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 19 different countries)

1/98

ECMM
European Confederation of Medical Mycology

CEMM
Confédération Européenne de Mycology Médicale

Message from the President

The ECMM is expanding and progressing. It now involves 19 countries, including Israel and Russia, encompassing about 3000 mycologists. Each annual congress gathers a bigger attendance showing happiness to meet and enthusiasm to share experience and hopes. The epidemiological study groups have started working and the first results will be presented at the next Congress in Glasgow 11-13 May 1998. Basic teaching of medical mycology will be a priority for 1998-1999. Clinical trials with new antifungal agents should be launched in 1998-1999 at the European level.

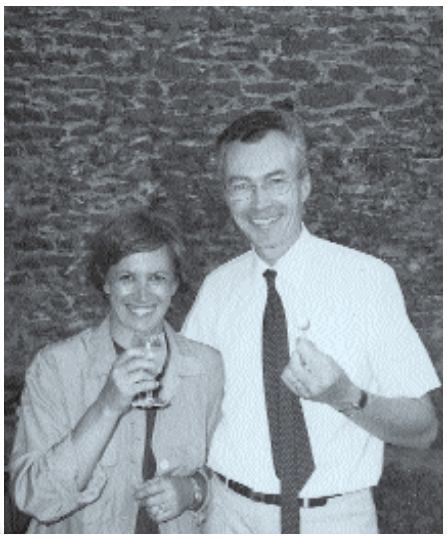
We were very happy to receive Professor McGinnis's letter (see below) recognizing the importance of our Confederation for mycology in Europe and in the world. This warmly encouraging letter from such a well known personality tells us that we are on the right track and means that our ambitious goals must be kept and reached. Our cooperative work, and our diversity are our strength and I am sure that we will overcome apparent slowness and transient difficulties.

Ideas and projects for further studies to be performed under the aegis of the ECMM are proliferating, and this is also an excellent sign. However, in order to successfully coordinate our actions and not disperse our efforts, the General Secretary must centralize any project or request for funding which needs the "stamp ECMM". Each research project must be presented to the Council by sending to the General Secretary a description that can be circulated to Council members before they meet to discuss it. The Council has the task of deciding if the project has the scientific validity and interest on the European scale for it to be recognized as an ECMM initiative.

Today we are still quite close to the creation of the Confederation. Beside the results which will soon be available I would like to point out that the ways and possibilities of working together, the adopted methodology, the objectives and the consciousness of the growing importance of mycology have already changed the mentality of Europeans mycologists.

With this second issue of the ECMM Newsletter I am pleased to thank Marianna Viviani for all the productive work she has done and I wish all you a prosperous New Year.

Bertrand Dupont



The following letter has been sent by Prof. Michael R. McGinnis, Chief Editor of "Medical Mycology" (formerly "Journal of Medical and Veterinary Mycology") to the ECMM General Secretary.

Dear Marianna: I want to thank you for sending me a copy of the first ECMM Mycology Newsletter.
The European Confederation of Medical Mycology is a fantastic first step towards uniting mycologists throughout Europe. As we approach the 21st century, there is a pressing need for our profession to have leadership. The ECMM, its working groups and congresses certainly have assumed that leadership role.
The list of affiliated societies is impressive and the ECMM Council clearly reflects all facets of mycology as well as geographic areas. The emphasis on epidemiological working groups is superb. By working together, information regarding the frequency of representative mycoses can be gathered from many different patient populations throughout Europe. Such information will help mycologists throughout the entire world.
The creation of the ECMM and seeing so many different mycologists working together is impressive.
With best regards,
Sincerely yours,

Michael R. McGinnis, Ph.D.

ECMM/CEMM
Mycology Newsletter

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Newsletter

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Membership 1997: 75
National meeting: Nov. 19-21, 1998, Cadiz
Journal: Revista Iberoamericana de Micologia

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National meeting: May 11-13, 1998, Glasgow (joint with ECMM Congress)
Newsletter

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Membership 1997: 45

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National meeting: September 17-20, 1998, Frankfurt/Oder

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National meeting: Dec. 10-12, 1998, Milano
Newsletter

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Membership 1997: 26

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Treasurer: D. Elad
Membership 1997: 80

Polish Dermatologic Society Mycology Section
President: E. Baran (*ECMM delegate*)
Secretary: J. Szepietowski
Treasurer: R. Bialynicki-Birula
Membership 1997: 89
National meeting: 2000, Poznan
Journal: Mykologia Lekarska (Medical Mycology)

Netherland Society for Human and Veterinary Mycology (NVMy)
President: J.F.G.M. Meis (*ECMM delegate*)
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Treasurer: R.W. Brimicombe
Membership 1997: 95
National meeting: April 21, 1998, Veldhoven

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President: S.A. Burova (*ECMM delegate*)
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Membership 1997: 25

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Secretary: D. Robbrecht, J. Boelaert
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ECMM delegate: D. Swinne
Membership 1997: 216
National meeting: March 21, 1998, Brussels

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Vicepresident: D. Chabasse, O. Morin, H. Koenig
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Treasurer: P. Boiron
Membership 1997: 360
National meetings: June 11-12, 1998 - Rennes
November 27-28, 1998, Paris
Journal: Journal de Mycologie Médicale

Swedish Society for Clinical Mycology
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Secretary: G. Pålsson
Treasurer: L. Edebo (*ECMM delegate*)
Membership 1997: 91
National meeting: April 23-24, 1998, Göteborg
Newsletter

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Turkish Microbiological Society Mycology Section
President: Ö. Ang
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Membership 1997: 21

Contents

Requirements for establishing a country-wide diagnostic service in Medical Mycology

The 13th ISHAM General Assembly, held in June 1997, passed a Resolution which stresses the problems related to the lack of adequate diagnostic services in Medical Mycology and indicates the remedial measures.
This Mycology Newsletter reports the Resolution together with the remarks of Prof. Johannes Müller, who proposed the Resolution at the ISHAM Assembly.

In most countries of the world the laboratory diagnostic service in Medical Mycology is far from being as perfect as it could be. Problems concern the number of laboratories, the number as well as the education of the staff members, the instrumental endowment of the laboratories, the budgeting of the service and, finally, the cross-relations to the other branches of Medical Microbiology. In these respects many otherwise well-developed countries must be regarded as developing countries.

From this specification the following topics are discussed:
1. the indispensable number of laboratories;
2. the workload and qualifications of the laboratory staff;
3. a reasonable hierarchy of medical mycological laboratories;
4. the cross-relations of Medical Mycology within Medical Microbiology.

This analysis essentially concerns handling of opportunistic fungal infections, since they are of considerable epidemiological significance and require urgent initiatives of being controlled.

A lot of data are available on the prevalence of opportunistic mycoses in patient groups with various underlying diseases. Very few data, however, exist on the overall incidence of opportunistic fungal infections in the total population. An epidemiological calculation assessed the dimension of opportunistic fungal infections at the rate of 500 per million population per year. This assessment is meanwhile supported by other surveys and should be true for the whole northern hemisphere, but only for a part of the southern hemisphere.

Candidosis is predominant at the rate of approximately 90%. A quota of approximately 10% is observed with aspergillosis, however, this portion may vary widely from place to place and is perhaps increasing due to the fact of constantly improving control of candidosis. All other opportunistic fungal infections, including cryptococcosis, fusariomycosis, trichosporomycosis, zygomycosis, but also the great diversity of emerging fungal pathogens do not constitute more than 1% of all opportunistic fungal infections.

The workload needed to detect these opportunistic fungal infections is calculated at a dimension of 50 000 clinical specimens of different kind per million population per year for cultural examination. A further dimension of 5000 specimens per year - blood serum and CSF probes mainly - are to be analysed for fungal antigens and antibodies coming from a total population of 1 million. These figures form the basis for further calculations concerning the structures and strategies of Medical Mycology.

For correct processing of a volume of 50 000 cultural and 5000 serological specimens two academically educated mycologists as well as five mycologically experienced technicians are imperative. This is based on good working conditions and a well-equipped, largely automatic controlled laboratory.

The final diagnostic output of these efforts is dependent on several preconditions, such as the mycological awareness of the clinician who is taking care of the risk patients, on the intensity of mycological survey monitoring, as well as on the mycological experience of the laboratory staff. Therefore, the diagnostic output will vary across a wide range from one laboratory to another. In our own experience the suspicion of a fungal infection was raised in 1 out of 30 specimens. A proven fungal infection was detected in 1 out of 120 clinical specimens. This is comparable to the diagnostic output of the bacteriologi-

cal laboratory working for the same background population.

