Mycology newsletter

The ECMM/CEMM Mycology Newsletter is mailed to the members of the national societies affiliated to the European Confederation of Medical Mycology (about 3000 in 23 different countries)

1/2006

ECMM
European Confederation of Medical Mycology
CEMM
Confédération Européenne de Mycologie Médicale

Our 13th anniversary

Last year a voting round among the Council membership for the new president of ECMM ended up with a close finish between several candidates. I have the honour of serving the Confederation for the next 3 years.

The road has been paved and widened by my three excellent predecessors Profs. Bertrand Dupont (1993-1999), Rod Hay (1999-2002) and Frank Odds (2002-2005). I congratulate them with the 13th birthday of ECMM and thank them for the creation of our confederation as it stands now. I see it as my task for the next years to come to construct side roads and connections to other areas of infectious diseases in Europe and bring basic mycology together with clinical mycology. Our Trends in Medical Mycology Congress is the starting point of the latter goal. The last year and this year we are blessed in Europe with two high quality mycology meetings, TIMM2 and the International Society for Human and Animal Mycology Congress. Profs. Markus Ruhnke and Georg Maschmeyer were responsible for the smooth and successful organisation of our bi-annual conference last fall in Berlin and Prof. Dupont, one of the founding fathers of ECMM, is preparing the world conference on mycology, ISHAM, coming June in Paris. And this is not all. Preparations towards TIMM3 in October 2007 in Torino, Italy have started and are on track. Our Italian colleagues Profs. Marianna Viviani and Claudio Viscoli, as national organizers, distributed the first announcement at the last European Society of Clinical Microbiology and Infectious Diseases meeting in Nice and you will hear more about Torino in the coming months. This year it is time to plan our first Educational meeting for 2008 and I urge National Societies to express their interest in hosting TIMM4 in 2009, to contact the secretary of ECMM via their Council Member.

Jacques F. Meis

The Council meeting in Berlin appointed Dr. Maiken Cavling Arendrup, President of the Nordic Society for Medical Mycology, in the Executive Committee for organizing the next two TIMM conferences together with Prof. Thierry Calandra as representative of the EORTC-Infectious Diseases Group. Everybody recognizes the necessity of a well designed and smoothly running website to enhance

(continued on page 4)

Contents

ECMM/CEMM
Mycology Newsletter

Editorial Advisory Board
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ECMM Affiliated Societies

(Information provided by the member Societies)

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Vicepresident, Head of Medical Section:
S.A. Burova
Secretary: A.Y. Sergeev *(ECMM delegate)*
Treasurer: V.M. Leschenko
Membership 2006: 246
Website: www.mycology.ru

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President: M. Rocha
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Secretary: M.L. Rosado *(ECMM delegate)*
Treasurer: M. Gardete
Membership 2004: 50

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Secretary: : F.J. Cabañes Saenz
Treasurer: F.L. Hernando Echevarría
President Medical Mycology Section:
J. Pemán García *(ECMM delegate)*
Membership 2006: 145
National meeting: Every two years.
A workshop meeting ("Forum Micológico") is scheduled the years between National Meetings
Journal: Revista Iberoamericana de Micología
Website:: www.reviberoammicol.com/AEM

Austrian Society for Medical Mycology (ASMM)/Österreichische Gesellschaft für Medizinische Mykologie (ÖGMM)
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Secretary: C. Lass-Flörl *(ECMM delegate)*
Vicesecretary: H.-J. Dornbusch
Treasurer: C. Speth
Vicetreasurer: K. Kuchler
Membership 2006: 122
National meeting: twice a year
Website: www.oegmm.at

British Society for Medical Mycology (BSMM)
President: E. M. Johnson *(ECMM delegate)*
General Secretary: R.P. Hobson
Meetings Secretary: E. Bignell
Treasurer: D.M. MacCallum
Membership 2006: 281
National meeting: March 18-20, 2007, Leeds
Newsletter: BSMM Newsletter
Website: www.bsmm.org

Bulgarian Mycological Society (BMS)
President: T. Kantardjiev *(ECMM delegate)*
Vicepresident: G. Mateev
Secretary: A. Kouzmanov
Treasurer: T. Velinov
Membership 2006: 49
Website: www.bam-bg.net

Committee for Medical Mycology of Czechoslovak Society for Microbiology (CSSM)
President: K. Mencl *(ECMM delegate)*
Secretary: P. Hamal
Treasurer: J. Gabriel
Membership 2006: 15
National meeting: 2007
Newsletter: Bulletin of CSSM

Danish Society for Mycopathologia
President: J. Stenderup *(ECMM delegate)*
Vicepresident: B. Andersen
Secretary: B. Knudsgaard
Treasurer: J. Stenderup
Membership 2006: 25
National meeting: twice a year
Newsletter: Report from the Danish Society for Mycopathology

Deutschsprachige Mykologische Gesellschaft e.V. (DMykG)
President: M. Ruhnke
Vicepresident: O. Cornely
Secretary: H. Chr. Korting
Treasurer: C. Hipler
ECMM delegate: M. Schaller
Membership 2006: 475
National meeting: September 7-9, 2006, Innsbruck
Journal: Mycoses
Newsletter: Mykologie Forum (4 issues/year)
Website: www.dmykg.de/start2.html

Federazione Italiana di Micopatologia Umana e Animale (FIMUA)
President: M.T. Montagna
Vicepresident: P.L. Viale
Secretary: F. Barchiesi
Treasurer: A.M. Tortorano
ECMM delegate: M.A. Viviani
Membership 2006: 160
Newsletter: FIMUA news
National meeting: November 9-11, 2006, Firenze
Website: www.fimua.it

Finnish Society for Medical Mycology
President: R. Visakorpi
Vicepresident: J. Salonen*(ECMM delegate)*
Secretary: L. Naire-Koivisto
Treasurer: O. Lindroos
Membership 2006: 86
Newsletter: Sienet ia Terveys (Fungi and Health)

Hellenic Society of Medical Mycology
President: G.L. Petrikkos
Vicepresident: G. Samonis
Secretary: A.M. Ziouva
Treasurer: O. Nikolatou-Galiti
ECMM delegate: E. Roilides
Membership 2006: 81
National meeting: June 2007
Website: www.hsmm.gr

Hungarian Dermatological Society Mycology Section
President: G. Simon *(ECMM delegate)*
Secretary: G. Fekete
Membership 2005: 59

Israel Society for Medical Mycology
President: E. Segal
Vicepresident: I. Polacek
Secretary: I. Berdicevsky *(ECMM delegate)*
Treasurer: D. Elad
Membership 2006: 60
National meeting: twice a year

Mycology Group of Bosnia Hercegovina
President: L. Ozegovic *(ECMM delegate)*
Secretary: M. Babic
Membership 2005: 19
National meeting: twice a year

Netherland Society for Medical Mycology (NVMy)
President: J.F.G.M. Meis *(ECMM delegate)*
Secretary: E.P.F. Yzerman
Treasurer: M.H. Dammer
Scientific Secretary: G. S. de Hoog
Membership 2006: 120
National meetings: October 2006, Nijmegen
Newsletter: NVMy Newsletter
Website: www.nvmy.nl

Nordic Society for Medical Mycology (NSMM)
President: M.C. Arendrup *(ECMM delegate)*
Vicepresident: M. Richardson
Secretary: P. Gaustad
Treasurer: D.M.L. Saunte
Membership 2006: 158
Newsletter: at web site
Website: www.nsmm.nu

Polish Dermatologic Society Mycology Section
President: E. Baran
Vicepresident: Z. Adamski, R. Maleszka
Secretary: J.C. Szepietowski *(ECMM delegate)*
Treasurer: R. Bialynicki-Birula
Membership 2006: 98
National meeting: 20-24 September 2006, Bialowieza
Journal: Mikologia Lekarska (Medical Mycology)

Société Belge de Mycologie Humaine et Animale/Belgische Vereniging Voor Menselijke en Dierlijke Mycologie
President: I. Surmont
Vicepresident: M. Lontie
Secretary: M. Van Esbroeck, K. Lagrou
Treasurer: M.-P. Hayette
Secrétaire des Séances: K. Lagrou
ECMM delegate: N. Nolard
Membership 2006: 179
National meeting: 28 October 2006, Leuven
Website: www.medmycol.be

Société Française de Mycologie Médicale
President: B. Dupont *(ECMM delegate)*
Vicepresident: N. Contet-Audonneau,
R. Grillot, C. Guiguen
Secretary: P. Roux
Treasurer: A. Datry
Membership 2006: 400
National meeting: November 24-25, 2006, Paris
Journal: Journal de Mycologie Médicale
Website: www.mycolmed.chez.tiscali.fr

Swedish Society for Clinical Mycology
President: J. Faergemann
Vicepresident: T. Kaaman
Secretary: L. Klingspor *(ECMM delegate)*
Treasurer: M.L. von Rosen
Membership 2006: 80
National meeting: Autumn 2006, Linköping

Swiss Mycological Group
ECMM delegate: M. Monod

Turkish Microbiological Society Mycology Section
President: Ö. Ang
Secretary: A. Ağaçfidan
Treasury: D. Yaylali
ECMM delegate: E. Tümbay
Membership 2006: 150
Newsletter: Bulletin of the Turkish
Microbiological Society

Our 13th anniversary

(continued from page 1)

communication in mycology in Europe. Prof. Frank Odds launched our site www. ecmm.org last year and Prof. Alexey Sergeev, council member on behalf of the All-Russian Academy of Mycology, took up the task of webmaster to professionalize the site.

Where does our speciality stand in clinical microbiology? Although much has changed for the better, mycology is still a minor player in infectious diseases in Europe. Bacteriology and virology are dominating the scene, also in media attention for example with regard to the avian flu. Although all of us know that there are far more casualties due to invasive fungal infections than to any of the sexy new diseases, mycology is hampered with much less public notice. How can we change this for the better? The German Society for Mycology already had a tradition of inviting the press for an update in fungal infections during their yearly meeting. Such a press conference was also arranged during the last TIMM in Berlin. Journalists appeared to be very interested in the field of mycology especially regarding the resistance development of fungi against existing drugs and the introduction of new generations of antifungals. But also the presentations of new findings at this meeting on the introduction of new emerging fungal infections into Europe such as *Cryptococcus gattii* from Vancouver Island and rare zygomycetes after the repatriation of European victims of the Tsunami disaster attracted attention.

