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)

1/99

ECMM
European Confederation of Medical Mycology

CEMM
Confédération Européenne de Mycologie Médicale

Message from the President

Six years ago the European Confederation of Medical Mycology was born. The idea was in the air since a few years and it was time to realize the project. There was immediately a great enthusiasm among the European Societies and Groups of Mycology and the first Congress was held in Paris at the Institut Pasteur on November 26, 1993. At the same time the Statutes and the goals of the ECMM were defined and adopted: the adventure was beginning.

As founder of the ECMM I had the great honor to be elected Chairman for two 3-year mandates, Lars Edebo was Treasurer during the same time and David Warnock was the first General Secretary. He had the merit of accomplishing a considerable work as, starting from nothing, all had to be done. After 3 years of fruitful mandate, Marianna Viviani was elected and brought her enthusiasm, her tenacity, ideas and devotion to the ECMM.

Already many objectives have been reached. All the Societies who were approached accepted to participate and are still present. Russia and Israel joined the Confederation and very soon we hope that Finnish Society of Medical Mycology will be the 20th member of the ECMM.

Our Congresses are held regularly with a large and increasing attendance. After Paris 1993, Brussels 1995, Lisboa 1996, Glasgow 1998, the next Congresses will be Dresden: 1999, Barcelona: 2000, Tel Aviv: 2001, Poland: 2002. Mycologists have the opportunity to meet each other during these meetings to exchange experience, to share advances and to establish scientific collaborations.

Working groups were constituted, particularly on epidemiology: candidemia, cryptococcosis, histoplasmosis, tinea capitis, nocardiosis and very interesting results have already been reported.

ECMM Newsletter, thanks to Marianna Viviani, is regularly issued and carries directly information to all members of the Societies belonging to the ECMM.

Fundings were obtained from pharmaceutical compa-

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Blue Grass band entertains the *Candida* barbecue at 5th Conference on *Candida* and Candidiasis (Report page 9)

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ECMM Council

Affiliated Societies

Associação Portuguesa de Micologia Médica (ASPOMM)
President: M. Rocha
Vicepresident: R.M. Velho
Secretary: M.L. Rosado *(ECMM delegate)*
Treasurer: M. Gardete
Membership 1999: 50
Newsletter

Asociacion Española de Micologia Seccion de Micologia Medica
President: J.M. Torres Rodriguez
Vicepresident: J. Ponton
Secretary: S. Santamaria del Campo
Treasurer: A.J. Carrillo Muñoz
President Medical Section: J. Cabañes *(ECMM delegate)*
Membership 1999: 89
National meeting: 2000
Journal: Revista Iberoamericana de Micologia

British Society for Medical Mycology (BSMM)
President: R.J. Hay *(ECMM delegate)*
General Secretary: R.A. Barnes
Meetings Secretary: D. Sullivan
Treasurer: G.S. Shankland
Membership 1999: 255
National meeting: April 25-27, 1999, Dublin, Ireland
Newsletter

Bulgarian Mycological Society (BMS)
President: T. Kantardjiev *(ECMM delegate)*
Vicepresident: G. Mateev
Secretary: A. Kouzmanov
Treasurer: T. Velinov
Membership 1999: 31
National meeting: November 19-20, 1999

Czech Mycological Group
ECMM delegate: A. Tomsíková

Danish Society for Mycopathologia
President: S. Gravesen
Secretary: L. Ravnborg
Treasurer: J. Stenderup *(ECMM delegate)*
Membership 1999: 45

Deutschsprachige Mykologische Gesellschaft e.V. (DMykG)
President: H. Bernhardt *(ECMM delegate)*
Vicepresident: H. Chr. Korting
Secretary: C. Seebacher
Treasurer: W. Fegeler
Membership 1999: 1100
National meeting: June 3-6, 1999, Dresden
Journal: Mycoses

Federazione Italiana di Micopatologia Umana e Animale (FIMUA)
President: E. Concia
Vicepresident: M.T. Montagna
Secretary: A. Persi
Treasurer: A.M. Tortorano
ECMM delegate: M.A. Viviani
Membership 1999: 160
National meeting: September 2000, Bari
Newsletter

Greek Mycological Group
ECMM delegate: O. Marcelou-Kinti

Hungarian Dermatological Society - Mycology Section
President: G. Simon *(ECMM delegate)*
Secretary: G. Fekete
Membership 1999: 37
National meeting: 2000

Israel Society for Medical Mycology
President: E. Segal
Secretary: I. Berdicevsky *(ECMM delegate)*
Treasurer: D. Elad
Membership 1999: 80

Polish Dermatologic Society Mycology Section
President: E. Baran *(ECMM delegate)*
Secretary: J. Szepietowski
Treasurer: R. Bialynicki-Birula
Membership 1999: 98
National meeting: 2000, Poznan
Journal: Mikologia Lekarska (Medical Mycology)

Netherland Society for Medical Mycology (NVMy)
President: J.F.G.M. Meis *(ECMM delegate)*
Scientific Secretary: G.S. de Hoog
Secretary: E.P.F. Yzerman
Treasurer: R.W. Brimicombe
Membership 1999: 137
National meeting: April 21, 1999, Veldhoven

Russian Society of Mycology
President: S.A. Burova *(ECMM delegate)*
Vicepresident: V.B. Antonov
Secretary: N.M. Vasilyeva
Treasurer: I.V. Kurbatova
Membership 1999: 25

Société Belge de Mycologie Humaine et Animale/ Belgische Vereniging Voor Menselijke en Dierlijke Mycologie
President: N. Nolard
Vicepresident: N. Lateur, E. Van Hecke
Secretary: P.E. Lagneau, J. Boelaert
Treasurer: F. Symoens
ECMM delegate: D. Swinne
Membership 1999: 180
National meeting: February 1999, Liège

Société Française de Mycologie Médicale
President: Cl. de Bièvre
Vicepresident: D. Chabasse, O. Morin, H. Koenig
Secretary: B. Dupont *(ECMM delegate)*
Treasurer: P. Boiron
Membership 1999: 360
National meetings: May 20-22, 1999, Strasbourg; November 26-27, 1999, Paris
Journal: Journal de Mycologie Médicale

Swedish Society for Clinical Mycology
President: J. Faergemann
Vicepresident: T. Kaaman
Secretary: G. Pålsson
Treasurer: L. Edebo *(ECMM delegate)*
Membership 1999: 105
Newsletter

Swiss Mycological Group
ECMM delegate: M. Monod

Turkish Microbiological Society Mycology Section
President: Ö. Ang
ECMM delegate: E. Tümbay
Membership 1999: 21

(Information provided by the member Societies)

Message from the President

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nies to finance certain actions.

