

Report March 2010

Fungiscope

Global Rare Fungal Infection Registry

Working group of the



Under the auspices of



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Abstract

Introduction

We are coordinating a global registry for cases of rare invasive fungal infections. Our objective is to broaden the knowledge on epidemiology, to determine the clinical pattern of disease, to describe and improve diagnostic procedures and therapeutic regimens, as well as to facilitate exchange of clinical isolates among the contributors.

Methods

Data entry is performed via a web-based registration system (www.clinicalsurveys.net) that focuses on demographic information, underlying diseases, risk factors, details on the infection (pathogen, localization, specimen collection) therapy and outcome.

Inclusion criteria include cultural, histopathological, antigen, or DNA evidence of invasive fungal infection. Infection due to *Aspergillus* spp., *Candida* spp., *Cryptococcus neoformans*, *Pneumocystis jiroveci*, Zygomycetes or any endemic fungal infection, such as coccidioidomycosis or histoplasmosis, as well as mere colonization or other non-invasive infection are exclusion criteria.

Results

By now, 146 cases of rare invasive fungal infections have been documented, including *Fusarium* spp., *Scedosporium* spp., *Acremonium* spp., *Alternaria* spp. as well as rare yeasts such as *Geotrichum capitatum*, *Rhodotorula* spp. and *Trichosporon* spp. Most patients were in an immunocompromised state as a result of their underlying disease, chemotherapy or transplantation.

Discussion

The clinical relevance of invasive fungal infections by rare fungi is increasing steadily. In a short period of time, actual cases from Europe, Asia and South America could be documented, showing a broad spectrum of pathogens.

Further investigators and coordinators are cordially invited to contribute to the success of Fungiscope.

Full protocol

Introduction

The incidence of invasive fungal infections is increasing worldwide. The etiology for this ongoing epidemiological development is not completely understood. However, major contributing factors are the increasing number of transplantation procedures around the world (estimated at 500,000 per year), a widening of the indications for intensive chemotherapy, and the growing number of other clinical conditions requiring immunosuppressive treatment.

Therapeutic standards have been developed for the most frequent invasive fungal infections, i.e. candidiasis, aspergillosis and cryptococcosis. However, the so called “rare fungi” are also a reason for the increased number of invasive fungal infections. Thus, clinicians are now facing infections due to a variety of different fungi without any reliable treatment recommendations. Therapeutic decision making is not evidence based.

Objectives

The main objective is to broaden the knowledge on epidemiology, diagnostic procedures and the clinical course of invasive fungal infections caused by unusual invasive fungi. This includes in detail:

1. To determine the fungal species causing invasive fungal infection in different parts of the world.
2. To determine the clinical pattern of disease and document procedures performed for confirmation of the diagnosis.
3. To describe the therapeutic regimens used and their efficacy.
4. To share clinical isolates among the contributors of Fungiscope.
5. To develop molecular biology tools for identification pathogens causing rare invasive fungal infections.

Study period

Start date: March 1, 2004

Patient definition

Inclusion criteria:

- Cultural, histopathological, antigen, or DNA evidence of invasive fungal infection

Exclusion criteria:

- Infection due to *Aspergillus spp.*, *Candida spp.*, *Cryptococcus neoformans*, *Pneumocystis jiroveci*, Zygomycetes
- Any endemic fungal infection such as coccidioidomycosis or histoplasmosis
- Colonisation or other non-invasive infection

In case of any uncertainty whether a specific patient can be included, please contact the chair.

Documentation

- The case report form (CRF) is an internet based form accessed through the following websites: www.fungiscope.net or www.ClinicalSurveys.net
- Demographic data
- Underlying conditions and immunosuppressive medication
- Diagnostic procedures
- Fungal species, organs involved
- Antifungals and other treatment modalities
- Response to treatment and survival at 14 and 30 days after diagnosis or cause of death including results of post mortem examination
- Registration in any other trial or registry. Can still be registered with Fungiscope, however, repetitive publication will be avoided or disclaimed.

After documentation, all cases are monitored and necessary queries sent out to the case contributors.