As the needs and opportunities in medical mycology are expanding, the demand for appropriately trained personnel must be met to deal with these new mycoses appearing in our hospitals. There appears to be a diminishing number of clinical mycologists available to face the increasing demand of proper diagnostic mycological facilities. In the UK, the medical mycology community recognized this potential treat and therefore the British Society for Medical Mycology under the leadership of Dr. Chris Kibbler started last year a post graduate course in Medical Mycology which is enthusiastically met by the participants. Web-based learning is an integral part of the course and this gives opportunities for sister organizations in Europe to learn from this pilot project. Furthermore our British colleagues organized a Clinical Mycology Network to ensure the availability of diagnostic clinical mycology throughout the UK. Can ECMM copy this approach for Europe? The future will tell.

Since the start of the European Confederation of Medical Mycology in 1993, mycology is gathering momentum, opportunities seem plentiful and with the extensive collaborations and new initiatives going on, I feel the future for our specialty looks bright.

Jacques F. Meis
ECMM President

The 3rd international congress on Trends in Medical Mycology (TIMM-3) will be held in Torino, Italy, from 28th to 31st October 2007. As usual, TIMM-3 will be organised jointly by the European Confederation of Medical Mycology and the Infectious Diseases Group of the European Organization for Research and Treatment of Cancer. TIMM has become an important reality in the field of fungal infections, a forum in which investigators from almost everywhere in the world can exchange research and opinions and gather to learn the most important advances in basic science and clinical research in mycology.

ECMM Working Group on *Candida* Infections in ICU Surgical Patients in Europe

Convenor

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Dear Colleagues,

It is my pleasure to inform you that 17 countries have declared their willingness to participate in this ECMM Intensive Care Unit (ICU) study in surgical patients. Names and email addresses of the co-ordinators from each country as well as detailed information of this study are presented below. The final questionnaire will soon be finalised and sent out to the national co-ordinators. It consists of one page for clinical data and the reverse page for the laboratory data to be filled in.

The study

An initial meeting of the ECMM ICU working group was held in Berlin, October 22, 2005, at the Trends in Medical Mycology 2 conference. The study is planned to start late spring 2006 and will be open for inclusion of patients (adults and children) over a 2-year period.

The aims of the survey are:

A) To expand our knowledge of the characteristics of surgical patients in the ICU with invasive *Candida* infection:

1. Type of preceding surgery
2. Underlying disease(s)
3. Risk factors
4. *Candida* species causing infection
5. Treatment

B) To gain more knowledge of the different diagnostic procedures and their sensitivity, i.e.:

6. The sensitivity of different blood culture systems and media to detect candidemia.
7. The detection time (in hours) for the different media to detect candidemia.
8. To determine if the source of blood for blood culture influences the sensitivity of detection of candidemia, i.e. peripheral vein or artery, CVL or Porth-a-Catheter.
9. The sensitivity of different blood culture systems and different media to detect candidemia with a concordant bacterial sepsis.
10. The possible sensitivity of different blood culture systems and different media to detect different *Candida* species.
11. To get more information about invasive *Candida* infections in the absence of a positive blood culture for *Candida* spp. For example: to characterise blood culture negative patients with other signs of invasive *Candida* infection, e.g. a positive culture for *Candida* from an abdominal abscess.

C) If possible, to determine the patient groups who could benefit from prophylaxis.

The goal for the study is to include 75 patients with invasive *Candida* infection (blood from culture positive and/or positive cultures from a normally sterile body site) from each participating country. The study will be open for inclusion for a 2-year period.

Lena Klingspor

ECMM Working Group participants

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ECMM Epidemiological Survey on Zygomycosis in Europe

Convenor

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Other investigators

A. Skiada
J. Meis
E. Roilides
J-L. Rodriguez-Tudela
A. Velegraki

The European Zygomycosis Survey Study is well under way. The year 2005 was a pilot year and now the cases are sent to us in a much more regular fashion. For 2006, the study is going to be funded by GILEAD.

We present a summary of the cases we received up to now. It should be noted that the information we have is preliminary in several cases, so this does not represent a final analysis.

Up to now, 58 cases of zygomycosis have been included in the database (Italy 15, Greece 13, Germany 13, Austria 5, Spain 4, Finland 2, Russia 2, Belgium 2 and Norway 2 cases). The underlying diseases of these patients are: hematologic malignancy in 29, diabetes in 6, corticosteroids in 15, transplantation in 6 and trauma in 3 patients. The site of the zygomycosis was lungs in 19 patients, soft tissues in 11 and heart in 2; 19 cases were rhinocerebral and 1 disseminated; in 6 cases site was not reported or was unclear.

A meeting of all the representatives and the interested participants has been arranged during the ISHAM congress in Paris. It will be held in Room 341 of Palais des Congres de Paris, Wednesday 28 June 2006 13.00-14.00 pm.

Call for new participants: If any physician in a country already participating in the study has a case of zygomycosis to submit, please contact your national co-ordinator. If any other country would like to participate in the study, there is still time. Please contact Dr. Petrikkos at petrikos@med.uoa.gr

Georgios L.Petrikkos

National co-ordinators

Country	*Co-ordinator*	*E-mail address*
Austria	*C. Lass-Floerl*	*Cornelia.Lass-Floerl@uibk.ac.at*
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Switzerland	*J. Bille*	*jacques.bille@chuv.hospvd.ch*
The Netherlands	*J. Meis*	*j.meis@cwz.nl*
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UK	*B. Jones*	*B.L.Jones@clinmed.gla.ac.uk*

ECMM Working Group on *Pseudallescheria/ Scedosporium* Infections

A meeting of the ECMM Working Group on *Pseudallescheria/Scedosporium* Infections was held at the 'Trends in Medical Mycology' in Berlin, October 2005. Seven lectures were presented covering aspects of epidemiology, ecology, virulence factors, phylogeny, serology and antifungal susceptibility. Full presentations are available on our Website www.Scedosporium-ECMM.com.

Several papers were recently published by members of our Working Group. Gilgado et al. (J. Clin. Microbiol. 43: 4930-4942, 2005), introduced new species close to *Pseudallescheria boydii* and sharing a clinical potential. Borman et al. (Med. Mycol. 44: 33-39, 2006) showed that the "pathogenic genus" *Polycytella* appears to concern a *Pseudallescheria* mutant, as was also presented independently in one of our earlier workshops. Several papers are in press or will soon be submitted, among which are large reviews of the literature on *P. boydii* and *Scedosporium prolificans*. Our next challenge will be to develop a standard diagnostic system to be used in the routine lab for rapid recognition of the different species. Several members are currently working on detection, isolation, and recognition of *Scedosporium* species.

Our next symposium will be a part of the 16th Congress of ISHAM (International Society for Human and Animal Mycology) in Paris, June 2006.

The full programme is available on: www.imedex.com/announcements/isham06.asp for information on ISHAM, please go to www.isham.org. Our session is on Thursday, June 29 in the afternoon. The program is given below.

Sybren de Hoog,

"Scedosporium, a complex of emerging opportunists"
to be held at the ISHAM Congress, Paris, France,
on Thursday June 29, 2006.

14.30 – 14.50
Laurence Delhaes[1], Wieland Meyer[2], Anne-Laure Banuls[3], Sharon Chen[4], Emilie Fréalle[1], Isabelle Durand-Joly[1], Chris Heath[5], Daniel Camus[1], Monica Slavin[6], Eduardo Dei-Cas[1], Tania Sorrell[2] *([1]EA 3609, Service de Parasitologie Mycologie, Département de Microbiologie, Université de Lille-2, Institut Pasteur, CHU de Lille, Lille-France; [2]Molecular Mycology Laboratory, Westmead Hospital and University of Sydney-Australia; [3] Centre IRD, Montpellier-France; [4]Centre for Infectious Diseases and Microbiology, Westmead Hospital, Sydney-Australia; [5]Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth-Australia; [6]Department of Infectious Diseases and Microbiology, Alfred Hospital, Melbourne-Australia)*
Molecular characterisation of *Scedosporium* populations.

14.50 – 15.10
Marc Pihet *(Host-Parasite Interaction Study Group, Laboratory of Parasitology-Mycology, Angers University Hospital, Angers, France)*
Biochemical characterization of a dipeptidylpeptidase from *Scedosporium apiospermum* and its encoding gene.

15.10 – 15.30
Jan Nedved, Miroslav Sulc, Jan Sklenar, Martin Zabka, Alexandr Jegorov, Marian Hajduch, Vladimir Havlicek *(Institute of Microbiology, Academy of Sciences, Prague, Czech Republic)*
Mass Spectrometry as an alternative tool for diagnosing fungal infections, applied to *Pseudallescheria*.

15.30 – 15.50
Enrique Marco de Lucas & Javier Arnáiz *(Servicio de Radiodiagnóstico, Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain)*
Radiologic findings of *Pseudallescheria* / *Scedosporium* infections.

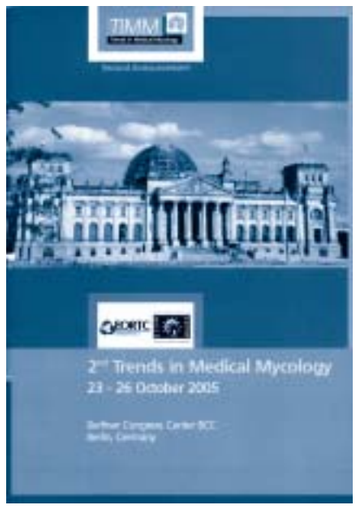
15.50 – 16.00
Wolfgang Becker *(Centraalbureau voor Schimmelcultures, Utrecht, The Netherlands)*
Molecular diversity of *Pseudallescheria boydii* using AFLP data.

Special report on...

Trends in Medical Mycology

Joint meeting of the 8th TIFI and 11th ECMM

EORTC ECMM CEMM



The second international congress on Trends in Medical Mycology (TIMM-2) took place in Berlin (Germany) from October 23 to 26, 2005. Over 1000 participants who came from 45 countries could found both an ambitious scientific program and the possibility to spend some nice moments in the city with a unique tradition of science, culture and politics.

Overall, 33 program parts with symposia, interactive morning sessions, plenary and poster sessions, oral presentation sessions, workshops and industry sponsored symposia gave everybody the opportunity to find his own topics of interest. Most sessions were devoted to antifungal treatment, emerging fungal pathogens, fungal infections in the different patient populations (immunocompromised host, children, haematology/oncology) and diagnostic methods. Special sessions were devoted to signal transduction, molecular methods, dermatomycology, host fungus relationship and allergy and mycotoxins.