A lot has already been accomplished and this has required considerable efforts. A lot remains to be done and our numerous projects are the witness of our vitality: the basic teaching of medical mycology is scheduled, a network of mycologists and clinicians is able to participate in large clinical trials with antifungal agents. All the working groups are open, any mycologist who wish to participate in any action, to develop any idea, is welcome.

In the next future we probably have to study collaborations with other organizations such as the Mycosis Study Group (MSG-USA), EORTC, ISHAM and other.

Among the very positive results of ECMM I would like to emphasize the creation of a national and European consciousness of being the Medical Mycology people. Societies or groups of Mycology were created or individualized from microbiology, they act and think for themselves, they realized that they represent an important, useful and powerful group.

At the end of my mandate as Chairman, I would like to express my warmest thanks to all Societies and their members, to the delegates from all countries and to the officers who make this adventure a successful reality. Good luck and prosperity to ECMM.

Bertrand Dupont

Quality Control in Mycology

Quality Control is universally recognised as fundamentally important in ensuring that diagnostic laboratories are performing appropriate tests at acceptable levels of competence. Moreover, it provides an invaluable means of educating laboratory staff in both specialist and non-specialist laboratories with the range and identifying features of pathogenic fungi isolated from clinical materials. The importance of Quality Control has grown significantly in recent years, because of increased numbers of superficial and deep-seated mycoses, the introduction of rapid identification test kits, and the relative shortage of suitable courses in diagnostic mycology.

In view of the incontestable and widely acknowledged need for monitoring performances of diagnostic laboratories, it is perhaps surprising that Quality Control programmes throughout Europe are so disparate, ranging from the well-established to the non-existent. The last issue of the Mycology Newsletter contained a keynote report by Dr. Alain Leblanc, describing the Mycology Quality Control programme in France. In this issue, Dr. Colin Campbell, Dr. Nicole Nolard and Prof. Danielle Swinne review existing programmes in the UK and Belgium.

One of the declared objectives of the ECMM is «to make the European mycological societies aware of the importance of Quality Control» and future issues of the newsletter will provide additional information on existing programmes in other European countries.

The value of Quality Control cannot be over-emphasized. One of the potential benefits arising from the formation of our Confederation is that it facilitates exchanges amongst its member societies and development of constructive cooperative activities. Quality Control as a means of improving knowledge and professional competence is a topic that is both timely and worthy.

Donald W.R. Mackenzie

The UK NEQAS scheme for quality assurance in Medical Mycology

The External Quality Assessment (EQA) scheme for medical mycology was set up in England and Wales in 1986 as a sub-division of the UK National External Quality Assessment Scheme (NEQAS) for microbiology and is run by the Quality Assurance Laboratory (QAL) in London and the Mycology Reference Laboratory (MRL) in Bristol. NEQAS coordinates EQA for all branches of pathology. Its management system consists of two levels of committees, made up of independent senior professional microbiologists. A "steering committee" directs the policy and ensures that the testing is relevant to modern laboratories. In addition an "advisory panel" monitors laboratory performance and offers help and advice to those laboratories showing consistently poor performance.

Strains of fungi to be used as simulated specimens are selected by the MRL and distributed by QAL to participant laboratories. There are three distributions per year, and clinical details are included to simulate the type of infection most often caused by the species. The participants are given three weeks to identify the fungi and return their results to QAL for assessment of a score.

Several levels of scoring are used, depending on the perceived difficulty of the individual fungus. For both "simple" and "difficult" species, the full score of 2 points is given if the fungus is fully identified, whether or not the laboratory states that it would have been referred to a specialist laboratory in practice. For "simple" specimens, laboratories returning the correct genus name with no specific epithet are awarded 1 point, but only if the laboratory has stated the intention to refer to a specialist laboratory. For species scored as "difficult" this category is given 2 points, and 1 point if there is no intention to refer. A third scoring level, "genus only", is used for those fungi which it would be unreasonable to expect the average clinical laboratory to fully identify (*Alternaria, Acremonium* etc.). These confer either 2 points or zero points. In addition to these specimens, rare pathogens are sometimes included as "educational" and are not scored.

As a further control, the scoring is cancelled if a fungus is identified by fewer than 80% of a group of "reference" laboratories, selected on past performance during the previous year.

There are now over 300 laboratories taking part in the UK NEQAS mycology scheme comprising 240 UK laboratories, many European laboratories and a few others worldwide.

Performance of participants over the thirteen years that the Mycology QA has been running varies according to the fungal species distributed. In general the level of expertise is higher with yeasts than with moulds. Some of the well-known yeast pathogens, such as *Cryptococcus neoformans*, *Candida albicans* and *C. parapsilosis*, are often correctly identified by over 90% of laboratories. This probably reflects the widespread use of commercial yeast identification kits.

However, too strong a dependence on these kits without knowledge of the morphology of the unknown yeast still accounts for a significant number of errors.

For instance, *C. krusei* was often reported as *C. inconspicua*, *C. glabrata* as *C. parapsilosis*, *Trichosporon beigelii* group as *Cryptococcus* species, and *Blastoschizomyces capitatus* as *C. krusei*. With the help of written comments following the distributions, and educational courses, the message seems to be getting through to the laboratories that kits must always be interpreted in the context of morphological characteristics. The last distribution of *C. glabrata* resulted in correct identification by 98% of UK laboratories.