Data analysis

The evaluation is descriptive, by causative organism. Diagnostic approach and response to therapy are compared by fungal disease. For differences between

subgroups χ^2 -test or exact test of Fisher is used with a $p < 0.05$ as limit for statistical significance, with a Bonferroni correction for multiple comparisons.

Strain collection/Fungithek

Isolates are sent to and stored by the reference laboratories, where formal identification is done based on culture and molecular biology results. Susceptibility patterns/MIC according to CLSI and/or EUCAST methods/MFC of the isolates are tested.

Tissue collection

Every effort should be made to obtain tissue samples. If fresh frozen tissue is not available, 10 slices of formaldehyde fixated tissue should be obtained.

Budgetary information

For evaluable patient documentations filled in by the participating center a compensation of € 100 each is paid. If the documentation workload is too high, centers are encouraged to ask the study office for personnel to be sent to the site. For isolates made available to the central laboratory an additional € 50 is paid.

Authorship

It is intended to publish each subset of this cohort at a time. Authorship will be restricted to those centers contributing patients or translational work to the subset published. From each contribution center there will be authorship positions available. This will extend to a maximum of three.

Patients registered until March 2010

Total documented: 146, for 18 cases completion of documentation pending

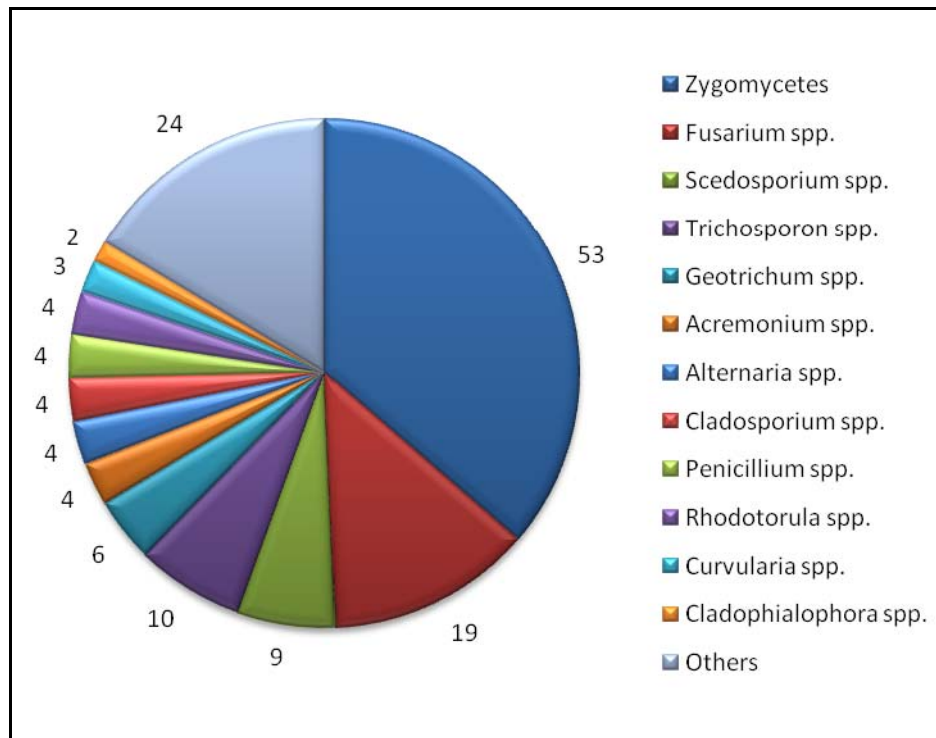


Figure 1: Distribution of 146 documented cases of rare invasive fungal infections

Publication Plan for 2010

April 10-13, 2010	20 th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, Austria
May 7-8, 2010	Paul-Ehrlich-Gesellschaft für Chemotherapie e.V., Spring Meeting of the “Sektion Antimykotische Chemotherapie”, Bonn, Germany
June 18-19, 2010	MSD Workshop „Infektionen in der Hämatologie“, Munich, Germany
June 23-26, 2010	10 th Congress of Infectious Diseases and Tropical Medicine, Cologne, Germany
September 12-15, 2010	50 th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), MA, Boston, USA
September 9-11, 2010	44 th Congress of German Society for Mycology (DMykG e.V.), Vienna, Austria
October 1-5, 2010	Annual Congress of the German Society for Hematology and Oncology (DGHO), Berlin, Germany