The first day started with three satellite symposia (sponsored by Gilead, Pfizer, Merck Sharp & Dohme) that concentrated on clinical approaches to the antifungal therapy today. The official opening ceremony was held by Markus Ruhnke and Georg Maschmeyer from Berlin who together with Bart-Jan Kullberg and Jacques F. Meis from Nijmegen formed the Executive Committee for this congress. This year the ECMM Drouhet lecture was given by Annemarie Polak from Switzerland who gave a presentation about the current aspects and history of antifungal combination therapy. Frank Odds as the president of the ECMM honoured the scientific career of Annemarie Polak. This ceremony was followed by an overview over the history of medical mycology in Germany given by the congress chairman Markus Ruhnke.

Every morning started with interactive case session followed by state-of-the-art plenary session. The first presentation, antifungal therapy in cancer patients, summarized the most important key points related to the therapy of fungal infections in cancer patients. We were reminded that fatality rates in patients with documented invasive aspergillosis had been significantly reduced by primary use of voriconazole as compared with amphotericin B. For those not tolerating or refractory to voriconazole or amphotericin B formulation complete or partial response could be achieved with caspofungin. Early detection of invasive aspergillosis and prompt start of an effective therapy are the most essential factors for treatment outcome. Invasive and oropharyngeal or esophageal candidiasis in cancer patients might be due to species other than *Candida albicans*, particularly *C. glabrata*, however, in patients not treated with fluconazole for prophylaxis, *C. albicans* is still predominant and therefore fluconazole may be effective in the majority of *Candida* infections in cancer patients.

After that overview we could continue with fungal infections in the severely ill patients or choose one of the parallel symposia: molecular mycology or antifungal pharmacology. It was very interesting to learn about biofilms, three-dimensional communities of microorganisms that develop attached to a surface. One of the distinctive features of *C. albicans* biofilms is their reduced susceptibility to an array of antifungals. Consequently biofilms represent an important cause of relapses after therapy. However as we learnt during the next days, especially echinocandins show a good efficacy in biofilms.

Some recent clinical studies were discussed on the first day. A multicenter trial of oral posaconazole vs. fluconazole was presented by Andrew Ullmann from Mainz (see report below). The study presented by Andreas Groll from Münster, on empirical antifungal therapy with liposomal amphotericin B (L-AmB), showed that it was a safe and effective preventive intervention against life-threatening invasive fungal infections in high-risk granulocytopenic pediatric cancer/HSCT patients. A significant lower incidence of IFI in neutropenic patients treated with low dose L-AmB for prophylaxis of IFI was observed by Olaf Penack from Berlin.

The first day ended with an integrated symposium sponsored by Astellas presenting once more a detailed overview of *Candida* infections with a special look at the pharmacokinetic of micafungin and its clinical relevance.

In the symposia on the second congress day, presentations regarding to the important problem of antifungal resistance were given by Thomas Edlind from Philadelphia who explained the function of MDR pumps in fungi contributing to the development of resistance mechanisms and Dominique Sanglard from Lausanne who summarized in detail all known mechanisms of antifungal resistance.

The afternoon symposium dealt with fungal infections of the central nervous system (CNS). From the initial sites of infection CNS involvement might arise from extension of sinus/ear infections or haematogenous spread. Autopsy studies indicate that the CNS is the second most frequent organ affected in invasive aspergillosis. CNS infections caused by filamentous fungi have an extremely poor prognosis. Stefan Schwartz from Berlin presented some data of a recent retrospective analysis of 81 patients with proven or probable neuroaspergillosis suggesting improved outcome after treatment with voriconazole.

Markus Ruhnke

The Drouhet Lecture was delivered by Annemarie Polak

From left to right: Jacques Meis, Gudrun Just-Nübling, Georg Maschmeyer

The integrated symposium of the second day sponsored by Schering-Plough focused on filamentous fungi and the role of posaconazole in treatment of invasive infections caused by these pathogens.

The positive and negative sites of new and old antifungals were the hot topic of the last congress day. Questions such as “When will amphotericin B die?”, “More echinocandins - better therapies?”, “New azoles - more options?” awoke a lot of interest among the participants and were discussed very intensively. This discussion created the basis for a trial of defining the roles of antifungal agents available today. At the end we looked behind the horizon with Christopher Hitchcock from Kent to imagine the antifungal development in the future.

Finally, during the lunch time break Walter Buzina from Graz gave us a beautiful presentation about “Fungi and art” telling us how the attributes of fungi as mind-altering psychedelic mushrooms, deadly poisonous toadstools, incredibly expensive delicacies or just beautiful-looking creatures, inspired numerous artists to immortalize fungi in artwork. Not to forget, 294 posters contributed to the scientific success of the 2nd Trends in Medical Mycology congress in Berlin 2005.

Markus Ruhnke
for the Executive Committee of TIMM2005

2nd Trends in Medical Mycology

Candida biofilms: what have we learnt so far?

Candida biofilms were a hot topic in TIMM2 and stimulated interesting discussion among the participants. Two pioneers of fungal biofilms, Julia Douglas and Mahmoud Ghannoum gave excellent overviews on the topic and where we stand today.

Dr. Ghannoum (University Hospital of Cleveland, USA) presented recent findings of his research work on *Candida* biofilms with two very eloquent talks enriched with impressive microscopy photographs. Dr. Ghannoum and his research team have developed a simple, clinically relevant, *in vitro* model of *Candida* biofilms on medical devices. Using various techniques, including fluorescence microscopy, confocal scanning laser microscopy, tetrazolium (XTT) and dry weight assays, they have been able to visualize and quantify *Candida* biofilms formed on silicone elastomer disks. As shown by Ghannoum's lab, *C. albicans* produces quantitatively larger and qualitatively more complex biofilm than other *Candida* species. On microscopy, *C. albicans* biofilms were found to be thick, had a uniform morphology and they consisted of a basal blastospore layer with a dense overlying matrix composed of exopolysaccharides and hyphae while *C. parapsilosis* biofilms had less volume and were comprised exclusively of clumped blastospores. Dr. Ghannoum also highlighted the importance of biofilms by non-*albicans Candida* species and as evidence for this he cited the first study, which compared clinical isolates, demonstrating that biofilm production by *C. albicans* isolates was significantly less frequent (8%) than that by non-*albicans Candida* species (61%). He also referred to an epidemiological study of his group, concerning a nosocomial outbreak of *C. parapsilosis*. They compared outbreak isolates with those obtained from sporadic infections and concluded that the outbreak clone produced more biofilm than all the other strains while no clear relationship was apparent for other putative virulence factors (adherence, phospholipase and proteinase production). *Candida* spp. in biofilm form were significantly more resistant to fluconazole than in planktonic form. Micafungin and anidulafungin as well as amphotericin B lipid complex showed minimal increase of their MIC's for biofilm forms as compared to planktonic *Candida* forms. In addition, Dr. Ghannoum described the development of a rabbit model of catheter associated infection with *C. albicans* biofilm and showed that antifungal lock therapy with liposomal amphotericin B and micafungin are effective treatment strategies for these infections.

Mahmoud Ghannoum


Emmanuel Roilides and Aspasia Katragkou

The mechanisms of antifungal drug resistance of *Candida* biofilms were thoroughly presented by Julia Douglas (University of Glasgow, UK). Dr. Douglas clarified that a variety of clinically important agents, such as amphotericin B, fluconazole, flucytosine, itraconazole as well as the newer azoles (voriconazole and ravuconazole) are ineffective against *Candida* biofilms. Explaining the phenomenon of reduced susceptibility of *Candida* biofilms to antifungal agents, she analyzed the potential roles of biofilm matrix material, slow growth rate of biofilm organisms and surface-induced genes coding for multidrug efflux pumps, integrating results of different *in vitro* biofilm model systems (ranging from a simple assay with catheter disks to more complex flow systems, such as perfused biofilm fermentor). Of note, she also mentioned the recent suggestion of Kim Lewis about "persister" cells as another contributory factor to biofilm resistance to killing. Overall, she concluded that the recalcitrance of *Candida* biofilm cells is not fully understood and in all probabilities it is a multifactorial phenomenon. Of the antifungal agents showing anti-biofilm activity, Dr. Douglas underscored the role of lipid formulations of amphotericin B, caspofungin and micafungin. Similarly, according to *in vitro* experiments conducted by her group, aspirin and other non-steroidal anti-inflammatory drugs possess potent anti-biofilm action. Finally, Dr. Douglas determined the promising role of two quorum sensing molecules that have already been identified in *C. albicans*, farnesol and tyrosol, which inhibit or promote hyphal formation, respectively. She suggested that "analogs of quorum sensing molecules might inhibit biofilm development and so they might represent a novel anti-infective strategy". Moreover, she concluded that the various secreted molecules could be implicated in the demonstration of antagonism by *Pseudomonas* spp. and *Candida* spp. within a biofilm.

Excellent insights into the molecular basis of *Candida* biofilms were presented by Christophe d'Enfert (Institut Pasteur, Paris, France). He presented results of the study of his group on the expression patterns that accompany biofilm growth in *C. albicans*. In their studies they observed that diverse *C. albicans* biofilms have homogeneous transcript profiles that differ from those of planktonic populations. Further, they identified a set of genes that are over-expressed in mature biofilms. In another study, by using a genetic screening strategy, they identified genes involved in biofilm formation in *C. glabrata*. They identified a new protein (Epa6p) which is the principal adhesin involved in biofilm formation in this yeast. Finally, they demonstrated that the kinase Yak1p is required for expression of adhesin genes and acts through a subtelomeric silencing machinery-dependent pathway.

Aspasia Katragkou
Emmanuel Roilides

2nd Trends in Medical Mycology

Infections in intensive care unit patients

Evidence is accumulating that invasive fungal infections pose a vital threat to critically ill ICU patients even in the absence of severe immunosuppression. Koenraad Vandewoude (Ghent University Hospital, Belgium) gave an overview on infections on the ICU and highlighted the problems on *Candida* spp. He pointed out, that adequate management is hampered by a problematic diagnosis and gave a survey on timely therapeutic strategies. Antifungal prophylaxis is based on type of underlying diseases with a high risk for invasive candidiasis; potential indications are bone marrow transplantation, liver transplantation, recurrent gastro-intestinal perforations or leakages, and surgery for acute necrotizing pancreatitis. Pre-emptive therapy can be recommended as basis of an individual risk profile including overt candidal colonization. Empiric therapy is started in patients with a risk profile for invasive candidiasis and is recommended in the presence of clinical signs of infection, but in the absence of a causative pathogen.