There are no identification kits for moulds, and expertise is learned only slowly. Some common species pose no problem. The common causes of tinea pedis, both *Trichophyton rubrum* and *T. interdigitale* (*T. mentagrophytes*) usually cause no problem, with over 80% of laboratories correctly identifying them. *Aspergillus fumigatus* was recognised by 82% in 1987, soon after the scheme started, and by 94% in 1998. In 1987 only 56% correctly identified *A. flavus*. At that time in the UK many laboratories knew little of *Aspergillus* species other than *A. fumigatus* and *A. niger* and possibly *A. terreus*. It is clear from the returns that green coloured *Aspergillus* spp. were difficult for many laboratories. Successive distributions of *A. flavus* in 1991, 1993 and 1995 show a steady improvement, with 64,73 and 83% of laboratories respectively returning correct identifications.

Many of the species distributed several times have shown the same type of improvement. The educational appeal of external QA is popular with the participants and is one of its greatest merits. The general ability of laboratories to recognise the less common dermatophytes is a good example of this learning aspect. Only 46% of laboratories identified *Trichophyton erinacei* in 1988, but 68% did so in 1993. *T. tonsurans* was identified by 44% of laboratories in 1987, but by 78% in

1998. One practical problem that has been encountered with the dermatophytes is the difficulty of lyophilising them without losing their essential gross morphological (and sometimes even microscopical) characters during the process. This particularly applies to the non sporulating species, and the MRL is currently examining alternative methods to overcome the problem.

Although scores for many fungal species have shown a gradual increase over several successive distributions of the same organism, the opposite has been true for *Scedosporium apiospermum*. Distributions of this species in 1989, 1992 and 1997 resulted in 85%, 67% and 57% of laboratories correctly identifying it respectively. One possible explanation is that the extra fungal genera now appearing in medical mycology texts as causes of opportunistic mycoses have given a wider range of possibilities than was possible with older books.

In conclusion, the UK experience of medical mycology EQA shows that it can be a useful management aid in the maintenance and even improvement of laboratory performance. However EQA is only worth doing if the participants are honest about their attitude to it and do not cheat. There are many ways for the unscrupulous to ensure that a laboratory performs well in a QA excercise. Obviously, to be an effective measure of the service available to the patient we should avoid such temptations. When used correctly and with honesty, it can indicate deficiencies in test procedures and their interpretation, and indicate areas for the training needs of laboratory workers in mycological expertise.

Colin K. Campbell

Quality Control in Belgium

In Belgium, two systems of quality control are currently available for laboratories of medical biology

External evaluation of quality (EEQ)

All the laboratories providing analyses of clinical biology within the scope of the regulations of the Belgian National Health Service have to be registered and therefore to participate regularly in the official programme of external evaluation of quality.

This control programme is dealing with: biochemistry, immunoassay, hematology, coagulation, immunohematology, non infectious and infectious serology, parasitology, microbiology, and allergy. The number of mycological samples sent is very limited: 6 freeze-dried fungal samples were distributed during the five last years. They included *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Candida krusei*, *Candida glabrata*, *Rhizopus microsporus* var. *rhizopodiformis*, and *Candida parapsilosis*.

The objective of this evaluation is clearly described in an article of a royal by-law: the objective of the external evaluation of the quality of clinical biology analyses is to determine the validity of the results of the analyses performed for each laboratory concerned, taking into account techniques, products, reagents and material used, comparing them among others to the results obtained by all the laboratories registered to perform the same analyses or groups of analyses. On the one hand, the evaluation aims to ensure the accuracy and improvement of the analyses of clinical biology for the benefit of public health. On the other hand it enables each laboratory to check their techniques and monitor their performances. Legal fees are also charged to the participants.

Specific quality assessment scheme for Medical Mycology

A second system of quality assessment and assistance for improving the quality of mycological identifications was also set up by the laboratory of Mycology of the Institute of Tropical Medicine in Antwerp a few years ago, and from October 1999 on will be working in collaboration with the Mycology section of Institute of Public Health in Brussels.

About 40 laboratories of clinical biology were willing to participate to a specific quality control programme for Medical Mycology. Five isolates (filamentous fungi or yeasts) from clinical origins are distributed each year. The species sent for four years are: *Pseudallescheria boydii*, *Paecilomyces variotii*, *Trichophyton verrucosum*, *Scopulariopsis brevicaulis*, *Geotrichum capitatum*, *Aspergillus terreus*, *Trichophyton tonsurans*, *Acremonium sclerotigenum*, *Alternaria* sp., *Exophiala jeanselmei*, *Rhizopus microsporus* var. *rhizopodiformis*, *Microsporum lange-ronii*, *Scedosporium prolificans*, *Onychocola canadensis*, *Microsporum praecox*, *Trichosporon mucoides*, *Curvularia clavata*, *Epidermophyton floccosum*, *Phoma* sp., *Paecilomyces lilacinus*, *Hormographiella aspergillata*. Annual fees are charged to the participants.

The purpose of the scheme is to help laboratories to monitor their own performance in Medical Mycology and also to check their knowledge in the fields of emerging fungal pathogens. Until now, the participants have not been requested to send their own identifications. After one month, the correct identifications are automatically sent by post by the organizing laboratory together with a file giving the morphological and physiological characteristics of the species and possibly recent literature references.

Nicole Nolard and Danielle Swinne

Thoughts towards standardization of European Quality Control

The ECMM Mycology Newsletter has carried out an enquiry among its affiliated Societies in order to verify the application of External Quality Assessment Schemes (EQAS) in their countries. Questions have been asked to all the Societies' delegates about the type, frequency and extent of the EQAS, and about the registration of the reagents and their post-marketing evaluation

Analysis of the information collected (12 out of the 19 countries returned the enquiry form) showed that in Europe the situation of EQAS in Mycology is quite varied. In particular, it shows that an EQAS in Mycology does not exist in isolation, but only exists as an appendix of surveys on bacteriology and parasitology, as shown by the scanty, quite insignificant number of mycological samples per year. The frequency of individual surveys varies from 1 to 4 per year. There is no harmonization with other EQAS. The pre-marketing evaluation of the reagents depends mostly on internal controls made up by the companies. The quality of commercially available reagents on the market is checked only in those countries where, after the registration, it can be evaluated through an EQAS.

This situation highlights the pressing need to establish, at a European level, an EQAS organized by a group of expert mycologists, functioning as a committee, who should define the guidelines and support necessary for all countries to reach, through EQAS, harmonization, though respecting their own regulations.