A desirable hierarchic system of medical mycological laboratories refers to a population of 10 million: ten labs should be doing basic routine mycology; above these, two laboratories of a Second Care status should supervise the routine laboratories concerning quality control, should offer more sophisticated, rarely used techniques for selected cases, and should perform regular basic education and be responsible for the documentation of individual casuistics. This pyramid should be headed by one Reference Laboratory competent for activities such as evaluation of techniques, co-operation in treatment studies, epidemiological data collection, development of strategies, higher education, standard setting, and culture collections. In big countries several Reference Laboratories should be specialised and co-operate together in a complementary manner.

In improving the control of opportunistic fungal infections ISHAM can practise the following strategy:

1. ISHAM should clearly define the indispensable needs for controlling opportunistic fungal infections.
2. ISHAM should make clear the institutional, budgetary independence as well as the creation of leading positions in adequate ranks are imperative for the success in promoting Medical Mycology.
3. The General Assembly of ISHAM should pass a Resolution on this matter as proposed addressed to executive bodies in national institutions involved in Health Care, but addressed also to the WHO.
4. This Resolution should serve as the reference basis for general as well as individual national initiatives to further developing of Medical Mycology in a given political entity.

Johannes Müller

RESOLUTION

passed by the 13th ISHAM General Assembly held on June 13, 1997, in Salsomaggiore Terme, Parma, Italy

To:
The World Health Organisation WHO
All National Ministres of Health
All Heads and Deciding and Executive Bodies of Medical Faculties and Medical Schools
All National Associations for Medical Mycrobiology
All National Associations for Medical Mycology

To whom it may concern

It is a fact:
that great progress has been made in medical science to cure previously fatal diseases, to alleviate serious health problems, both acute and chronic, and to prolong human life

but, on the other hand, it must be recognized:
that a considerable and increasing number of individuals whose lives are saved or prolonged due to treatment of their underlying diseases, are falling victim of opportunistic, life-threatening, deep-seated fungal infections. This is despite the fact that, potentially, these diseases can be diagnosed and treated successfully. The great majority of deaths due to fungal infections results from the world wide lack of adequate and sufficient diagnostic services in medical mycology.

The International Society for Human and Animal Mycology (ISHAM), therefore, urgently calls on all Authorities responsible for health care in the widest sense to take remedial measures to deal with this deficiency.

Such remedial measures are:

1. To create permanent positions for academically educated medical mycologists running Routine Diagnostic Laboratories together with appropriately equipped facilities. The minimum requirement are for two such positions per million population.
2. To create permanent positions for technicians experienced in medical mycology to deal with routine diagnosis of opportunistic fungal infections. The minimum requirements are five such positions per million population.
3. To establish Mycology Reference Laboratories for opportunistic fungal infections, to be responsible for epidemiology, education, quality control and evaluation of diagnostic procedures, as well as for therapy. The minimum requirements are one such Reference Laboratory per ten million population.
4. To establish and recognize a clear status for Medical Mycology as a subject in its own right that has both institutional and budgetary independence from other branches of Medical Microbiology, such as Bacteriology, Parasitology and Virology. This is essential in order to guarantee a permanent, advanced and productive mycological service of the highest possible standard for the benefit of patients with life threatening fungal disease.

J. Müller, President of ISHAM
E.G.V. Evans, General Secretary of ISHAM

Epidemiological Working Groups of ECMM

The epidemiological studies announced in the previous Mycology Newsletter have been initiated. Most of the national coordinators have been named and many of them have started work, collecting data and strains. Great efforts are now required to improve communications at the national level. To facilitate contacts for those who wish to participate to the studies, the name and address of the national coordinators for each study are reported in the following pages, together with some comments by the convenors to enhance the understanding of the project.

It is now the coordinators' task to stimulate participation in their own country and help participants in filling the forms, sending the strains, and so on. The coordinators are charged with an important role. Their supervision and assistance to the participants have to be constant throughout the survey period.

There is a pressing need for epidemiological data showing the importance of the morbidity of fungal infections, their frequency and their distribution at a European level. This information will greatly contribute to improved preventive measures and to the design of therapeutic guidelines. At the same time, it will be possible to draw a map of the mycological structures of European countries, to recognize the number of laboratories in relation to geographical region and population, to identify the level of the laboratories and the degree of mycological training of their staff. This is an effective way to contribute to the development of Medical Mycology in the European continent, starting from those regions with greatest mycological requirements.

In the course of the study the interactions among mycologists, and between mycologists and clinicians, can be expected to stimulate complementary researches at national or regional levels which may enrich the data produced by the ECMM epidemiological survey. The results of these national complementary studies could be published in the same issue of the journal in which the ECMM survey will be printed.

Confidence in correct collaboration is required for the success of these studies. For this reason convenors should refer to the "Rules for Epidemiological Working Groups", reported in the previous number of the Mycology Newsletter. In particular, these "Rules" are intended to protect ownership of the isolates. Those who will receive and maintain the strains have already agreed to the "Rules". Thus, they will recognize the ownership to those who have sent the strains. The strains will be lodged in a restricted culture collection in the Institutions which run a public culture collection. This restriction will be removed after the final paper of the ECMM survey has been submitted for publication. Of course, the owner can use his isolate for any research as long as it does not interfere with the ECMM epidemiological study.

I am sure that the participation will be large and enthusiastic in all the 19 countries of the ECMM. Those who are interested in joining these studies can rely on full assistance from the national coordinators, the convenors of the studies, as well as the ECMM delegates of the mycological societies (see the list pag. 3 and 2) and of course of the ECMM General Secretary.

Maria Anna Viviani

Notice

The national coordinators listed in the following pages are asked to check accurately their data and report any error or omission to the ECMM General Secretary:

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Epidemiological Survey of Cryptococcosis in Europe

National coordinators of the Working Group on Cryptococcosis

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Epidemiological Survey on Histoplasmosis in Europe

Notes for participants

Study period: The histoplasmosis survey will run for 2 years from January 1st, 1998 prospectively and 3 years retrospectively.

Prospective survey (January 1998 - December 1999): When a case of histoplasmosis is diagnosed, a survey form should be filled in detailing the clinical information, any histological information on the appearance and size of the yeasts (*Histoplasma capsulatum* var. *capsulatum* or var. *duboisii*) and, very importantly, any travel history. These forms can be obtained from your national coordinator. The form and the isolate of *Histoplasma* (if available) should then be sent to your national coordinator, who will carry out a brief characterisation of the isolate. Remember that in many European countries there are postal regulations on the safe packaging of dangerous pathogens such as *Histoplasma*; make sure that the culture is securely packaged before you send it by post. Cultures should always be sent in sealed test-tubes or universal containers (preferably plastic) and never in Petri dishes.

Retrospective study (January 1995 - December 1997): Obviously, isolates may not be available for the retrospective part of the survey. But please complete the survey form as fully as possible for each case.

***H. capsulatum* isolates**: It is not our intention to keep the isolates collected in the study. Therefore, please keep your own isolates if you think that they are of interest.

Collection and processing of data: Data from the retrospective study should be compiled as soon as possible and sent to the national coordinators. For the prospective study send the informations as the cases arise. The national coordinators will forward the epidemiological information to the European convenor, Prof. E.G.V. Evans, for analysis.

Further information can be obtained from
Prof. E.G.V. Evans
(E-mail: e.g.v.evans@leeds.ac.uk)
or Dr. H.R. Ashbee
(E-mail: h.r.ashbee@leeds.ac.uk)
Tel. +44 113 233 5590
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National coordinators of the Working Group on Histoplasmosis

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Epidemiological Survey of Nocardiosis and other Aerobic Actinomycetes Infections in Europe

Notes for participants

Dear Colleague,

The "Epidemiological survey of nocardiosis and other aerobic actinomycetes infections" is in place in 8 European countries since July 1997: Bulgaria, France, Greece, Italy, Russia, Switzerland, The Netherlands, United Kingdom.

Because of the small number of cases of aerobic actinomycete infection observed in each country, a significant survey of such infections will be performed only when all European countries will be represented.