Marcio Nucci (University Federal, Rio de Janeiro, Brazil) evaluated the role of optimal catheter management in patients with fungemia. He commented that until now it is not evident whether patients with candidemia benefit from central venous catheter (CVC) removal and whether CVC removal is associated with decreased mortality. He did a literature research regarding this topic and found only 23 studies (1966-2004) dealing with CVC removal and survival. A strong association between CVC removal and lower mortality was evident in only one study. In another trial persistent candidemia was associated with higher rates of total complications, but the death rates were not statistically different. Dr. Nucci concludes that despite these limitations, it seems reasonable to change CVC in patients with candidemia.


Cornelia Lass-Flörl

Elie Azoulay (Hôpital Saint-Louis, Paris, France) gave an overview on the role of a positive *Candida* culture in tracheal secretions. He pointed out that fungi colonize the gastrointestinal tract and spread along the respiratory tract, resulting in positive endobronchial specimens yet lack of pneumonia. In two studies on ICU patients, 85% showed respiratory specimens positive for *Candida* and lack of invasive diseases. Yet, endobronchial specimens yielding *Candida* remain clinically relevant as indicator for 'relative' immunodepression. He concluded, that the estimation of the colonization index, which is known to correlate well with secondary emergence of systemic candidiasis is helpful in making decision on therapy. He suggested the use of prophylactic and pre-emptive treatment.

Aspergillus may also pose a threat to this patient population. Koenraad Vandewoude noted that invasive aspergillosis is increasingly recognized as disease in critically ill ICU patients. In a single center study in a medical ICU, with strict application of the EORTC/MSG criteria, an incidence of 6,7% was found, with pulmonary involvement in most cases. The most frequent underlying condition was COPD requiring chronic systemic steroids. The presence of *Aspergillus* spp. in respiratory tract should not be discarded in the absence of typical host risk factors, but should urge for prompt CT-scan, broncho-alveolar lavage, and lung biopsy if appropriate.

Lena Klingspor (Karolinska University Hospital, Huddinge, Sweden) gave an overview on the value of non-culture fungal diagnosis in intensive care patients. She underlined, that the polymerase chain reaction (PCR) offers great promise for the rapid diagnosis of fungal infections. A real-time assay for *Candida* and *Aspergillus* spp. using a robot for automated extraction of DNA was established in her laboratory. MagNa Pure LC was used for automated extraction of DNA, the whole assay takes approximately 5–6 h to perform; prospective studies evaluating the potential benefits of early therapy based on real-time PCR are ongoing at the Karolinska University Hospital Huddinge. Another pyrosequencing technology for short to medium length sequences was developed in her laboratory for rapid typing *Candida*, *Cryptococcus*, *Saccharomyces* and *Aspergillus* to species level.

Cornelia Lass-Flörl

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Update on antifungal resistance

Juan Luis Rodríguez Tudela (Instituto de Salud Carlos III, Majadahonda, Spain) gave an overview on the advances in developing susceptibility testing standards and discussed the contribution of these methodologies in assessing the clinical importance of susceptibility testing and in epidemiology. The Clinical Laboratory Standards Institute (CLSI), formerly NCCLS, was the first to create antifungal susceptibility standards for yeasts and filamentous fungi. Subsequently, the Antifungal Susceptibility Testing Subcommittee of the European Committee on Antibiotic Susceptibility Testing produced their own European Standards: One on detecting antifungal resistance of glucose fermenting yeasts (Edis 7.1) and one, currently at the final phase, for detecting filamentous fungi resistance.

The established antifungal susceptibility methodologies were the corner stone of numerous epidemiological studies aiming to determine the rate of antifungal resistance within the population of human fungal pathogens. For high incidence fungal pathogens, these studies reveal whether certain species maintain their primary susceptibility pattern or whether they develop secondary resistance. By contrast, for low incidence fungal pathogens the majority of available data are derived from passive surveillance studies, which despite their limitations have identified those strains, species or genera with high MICs to antifungal drugs. Such susceptibility and epidemiology-instigated studies can reveal the mechanisms of resistance in isolates with high MICs compared to those displaying low MICs.

The subject matter on the new developments on resistance of fungal pathogens to antifungal drugs dealt with an important aspect of antifungal resistance research (Dominique Sanglard, University Hospital Lausanne, Switzerland). Active research undertaken over the past years has contributed in elucidating the molecular basis of antifungal drug resistance in fungal pathogens, especially against the class of azole antifungals. Detailed genome analysis studies on azole-resistant isolates have allowed comprehensive analysis of the impact of resistance on gene expression, as resistance mechanisms to azoles are also linked with upregulation of multidrug transporter genes. A new *Candida albicans* transcription factor located near the mating type locus on chromosome 5, the transcriptional activator *TAC*1 of the CDR genes, is involved in the regulation of *CDR*1 and *CDR*2 ABC transporters, which mediate azole resistance. Also, reduced azole susceptibility is recorded in *C. dubliniensis*, genotype 3 (identified by sequencing of the rRNA internal transcribed spacer region), that is associated with increased expression of the multidrug transporters CdCDR1 and CdCDR2.

The exciting developments on the coordinate upregulation of multidrug transporters involved in *C. glabrata* azole resistance and the experimental evidence for upregulation of a *C. glabrata* homolog Pdr1 transcription factor in azole-resistant isolates were also incorporated in the session covering Antifungal Resistance (Thomas Edlind, Drexel University College of Medicine, Philadelphia, USA).

In the Pfizer sponsored symposium entitled "Defining the roles of new antifungal agents", Mahmoud Ghannoum (University Hospital of Cleveland, USA) focussed on the question on what susceptibility data tell us about the new antifungals. As new antifungal agents have been approved in the recent years, standard procedures for testing susceptibility had to be employed and evaluated. Interlaboratory comparison of results for susceptibility testing with caspofungin against *Candida* species generated consistent MIC data by visual "prominent growth reduction" (MIC2) end points read at 24 h in RPMI or antibiotic medium 3. For *Aspergillus* species reproducibility of caspofungin minimum effective concentration end point determinations gave excellent reproducibility unlike the MIC end point reproducibility data. For the newer azoles voriconazole and posaconazole quality control data and reference guidelines for the filamentous fungi according CLSI broth microdilution susceptibility method (M38-A) have been produced. Also, studies on the correlation of MICs with outcome for *Candida* species tested against voriconazole may soon lead to establishing relevant interpretive breakpoints. MIC distribution data, integrated with pharmacokinetic and pharmacodynamic parameters, contribute in the development of interpretive breakpoints provided there is evidence for the relationship between *in vitro* activity with the *in vivo* and clinical studies. Currently, *in vitro* and clinical studies investigate use of newer antifungals in combination therapy.

In the integrated symposium sponsored by Schering-Plough entitled "Unravelling the issues in filamentous fungi: The role of newer antifungals" the emerging trends in the prevalence and resistance profiles of filamentous fungi were comprehensively discussed (Paul Verweij, Radboud University Nijmegen Medical Centre, The Netherlands). It was stressed that the changing spectrum of fungal infections in immunocompromised patients due to the emergence of unusual and rare pathogens such as other than *A. fumigatus* (*A. flavus*, *A. terreus*, *A. niger*, *A. versicolor*) and *Scedosporium*, species presents a clinical challenge. Moreover, many of these pathogens may possess either natural or acquired resistance after exposure to therapy. Then again, the use of antifungals such as fluconazole though contributed in a decrease of invasive candidiasis has raised the numbers of patients infected by *Aspergillus* species. Subsequently, the introduction of voriconazole though improved treatment of aspergillosis has surfaced the issue of breakthrough zygomycete and other rare mould infections. The change in the spectrum of fungal pathogens transpired progress in diagnostic approaches, especially in invasive aspergillosis, but it was pointed out that laboratory diagnostic options for other moulds remain scarce. Besides diagnostics, it was noted that the shift in pathogens is perceived in conjunction with the availability of the new broad-spectrum antifungal agents, such as the novel triazole posaconazole, which shows potent *in vitro* antifungal activity against a wide range of yeasts and moulds. Although resistance has been described with chronic use of azoles, in particular with itraconazole, azole resistance in acute invasive aspergillosis is very rare. It was concluded that, in addition to *Aspergillus*, posaconazole exhibits *in vitro* activity against fungi of major clinical importance, such as the *Zygomycetes*, *Fusarium* and *Scedosporium* species and that pre-clinical trials revealed promising efficacy in experimental models of invasive fungal infection.

Aristea Velegraki

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New antifungal drugs and treatment strategies

The congress enabled participants to report new data and debate ideas on the management of severe fungal diseases. The discussion on their treatment included consideration of the possible place of new antifungal drugs in future treatment strategies, the potential use of combination therapy and immunological approaches to fungal infection.

In a presentation on the treatment of invasive aspergillosis, Raoul Herbrecht (University Hospital of Strasbourg, France) said that despite the significant progress marked by the introduction of newer antifungal agents such as voriconazole, caspofungin and micafungin, mortality in patients with this infection remains high. Even with the best available first-line treatment (voriconazole), mortality at 12 weeks is 29% (compared with 42% with amphotericin B, which is associated with significant toxicity). There is still a need to try to improve therapeutic strategies. Emphasising the importance of early treatment, Prof. Herbrecht said that if treatment is started when infection is "possible", i.e., before confirmation, survival at 12 weeks is 58%. In contrast, 12-week survival is 43% if treatment is not started until the patient has "probable" or "proven" infection.

Andrew Ullmann (Johannes Gutenberg University, Mainz, Germany) emphasised the high risk of

invasive fungal infection in allogeneic haematopoietic stem cell transplant (HSCT) recipients. Current prophylaxis options for HSCT recipients have some limitations. With fluconazole, there is an increasing prevalence of resistant *Candida* spp and the drug is not active against moulds; itraconazole is associated with poor tolerability and erratic bioavailability, and breakthrough zygomycosis has occurred during voriconazole use.