This committee should prepare a unique schedule for sending results, giving directions about strains or other materials to be sent in all countries to the laboratories of different countries, and assuming responsibility for training courses.

In this way, after each EQAS mailing, a great number of comparable data will be available, not only on the performance of each laboratory but also on the reagents utilized. This may highlight their correct use for obtaining the best diagnostic efficacy. At each country level, an expert mycologist should be involved in the organization of the EQAS. Beside implementing the guidelines proposed by the ECMM committee, he/she should supervise statistical evaluation of the results, prepare the technical report (that will include comments on the results) and the make recommendations based on the data collected, and finally define the technical procedures needed to achieve standardization.

This approach provides a unique means to begin a systematic process of standardization that evaluates not only the operative procedures and diagnostic interpretation, but also the reagents and the instruments used in the daily routine. We will then obtain the concrete advantage of effective diagnosis at a minor cost.

Emanuela Soresini

Summary of replies to an inquiry form sent to ECMM Delegates

	Belgium	France	Germany	Hungary	Israel	Italy	Poland	Portugal	Russia	Spain	The Netherlands	United Kingdom
EQAS												
National	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes
Mandatory (M) / Facultative (F)	M*	M	M	F	–	–	–	F	F	F	F	F
Regional	No	No	No	No	No	Yes*	No	No	Yes	Yes**	No	No
Mandatory (M) / Facultative (F)	–	–	–	–	–	M*	–	–	F	F**	–	–
Type of control & frequency per year												
Identification (n. strains per each mailing)	once (1)	twice (1)	twice (1)	once (1)	–	once (1)	–	3 times (1)	◊	4 times (1)	twice (1)	3 times (4)
Serology	–	–	twice	once	–	–	–	–	◊	–	–	4 times
Susceptibility test	–	–	–	once	–	–	–	–	◊	–	–	–
Assay of antifungal drugs	–	–	–	–	–	–	–	–	◊	–	–	12 times
Dermatological methods	–	starting	–	–	–	–	–	–	◊	–	–	–
Reagents												
Registration mandatory	No	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No
requiring internal evaluation	–	Yes	–	Yes	–	–	Yes	Yes	Yes	Yes	–	–
external evaluation	–	Yes	–	–	–	–	Yes	–	Yes	–	–	–
Evaluation after marketing	No	No	No	No	No	No	No	Yes	Yes	No	No	No
internal	–	–	–	–	–	–	–	Yes	Yes	–	–	–
external	–	–	–	–	–	–	–	–	Yes	–	–	–

* A national facultative QC is organised in Belgium by the Institute of Tropical Medicine in Antwerp
* Lombardia, Piemonte, Toscana
** Catalonia (type and frequency not specified)
◊ Not specified

STATUTES
OF THE EUROPEAN CONFEDERATION OF MEDICAL MYCOLOGY
CONFEDERATION EUROPEENNE DE MYCOLOGIE MEDICALE
(ECMM / CEMM)

ARTICLE 1
Name of the Confederation
The Confederation shall be called the European Confederation of Medical Mycology (ECMM) or Confederation Européenne de Mycologie Médicale (CEMM), and is hereinafter referred to as 'The Confederation'.

ARTICLE 2
Location of Office
The official office of the Confederation shall be situated in France at the Institut Pasteur, 28 rue du Docteur Roux, 75015 Paris.

ARTICLE 3
Objects
The Confederation is established for the purpose of:
(a) Promoting the science and practice of all aspects of medical mycology throughout the European continent.
(b) Initiating, facilitating and coordinating research and other scientific activities on an international basis throughout Europe.
(c) Facilitating the discussion and dissemination of the results of international collaborative research.
(d) Promoting scientific meetings and training courses.
(e) Collaborating with other organizations which are established for similar objects.

ARTICLE 4
Membership of the Confederation
Membership of the Confederation shall be open to all suitable national societies and groups throughout the European continent which are established for similar objects to the Confederation.
Applications for membership of the Confederation must be approved by the Council. Societies and groups wishing to join the Confederation must submit a request in writing to the General Secretary of the Confederation.
At the discretion of the Council of the Confederation, national societies and groups not situated within the European continent may be admitted to membership of the Confederation.

ARTICLE 5
Administration
The Confederation shall be governed by an Executive Committee and a Council.
The Executive Committee shall consist of a Chairman, a General Secretary, a Treasurer and two other members representing the national societies that will act as hosts for the next two meetings of the Confederation.
The Chairman, General Secretary and Treasurer shall be elected for a term of three years and shall be eligible for a further term of three years. These Officers shall be elected from among the members of the Council of the Confederation. In the event of a vote being tied, the successful candidate shall be decided by drawing lots. These Officers, when elected, shall remain delegates, members of the Council, for at least three years.
The Executive Committee shall prepare the agenda for meetings of the Council of the Confederation and, between meetings, shall be empowered to act on behalf of the Confederation. It shall report any such actions to the next meeting of the Council.
The Council of the Confederation shall meet at least once each year, normally during the annual scientific meeting of the Confederation. The date of the meeting shall be announced at least two months before the meeting. With the exception of changes to the Statutes (see Article 9), all decisions of the Council shall be settled by a simple majority vote of those delegates present and voting. In the event of a vote being tied, the matter shall be decided by drawing lots.
Membership of the Council shall consist of one delegate representing each of the constituent national societies and groups. A delegate who cannot attend a meeting of the Council may appoint a substitute. It shall be for the constituent societies and groups to determine how their delegate should be chosen. A delegate, once chosen, shall remain a member of the Council for at least two years.

ARTICLE 6
Finance
The Confederation is an international non-profit making scientific association. Constituent national societies and groups shall pay an annual subscription depending on the number of their members, the amount being determined by the Council of the Confederation.
The Executive Committee of the Confederation shall be empowered to approach other organizations for financial support to further the objects of the Confederation.

ARTICLE 7
Scientific Meetings
A scientific meeting, relating to the objects of the Confederation, shall be arranged at least once each year by the Executive Committee. The meeting shall be held in a different European country each year, the host country being chosen by the Council from among written proposals submitted by constituent national societies or groups. Such proposals must be submitted to the General Secretary at least two calendar years before the year in which the meeting is to be held.
In years in which a Congress of the International Society for Human and Animal Mycology (ISHAM) is to be held in Europe, the Council of the Confederation shall be empowered, should it so decide, to cancel the annual meeting of the Confederation.

