure**

**Nosocomial**
- Due to a break in or contamination of hospital water system
- Due to a break in HEPA filtration system
- Due to construction or demolition work in the hospital or near by
- Due to occupational or leisure activities developed leading to direct exposure to high amount of conidia

*Important to understand the epidemiology of Aspergillus in the different hospital wards housing high risk patients.*

**Community acquired**
- Due to the air quality/Aspergillus burden in the patients’ houses
- Due to occupational or leisure activities developed leading to direct exposure to high amount of conidia

Adapted from: Praz-Christinaz et al. (2007). Transplant Infect Dis; 9: 175-181
Aspergillus in hospital environment

1 year study: 101 air and 99 surface samples (impaction method and swabbing)

- From all samples, 548 fungal isolates were obtained
- Aspergillus was the most frequently fungal genera found (19.7%)

- 25 different species of Aspergillus were identified by β-tubulin and calmodulin sequencing, and a high percentage of cryptic species (i.e., not sensu stricto) was found (59%)

Among the tested isolates, sections *Circundati, Versicolores* showed isolates – namely cryptic species - with reduced susceptibility to some of the antifungals used as clinical therapeutics.

### Table: MICs of various species

<table>
<thead>
<tr>
<th>Source</th>
<th>Ward</th>
<th>Species</th>
<th>MIC AMB (µg/mL)</th>
<th>MIC ICZ (µg/mL)</th>
<th>MIC VCZ (µg/mL)</th>
<th>MIC PCZ (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. sidowii</em></td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>surface</td>
<td>Hematology</td>
<td><em>A. sidowii</em></td>
<td>4</td>
<td>&gt;8</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. sidowii</em></td>
<td>4</td>
<td>4</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>surface</td>
<td>Hematology</td>
<td><em>A. versicolor sensu stricto</em></td>
<td>2</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. venenatus</em></td>
<td>2</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. tubiaensis</em></td>
<td>1</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>surface</td>
<td>ICU</td>
<td><em>A. phoenicis</em></td>
<td>1</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. niger sensu stricto</em></td>
<td>1</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. niger sensu stricto</em></td>
<td>1</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>surface</td>
<td>ICU</td>
<td><em>A. persii</em></td>
<td>4</td>
<td>4</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>air</td>
<td>ICU</td>
<td><em>A. persii</em></td>
<td>3</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. sclerotium</em></td>
<td>2</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>A. sclerotium</em></td>
<td>2</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>ICU</td>
<td><em>A. sclerotium</em></td>
<td>4</td>
<td>8</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>ICU</td>
<td><em>A. westerdijkae</em></td>
<td>&gt;8</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>ICU</td>
<td><em>A. westerdijkae</em></td>
<td>&gt;8</td>
<td>4</td>
<td>≤0.25</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>ICU</td>
<td><em>A. flavus sensu stricto</em></td>
<td>2</td>
<td>2</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>surface</td>
<td>ICU</td>
<td><em>A. flavus sensu stricto</em></td>
<td>2</td>
<td>2</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>surface</td>
<td>ICU</td>
<td><em>A. flavus sensu stricto</em></td>
<td>2</td>
<td>2</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>Emmericella nidulans</em></td>
<td>2</td>
<td>2</td>
<td>≤0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>air</td>
<td>Hematology</td>
<td><em>Emmericella nidulans</em></td>
<td>2</td>
<td>2</td>
<td>≤0.25</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Clear differences were found between the susceptibility of clinical and environmental isolates.

For AMB and PCZ, significant higher values in environmental isolates

4 environmental isolates with MICs \( \geq 8 \) µg/ml to PCZ + MICs \( \geq 8 \) µg/ml to ITC:
- 1 isolate from beach sand,
- 1 isolate from poultry
- 2 isolates from swineries

Other than A. Fumigatus: Versicolores, Nidulantes and Aspergilli sections)
The problem of antifungal resistances in *Aspergillus* related to occupational exposure

**EXPOSURE** to high levels of environmental isolates with intrinsic / less susceptibility to antifungals

**EXPOSURE** to environmental isolates with induced azole-resistance (secondary resistance): in agricultural settings – PESTICIDES/OTHER FUNGICIDES???


Final considerations...

- Strategies to avoid Aspergillus exposure of the worker in contaminated occupational settings and these include: engineering, sampling and control, as well usage of personal protective equipment.

- Aspergillus occupational exposure is a public health problem that should be managed properly.

The molecular study of Aspergillus epidemiology (including the identification of cryptic species) and determination of the susceptibility profile of environmental isolates may contribute to the prevention of diseases associated to occupational exposure.
Acknowledgements

Cristina Veríssimo
Helena Simões
João Brandão
Carla Viegas
Elisabete Carolino
Susana Viegas
Anita Q. Gomes
David A. Stevens
Karl V. Clemons

Reference Laboratory for Parasitic and Fungal Infections, Infectious Diseases Department
National Health Institute Dr. Ricardo Jorge, Portugal

GIAS, ESTeSL - Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa, Lisbon, Portugal

California Institute for Medical Research, San Jose, CA, United States
School of Medicine, Stanford University, Stanford, CA, United States
Thank you!!!

Hope to receive you again in Lisbon!!!