Dr. Ullmann reported for the first time the results of a 90-centre trial comparing posaconazole and fluconazole for prophylaxis of invasive fungal infection in allogeneic HSCT recipients with graft versus host disease. Patients were randomised (double blind, double dummy) to receive posaconazole suspension 200mg three times a day (301 patients) or fluconazole capsules 400mg once daily (299 patients). Treatment was given for 112 days (16 weeks) or until a pre-specified endpoint was reached. Dr. Ullmann reported that at the end of the study period, posaconazole was superior to fluconazole in preventing proven or probable invasive aspergillosis (7 cases vs 21 cases, P=0.006) and as effective as fluconazole in preventing all invasive fungal infections (16 cases vs 27 cases, P=0.074). While patients were receiving study drugs (a mean of 80.3 days for posaconazole and 77.2 days for fluconazole), posaconazole was superior in preventing both aspergillosis (3 cases vs 17 cases, P=0.001) and invasive fungal infections overall (7 cases vs 22 cases, P=0.004). Mortality due to invasive fungal infections was lower with posaconazole. Both drugs were well tolerated.

Dr. Ullmann noted that this is the first randomised trial showing efficacy of antifungal prophylaxis in this high-risk patient group. David Denning (University of Manchester, UK), who chaired the symposium, suggested that the trial will change practice in this area.

Several speakers at the congress commented on the potential use of combination antifungal therapy. Markus Ruhnke (Humboldt University, Berlin. Germany) said that monotherapy against invasive candidiasis gives response rates of around 70% and monotherapy for invasive aspergillosis gives response rates of 50% with the best available treatment (voriconazole), while response rates in neutropenic patients are even lower. “We probably do need combination therapies,” he said.

Georg Maschmeyer (Klinikum Ernst von Bergmann, Potsdam, Germany) said that preclinical studies have shown additive or synergistic antifungal activities, particularly between echinocandin antifungals and azoles. But caution is required as there have also been reports of antagonism between azoles and amphotericin B. Potential disadvantages include possible antagonism, drug interactions, increased toxicity and higher costs. He added that prospective clinical trials are now urgently needed to assess whether combination therapy can improve clinical outcome.

Bart-Jan Kullberg (Radboud University Nijmegen Medical Centre, The Netherlands) explained that the high failure rate with current treatments for invasive fungal infections has led to renewed interest in the idea of stimulating the host immune system as a treatment strategy. Regarding use of pro-inflammatory cytokines, he said that interferon gamma has been given to boost the immune system in HIV patients with acute cryptococcal meningitis receiving antifungal therapy and has led to improved response. In addition, he has completed a study in which non-neutropenic patients with candidemia received fluconazole, with or without G-CSF. Duration of infection fell from 21 to 14 days with the G-CSF treatment and the cure rate was improved. “This approach is experimental but indicates we are on the right track,” he said.

As an example of passive vaccination, Prof. Kullberg cited UK work with Mycograb (antibody against fungal heat shock protein 90) in patients with candidemia. Response was significantly better when the antibody was given with amphotericin B than with the antifungal drug alone, although there was more toxicity in the antibody arm.

Active vaccination is still some way off, but researchers are starting to understand the mechanisms by which host cells recognise fungal pathogens, Prof. Kullberg explained. The idea with this strategy will be to stimulate specific receptors to boost the immune system before the patient enters the “risk” situation. If a vaccine could be developed that worked quickly, it might be given to people at high risk of fungal infection, such as those who go in to ICU, or who are undergoing transplantation or major abdominal surgery.

Joanna Lumb

EORTC ECMM CEMM **2nd Trends in Medical Mycology**

Dermatomycology

This symposium, chaired by H.C. Korting and R. Baran, focused on essential and up-to-date issues of widespread human mycoses: dermatophytosis, *Malas-sezia* infections and onychomycosis.

Peter Mayser (Justus Liebig University, Giessen, Germany) described the new methabolic pathway in species of *Malassezia*, agents of pitiryasis versicolor and a possible cause for a variety of other cutaneous conditions. Dr. Mayser and coworkers have shown recently that tryptophan-utilising strains of *M. furfur* produce a range of pigments and fluorochromes with pharmacological properties of special interest, such as UV-protection, inhibition of inflammatory reaction,

Alexey Y. Sergeev

induction of apoptosis in melanocytes and cytochrome p450 in keratinocytes. The relevance of the genes, encoding these substances, to pathogenesis of pityriasis versicolor was investigated. Several elements of indol metabolic pathway, detected in skin scraping from patients, were also found in phylogenetically related basidiomycete *Ustilago maydis* and ascomycetous yeasts, species with genomes already sequenced. Those findings facilitate research and offer new insights in our understanding of *Malassezia* species and their role in human pathology.

Jacek C. Szepietowski (University of Medicine, Wroclaw, Poland) reviewed clinical and diagnostic aspects of tinea faciei, the disease often misdiagnosed by dermatologists. Tinea faciei appears to be more common today, and may account up to 19 per cent of all dermatophytic infections. Causative agents of tinea faciei vary from *Microsporum canis* to antropophylic *Trychophyton* spp., resulting in different epidemiological and clinical patterns. Tinea faciei may manifest atypically, mimicking conditions like rosacea, seborrheic dermatitis or lupus erythematosus. As many as 70 per cent of patients with tinea faciei are misdiagnosed initially. Thus, the possibility of facial dermatophyte eruptions should be expected in everyday practice and not underestimated.

Gabriele Ginter-Hanselmayer (Medical School of Graz, Austria) focused her talk on the treatment of tinea capitis – the dermatophyte infection with increasing incidence and variable etiology. Griseofulvin, considered to be a drug of choice in tinea capitis for more than four decades, has proved to be highly efficacious and safe. Trials with newer antifungals, terbinafine, fluconazole and itraconazole, have demonstrated comparable efficacy and safety, offering better compliance and shorter treatment courses. Modern choice of antifungals in tinea capitis deals with questions of etiology (higher dosages or longer treatment for terbinafine and fluconazole in *M. canis* infection), bioavailability and safety in pediatric population.

Alexey Y. Sergeev (All-Russian National Academy of Mycology, Moscow, Russia) provided an update on onychomycosis and recent advances in diagnosis, treatment and prevention. Onychomycosis today appears to be the most common form of tinea infections, affecting at least 5 per cent of adult urban population. Often neglected, self-treated or diagnosed late, onychomycosis may last for decades, resulting in multiple and extensive nail involvement. Severity of onychomycosis may explain failures of antifungal treatment, necessitating differential treatment approaches and combination therapy. Direct PCR probes have been developed recently to detect the main causative agents of onychomycosis in the nails, and the clinical study presented reports higher accuracy in diagnosing tinea unguium when compared to conventional methods. Newer prevention strategies, including awareness campaigns and distant education, reveal “hidden” patients and provide early admissions with better outcomes.

Alexey Y. Sergeev

The Congress Dinner was held at the Schlüterhof, in the Berliner Castle, the oldest and biggest antique courtyard in Berlin

The ECMM Young Investigators Travel Award

Elisabete Ricardo (on the right) from Porto University, Portugal, was awarded the 2005 ECMM Young Investigators Travel Award

I'm a biochemist and a Master Degree student in the Microbiology Laboratory at the School of Medicine in Porto University, Portugal. For me it was an enormous surprise and even a great honour to receive the Young Investigators Travel Award for my poster presentation entitled "Reversion of resistance of *Candida* due to efflux: a phenotype and genotype study" (authors: Cidália Pina-Vaz, Sofia Costa-de-Oliveira, Elisabete Ricardo, Acácio Rodrigues Gonçalves) presented in the 11th Congress of ECMM, 2nd Trends in Medical Mycology, October 2005, Berlin, Germany and also published in a supplement of "Mycoses". It was my first presenting poster and my first international congress, so the award had a special meaning in my personal life as a beginning researcher.

I mostly work with *C. albicans*, studying gene expression profiles associated with resistance mechanisms involving efflux pumps, one of the main research topic. In our laboratory we also work with all *Candida* spp, a human fungal pathogen that could cause candidemia in imunocompromised individuals as well as filamentous fungals like *Aspergillus* spp, its mechanisms of virulence and its susceptibility.

Candida species are the most common opportunistic yeasts, especially *C. albicans*. It causes oral, vaginal and systemic infections with high morbidity. Such infections are associated with immune disorders, endocrine abnormalities and unrestricted use of large spectrum antimicrobians. Candidoses are usually treated with antifungals, being the most widely used the azoles like fluconazole, itraconazole and voriconazole (Smith e Edlind, 2002). There are several mechanisms of azole resistance in *C. albicans*: reduced accumulation of drugs through active efflux (over expression of genes like CDR1, CDR2 and MDR1), alteration or overexpression of the target enzyme 14α – sterol-demethylase, encoded by ERG11, and loss of function downstream mutation in the ergosterol pathway (defective ¢-5, 6-desaturase encoded by ERG3). Frequent cross-resistance also stresses the need for developing new therapeutic alternatives.

I'm focusing my work on the study of CDR1 and CDR2 gene, which belong to the family of ABC transporter genes that encode ATP-dependent efflux pumps, over expressed in many azoles resistant clinical isolates. The primary aim of my research is to determine differences in gene expression profile in clinical isolates of *C. albicans* clinical isolates, in a central hospital, exhibiting different phenotypes (susceptible and resistant, determined by the Clinical Laboratory Standards Institute, formerly CLSI) and try to understand the molecular mechanism involved. It has already been described in some clinical isolates, with the resistance mechanism associated to efflux, a considerable increase in CDR1 and CDR2 expression, but little is known about how the regulation of expression proceeds and if this is an intrinsic characteristic of the resistant strains or if they acquire it. We just know that resistant strains have over expression of them, so it would be very important to understand what's going on in the cells. *C. albicans* genes encode other efflux pumps but these seem to be the most important and prevalent in resistance.

Flow cytometry is also used in our laboratory to provide consistent results concerning the susceptibility of *Candida* to fluconazole in a few hours. Using the fluorescent stain FUN-1, allows classifying *Candida* strains as susceptible, susceptible dose dependent or resistant to fluconazole. We can even predict the resistance mechanism associated with a certain isolate by blocking efflux pumps and register differences in the fluorescence signal. This technique also helped to clarify the mode of action of some non – antifungals, such as local anaesthetics, sex hormones or ibuprofen as potential blockers for efflux pumps reverting resistance in clinical isolates.

Particularly, the results of the awarded poster strongly suggest that ibuprofen, a potent anti-inflammatory and analgesic drug, might have a future role in therapy of candidoses, with association with a classical antifungal drug like fluconazole.

I would like to thank Drª Cidália Pina-Vaz and Dr Acácio Rodrigues for the opportunity to work with them and for trusting on me; I would also like to thank all my laboratory colleagues in Microbiology Laboratory for all the support.

And off course, to the ECMM group, I congratulate for the magnificent congress in Berlin, where I had the opportunity to talk and mostly learn with so many important researchers, directly or indirectly through the different sessions presented. It was a really enjoyable experience.