ARTICLE 8
Exchange of Information
It shall be the task of each constituent national society or group to distribute to its members relevant information received from the Executive Committee or Council of the Confederation.

ARTICLE 9
Change of Statutes
Alteration of the Statutes of the Confederation shall be made only at a meeting of the Council. Any such proposal must be submitted in writing to the General Secretary not less than three months before the meeting and shall be circulated with the notice of that meeting. For adoption a two thirds majority of those present and voting is required.

November 1993

Special report on...

by
Frank Odds

5th Conference on Candida and Candidiasis

The Fifth Conference on Candida and Candidiasis, organised by American Society for Microbiology, was held on March 1-4, 1999 in Charleston, South Carolina

with nine Charleston snapshots

The numbers tell the story. The fifth ASM Conference on *Candida* and Candidiasis, with more than 330 participants, was the best attended ever. In the course of four full days, the attendees heard 52 oral presentations and saw 160 posters. The scale of the meeting reflects the still unchallenged position of *Candida* species as the most frequent and most cosmopolitan of all fungal pathogens. The depth and sophistication of the research presented indicate the enormous scientific excitement that *Candida* still inspires. Contributors from European countries accounted for 29% of the lectures, 29% of the posters and 27% of the audience.

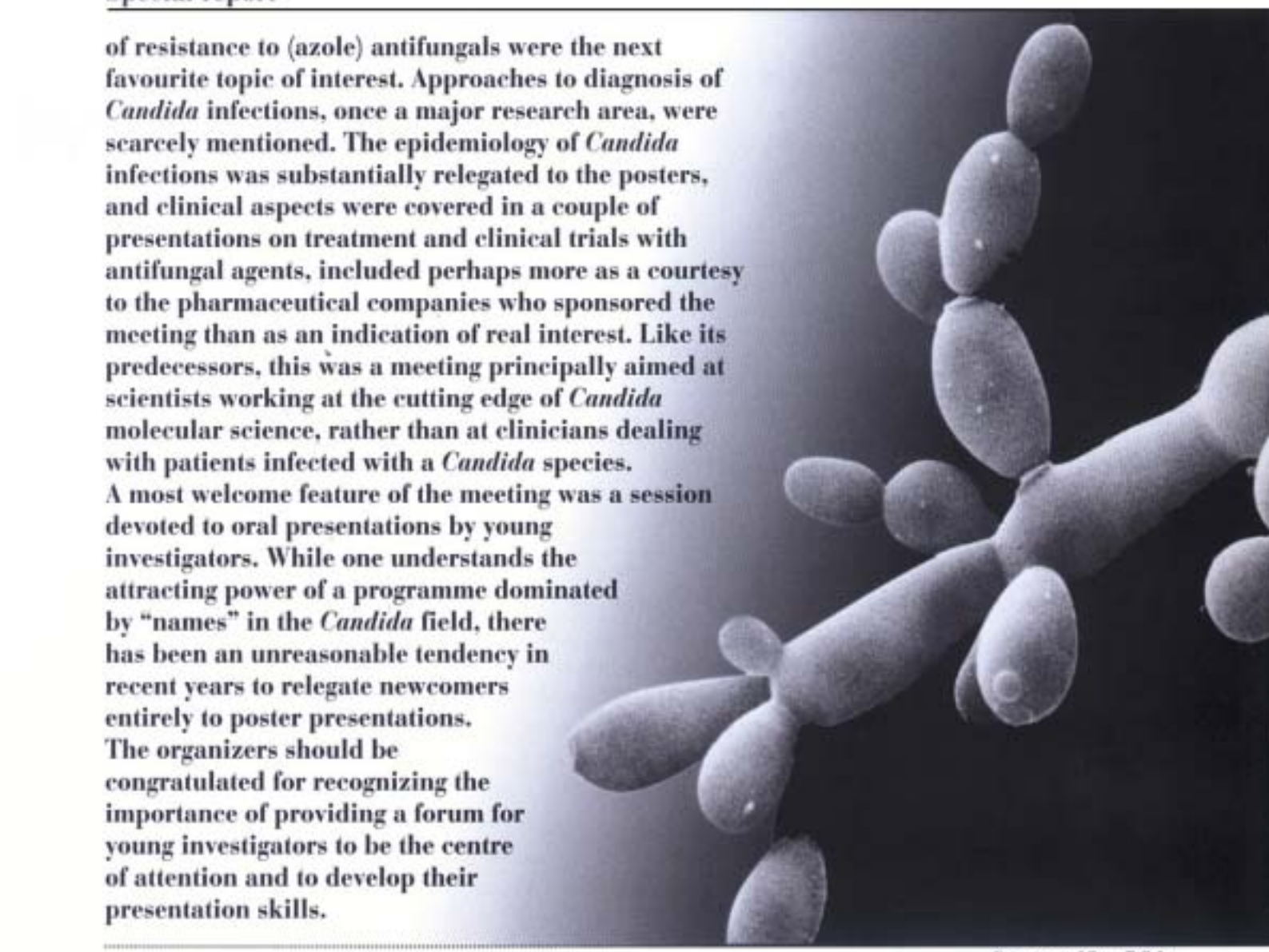
The venue for this year's meeting was Charleston, South Carolina. This is a city that has survived earthquakes and hurricanes to preserve a unique state of old-world charm in a country almost obsessively devoted to replacement of the past with things brash and new. No steel-and-concrete architecture dominate the Charleston skyline. The pace of life is gentle, calm, polite and orderly. Reviews, overviews and news of all things candidal were presented in the venerable Hibernian Hall under the watchful gaze of portraits of those who lived and died in Charleston long before anybody ever heard of genomics, transmembrane domains or virulence factors. With its many excellent restaurants and a closing barbecue with bluegrass hoe-down, Charleston provided a warm social atmosphere for its mycological visitors.