At this date, there has been no spontaneous candidature from members of Belgian, Danish, German, Hungarian, Israeli, Polish, Portuguese, Spanish, Swedish or Turkish Societies. I should be very grateful if the ECMM delegate of each country could contact as soon as possible one selected member of his National Society that could be interest-

ed to act as national coordinator of this study. The latter will be responsible for stimulating participation of various researchers in his own country in order to collect a sufficient number of cases and collate, check and transmit the data to the convenor. Candidates for the role of national coordinator should promptly inform me of his/her availability.

A presentation of this 2-year study, the "Rules for epidemiological Working Groups" and the case record form were published in the first issue of the ECMM Newsletter.
I thank you warmly your collaboration

Patrick Boiron

National coordinators of the Working Group on Nocardiosis

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Epidemiological Survey on Candidemia in Europe

Notes for participants

At the present time, the "Epidemiological survey of candidemia" is in place in 17 European countries since the last quarter of 1997 (see the table of participating countries below). Thus I thank all the spontaneous candidatures from members of ECMM Affiliated Societies for this study.

Compared with the other ECMM studies, the candidemia survey presents some peculiarities and some specific points must be clarified.

Aim of the study: the main purpose of the candidemia survey is not to be exhaustive at the country level but to be exhaustive at the level of each participant hospital.

- In practice, this means to declare all the candidemias diagnosed in the participating hospitals during the two year period of the survey, to fill the forms in completely and to properly maintain the strains.

- So in each country, the national coordinator has to identify the institutions where the collaboration of a skilful mycologist is available.

- For each participating hospital, some general information is needed such as the number of admitted patients in the period of the survey, the type of hospital, the presence and size of units receiving patients at risk of fungal infection (oncohematology, organ transplantation, intensive care, neonatalogy etc.).

Processing and collection of data and strains: for this prospective study, information and strains must be sent to the national coordinator every second month. The national coordinator will check and transmit the epidemiological information to the European convenor (Prof. R. Grillot) for analysis, but will keep the yeast isolates until the end of the ECMM study for potential study proposed to the ECMM Council.

Exploitation plan of the study: more than one thousand candidemia cases will probably be collected during the study, as it involves 17 countries and probably 100-200 participants. Of course, so many people could not be co-authors of the published paper at the European level. So the following propositions are offered:

The analysis of the epidemiological data from the participant countries will be presented according to the "Rules" published in the ECMM Mycology Newsletter 0/97 (names of the convenor and coordinators listed according to the proposed order). The Institution and the name of the mycologist involved in the study (one for each Institution) will be reported in a box.

Results of this epidemiological study can be exploited at a country level by each national coordinator, but not before the publication of the ECMM paper. All the participants of the national study could be co-authors, this being under the responsibility of the national coordinator.

I hope warmly this study will be very successful.

Further information about filling of the forms, storage of strains can be obtained from Prof. Renée Grillot:
E-mail: renee.grillot@ujf.grenoble.fr
tel: +33 4 7676 5350, fax: +33 4 7676 5656.
Please let me know also your comments about this letter and the study.

Again many thanks for your collaboration

Renée Grillot

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Epidemiological Survey on Tinea Capitis in Europe

Notes for participants

The tinea capitis survey is now underway. National coordinators have been chosen; in a few instances countries have opted to have two individual responsible for gathering data. The objective has been to provide information on the number of confirmed cases for the year 1997 and if possible also for the year 1987. These are then broken down into different species. The survey questionnaire has been written in order to analyse the data with the Epi Info programme. In addition respondents have been asked to identify the main source of their laboratory material, in particular whether they receive material for reference purposes or for routine diagnosis. The questionnaire also seeks to gather information of a more general nature such as the usual treatments given in each country or area and whether particular ethnic or social groups are affected.

The process: national coordinators have been sent details of individuals or laboratories who have expressed an interest in participation and these should forward completed forms to the national coordinators. Others who would like to participate should contact the national coordinator for a copy of the survey form. All forms will then be forwarded to the European convenor, Professor Rod Hay or Dr. Wanda Robles:
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Tel +44 171 928 9292 ext 1374.

Roderick Hay

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See you in Glasgow at the

4th Congress of the ECMM
11th - 13th May 1998

organized by the British Society for Medical Mycology

Scientific programme: 1. Antifungals/Resistance in AIDS - 2. Neutropenics/Non AIDS Resistance? - 3. Virulence Factors in Fungi - 4. Respiratory Mycosis - 5. Molecular Mycology 6. Fungal Cell Walls - 7. Dermatological Mycology - 8. Molecular Immunology.
The 9th session will be entirely dedicated to preliminary reports on the prevalence of fungal infections in Europe from the convenors of the epidemiological working groups of ECMM.

Information: Caterpoint>, PO Box 2714, Bearsden, Glasgow, Scotland G61 4LW, UK
Tel/Fax: +44 7000 627123 - E-mail: caterpoint@colloquium.co.uk
Deadline for receipt of abstracts: 30th January 1998

The Deutschsprachige Mykologische Gesellschaft will host the 5th ECMM Meeting in Dresden

The Deutschsprachige Mykologische Gesellschaft (Germanophone Mycological Society) is a scientific association of medical mycologists working in germanophone Central Europe (Austria, parts of Switzerland, Luxembourg, Germany).

This is a region of remarkable historic events in medical mycology. J.L. Schoenlein and Remak as early as in 1893 characterised ringworm of a disease of fungal origin. In the same year B. von Langenbeck and F.T. Berg demonstrated *Candida albicans* to be the causative agent of thrush. C.F. Eichstedt in 1846 characterized pityriasis versicolor as a fungal disease. The pathologist R. Virchow in 1856 created the term "mycosis" and described aspergillosis in histopathological terms. In 1894 A. Buschke and O. Busse described cryptococcosis and its causative agent *Cryptococcus neoformans* at the same time and independently from F. Sanfelice in Italy.

This tradition was continued in the 20th century in research, teaching and routine diagnostics. H.P.R. Seeliger was a pioneer in characterizing fungal antigenicity and developing mycoserology. The state of the art in medical mycology of the mid 1950's was edited in monographic treatises in Jadassohn's Handbuch der Haut- und Geschlechtskrankheiten - a standard opus printed in German by leading specialists.

The Deutschsprachige Mykologische Gesellschaft (DMykG) was founded in 1961 by Hans Götz, bringing together the medical mycologists of germanophone Central Europe to a scientific community. In 1990 the mycologists of the former German Democratic Republic were able to join this Society as well. At present the DMykG has 1197 members, approximately 400 of them being active scientists in all branches in clinical medicine, medical microbiology, universities, research units and industry.

The Society is governed by an executive committee consisting of the President, the Vicepresident, the Secretary and the Treasurer, elected for a period of 3 years each. At present the following members are holding offices:
President: Prof. Dr. Hannelore Bernhardt, Head of the Departement of Clinical Microbiology at the University of Greifswald;
Vicepresident: Prof. Dr. H.C. Korting, Department of Dermatology, University of Munich;
Secretary: Prof. Dr. C. Seebacher, Head of the Department of Dermatology, Hospital Dresden-Friedrichstadt;
Treasurer: PD Dr. W. Fegeler, Institute of Medical Microbiology, University of Münster.

The Society is organising one scientific meeting each year in varying places. The presented volume comprises at average one hundred oral and poster contributions per meeting.

The DMykG is running two working groups:
1. The study group "Clinical Mycology" dealing with clinically-orientated diagnostics, quality control, case documentation and epidemiology; currently 25 members are involved with two annual meetings.
2. The study group "Mycological Laboratory Diagnostics" dealing with exchange of laboratory experience and with training, with 30 active members holding one meeting per year.

The DMykG has established in 1991 the Forschungsförderpreis to be awarded annually. The prize-winners up to now were: R. Rüchel, Annemarie Polak, H.T. Heidemann, H.C. Korting, R. Kappe, Margarete Borg-v. Zepelin, M. Ollert.

The DMykG Honorary Membership is awarded for outstanding longterm contributions to the Society and to the domain of medical mycology. The Johann Lucas Schönlein-Plakette can be awarded for outstanding merits in medical mycology.

The journal "mycoses" formerly "mykosen" (1958-1987), founded by E. Langer, grew out of an appendix of a German dermatological journal to a reputed periodical in English, specialized in medical mycology; it is not legally, but by history linked to the DMykG and is accepting articles from authors all over the world.