Publications and presentations

- Dec 11, 2009 M.J.G.T. Rüping, W.J. Heinz, A.J. Kindo, V. Rickerts, C. Lass-Flörl, C. Beisel, R. Herbrecht, Y. Roth, G. Silling, A.J. Ullmann, K. Borchert, G. Egerer, J. Maertens, G. Maschmeyer, A. Simon, M. Wattad, G. Fischer, J.J. Vehreschild, O.A. Cornely
Forty-one Recent Cases of Invasive Zygomycosis from a Global Clinical Registry
J Antimicrob Chemother. 2010 Feb;65(2):296-302
- October 18-21, 2009 4th Trends in Medical Mycology (TIMM), Athens, Greece
- October 7-11, 2009 18th Congress of the European Academy of Dermatology and Venerology (EADV), Berlin, Germany
- October 2-6, 2009 Annual Congress of the German Society for Hematology and Oncology (DGHO), Mannheim, Germany
- September 17-19, 2009 11th Congress of the German Society for Anaesthesiology and Intensive Care (DGAI), Berlin, Germany
- September 12-15, 2009 49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), CA, San Francisco, USA
- September 9-12, 2009 Weimar Sepsis Update, Weimar, Germany
- September 3-5, 2009 43th Congress of German Society for Mycology (DMyKG e.V.), Cologne, Germany
- May 25-29, 2009 17th Congress of The International Society for Human and Animal Mycology (ISHAM), Tokyo, Japan
- May 16-19, 2009 19th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Helsinki, Finland
- March 12-14, 2009 9th Congress of Infectious Diseases and Tropical Medicine, Freiburg, Germany
- March 4-6, 2009 19th Focus on Fungal Infections, Fort Myers, FL, USA

February 7, 2009	Posaconazole Clinical Update Meeting, Miami, FL, USA
June 26-28, 2008	International MASCC/ISOO Symposium, Houston, Texas, USA
June 22-25, 2008	15 th Symposium on Infections in the Immunocompromised Host, Thessaloniki, Greece
June 19-22, 2008	13 th International Society for Infectious Diseases, Kuala Lumpur, Malaysia
April 19-22, 2008	18 th European Congress of Clinical Microbiology and Infectious Diseases, Barcelona
March 29-April 2, 2008	114 th Congress of the German Society for Internal Medicine, Wiesbaden, Germany
March 6-8, 2008	9 th Focus on Fungal Infections, San Antonio, USA
February 16-20, 2008	12 th Symposium on Acute Leukemia, Munich, Germany
September 6-8, 2007	International Congress of the German Mycological Society, Berlin, Germany
April 19-20, 2007	Gilead Clinical Studies Workshop, Munich, Germany
February 27-March 1, 2008	9 th Congress of Infectious Diseases and Tropical Medicine, Innsbruck, Austria

Innovations

1. Prof. Sybren de Hoog from the CBS Fungal Biodiversity Center, Institute of the Royal Netherlands Academy of Arts and Sciences (KNAW) has begun to carry out all molecular genetic analyses.
2. A revised version of the eCRF has been programmed and put online in November 2009.
3. An online tool for researching the database will be developed in 2010.
4. A co-operation with the MSG Phaeohyphomycoses Study Group has been confirmed.

As shown above, a large number of high quality publications has been generated from Fungiscope, particularly since 2008. In addition, the increasing number of collected clinical cases, isolates and histopathological samples, has allowed us to establish a network of valuable contributors who are now beginning to initiate sub-projects, e.g. Prof. Sybren de Hoog from the CBS Fungal Biodiversity Center and the MSG Phaeohyphomycoses Study Group.

Given this promising development, we aim to further expand the Fungiscope network and to consolidate newly initiated sub-projects within the next years.

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