As in most scientific fields, certain themes tend to predominate in a conference devoted to a single microbial pathogen. The major emphasis this year was unquestionably the effects of engineered gene disruptions on virulence, adhesion and morphogenesis in *Candida albicans*. Molecular mechanisms

of resistance to (azole) antifungals were the next favourite topic of interest. Approaches to diagnosis of *Candida* infections, once a major research area, were scarcely mentioned. The epidemiology of *Candida* infections was substantially relegated to the posters, and clinical aspects were covered in a couple of presentations on treatment and clinical trials with antifungal agents, included perhaps more as a courtesy to the pharmaceutical companies who sponsored the meeting than as an indication of real interest. Like its predecessors, this was a meeting principally aimed at scientists working at the cutting edge of *Candida* molecular science, rather than at clinicians dealing with patients infected with a *Candida* species.

A most welcome feature of the meeting was a session devoted to oral presentations by young investigators. While one understands the attracting power of a programme dominated by "names" in the *Candida* field, there has been an unreasonable tendency in recent years to relegate newcomers entirely to poster presentations.

The organizers should be congratulated for recognizing the importance of providing a forum for young investigators to be the centre of attention and to develop their presentation skills.



By courtesy of Garry T. Cole

Genomics of *Candida albicans*

Sequencing of the whole *C. albicans* genome is proceeding apace. The public *Candida* genome project, thanks mainly to the efforts of Stewart Scherer (Stanford) and Pete Magee (University of Minnesota), is on target to provide full (10x) coverage of the DNA base sequence of all eight *C. albicans* chromosomes by the end of the year 2000. The extent to which commercial sequencing efforts have covered the genome is unknown. Several pharmaceutical companies have bought into the Incyte Pathoseq project, and Incyte claim to have 5901 contiguous *C. albicans* sequences in their database. Of course, contigs alone do not indicate the success of a sequencing project. The 59 contigs claimed by the Scherer/Magee project include one that represents the entire DNA sequence of the smallest *C. albicans* chromosome (number 7): to claim just eight contigs, each representing a single entire chromosome, would be the ultimate goal!

From both genomics studies and from speakers who are studying mechanisms of *C. albicans* gene regulation, we now know that the fungus indulges readily in chromosome reassortments and rearrangements, even to the extent of apparently being able to delete or multiply individual chromosomes as a means of up- and down-regulating pathways. Mid-repeat sequences result from uneven chromatid exchange, and can differ in length by up to 50 kb. This phenomenon provides the basis of strain typing by DNA fingerprinting in *Candida* species.

Morphogenesis in *Candida albicans*

The change of *C. albicans* morphology from yeasts to hyphae involves an increase at least a two-fold in expression for more than 1400 genes including 40 genes whose expression increases more than five-fold, according to Mark Egerton, whose colleagues at Incyte have used DNA expression matrices to study the phenomenon. Regulation of the yeast-to-hypha transition must involve at least three different gene pathways, with others possibly still to be recognized, if one puts together the results presented in several talks and posters. For those of us who spent a large part of the 1970's and early 1980's carefully defining and quantifying *C. albicans* cell morphologies and the conditions that lead to their formation, it is perhaps disappointing to find that almost everybody now studying morphogenesis at the molecular level seems to assume both that hypha formation is an essential pathogenic event and that colonies with hairy fringes on plates incubated at 25 °C are adequate proof of hypha formation. Indeed, some presenters did acknowledge that gene knockouts that affected colony fringe development on and in agar did not always lead to morphological differences in cells grown in serum and other fluid media at 37 °C.

Pathogenicity determinants of *Candida albicans*

Genes that code for putative virulence in *C. albicans* have become almost too numerous to count. Among many others, knockouts of genes including *MNT1* (codes for mannosyl transferase), *HWP1* (hyphal wall protein), *PLB1* (phospholipase B), *HK1* (histidine kinase), *PMT1* and *PMT6* (putative protein-mannosyl transferases), *RBF1* (transcription factor), *CAP1* and *CAP2* (regulate production of drug efflux pumps), *HOG1* (involved in morphological responses to osmotic stress) and *CLA4* (regulates continuous polarized growth) result in strains that show lower lethality for mice than their parent strains when injected intravenously. These examples come entirely from the oral presentations; others were presented in posters. If all these and the many previously published genes that diminish mouse lethality in *C. albicans* are regarded as a whole, one possible conclusion is that many or most disturbances of normal gene function in the fungus tend to produce a generally, rather than a

Keep it in the family!

Dr. Peter Staib

Considering the small size and recent origins of the specialist medical mycology field, it is perhaps remarkable how often sons have followed fathers into fungal disease research. The earliest example, in Russia, was that of P.N. Kashkin, whose son also became a medical mycologist: both worked in the *Candida* field. Similarly, R. Negroni, the well-known mycologist from Argentina, is the son of P. Negroni, who contributed substantially to basic research into paracoccidioidomycosis. In Denmark, J. Stenderup has followed his father, A. Stenderup, into research and diagnostic mycology.

Astonishingly, in Charleston, three new sons of famous mycological fathers attended. Peter Staib, from Germany, is the son of Friedrich Staib, who was the first to demonstrate extracellular proteolytic activity in *C. albicans*. Kenneth Nickerson's father, Walter J. Nickerson, pioneered biochemical research into *C. albicans* dimorphism in the 1950's and 1960's. Finally, Scott Kobayashi, from the U.S.A., is the son of George S. Kobayashi, whose research into histoplasmosis and *Candida* infections is internationally acclaimed.

Does anyone have a daughter who might be interested in following father or mother into the world of fungal diseases? We seem to need some gender balance here!

specifically, disadvantaged cell phenotype, which fails to survive the initial phagocytic clearance onslaught that follows intravenous injection in mice.

More refined approaches to determining virulence roles was exemplified by the lecture from Bernhard Hube (Hamburg), who gave an update on one of the earliest studied among *C. albicans* virulence factors: secretion of proteolytic enzymes. Ten different secreted aspartyl proteinases are encoded by the genes *SAP1* to *SAP10* in *C. albicans*. They are differentially expressed under different environmental conditions *in vitro*, and differential expression has now been shown *ex vivo* in a model of reconstructed human epithelium, and *in vivo* in a rat model of vaginal *Candida* infection, a mouse model of intraperitoneal infection, and even in saliva samples from patients with and without oral *Candida* infections. There is evidence suggesting that expression of some *SAPs* may be altered to compensate for deletion of one or more of the others, although only *SAP4-SAP6* are consistently expressed in combination.