Thank you so very much for giving me the opportunity to take my work abroad through the Young Investigators Travel Award.

Elisabete Ricardo

About the ECMM Young Investigators Travel Award

To poster presenters and speakers of the 12th ECMM Congress in Torino

ABOUT THE AWARD

The ECMM Young Investigators Travel Award facilitates young, nonestablished investigators in medical mycology to make educational or practical study visits to medical mycology oriented departments or institutions in other European countries. As a rule, the Awardee will be selected from among those presenting a poster in the annual ECMM Congress. An outstanding oral presentation may also be considered.

The presentations are judged by a Prize Committee on the basis of the scientific quality, including novelty, reliability and significance, of the Awardee's presentation. The sum of the Award is presently 1000 EUR, to support the travel and living costs of one week. The institute visited is freely selected by the Awardee.

Eligibility: The Award is meant for young (not older than 35 years) persons who are citizens of European countries or work in Europe. The Awardee should not hold an established (other than grant-funded) post in medical mycology. It is also wished that the Awardee is a member of a national society or at least aims to apply for membership. Eligible first or presenting authors are preferred, but an outstanding team may be selected if it can direct the Award to junior coauthors who are eligible.

Those individuals and teams wishing to be considered as candidates of the Award in the 12th Congress of the ECMM in Torino, 2007, are kindly asked to fill this form and submit it to the Congress Secretariat at first convenience.

AUTHORS' STATEMENT

- Concerning our presentation, titled: .....

.....

- By authors (please mark the presenting author): .....

.....

Presented ☐ As a poster / ☐ Orally (*Tick square as appropriate*);

Yes, we wish that our presentation is considered as a candidate for the ECMM Young Investigators Travel Award. Our presentation meets the eligibility criteria as follows (*tick all squares that are appropriate*):

1) The following team members are aged 35 years or less:
☐ First author
☐ Presenting author
☐ Other coauthor(s) (*who?*)

2) The following team members do not hold an established position:
☐ First author
☐ Presenting author
☐ Other coauthor(s) (*who?*)

3) The following team members are citizens of, or work in, a European country and are either members of a ECMM member society or willing to submit a membership application if selected.
☐ First author
☐ Presenting author
☐ Other coauthor(s) (*who?*)

To be signed by the first or presenting author:

Date ..... / ..... 2007, ...

To be submitted as paper, fax or email to the Congress Secretariat (Congress Care, Muntelbolwerk 1, P.O. Box 440, 5201 AK's-Hertogenbosch, The Netherlands, fax: +31 73 690 1417, e-mail: info@congresscare.com. To facilitate handling, we kindly recommend submission before October 15th, 2007. However, forms given at the Congress registration desk at latest October 28th, will be considered.

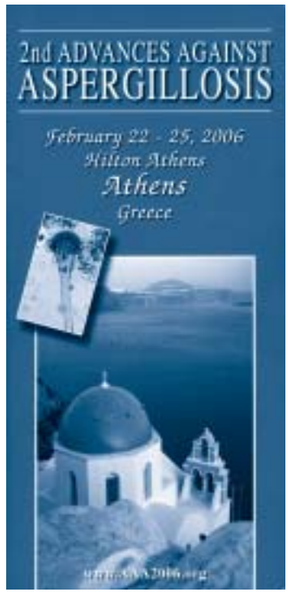
ECMM Executive Committee

Special report on...

2nd Advances Against Aspergillosis

The sculpture in front of the Hilton Hotel, venue of the 2nd AAA conference, is a work of Constantine Varotsos, who made out of glass his "Runner" depicting the hectic life of people in Athens

The 2nd Advances Against Aspergillosis international meeting was held at the Hilton Athens in Athens, Greece, February 22-25, 2006. For this year's meeting there were 442 registrants from 44 countries in attendance, a substantial increase from the inaugural meeting held in 2004.



The scientific program proved busy and comprehensive with 10 plenary sessions and 4 satellite symposia totalling more than 60 different speakers. In addition, two poster sessions were held to accommodate presentation of the 157 posters accepted for presentation. Abstracts on CD were distributed free to all registrants. The hoped for growth over the inaugural AAA 2004 meeting was the presentation of even greater scientific content, as indicated by the larger number of posters and more registrants and more detailed discussions and this goal clearly was attained. Moreover, several debates tackling the difficult issues of diagnosis and empiric antifungal therapy, occurred during the meeting.

Two awards for excellence were presented by David A. Stevens. The Young Investigator award was presented to S. Turnbull for her presentation of poster P015 "Transcript profiling of the murine immune response to *Aspergillus fumigatus*." Authors: Turnbull S., Armstrong-James D., Bignell E., Rogers N., Rogers T., Haynes K. Molecular Mycology, Imperial College, Hammersmith Hospital, London, UK. The best overall abstract award was chosen for presentation in an oral session along with four other submitted abstracts. The talk was given by K. Buckland and the abstract is entitled "Intrapulmonary TREM-1 expression confers significant protection against chronic fungal asthma in mice by promoting clearance of *A. fumigatus*." Authors: Buckland K.F., Carpenter K.J., Xing Z., Aoki N., Hogaboam C.M.; University of Michigan, Ann Arbor, MI, USA; McMaster University, Hamilton, ON, Canada; Asahikawa medical College, Asahikawa, Japan. Each of these individuals is to be congratulated for the high quality of their science and for their superb presentations.

In addition, 34 travel scholarships were awarded to deserving individuals to enable them to attend and further enhance their careers. These scholarships were possible because of the generous donations made to the meeting by industry and private foundations and individuals, including Schering-Plough Research Institute, ISHAM, Mira Vista Diagnostics, Foundation for Research in Infectious Diseases, David A. and Julie A. Stevens, and Advances Against Aspergillosis. In addition, the meeting' organizers and scientific committee are grateful to the 13 sponsors and their generous support (For a list of the sponsors and the program of the meeting go to http://www.aaa2006.org/2006/index.php).

The social events of the meeting began with a Welcome Reception on Wednesday evening to encourage the congeniality of meeting old friends once again and meeting new colleagues. On Friday evening the conference dinner was held at the "The Old Stables", where attendees were provided plenty of excellent Greek cuisine and drink, as well as displays of folkloric dance and music. All of the attendees appeared to enjoy the evening immensely.

A preliminary planning meeting was held to discuss possible venues and program material for AAA 2008. To date the AAA 2008 meeting will be held in the United States, likely Jan/Feb 2008, dates and location to be announced in summer 2006. In AAA 2008 the program will work to present complete issues and topics in "bench to bedside" in single sessions. The meeting Chairs and scientific committee truly wish to fulfill the needs of the *Aspergillus* community and as such, the continued success of this conference relies on the community's support. We seek the continued support and welcome comments on the content, suggestions for 2008 topics, and ways to improve the meeting.

Comments and suggestions can be emailed to Drs.:
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or Clemons (clemons@cimr.org).
We look forward to an even better conference in 2008.

Karl V. Clemons
William J. Steinbach
David W. Denning
David A. Stevens

George L. Petrikkos and David A. Stevens

David W. Denning

Karl V. Clemons

The complete 2006 conference syllabus as a PDF file, as well as meeting updates and information for the 2008 conference, will be available at the conference website

www.advancesagainstaspergillosis.org

In addition, a supplement of speaker's papers from the 2006 meeting will be published in Medical Mycology in 2006 or 2007.

2nd Advances Against Aspergillosis

Clinical issues with aspergillosis

From left to right: John Bennett, Archie Prentice, Raoul Herbrecht and Thomas Walsh during the debate on methodology appraisal of clinical trials

Drug interactions in IA

The need to be alert to the possibility of serious drug interactions when treating patients with IA was emphasized by Russell Lewis (University of Houston, USA). The magnitude and clinical impact of these interactions were not always predictable, and lead to a need for individualized case management.

Dr. Lewis commented that all azoles had potential for drug interactions. But there were clinically important differences between the drugs. While most azoles were metabolized through phase 1 (CYP-mediated oxidative) metabolism, posaconazole was metabolized primarily through phase 2 mechanisms. Posaconazole, like other azoles, is a potent inhibitor of CYP3A4 but not a major substrate, so the interaction profile was different from the other azoles. "You have to know the interaction profiles of each drug. You cannot make generalizations that all azoles will interact with a particular drug," stated Dr. Lewis.

Drug interactions that were always significant were those that affected agents with a narrow therapeutic index (e.g., immunosuppressants such as tacrolimus, chemotherapy such as vinca alkaloids) and those that increased the metabolism of antifungals (potentially resulting in ineffective treatment, such as rifamycins and phenytoin).

Also important were interactions leading to prolongation of the QTc interval. There was no doubt that antifungals, especially older azoles, could inhibit potassium channels in the heart which could lead to significant QTc prolongation and rare events of torsade des pointes arrhythmia. Ketoconazole and itraconazole had a significant risk: not only did they inhibit the metabolism of some drugs that carried high risk for torsade des pointes, they also had inherent inhibitory activity on heart tissue themselves. Many patients were taking several drugs that could prolong the QTc interval and it could be that adding an antifungal "pushes them over the edge" to arrhythmia, Dr. Lewis said.

Clinical trial methodology

In a session on clinical trial methodology, Patricia Ribaud (Hôpital Saint-Louis, Paris, France) discussed the challenges of patient recruitment for IA trials. "The main challenge is inclusion of the maximum number of patients for the minimum length of time," she said.

One problem was that IA was not a frequently diagnosed disease: the TRANSNET surveillance programme of infection in transplant patients showed approximately a 2% incidence of IA. Also, most recent trials tended to be non-inferiority trials and these needed many more patients than superiority trials.

Recruitment would be improved by better diagnostic tools (at present, probably over 50% of cases were undiagnosed before death). Also worth considering were "creative" trial endpoints, such as time to response or time to progression, and use of surrogate markers, such as changes in galactomannan index. This might allow shorter studies and fewer patients, Dr. Ribaud said.

Georg Maschmeyer (Humboldt University, Potsdam, Germany) spoke about the problems of defining clinical failure for salvage studies. His hypothesis was that many patients who entered a salvage trial were not really clinical failures but might be "pseudo-failures." In some cases, benefit would then be falsely attributed to a second drug when the patient would have improved if the first drug had continued. Prof. Maschmeyer also noted that salvage therapy might in fact be combination therapy: for example, patients switched to salvage antifungal after primary therapy with high-dose liposomal amphotericin B would be getting combination therapy because of the persistence of high drug tissue concentrations.