Dresden, the place of the 5th ECMM Meeting to be held in 1999, is one of the major cities in Germany, the capital of Saxonia. Lovely situated at the Elbe River, this town was always a focus of cultural activities of all facets. Newly reconstructed it is endowed with all necessary facilities to organise congresses and to host guests, offering a sympathetic ambient to foreigners. The organizers of the 5th ECMM Meeting, Prof. Dr. Renate Blaschke and Prof. Dr. C. Seebacher as well as the DMykG with an enthusiastic young generation of germanophone researchers are looking forward to hosting European mycologists in 1999 in Dresden.

Johannes Müller

Special report on...

by
Donald W.R. Mackenzie

Trends in Invasive Fungal Infections 4

The first Trends in Invasive Fungal Infections meeting was held in Nijmegen in 1991. This was followed by meetings in Manchester (1993), and Brussels (1995). The series is now well-established and highly successful, providing a forum for the presentation and exchange of information on a range of aspects including the aetiology, recognition, and management of invasive mycoses. The format of previous meetings was retained, with lectures on clinical topics, poster sessions and a generous allotment of time for formal and informal discussions.

One programme innovation was the inclusion of management seminars. In each of these, a young clinician supported by a senior chairman and an expert familiar with the clinical setting presented a case to the audience. Each case was presented as it occurred clinically, sometimes with incomplete data. The intention was to describe realistically how the patient's history evolved, and stimulate discussion of the basis of clinical decisions on management and on the resolution of controversial points.

Another innovation was the introduction of workshops. The first, preceding the meeting, was on laboratory mycology, and was presented by Dr. J. Torres Rodriguez. The second type involved sponsored working luncheons on management and testing for antifungal resistance.

The meeting was held between 6-8th November in the Hotel Arts of Barcelona, Spain. The programme included seven formal sessions with 19 presentations, two expert working luncheons with 5 presentations, and three management seminars. Attendance was in excess of 500.

Note from reviewer

This is the first meeting attended since my retirement in 1992. During the past five years my contact with medical mycology has been restricted, although a limited monitoring of the literature has been maintained. In returning to the conference scene, there were two immediate reactions. The first was that many of the problems of 1992 remained problems in 1997. Thus, amphotericin B was still the primary choice for many infections, flucytosine was still in use, laboratory diagnostic aids were still not reliable and were at times unhelpful. Much of the programme seemed to deal with familiar topics and familiar problems. Changes in the interim appeared to be incremental rather than abrupt, evolutionary rather than revolutionary.

On the other hand, there were several topics that had emerged or become prominent in the past five years. The Trends meetings themselves constituted one. This has provided a very valuable forum to review the situation and to provide updates for clinicians. Substantial progress has obviously been made in defining the parameters for usage of fluconazole, itraconazole and amphotericin B. A range of new therapeutic approaches and agents were now being developed. The overall picture regarding opportunistic mycoses in patients with AIDS had changed significantly with the advent of protease inhibitors.

Many of the speakers were being heard by me for the first time. There was much that was new and exciting for me. One of the session convenors ironically announced that he was banning the convention of starting talks with thanks to the organizers and sponsors, and suggested that organizers should thank people like us for coming to the meeting. I thought this was going a little too far. It is a mutually beneficial association, surely, and certainly was at this Trend meeting. Whoever was responsible for its success - speakers, organizers, or sponsors - deserves great credit for making the occasion such a successful one.

It would be invidious to apportion credit, so let the record stand that this was a highly successful meeting, a splendid venue, and a delight from beginning to end.

chaired by
D.W. Denning and M. Akova

Session I

Prevention and early empiric therapy: risk assessment

The scientific programme opened with a paper by P. Ljungman on the implications of CMV infection for fungal infections. CMV infection has been shown to be a risk factor in bone marrow and organ transplant patients. Possible mechanisms include cytokine production that might upregulate reactivity to allo antigens, increasing the risk of rejection. Induced immunosuppression could lead to build up in the amounts of virus, establishing a vicious cycle. Allogenic bone marrow recipients with CMV infections might suffer chronic graft-versus-host reactions through an autoimmune mechanism involving cytotoxic antibodies, thereby prolonging the need for corticosteroid treatment, and increasing the possibility of invasive aspergillosis. Neutropenia associated with CMV-induced cytokine production or treatment with ganciclovir have also been recognized as a risk factor.

B.E. de Pauw described strategies for prophylaxis and empiric therapy in neutropenia. General hygienic measures are commonly practised to reduce fungal load in the patient's environment. Prophylaxis with fluconazole appears to be effective in patients receiving bone marrow transplants. Results with itraconazole seem less favourable but in its new formulation is better absorbed. The incidence of invasive pulmonary aspergillosis is apparently reduced by aerosolized amphotericin B, but prospective randomized studies showed no decrease in prevalence or increase in survival. The use of intravenous amphotericin B in prophylaxis studies, and new lipid formulations of the drug in patients receiving bone marrow transplants have not resulted in marked reduction in invasive fungal infections. Therapeutic doses of amphotericin B are required to protect patients with proven aspergillosis from recrudescence during later episodes of antileukemic therapy or bone marrow transplantation. Itraconazole might provide protection between episodes of neutropenia. It was suggested that most patients would receive antifungal therapy for 4-6 days during unexplained fever unresponsive to antibacterial agents. The optimal moment for empiric therapy to begin has not yet been fully established.

P. Ribaud and E. Gluckman described their experience with prevention of fungal infection after allogenic bone marrow transplantation. Serious invasive fungal infections can become manifest from the day of transplant to several months thereafter. *Candida* infections are generally seen during the aplastic phase, while mould infections usually occur after hematological recovery. Between 10-20% of bone marrow transplant patients will develop invasive fungal infections, and more than half will die from it. Reduction in the environmental exposure to fungi is not widely adopted, apart from asepsis to prevent candidosis and HEPA filters for prevention of aspergillosis. Optimal protocols for prophylaxis have not yet been established. Recent problems include the increased numbers of infections with non-*albicans* species of *Candida*, and species of *Aspergillus* other than *A. fumigatus*.

Current approaches which may improve the problems associated with invasive fungal infections include controlled prophylaxis studies, monitoring for fungal resistance, more effective methods for immune reconstitution, and prevention of graft-versus-host reactions.

Session II

chaired by
G. Prentice and A.M. Sugar

Candidiasis* and aspergillosis

A. A. Fauser and M. Rudolphi described studies on the prophylactic use of hematopoietic growth factors in reducing the incidence of fever and complications of mycotic infections in patients with cancer.
The therapeutic use of recombinant human granulocyte-macrophage colony stimulating factor in combination with antibiotics was studied in patients with febrile neutropenia. Beneficial effects were observed in some cases. It is suggested that recombinant human growth factors in combination with antifungal drugs may have a role in the management of invasive fungal infections in cancer patients and bone marrow recipients.

C. Viscoli reviewed the changing epidemiology of invasive candidosis as a cause of morbidity and mortality in immuno-compromised patients. Studies from the USA, Europe and Taiwan provide evidence for increases in incidence of autopsy-confirmed invasive fungal infections from 2 to 7%. Fungemia may account for some 10% of bloodstream infections. Data were provided from a recent study of candidemia in cancer patients undertaken by the Invasive Fungal Infection Group of the European Organization for Research and Treatment of Cancer (EORTC). With the object of evaluating factors associated with *albicans* versus non-*albicans* aetiology, and post-candidemia survival, a surveillance was made of candidemias occurring over a two year period in 30 cancer centres. Within this period, 249 episodes were reported. Non-*albicans* candidemia accounted for 30% of episodes in patients with solid tumours and in 64% of those with hematological malignancies ($p<0.001$). In tumour patients, only neutropenia was significantly associated with non-*albicans* candidemia, whereas in hematological patients, significance was also related to acute leukaemia and antifungal prophylaxis. The overall mortality within 30 days was 39%. Univariate analysis showed that *Candida glabrata* was the species associated with the highest risk of death. Multivariate analysis showed that the risk of death was associated with age and severity of the underlying condition for both groups. Additional factors amongst hematological patients included allogenic bone marrow transplant, septic shock, and lack of antifungal prophylaxis. Reduced mortality was associated with antifungal prophylaxis.