Lois Hoyer (University of Illinois) has extended her research on the ALS gene family in *C. albicans*. This is a group of genes coding for surface proteins that contribute to the adhesion of the fungus to epithelial surfaces. Dr. Hoyer's imaginative use of cartoons of human figures, with the colours of hair and clothing indicating similarities and sizes of gene sequences, was a particularly painless way of conveying complex information in a listener-friendly manner. Another novel finding concerning the adhesion of *C. albicans* to surfaces came from Paula Sundstrom (Ohio State University), who has found that a surface protein in the fungus, encoded by the gene *HWP1*, serves as a substrate for epithelial transglutaminase enzymes, that can covalently cross-link the fungal protein to epithelial proteins. Dr. Sundstrom has not been able to detect any transglutaminase activity produced by *C. albicans* itself. This observation contrasts curiously with that of Rafael Sentandreu (University of València), who devoted a portion of his presentation to his characterization of *C. albicans* transglutaminase activity.

In a meeting that was overwhelmingly dominated by research on fungal gene function and regulation, the relevance of the host as a primary factor influencing the status of *C. albicans* as commensal or pathogen was not overlooked. Several speakers reminded their audience of the complexity and significance of leukocytes and their cytokine products in determining whether or not *C. albicans* is able to colonize and invade a mammalian host.

What did others think?

To provide readers with opinions other than those expressed in the full review above, we contacted 14 European attendees at Charleston to learn their reactions to the *Candida* meeting. The people we asked represented veteran *Candida* specialists as well as postgrads and postdocs new to the field. We also tried to get representatives from a good selection of the European countries represented at the Charleston. Our warmest thanks for their help go to the following: Dr. Angel Dominguez, Salamanca, Spain; Dr. Françoise Dromer, Paris, France; Ms. Samantha Donnelly, Dublin, Ireland; Dr. Jose F. Garcia-Bustos, Madrid, Spain; Mr. Mo Kamran, London, UK; Dr. Hans Kapteyn, Amsterdam, The Netherlands; Dr. Bart-Jan Kullberg, Nijmegen, The Netherlands; Dr. Marc Logghe, Gent, Belgium; Dr. Michel Monod, Lausanne, Switzerland; Dr. Justin M. O'Sullivan, Canterbury, UK; Dr. Daniel Poulain, Lille, France; Professor Tom Rogers, London, UK; Dr. Peter Staib, Wurzburg, Germany; Dr. Derek Sullivan, Dublin, Ireland and Ms. Lynn Thomson, Aberdeen, UK.

Mechanisms of *Candida* drug resistance

Clinical resistance of *Candida* species to antifungal agents, particularly fluconazole, has clearly become a therapeutic problem. More than one speaker commented on a rising prevalence of fluconazole resistant *Candida* isolates, though this statistic has to be seen against a background of generally falling prevalence of *Candida* bloodstream isolations, particularly among neutropenic patients where antifungal prophylaxis is often used. The quality of laboratory susceptibility testing of *Candida* species against azole antifungal agents has become as good as that for antibacterial agents, according to John Rex (Houston, Texas). Combination of pharmacokinetic parameters for an agent with *in vitro* susceptibility data may improve the clinical predictive value of such tests.

The discovery of multi-drug resistance pumps located in fungal cell membranes has generated considerable research activity. The families of "ATP-binding" and "major facilitator" pumps are growing rapidly (at least 7 of the former and 3 of the latter have

been studied and more are being discovered) and their regulation by gene expression is being characterized. It remains a mystery as to exactly why the membranes of living cells are blessed with enzymes that specifically remove an exogenous molecule such as fluconazole, which is surely far too recent on the evolutionary scale to have played any part in their appearance. However, one intriguing possibility was raised by Rajendra Prašad (New Delhi), who linked the pumps with the enzymic translocation activities ("flippase", "floppase" and "scramblase") that maintain the asymmetry of distribution of different phospholipids between the outer and inner plasma membrane monolayers.

Other topics presented

These "nutshell" summaries of much of the research presented in Charleston fail to do justice to the scope and extent of the full programme. Grouping disparate pieces of research under broad headings inevitably omits occasional highly individual contributions. For example, Jack Sobel reminded us that vulvovaginal *Candida* infections afflict women just as regularly as they ever did. He stressed the needs for a rapid and specific diagnostic test and for a fungicidal agent active against all the pathogenic *Candida* species. Karl Miletti showed that *C. albicans* possesses ribozymes with the potential to be useful antifungal targets. Mick Tuite described his research on the structure of the tRNA that causes *C. albicans* to misread the codon CUG as serine instead of leucine. Jack Edwards gave a splendid historical overview of the work of the US Mycoses Study Group in organizing clinical trials of antifungal agents.

Lies, damned lies, and statistics

Our group of contactees was too small to permit any statistical analysis of their comments, except to conclude that there was 100% agreement that the Charleston meeting was generally a success and much enjoyed by everyone ($P<0.000001$). Nobody showed a negative reaction of a type that suggested they felt had wasted their time or their money by attending. When we asked which presentations they had particularly enjoyed, each of our 14 interviewees usually tended to mention the subject areas in which they already had the greatest interest. Attempts to stratify the group by relative length of experience in *Candida* research failed to reveal any significant differences in attitude. (A few individuals were surprised at the venerability of their *Candida* experience when we asked them how long they had worked in the field. They had not realized how fast the years had passed, obviously because they found that little yeast so much fun!)

Discovering new blood

The one thing most often mentioned as a positive feature of the Charleston conference was the session presented by young scientists. Five of our interviewees (young and old) described this session very favourably and it is clearly something to be repeated. For those of you who may have wondered why you often seem to see the same old people presenting the same old stuff at every mycology meeting, the answer is that meeting organizers fear nobody will turn up unless the programme is dominated by speakers with established reputations to draw the crowds. While there may be a grain of truth in this notion, Charleston clearly proved that a mixture of seasoned (does that sometimes mean "peppery") speakers and a forum for new faces tends to make everyone feel happy.