He suggested that future salvage studies might ideally have three arms: continued primary antifungal (unless clearly inappropriate, e.g., resistance) vs. primary antifungal plus salvage antifungal vs. salvage antifungal alone.

Prof. Maschmeyer thought there was need "to cool down a bit" and not keep switching antifungals. He commented: "We have to distinguish between our nervousness and the reality." It had not really been shown that a switch of drug was of benefit to a patient with IA who had failed full-dose modern antifungal treatment.

Pre-emptive antifungal therapy

Monica Slavin (Royal Melbourne Hospital, Australia) discussed a new approach to antifungal therapy in high-risk patients, using "pre-emptive" therapy guided by new diagnostic tests. In addition to prophylaxis for high-risk patients, the standard approach was empiric antifungal therapy, prompted by fever that was not responsive to broad-spectrum antibiotics in a neutropenic patient. "We are comfortable with this approach but there are some problems," Dr. Slavin said. For example, empiric therapy involved treating many patients who were not going to develop infection. "Are we over-treating 90% of patients to treat the 10% who have an invasive fungal infection?" Conversely, an increasing proportion of invasive fungal infections (IFIs) occurred in the absence of febrile neutropenia (e.g., in patients with graft versus host disease) thus patients could miss out on therapy. That said, Dr. Slavin concluded, there was no doubt that outcome was better if treatment was started before infection was well established. "The ideal is to target early treatment to patients who absolutely need it. To do this, we need better understanding of how to interpret results of the non-culture diagnostic tests and work out which one, or which combinations, will be best for surveillance of patients," Dr. Slavin said.

These non-invasive rapid IA diagnostic tests include detection of *Aspergillus* antigens, such as galactomannan and beta-D-glucan, and PCR-based assays to detect *Aspergillus* DNA. There are still a number of problems with the tests but speakers at the conference were largely optimistic that they would be useful.

Dr. Slavin said that a study had just started in Australia — the ASPID study — looking at the impact of using PCR and galactomannan to guide antifungal therapy in patients undergoing allogeneic stem cell transplant or chemotherapy for acute leukemia. The control group was receiving the standard fever-driven approach to starting treatment. "The aim is to see if we can reduce our use of empiric antifungal therapy," she explained.

Allergic aspergillosis

Aspergillosis is classified into three groups: invasive aspergillosis, chronic aspergillosis, and allergic aspergillosis. One of the major allergic diseases is allergic bronchopulmonary aspergillosis (ABPA), a hypersensitivity disease of the lungs. The evidence base for treatment of ABPA was discussed by Richard Moss (Stanford University, Palo Alto, USA). He emphasized the paucity of trial data, which was related in part to the fact that patients tended to be treated as outpatients which made trials more difficult.

Oral steroids remained the mainstay of treatment but astonishingly had never been evaluated in a randomized controlled trial, and had high toxicity. An important recent advance had been the use of itraconazole as an adjunct to steroids. There was trial evidence indicating that the antifungal had steroid-sparing effects and may have independent anti-inflammatory activity in this disease. "Evidence on itraconazole, while not overwhelming, is compelling enough to consider it as standard therapy in both asthma and cystic fibrosis patients with ABPA," said Dr. Moss, who pointed out that risk of ABPA was now known to be higher in cystic fibrosis than in asthma.

There were limited data on other treatments, and no large controlled trials. Possibilities included inhaled steroids as alternative to systemic steroids – there was "a crying need" to find out if this was effective, Dr.Moss said. Newer azoles, IV pulse steroids, and nebulized amphotericin B were also possibilities.

Joanna Lumb

2nd Advances Against Aspergillosis

Pathogenesis

One of the oral sessions was dedicated to pathogenesis of aspergillosis, and a number of poster presentations dealt with aspects of pathogenesis. One of the interesting facets of the meeting was the high level of interest in secondary metabolites of *Aspergillus* species and the roles that these interesting compounds might play in pathogenesis, as well as how they might be exploited for identification. Nancy Keller (University of Wisconsin, Madison, USA) presented her work on the transcriptional regulator LaeA and its role in regulating expression of secondary metabolites in the gliotoxin pathway in *A. fumigatus*. Deletion of *lae*A influences the expression of *pks*P and *rod*A, as well as virtually eliminating gliotoxin production. The resulting mutants have decreased virulence in a mouse model. However, deletion of *gliZ*, a Zn-finger transcriptional regulator specific for the gliotoxin pathway does not lead to decreased virulence in the mutant. In addition, two posters presented data examining the role of gliotoxin in patho-

Judith Rhodes

genesis using mutants deleted for the gene *gliP*, the non-ribosomal peptidase that catalyzes the first step in gliotoxin synthesis. In the genetic background of strain Af293, Robb Cramer (Duke University Medical Center, Durham, USA) did not find in alteration in virulence, whereas June Kwon-Chung (National Institutes of Health, Bethesda, USA), working the B-5233 background, did see a reduction. Clearly, more work needs to be done to understand the biological effects of the end products, as well as some of the intermediaries, of these highly conserved metabolic pathways.

Studying the host side of the pathogenesis equation, Scott Filler (Harbor-UCLA Medical Center, Torrance, USA) presented his *in vitro* model for angio-invasion in aspergillosis. By examining cytokine profile from endothelial cells grown in transwells, Dr. Filler's group showed that endothelial cells sense whether the hyphae are penetrating them from the luminal side or the abluminal side, and respond differently to the interaction. Penetration from the luminal side actually causes more damage to the endothelial cells.

The interaction of the alveolar macrophage with the conidia of *A. fumigatus* was the focus of Oumaïma Ibrahim-Granet's presentation (Institute Pasteur, Paris, France). She has previously shown that alveolar macrophages efficiently ingest and kill the conidia, and here she expanded that observation to show that activation of the ERK MAP kinase pathway is essential for this response. Treatment of the macrophages with corticosteroids blocked the ERK activation, presumably one of the mechanisms by which corticosteroid treatment predisposes patients to invasive aspergillosis. These presentations are only some of the highlights of the meeting concerning pathogenesis. They illustrate not only how far we have come in understanding some of the underlying factors contributing to the pathogenesis of disease, but also many of the continuing challenges that lie ahead of us.

Judith Rhodes

2nd Advances Against Aspergillosis

Laboratory diagnosis of invasive aspergillosis

Thomas Rogers

The Advances Against Aspergillosis Conference again provided an important forum for updating the situation on diagnosis of invasive aspergillosis (IA). So far the development of a reliable diagnostic test has proved elusive.

Dimitrios Kontoyiannis (University of Texas, Houston, USA) gave a useful review lecture which set out the current challenges associated with diagnosis. Late diagnosis is often the case and this almost certainly contributes to delay in giving effective antifungal therapy and leads to poorer outcomes for patients. He believes that over a third of cases of IA are still first diagnosed at postmortem. He pointed to the progress that has been made with publication of the widely accepted EORTC/MSG diagnostic criteria (which are in the process of being updated) although these really only apply to the setting of haematological malignancy treatment and are intended for use in research protocols.

Histological diagnosis is the gold standard but this is usually cannot be achieved. High resolution CT scans have probably made the greatest impact in recently improved clinical diagnosis, and even though characteristic abnormalities on a scan are not specific to aspergillosis they are nevertheless indicative of an invasive pulmonary fungal infection which in most centres is likely to be IA.

Within the diagnostic laboratory the focus has been on validation of non-culture based tests. Those commercially available are the *Aspergillus* Platelia test for detection of *Aspergillus* galactomannan (GM), and 1-3 beta-D-glucan (BDG) detection which is not specific for *Aspergillus*. The utility of the GM test was debated by Johan Maertens (University Hospital Gasthuisberg, Leuven, Belgium) and Paul Verweij (Radboud University Nijmegen Medical Center, The Netherlands). Dr. Maertens has shown in his patients that GM detection is a valuable diagnostic tool achieving high sensitivity and specificity. He pointed to the problems of including cases of possible IA in sensitivity analyses which made the test look less good in other published studies. Dr. Verweij has also published extensively on this test. He reviewed the problems that have been encountered with its use highlighting causes for false positive results and identifying the need for an agreed lower positive/negative cut off which the manufacturer is addressing.

Minoru Yoshida (Teikyo University School of Medicine, Kawasaki, Japan) presented data on the clinical evaluation of the BDG assay of which two are commercially available with slightly different

Paul Verweij (on the left) and Johan Maertens

protocols. Much of the early experience was from studies conducted in Japan but more recently there have been studies published from other countries which confirm the promising initial data. Dr. Yoshida felt that even though BDG detection is not specific to IA this is not a barrier to its inclusion in patient management protocols eg, empirical antifungal therapy in febrile neutropenia. He also showed data on how the test can be used to monitor the efficacy of therapy.

Lewis White (University Hospital of Wales, Cardiff, UK) gave a well structured lecture on where things stand with PCR assays for diagnosis of IA. The priorities are to determine the most appropriate 1) specimen to test, 2) extraction method, 3) assay design, with particular attention to minimising oligonucleotide cross hybridisation, 4) PCR platform and 5) reporting strategy.

It was somewhat disheartening to hear that automated extraction has not yet replaced labour-intensive manual protocols because there is no machine optimally designed for fungal DNA extraction although Dr. White is himself evaluating several commercially available systems. Real time PCR is now preferred but available platforms have differing performance which makes the choice of PCR platform crucial in developing a reliable assay. Dr. White is leading a consensus group which is working to establish an agreed protocol that addresses the above issues with the aim of getting PCR incorporated into consensus diagnosis criteria.

Emmanuel Roilides (Aristotle University of Thessaloniki, Greece) gave a talk on early diagnosis of IA in children. He advocated caution in using the above tests in young children because of the limited experience with their use and the problem of false positive and negative results with the GM assay.

Peter Donnelly (Radboud University Nijmegen Medical Centre, The Netherlands) reviewed the EORTC/MSG diagnostic criteria in the context of their intended use in clinical treatment trials in haematological malignancy patients. He highlighted recently identified problems with the probable and proven IA categories which tended to exclude cases of IA, while the possible IA category was likely to include too many cases that turned out not to be IA. Dr. Donnelly indicated that the revised guidelines would likely include more of the laboratory diagnostic markers discussed above although it will be interesting to see what tests are recommended.

The overall impression is that progress is being made with diagnostic tests. More laboratory validation is needed, based on consensus studies, to determine the optimal protocol; the treatment setting needs to be carefully identified; and these tests need to be studied on a prospective basis in research trials which adopt the internationally agreed diagnostic criteria.