J.D. Sobel presented a comparison between oral and vaginal candidosis, with special reference to differences in their pathogenesis and management. Features common to both forms of disease include levels of colonization in healthy adults and immuno-compromised hosts, in diabetics and in patients receiving antimicrobial agents: the range of clinical expressions is comparable. *C. albicans* is the predominant cause of oral candidosis in otherwise healthy subjects, in contrast to vaginal candidosis, where the frequency of non-*albicans* species is higher. Mixed infections with *Candida* spp. are common in oral forms of the disease, but rare in vaginal candidosis. Oral candidosis is apparently hormone independent, unlike vaginal disease, which is common in post-menopausal women. In patients with AIDS, oropharyngeal candidosis is common in contrast to *Candida* vaginitis which is less common, and which does not have the same prognostic significance. Resistance to antifungals appears to be common in immunocompromised patients with oropharyngeal candidosis, but not with vaginal candidosis. Differences in epidemiology, pathogenesis, associated species and response suggests that they represent strongly contrasting clinical entities.

J.E. Edwards reviewed treatment guidelines for candidosis recommended by a consensus conference of 22 experienced investigators from the USA, Europe and Japan. Majority agreement was reached on several key questions. It was agreed that all patients, neutropenic or non-neutropenic should be treated with an antifungal. For patients whose isolates were not resistant to fluconazole and who had no evidence of hematogenous seeding, treatment with fluconazole was universally recommended. If fluconazole had been used previously, most investigators recommended a regimen that included amphotericin B. Doses of flucytosine, when used in combination with amphotericin B, were 100 mg/kg/day, with recommended blood levels of 51-100 µg/mL. Most investigators would change non-surgically implanted lines in patients with one or more blood cultures positive for *Candida*. There was unanimous agreement that antifungal prophylaxis should not be given on a routine basis to neutropenic patients, but should be reserved for non-neutropenic patients at high risk for candidemia. When empiric treatment was indicated, on the basis of isolation of *Candida* species from sputum or urine of non-neutropenic patients, fluconazole was generally recommended. Fluconazole was also recommended for treatment of candidal infections in neutropenic and non-neutropenic children. Consensus opinion on the duration of follow-up for both neutropenic and non-neutropenic patients who develop candidemia is 3 months. Other key questions considered include management of candidal cystitis and chronic disseminated candidosis. For further details see Edwards J.E. et al., Clinical Infectious Diseases, 1997, 25, 43-59.

M.E. Ellis spoke on the manage-

* *The Editorial Board decided to adopt the term "candidosis".*

ment of acute invasive aspergillosis. In the past, only 33% of cases have had a successful outcome. Some improvements have been made by reducing delays between diagnosis and start of treatment, by the availability of improved therapeutic regimens and by improvement of host defence mechanisms. Regular use of chest CT scans for detection of pre-cavitary haloes has increased survival rates to >70%. The value of liposomal and lipid formulations of amphotericin B has not yet been fully determined: EORTC studies have shown comparable results with amphotericin B at 1 mg/kg and AmBisome at 4 mg/kg. In comparative studies with amphotericin B and lipid amphotericin B for treatment of invasive fungal infections, greater success was obtained with lipid formulations (50% versus 24%, p = 0.03). On the basis of these comparative studies, itraconazole, despite its pharmacologic variability, had a role in the primary management of less ill patients, in secondary treatment after amphotericin B therapy, in salvage treatment and in cerebral invasive aspergillosis. The role of combination therapy, such as itraconazole plus amphotericin B has not yet been clearly defined, although commonly employed. Surgery remains of proven value in treating pulmonary hemoptysis associated with aspergillosis, and endocarditis. Immunomodulation with GM-CSF is under investigation, but its role remains uncertain. Future comparative studies are directed towards international multicentre cooperation, with comparable patient groups and standardization of parameters for diagnosis and response.

chaired by
M.D. Richardson and G. Freitas

Session III

New diagnostic techniques

J. Bille reviewed methods for the molecular diagnosis of candidosis. Such procedures should provide earlier detection of *Candida* in clinical specimens, faster identification of clinical isolates, and a basis for monitoring drug susceptibility and response to therapy. The range of variables for genomic amplification procedures is wide. Most studies have focused on DNA extracted from differing dilutions of yeasts, rather than from clinical materials. Maximal sensitivity is in the order of 1 colony forming unit (10-20fg of yeast DNA). Recently published data suggest that in patients with candidemia or invasive candidosis, sensitivity and specificity values close to 100% can be achieved, and that it is feasible to differentiate between responses and failures to respond. Although promising, molecular procedures remain largely experimental, and have not yet superseded conventional approaches.

J.F. Meis and P.E. Verweij spoke on the microbiological diagnosis of invasive aspergillosis in cancer patients. A definitive diagnosis is established only by demonstration of the agent in biopsy material, and its isolation in culture. Such invasive diagnostic procedures, however, are usually not practicable in patients at risk of invasive aspergillosis. Isolation of *Aspergillus* spp. from respiratory secretion of such patients provides evidence for a presumptive diagnosis, and justification for the start of treatment. The sensitivity of positive cultures is unacceptably low, and additional laboratory procedures based on antigen detection have been developed as ancillary diagnostic tools. Daily examinations of serum and other body fluids and radiological investigations of patients identified as at risk should lead to early diagnosis of invasive aspergillosis.

Bettina Lundgren described the clinical use of PCR in the diagnosis of *Pneumocystis carinii* pneumonia. DNA amplification by PCR appears to be more sensitive than conventional methods for detecting *P. carinii* in samples with low numbers of the agent. It offers no clear advantage in the examination of bronchalveolar lavage specimens, because of the high sensitivity (95%) of conventional methods. Detection of *P. carinii* in samples of induced sputum by immunofluorescent staining, however, has a variable sensitivity (45-78%). Since good quality induced sputum requires experienced personnel and a cooperative patient, a higher detection rate is required. With PCR the sensitivity can approach 100%. In recent studies, the agent has been detected by PCR in oral washes with isotonic saline, with sensitivity rates of 70-99%. Additional studies have been made with PCR for detection of *P. carinii* in serum and peripheral mononuclear cells, but results have been conflicting, with success rates varying from 0-98%. Further studies are justified on the basis of the high sensitivity of PCR, and for its potential value in patients where invasive diagnostic procedures are not practicable.

T. Obayashi described the G-test for the diagnosis of fungal infections. This is based on the fact that (1→3)-β-D-glucan is a constituent of the cell wall of fungi other than *Zygomycetes*, but is not found in cells of other microorganisms (bacteria, rickettsiae and viruses), or humans. Presence of the polysaccharide would therefore be a good indicator of systemic fungal infection, if detectable in blood or other normally sterile body fluids. Its detection is achieved by activation of Factor G, a coagulation factor of the horseshoe crab (Limulus). Results of the test with glucans isolated from

various pathogenic fungi are dose-dependent. The test can be automated, giving a result within 30 minutes. Digestion studies with (1→3)-β-D-glucanase showed that blood from patients with invasive mycoses contained β-glucan. A positive result was obtained in the blood of 39 of 41 febrile episodes in patients with mycoses, but in none of 59 non-fungal episodes. Sensitivities and specificities were 90% and 100% respectively. Some false positive results were observed in patients receiving hemodialysis, or infusions of fractionated blood products such as albumen and gamma-globulin.

Session IV

chaired by
E.G.V. Evans

Cryptococcosis

B.R. Speed spoke on patterns of *Cryptococcus neoformans* disease and its varieties. Differences have been shown between the two varieties for epidemiology, clinical features, laboratory, radiological findings, outcomes and immune responses. Var. *neoformans* is associated with immunosuppressed patients, whereas var. *gattii* affects immunocompetent hosts. Among the characteristics of infections with var. *gattii*, are visual loss in patients with CNS infection, and concomitant CNS and pulmonary disease with nodular mass lesions in the lungs, compared to the more diffuse and widespread disease in infections caused by var. *neoformans*. Patients from rural areas are more likely to be infected with var. *gattii*. Ring enhancing cryptococcomas on CT brain scans are more likely in patients with normal immunity; multiple lesions are commoner in var. *gattii* infections. Mortality is higher in patients infected with var. *neoformans*, but var. *gattii* infections tend to develop more complications and sequelae and to require more protracted treatment. The disease and its clinicopathological features are the result of a host-parasite interaction that is dependent on both the variety causing the infection and the immunological status of the patient.

D.A. Stevens presented a paper on treatment of cryptococcosis. In the management of meningitis associated with AIDS, 25-50% of patients failed to respond to conventional amphotericin B. Moreover, there was a relapse rate of 17-90%. Encouraging results have been obtained with both fluconazole, at doses of not less that 400 mg/day, and itraconazole, but recrudescences were inevitable. In studies organized by the Mycoses Study Group AIDS Clinical Trials Group, responses to fluconazole and amphotericin B were equivalent, with less toxicity in patients receiving fluconazole. Reports of lower relapse rates in patients receiving secondary prophylaxis with fluconazole led to studies (California Cooperative Treatment Group) revealing the superiority of fluconazole to placebo, and its equivalence to once weekly amphotericin B, with reduced toxicity. A recent Mycoses Study Group trial showed that after a two week induction course of amphotericin B, comparable results were obtained with both fluconazole and itraconazole. The latter drug, however, was found to be of less value in subsequent maintenance. The recommended regimen for treatment of cryptococcosis in patients with AIDS is as follows: two weeks of intravenous amphotericin B (1 mg/kg) plus flucytosine (150 mg/kg/day) with monitoring of flucytosine levels, followed by eight weeks of fluconazole or itraconazole at 400 mg/day, then lifelong maintenance with fluconazole. New approaches include high dose fluconazole or combined fluconazole-flucytosine, potentiation of conventional therapy with IFN-gamma, or adjunct use of monoclonal antibody. The future role of new formulations of amphotericin B, such as ABCD or liposomal amphotericin B is unknown, although they have been shown to be effective in experimental infections.

Session V

chaired by
J.M. Torres Rodriguez and P. Martino

Newly emerging and challenging fungal infections

V. Krcmery reviewed treatment of infections with unusual fungi in patients with leukaemia. In recent years, an increase has been seen in the numbers of infections caused by yeasts other than *Candida* species. These include *Malassezia furfur, Trichosporon spp., Rhodotorula rubra, Hansenula anomala, Saccharomyces cerevisiae, Clavispora lusitaniae, Torulopsis glabrata, Geotrichum candidum*, and non-*neoformans* cryptococci. In major hematology centres in Europe and the USA, the proportion of non-*Candida* yeasts increased from 1-5% in 1980 to 10-25% after 1990. Insufficient data are available to determine whether or not associated mortality is higher than with *Candida* spp. (30-40%) or filamentous fungi (50-70%).

W.G. Merz spoke on *Penicillium marneffei* infections. Hundreds of cases have been reported in the wake of the HIV epidemic, mainly in southern Asia. The organism is associated with bamboo rats but animal-to-human transmission probably does not occur. The environmental niche is unknown. The associated disease is disseminated, with fever and secondary skin lesions in HIV+ individuals with CD4 counts ~ 50. Diagnosis can be made by antigen detection, histopathology, or isolation of the agent from skin biopsies, blood, bone marrow or lymph node specimens. The organism is seen in vivo as intracellular yeasts, distinguished from *Histoplasma capsulatum* by the occurrence of fission. In treating the disease, some success has been obtained with amphotericin B and itraconazole, but long term maintenance with itraconazole may be necessary.

An overview of pigmented fungal pathogens (black and brown fungi) was provided by M.G. Rinaldi. Infections caused by such agents are, with some exceptions, correctly termed phaeohyphomycoses. The pigmentation in most instances is caused by the presence of melanin in the cell wall. Presence of melanin in fungal elements seen in histopathological preparations can be revealed by use of the Masson stain. Some 80 species have been associated with phaeohyphomycosis. The causal agents include both yeast and mould forms. Most are moulds lacking a sexual phase, placed in the *Hyphomycetes*. The diseases they cause range from superficial to deep, and may occur in both immunocompetent and immunologically compromised individuals.

B. Dupont reported the findings by the French Study Group on Histoplasmosis on diagnosis and management of imported histoplasmosis. Cases occurring in France over the past 25 years were analyzed retrospectively. Only those confirmed by histopathology were included. Infections with *H. capsulatum* var. *duboisii* were confirmed in 26 cases. Apart from one laboratory-acquired infection, all had originated in Central or West Africa. The commonest locations were lymph nodes, followed by skin, lungs and bones. Most were treated with amphotericin B and/or ketoconazole. Revealed by the survey were the value of surgery and the high rate of relapse. In individuals not infected with HIV, 43 cases were recorded, 38 of which were in Caucasian patients. Most had acquired the disease in Central or South America. Mean duration between return to France and onset of overt infection was 18 months. The commonest form of treatment was ketoconazole, others being treated with amphotericin B or itraconazole. There were 51 cases in HIV+ patients, mostly (31) in Caucasians who had acquired histoplasmosis in South and Central America. Histoplasmosis was an AIDS-defining illness in 53% of cases. Predominant locations were lungs and skin, and the commonest form of therapy was intravenous amphotericin B.

R. Miller spoke on the management of *Pneumocystis carinii* pneumonia. The illness remains common in patients unaware of their HIV serostatus, or who decline or are intolerant of *P. carinii* pneumonia prophylaxis and retroviral combination therapy. The drug of choice remains co-trimoxazole, which produces a response in 85% of patients. Uncertainties remain about the role of salvage therapy, the use of adjuvant steroids and optimal dosing.

chaired by
D.A. Stevens and E. Roilides

Session VI

Antifungal resistance

J.L. Rodriguez Tudela spoke on correlations of antifungal susceptibility testing with clinical outcome. Development of the Macrodilution Reference Method M27 for susceptibility testing of yeasts has provided a satisfactory basis for attempting to correlate in vitro results with clinical outcome. Such studies are complex, because so many factors can influence the clinical outcome. Results to date have not yet clearly demonstrated the clinical relevance of susceptible and resistant isolates. However, although low MICs do not guarantee successful outcomes and high MICs do not indicate that treatment will always fail, infections with a resistant agent are less likely to respond than those caused by one that is susceptible. Current approaches involve the development of strategies for correlating in vitro results with clinical outcome, and determination of optimal breakpoints in the in vitro tests.

J.N. Galgiani, spoke on amphotericin B resistance. Most fungal pathogens are considered to be sensitive to amphotericin B, apart from species such as *Candida lusitaniae*, *Trichosporon beigelii* or *Pseudallescheria boydii*, which have reduced levels of membrane ergosterol. Not all infections caused by susceptible species respond to treatment with amphotericin B, failure possibly relating to host factors. The significance of intrinsic amphotericin B insusceptibility is not yet clear, for methods have not been available for identification of amphotericin B resistance. E-test appear to be promising for detecting resistance in yeasts, and investigations on the frequency of amphotericin B resistance may be helpful in specific clinical settings, such as bone transplantation and other units with high usage of polyene therapy. Azole resistance may be associated with reduced susceptibility to amphotericin B by decreasing ergosterol content of the cell membrane. The possibility that azole resistance may reduce efficacy of treatment with amphotericin B warrants investigation.

S. Kelly dealt with mechanisms of azole resistance in *Candida*. Studies on resistance have been made at the molecular level in clinical isolates of yeasts, including *C. albicans*, *C. glabrata*, and *C. tropicalis*. Sequential isolates of *C. albicans* showing increased resistance to azoles failed to accumulate fluconazole. This was linked to the

overexpression of efflux multidrug transporter genes belonging to the classes of ABC (ATP binding cassette)-transporters and Major Facilitators, which mediate cross-resistance to all azole derivatives or specific resistance to fluconazole, respectively. In *C. glabrata*, acquired resistance is mediated mainly by overexpression of a specific ABC-transporter gene. Other mechanisms of azole resistance include changes in affinity of azoles for their cellular target, namely, a cytochrome P450, which is involved in the 14a-demethylation of lanosterol (CYP51A1). Several mutations have been observed in CYP51A1 genes from azole-resistant *C. albicans*, although to date they have not all had the same effect on the binding of azoles. Such mutations could simultaneously occur with the efflux of azole antifungals, producing a different pattern and degree of resistance when measured in vitro. Cross-resistance mediated by the involvement of efflux multidrug transporters could occur in structurally unrelated compounds, including alternative or new antifungals.