Thomas Rogers

During a coffee break: June Kwon-Chung (on the right), Robert Samson (on the left), and William Steinbach (in the background)

Host-response and immunity: The cellular Toll-like receptors

Luigina Romani

Host factors determining the host–pathogen interaction are crucial for the reaction pattern leading to the threat of nosocomial fungal infections. Potential fungal pathogens need to be recognized early by the host's innate immune system in order to successfully mount a defence reaction. The recently identified family of Toll-like receptors (TLRs) represents the major group of cellular signalling receptors for pathogens. *Toll* is a Drosophila protein involved in fungal defence and control of embryonic development. Human homologues to *Toll* exist and are termed Toll-like receptors. Although the term "molecular pattern" is currently widely used, it is not yet clear whether molecular *patterns* are recognized by this system or whether certain microbial molecules initiate the innate immune response. There is growing evidence that variations within the genes of the family of these innate immune receptors may account in part for the inherited differences in infectious disease susceptibility. The current state of these analyses in response to *Aspergillus* was discussed at the recent 2nd Advances Against Aspergillosis and is summarized here.

In one Meet the Professor Session, Luigina Romani from the University of Perugia, Italy, highlighted recent findings on the TLRs and TLR-dependent signal transduction pathways that are selectively activated by the fungus. The early recognition system is largely brought about by TLR expressed on polymorphonuclear neutrophils (PMNs) and dendritic cells (DC). PMN recognition of *Aspergillus* occurs in a morphotype-dependent fashion, through the activation of different TLR signalling pathways. By affecting the balance between fungicidal oxidative and nonoxidative mechanisms, pro- and anti-inflammatory cytokine production and apoptosis versus necrosis, TLRs ultimately impact on the quality of microbicidal activity and inflammatory pathology. This translated *in vivo* in the occurrence of different patterns of fungal clearance and inflammatory pathology. Although TLRs signalling in response to *Aspergillus* may result in contrasting outputs in different types of effector cells, it is reasonable to believe that manipulation of TLRs by selective agonists might provoke divergent sequences and magnitudes of functional responses, so that diverse outcomes ultimately may transpire. Indeed, liposomal amphotericin B, in addition to its intrinsic antifungal activity, may activate antifungal resistance by activating TLR4 in PMNs. These studies provide a rationale to stimulate or inhibit specific classes of TLRs as a means of enhancing both innate and antigen-specific immunity to fungi. Indeed, IL-12 production by DC in response to *Aspergillus* conidia required the MyD88 pathway with the implication of distinct TLRs, whereas the production of IL-10 was largely MyD88-independent. Therefore, TLR collaborate with other innate immune receptors in the activation of DC against the fungus through MyD88-dependent and -independent pathways. Moreover, thymosin alpha 1, a naturally occurring thymic peptide, induced maturation and IL-12 production in DC pulsed with *Aspergillus*, an effect mediated by distinct TLRs. It is of interest that TLR gene expression on DC could be affected upon fungal exposure in a morphotype-dependent manner and that the TLR9 agonist CpG-ODN could convert an *Aspergillus* allergen to a potential protective antigen suggesting the potential for TLRs agonists to act upon the degree of flexibility of the immune recognition pathways to *Aspergillus* antigens and allergens.

Oumaïna Ibrahim-Granet (Institute Pasteur, Paris, France) examined the TLRs and TLR-dependent signal transduction pathways that are selectively activated by the fungus in alveolar macrophages. The ERK MAPK pathways were promptly activated upon the exposure to conidia, *in vitro* as well as *in vivo*. Surprisingly, however, *in vivo* studies ruled out a plausible role for TLRs in the activation of the ERK MAPK pathway. Although the obvious conclusion was that TLRs expressed on alveolar macrophages may not be essential for the early control of the fungus in condition of immunocompetence, the findings of Frank Ebel (Max von Pettenkofer- Institut, Munich, Germany) added complexity to the system. He showed that TLR2, more than TLR4, is essential for efficient phagocytosis of *Aspergillus* conidia by alveolar macrophages. This occurred by interaction with dectin-1, a non TLR receptor specifically recognizing fungal beta 1, 3-glucan. Thus, recognition and phagocytosis of the fungus are the joint effort of TLR and mantle recognition receptors.

The discovery of genetic variations of these proteins caused by single nucleotide polymorphisms has led to first studies aimed at elucidating a potential link between genomic variation of the host and susceptibility to infections. This field of research may lead to important new strategies to combat nosocomial infections. Further elucidation of the molecular events involved in pattern recognition will most likely lead to the introduction of novel diagnostic tools and eventually to the development of novel intervention strategies in severe fungal infection and sepsis.

Luigina Romani

Fungi and allergy

Unfortunately I missed the first congress on Advances Against Aspergillosis held at San Francisco on 2004 due to an overlap with the hunting season in the Swiss Alps, but I realize now that this was a big mistake. The second Advances Against Aspergillosis meeting in Athens was a highlight covering the many faces of research related to this complex field. Of course, one of the most important topics giving rise to deep discussions was centred on the completion of the *Aspergillus* genome projects, which will directly or indirectly influence our whole research activity on aspergillosis during the coming decades. Consequently, plenary session 7 dedicated to "Genomics and Post-genomics" was the most important for me and, perhaps, also for many other participants. I am looking forward to see the impact of this fantastic tool in *Aspergillus* research at the next AAA-meeting. The availability of the whole genome sequence will surely speed up identification of important diagnostic and therapeutic targets to be evaluated in a concentrated pharmacogenomic effort implementing all technologies involved in post genomic research projects.

Reto Crameri

Of special interest for me were the oral presentations and posters dedicated to allergy and it will not be possible to summarize all I have learned in a short note. It is evident and known for many years, that allergy to fungi in general, and to *A.fumigatus* in particular, affects almost exclusively patients suffering from asthma or cystic fibrosis, and a subgroup of sensitized patients might develop allergic bronchopulmonary aspergillosis as pointed out by Alan P. Knutsen (Saint Louis University, USA). Allergic bronchopulmonary aspergillosis (ABPA) is a Th2-mediated hypersensitivity of the lung due to bronchial colonization with *A.fumigatus* resulting in intense inflammatory responses with severe consequences for affected patients. Although *Aspergillus* is associated with often lethal invasive diseases in immune compromised hosts, it is a far more common agent of allergy and asthma, as pointed out by Paul Bowyer (University of Manchester, UK), and this aspect has been neglected for a long time. The real problem about fungal allergy is that while everybody is aware of the existence of the phenomenon, epidemiological data allowing estimation of the dimension of the problems related to fungal sensitization is almost lacking. Exact determination of the incidence of fungal sensitization would require the availability of internationally recognized standardized fungal extracts which, unfortunately, are not available, to be used in extended skin-test surveys. As long as each laboratory uses its own in-house made extract or commercially available extracts that are

subject to large batch-to-batch variation to perform *in vitro* and *in vivo* experiments, it will not be possible to compare the results obtained. I am convinced that the majority of the discrepancies reported between different studies are traceable to substantial differences on the quality of the extracts used to conduct the studies. Cloning, production and characterization of *A.fumigatus* allergens might strongly contribute to improving the diagnosis of sensitization as I pointed out in my own presentation. Unfortunately, most of the research projects are still conducted with uncharacterized extracts limiting their scientific value. Because a correct treatment anticipates a correct diagnosis of the disease, which in the case of fungal allergy is based on insufficiently characterized extracts, it is not astonishing that clinical trials aimed to treat *A. fumigatus*-related allergy by immunotherapy are inconclusive. Better results have been obtained with symptomatic treatments of ABPA (and partly allergy) with glucocorticosteroids as elegantly summarized by Richard B. Moss (Stanford University, Palo Alto, USA) during his critique of trials in ABPA and fungal allergy. However, also in this regard data available from the literature are fragmentary and partly contradictory. Although asthmatic patients suffering from ABPA can be successfully treated with glucocorticosteroids, the situation in CF-patients affected by ABPA is much more confusing. Despite combined use of oral steroids and itraconazole reported in many studies, a demonstration that these interventions are effective needs further substantiation. The work to be done to understand immunologic responses to fungi in detail in both, healthy and allergic individuals is still long and challenging.

From my point of view the AAA congress in Athens has highlighted the weakness of the approaches currently used in diagnosis and treatment of fungal allergies, evidenced the need for coordinated action starting from the standardization of the reagents to be used up to the need for the definition of consensus regimes of treatment, and underlined the potential of the genome project to speed up rapid progress in the field. I can not imagine a better outcome from a congress and I am grateful to the organizers for the tremendous amount of work done to create an international discussion platform which, I am absolutely sure about this point, will not fail to strengthen existing and start new collaborations in the field of aspergillosis.

Reto Crameri

Music and dance during the conference dinner at "The Old Stables"

PAMMS 2007

2nd Pan African Medical Mycology Society Conference

FIRST ANNOUNCEMENT

PAMMS 2007

Cape Town International Convention Centre (CTICC)

Cape Town, South Africa

6-8 May 2007

A successful first meeting ("Medical Mycology: The African Perspective") was held at the Hartenbos Beach Resort near Mossel Bay in the Western Cape, South Africa on 25 January 2005 (see Mycology Newsletter 1/2005). The Pan African Medical Mycology Society (PAMMS) was inaugurated during this meeting and a steering committee consisting of Hester Vismer (Cape Town, South Africa), Ifeoma Enweani (Ekpoma, Nigeria) and El Sheikh Mahgoub (Khartoum, Sudan) was elected to manage PAMMS during its first few years.

The second meeting of the PAMMS in Cape Town will be held at the Cape Town International Convention Centre (CTICC). The Conference will provide medical mycologists from Africa with a unique opportunity to present their latest research findings, to foster collaboration and to establish long-term relations between scientists from Africa and abroad. A PAMMS General Meeting will be held to elect a new executive committee and to discuss, amongst other aspects, the draft constitution of the society. Invited speakers from the African continent and speakers from outside Africa, working on topics concerning African fungi will participate in the meeting. Poster presentations will also form an important part of the programme.

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Microbes: then, now and hereafter

IUMS 2008 İSTANBUL

IUMS Meetings of the Three Divisions of the International Union of Microbiological Societies 2008

XII. International Congress of Bacteriology and Applied Microbiology

5-9 August 2008, Istanbul

XII. International Congress of Mycology

5-9 August 2008, Istanbul

XIV. International Congress of Virology

10-15 August 2008, Istanbul

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