Kelly also reviewed mechanisms of resistance in *Cryptococcus* with particular reference to amphotericin B and fluconazole. Amphotericin B binds to membrane ergosterol but other sterols can substitute for ergosterol and cause resistance. Fluconazole resistance mechanisms have been demonstrated in clinical settings, involving altered drug accumulation, and by mutation of sterol 5,6-desaturase. This event, observed in *C. albicans*, shows the pivotal importance of one sterol (14-methyl-3,6-diol) in the mode of action of fluconazole. Desaturase mutants fail to accumulate the diol. They do grow, but their deficiency in ergosterol synthesis also renders them cross-resistant to polyenes. In contrast to *Candida*, a major product of treatment of *Cryptococcus* is not accumulation of the diol but an earlier precursor ketosteroid. Recent reports have been published on the isolation of fluconazole and amphotericin B resistant mutants from clinical materials: one type of resistance to amphotericin B is unrelated to sterols. Additional studies have shown that heterogeneity exists in *C. neoformans*, some strains failing to accumulate ergosterol and having increased resistance to amphotericin B without prior selection.

D.W. Warnock spoke on antifungal drug susceptibility testing and resistance in *Aspergillus*. Standardized methods for in vitro testing have been developed for *Candida* spp. and *C. neoformans*, and good evidence now exists for a correlation between MIC values and therapeutic outcome in human and experimental animal infections. On the contrary, attention to date with moulds has concentrated on selection of optimal cultural conditions, rather than correlation with clinical outcome. In his work, isolates of *A. fumigatus* were obtained from cases with a documented therapeutic outcome, and attempts were made to determine the in vitro conditions which best discriminated between two isolates from clinical failures and four cases which responded to itraconazole. Broth and agar dilutions of five media were assessed. Optimal conditions for broth microdilution included RPMI medium with L-glutamine buffered with MOPS to pH 7, a spore concentration of 10^6 per mL, and incubation at 35°C for 48 hours. Standardization of the test made it possible to generate reproducible MICs for *Aspergillus* spp. that correlated with therapeutic outcome in a neutropenic mouse model of invasive aspergillosis. Two different mechanisms of resistance to itraconazole have been identified in the clinical isolates of *A. fumigatus* studied. One involves a mutation to the target 14a-demethylase enzyme: the other is characterized by markedly lower levels of intracellular itraconazole, possibly caused by overexpression of an efflux pump.

Session VII

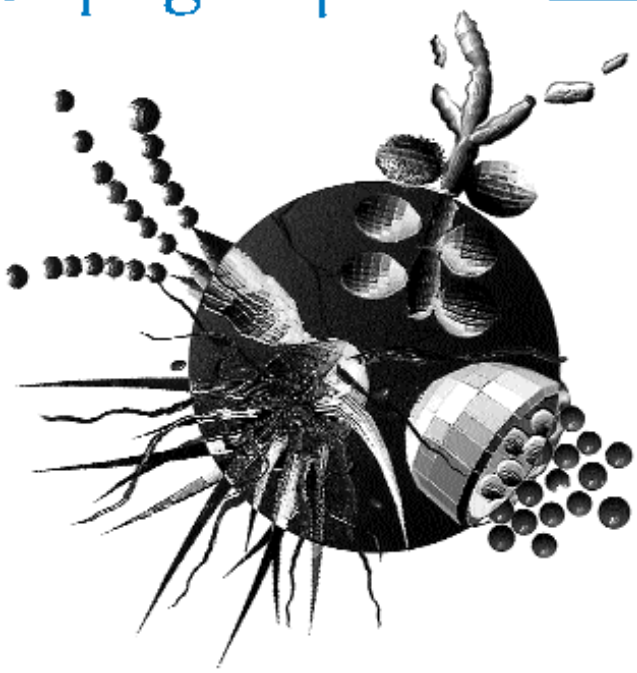
chaired by
B.E. de Pauw

New antifungals

Two papers in the final session briefly reviewed new drugs and therapeutic approaches. In the first, T.J. Walsh spoke of the wide range of antifungal agents presently being developed and evaluated. Terbinafine, long established for the treatment of cutaneous mycoses, may have some value in the management of systemic fungal infections. The expanding armamentarium of antifungals is accompanied by an increase in the number of potential targets. These include b-glucans (echinocandin, pneumocandin), chitin (nikkomicin, polyoxin), and mannoproteins (pradimicins and benanomicins).
Nikkomicin is being evaluated in a Mycoses Study Group trial. One new approach involves antimicrobial peptides derived from human cells. Augmentation of host defence mechanisms by colony stimulating factors continues to attract attention. The area is an exciting one and new strategies can be anticipated.

D.W. Denning described the new generation of antifungals. The list is lengthy, but some were singled out for mention. Voriconazole is a lipophilic broad spectrum azole in phase III development, with both intravenous and oral formulations. Amongst those at phase II development are SCH 56592, which has anti-*Aspergillus* activity, LY 303 366 and pneumocandin (L 743 872). The latter two agents act against the fungal cell wall and in vitro are rapidly fungicidal. Also in phase II/III development is liposomal nystatin, which may have a role in invasive aspergillosis. Other products under development include BMS 207147, TAK 187, Nikkomicin Z, UR 9825, and sordarin, an inhibitor of elongation factor 2.

FOCUS on fungal infections 8



The 8th edition of Focus on fungal infections, chaired by Drs. Elias J. Anaissie and Michael G. Rinaldi, will be held March 4-6, 1998, in Orlando, Florida. This series of meetings has evolved into what are perhaps the most authoritative meetings on the topic of invasive fungal infections. Each year "Focus" provides a forum where a growing number of experts, leading investigators, practicing infectious diseases specialists and laboratory microbiologists review the state of the art and present their newest data on the diagnosis and management of severe fungal infections.

Besides overview lectures, podium and posters presentation, the program features several Point-Counterpoint sessions, where the most controversial topics will be debated by supporters of diametrically opposing views. A Mycology Workshop which focuses on the culture and identification of selected medically-significant fungi, will be held at the start of the meeting.

The program of the 8 sessions of this 1998 edition is organized in order to integrate the most recent mycological research data into the daily practice of clinicians and laboratorians.

Session 1: Mycoses and HIV infections: the big change?
chaired by W.G. Powderly

Lectures by Peter G. Pappas and Robert A. Larsen

Point-Counterpoint: Are fungal infections in HIV patients becoming less prominent/important?
- Yes, they are definitely less prominent (Charles P. Farthing)
- No, they still incite as much grief as previously (Alan M. Sugar)

Session 2: Recent developments in selected mycoses
chaired by S.E. Sanche

Lectures by Mary H. White, Thomas J. Walsh, Michael G. Rinaldi, and David S. Bauman

Session 3: Superficial and cutaneous mycoses
chaired by S.G. Revankar

Lectures by Roderick J. Hay and Timothy G. Berger

Session 4: Opportunistic Mycoses
chaired by J.W. Hiemenz

Lectures by Nina Singh, Elias J. Anaissie, and William R. Jarvis

Session 5: Current happenings in antifungal therapy
chaired by W.E. Dismukes

Lectures by Frank C. Odds, Lisa Saiman, and Richard W. Yee

Point-Counterpoint: The Tale of the Sage Professor and the Very Bright Infectious Disease Fellow - The appropriate use (or not) of lipid formulations of polyenes
- The Sage Professor (Donald A. Armstrong)
- The Very Bright Infectious Diseases Fellow (John H. Rex)

Session 6: Antifungal resistance - The continuing saga
chaired by M. Hong Nguyen

Point-Counterpoint: The Pattersons at breakfast - A year later
- Resistance to antifungals is still no big deal (Thomas F. Patterson)
- Quite the reverse, dear, resistance to antifungals has become an entrenched, legitimate clinical concern (Jan E. Patterson)

Session 7: Therapeutic potpourri
chaired by J.F. Toney

Lectures by John R. Graybill and John R. Wingard

Session 8: Laboratory-clinical correlations
chaired by M.A. Ghannoum

Lectures by Michael A. Pfaller, William G. Merz, Michael A. Saubolle, and Richard F. Hector

Abstracts submission deadline

Abstracts for posters must be submitted by February 2, 1998 at Imedex USA, Inc.,
70 Technology Drive, Alpharetta, GA 30005-3969 USA
Fax +1 770 751 7334, Tel +1 770 751 7332
E-mail: meetings@imedex.com
Abstract forms are provided by Imedex, at request.

Registration fee: US $ 200 (by February 2)
US $ 300 (by February 25)
US $ 350 (on site)

Mycology Courses in Europe (1998)

BELGIUM

Course on Medical and Veterinary Mycology *(every year)*

Organizers: Proff. D. Swinne and I. Surmont (lectures/aerobiology: Drs. N. Nolard, M. Detandt)
Address: Institute of Tropical Medicine, Nationalestr. 155, M-2000 Antwerpen, Fax +32 3 2161431
Duration - date: 5 months (one full day/week) - February to June
Hours theory/practice: Theory 30h/practice 70h
Admitted participants: 20
Scientific programme: Morphology, classification, identification of filamentous fungi and yeasts. Superficial, subcutaneous and deep mycoses: clinical forms, aetiology, ecology, epidemiology, diagnosis and treatment. Overview on mycotoxines and fungal allergy
Certificate: Diploma

Cycle de Formation Moisissures et Allergies *(every year)*

Organizers: Dr. N. Nolard, Institut Scientifique de la Santé Publique Louis Pasteur (ISP), Section de Mycologie, 14 rue J. Wytsman, 1050 Bruxelles, Belgium, Fax +32 2 642 5519 and Dr. O. Massot, Centre Européen Médical et Bioclimatique de Recherches et d'Enseignement Universitaire, 40 rue J. Bayle, 05100 Villard S-Pancrace, France, Fax +33 4 9220 1303
Address: ISP, 14 rue J. Wytsman, 1050 Bruxelles, Belgium
Duration - date: 10 jours - November 1998
Admitted participants: 12
Certificate: Diploma

BULGARIA

Course on Diagnosis of Systemic Mycoses

Organizer: Prof. T. Kantardjiev
Address: National Center of Infectious and Parasitic Diseases, 26 Yanko Sakazov Blvd., Sofia 1504
Duration - date: 10 days - April 6, 1998
Hours theory/practice: Theory 50h/practice 20h
Admitted participants: 10
Certificate: Diploma

FRANCE

Cours de Mycologie Médicale *(every year)*

Organizer: Dr. Cl. de Bièvre
Address: Institut Pasteur, 28 Rue du Dr. Roux, 75015 Paris, Fax +33 1 45688420
Duration - date: 8 weeks - April 20-June 15, 1998
Hours theory/practice: Theory 100h/practice 100h
Admitted participants: 20
Scientific programme: Clinical and mycological features of deep-seated and superficial mycoses. Diagnosis, treatment, identification
Certificate: Diploma Institut Pasteur and Université Paris VI Paris VII

GERMANY

Course on Clinical Mycology *(every year)*

Organizer: Dr. K. Tintelnot, Robert-Koch-Institut, Bundesgesundheitsamt, Nordufer 20, 13353 Berlin
Address: Working Group "Clinical Mycology" of DMykG, Fax +33 1 45688218
Duration - date: 2 days - February 13-14, 1998
Hours theory/practice: Only theory
Admitted participants: 25
Scientific programme: Antimycotic susceptibility tests. Identification of yeasts. Immunological diagnostic of candidose opportunistes, *Aspergillus*

Course on Experimental Mycology *(every year)*

Organizer: Dr. H.-J. Tietz, Zahnarzt, Facharzt für Mikrobiologie, Hautklinik der Charité, Schumannstr. 20/21, 10117 Berlin
Address: Working Group "Micological Laboratory Diagnostics" of DMykG
Duration - date: 2 days - October 1998
Hours theory/practice: Only theory
Admitted participants: 30
Scientific programme: Identification of yeasts and dermatophytes

GREECE

Short Course on Laboratory Diagnosis of Fungal Infections

Organizers: Prof. N.J. Legakis and Dr. A. Velegraki
Address: c/o Dr. A. Velegraki, Dept. of Microbiology, Medical School, University of Athens, Mikras Asias 75-77, Goudi, 115 27 Athens, Fax +301 7709180
E-mail: avelegra@acropolis.net
Duration - date: 2 days - March 30-31, 1998
Hours theory/practice: Theory 5h/practice 9h
Admitted participants: 20

POLAND

Course on Dermatological Mycology *(every year)*

Organizers: Prof. R. Maleszka and others
Address: Oddzial Dermatologiczny Szpitala MSW, ul. Dojazd 34, 60-631 Poznan
Duration - date: 5 days - September 7-11, 1998
Hours theory/practice: Theory 12h/practice 36h
Scientific programme: Dermatomycoses (description of the fungi, biology, clinical description, laboratory diagnosis, treatment)
Certificate: Certificate (after examination)

Advances in Mycologic Dermatology

Organizers: Prof. E. Baran and others
Address: Clinic of Dermatology, 50-368 Wroclaw, Chalubinskiego 1
Duration - date: 3 days - April 2-4, 1998
Admitted participants: 10
Hours theory/practice: Theory 12h/practice 10h
Certificate: Diploma

PORTUGAL

Course on Medical Mycology *(every year)*

Organizers: Drs. M. Rocha, R. Velho, L. Rosada, J. Brandão, I. Costa
Address: ASPOMM, Centro de Dermatologia, R. José Estêvão 135, 1150 Lisboa, Fax +351 1 3522359
Duration - date: 3 weeks - March 18-April 3, 1998
Hours theory/practice: Theory 35h/practice 42h
Admitted participants: 10
Scientific programme: Mycosis: Clinical, epidemiology and treatment. Study of pathogenic fungi and actinomicetes: Laboratory study, molecular biology and antifungal sensitivity. Veterinary Mycology. Food Mycology. Quality Control in Mycology
Certificate: Diploma

SPAIN

Course on Medical Mycology *(every year)*

Organizer: Dr. Josep M. Torres-Rodriguez, Unitat de Microbiologia, Institut Municipal D'Investigació Mèdica, c/ Aiguader 80, 08003 Barcelona, Fax +34 3 221 3237
Address: Departamento de Microbiologia, Fac. Medicina "UDIMAS", Universidad Autonoma de Barcelona
Duration: 3 weeks
Hours theory/practice: Theory 65%/practice 35%
Admitted participants: 15
Certificate: Diploma

Practical Course on Identification of Food-borne Fungi and Micotoxins *(every two years)*

Organizer: R. Canela, J.Cano, M.J. Figueras, J. Gené, J. Guarro, V. Sanchis, N. Sala, M. Torres, R. Viladrich, A. Ramos, I. Vinas, J.M. Guillamon
Address: Unidad de Microbiologia, Departamento de Tecnologia de Alimentos, Escuela Tecnica Supérior de Ingénieria Agraria de Lérida, Universidad de Lérida
Duration - date: 1 week - 1998
Hours theory/practice: Theory 10h/practice 30h
Admitted participants: 14
Scientific programme: General characteristics of the fungi. Identification of the common food-borne fungi. General techniques for detection and quantification of mycotoxins in food
Certificate: AEM Certification

SWEDEN

Course on Medical Mycology

Organizers: Drs. L. Edebo, J. Faergemann
Address: Sahlgrenska University Hospital, Dept. of Clinical Bacteriology, Guldhedsgatan 10, 413 46 Göteborg, Fax +46 31 604975
Duration - date: 2 days - September 1998
Admitted participants: 12
Scientific programme: Fungal taxonomy. Structure and metabolism. Molecular biology of fungi. Identification of medically important fungi. Diagnosis of mycotic infections. Antifungal agents. Mechanism of action. Pharmacokinetics.
Certificate: Diploma

THE NETHERLANDS

Course on Medical Mycology *(Dutch language edition)*

Organizer: Centraalbureau voor Schimmelcultures, Baarn
Address: CBS, Oosterstr. 1, Baarn, Fax +31 3554 16142
Duration - date: 3 weeks - April 1998
Admitted participants: 25
Scientific programme: Biodiversity in medical mycology. All major species and their clinical pictures are treated
Certificate: Diploma

Course on General Mycology *(English language edition)*

Organizer: Centraalbureau voor Schimmelcultures, Baarn
Address: CBS, Oosterstr. 1, Baarn, Fax +31 3554 16142
Duration - date: 3 weeks - March16- April 2, 1998
Hours theory/practice: Theory 30h/practice 75h
Admitted participants: 25
Scientific programme: Classical mycology course on biodiversity and taxonomy including one day medical mycology
Certificate: Diploma