That mixture used to be the norm up to about 15 years ago. Perhaps we should be glad to return to it. After all, many of our interviewees did mention at least one invited speaker they felt gave a weak presentation; so inviting the heavy brigade is not a sure-fire guarantee of success!

Putting faces to names

Four of our panel specifically commented on the pleasure of being able to meet people in the field in person and informally. The present author feels that has always been the major attraction at a meeting, and that aspect of conferences is possibly the one that everybody appreciates most. But don't let anybody tell you things could be done just as well by putting everybody together in a room with food and drink and leaving them to it. Those lectures and posters are the true catalysts for the conversations that happen in the social periods: learning what people are doing (then saying what you think or know about it) is the way we all get new ideas and new insights.

What *wasn't* covered in Charleston

None of our panel of 14 candidologists complained there was not enough molecular biology on the menu at Charleston. Indeed, one specifically mentioned he would have been happy with less molecular biology to accommodate more of other topics. It was areas such as epidemiology (two mentions), pathophysiology and diagnosis of candidal disease that some attendees would have preferred to see more in evidence. Jose Garcia-Bustos and Angel Dominguez, relative newcomers with fewer than five years of *Candida*-wrangling behind them, both pointed out that there was a noticeable degree of overlap and redundancy between speakers for some of the topics. Maybe more attention could be paid at the next Candida Conference to reducing the overlap and thus finding time to broaden the scope. Derek Sullivan commented that a topic like epidemiology is a reminder to us all just why we get interested in the molecular biology of our favourite yeast-beast in the first place!

Comments and conclusions

Not everything presented at the Charleston meeting was good, but the good science greatly exceeded the weak. There were far too many posters on display to be absorbed in detail (166 of them with just 270 minutes formally assigned to view them), but too many is a healthier sign than too few. The present fashion for blunderbuss gene-hunting in *Candida* science is likely to transform gently into a more refined examination of those genes and regulation pathways that can be most directly and emphatically associated with disease states in humans. Interactions of genetically modified strains with host leukocytes secreting specific cytokines/interleukins will inevitably become an approach to novel research in the not-too-distant future. There are clear signs that different laboratories are now cloning the same genes and giving them different names (indeed, not all labs yet use the same numbering system for *C. albicans* chromosomes!). But all this only reflects an underlying enthusiasm that, as Tom Walsh (NCI) pointed out in his closing remarks, seems to have attracted an impressively large number of young investigators into the field. Long may this trend continue!

Cost considerations

Attending a meeting like the one in Charleston is not a cheap proposition. High cost was a factor that caused several attendees to comment. Bart-Jan Kullberg pointed out that a "spoke" city like Charleston costs more to reach from abroad than one of the "hubs" that is directly connected by flights to European capitals.

Marc Logghe commented on the high price of the Conference hotel. That is sometimes a very frustrating matter. Meeting organizers nowadays usually have to reserve a minimum block of rooms to support their booking of a particular site. The financial consequences of not filling those rooms then makes the organizers less enthusiastic in their advertising to mention the fact that there may be much cheaper accommodation just a short walk away from the chosen hotel.

Nobody really complained of poor value for money in Charleston. Indeed, all our interviewees seemed to like the city a lot (hard to imagine any other reaction: it was charming!). However, Françoise Dromer would like to have received a notepad and pen in the registration materials, and Tom Rogers suggested having a working breakfast included in the registration fee, to bring people together earlier. That notion may be less popular with Mo Kamran, who felt that a 9 a.m. start would be more welcome than the 8 a.m. kick-off in Charleston, to allow for a little more physiological adjustment after a busy social programme the night before.

In their own words

«As a postgraduate student I find that sometimes the amount of information in my own area of interest can be overwhelming, never mind topics outside my area. The meeting provided a lot of information in a condensed form that was easy to absorb. I felt that most of the speakers were excellent and easy to understand.» (Samantha Donnelly, postgraduate student)

«It was very interesting to have information on what's going on in a field where I knew nothing without having to get a headache by reading the corresponding papers.» (Françoise Dromer, physician and senior scientist)

«Having a conference specifically related to *Candida* and candidosis is an excellent idea since it provides a somewhat unique opportunity to meet and socialise with others from the field.» (Mo Kamran, postgraduate student)

«It was a great meeting; *Candida* research is progressing very fast, and was covered generally well.» (Hans Kapteyn, postdoctoral researcher)

«The cheese and wine poster sessions are excellent... this way to convert dull poster sessions into a fruitful scientific market place should be an example for other meetings.» (Bart-Jan Kullberg, Associate Professor of Medicine)

«Everything is nice, big and beautiful but one is definitely more polite, let's say "civilized", in traffic compared to Belgium.» (Marc Logghe, research scientist, on his first impressions of the USA)

«These meetings are unique in giving a snapshot of research directions at a given time and are completely different each three years.» (Daniel Poulain, research team director)

«Maybe have a similar meeting on *Aspergillus* some time?» (Professor Tom Rogers, infectious diseases specialist)

«I got lots of good ideas and also could help others. A very important experience for a young scientist like me; I really learned much.» (Peter Staib, research scientist)

Perhaps the most succinct summing-up

«I really enjoyed the meeting and found it an excellent way to keep abreast with the latest developments in the *Candida* field.» (Lynn Thomson, postgraduate student)

4th International Conference on Cryptococcus and Cryptococcosis

A well recognized scientific appointment which every three years reviews the state af art and presents the newest research data of this important area of medical mycology.
The 4th edition, organized by R.J. Hay, A. Hamilton, K. Haynes, and K.J. Kwon Chung, will be held September 12-16, 1999, in London, at The Royal Society.

Session I:
Molecular biology and biochemistry I
Lectures by B.L. Wickes, J. Heitman, Y.C. Chang, J.A. Alspaugh, J.R. Perfect

Session II:
Cryptococcosis: clinical perspectives
Lectures by R.A. Seaton, W.G. Powderly, T.C. Sorrell, P.G. Pappas

Session III:
Immune responses in cryptococcosis
Lectures by S.M. Levitz, L.A. Pirofski, A. Vecchiarelli, K. Kawakami, T.R. Kozel, M.D. Scharff, C.H. Mody

Session IV:
Pathogenesis and host responses
Lectures by G.B. Huffnagle, D.L. Goldman, M.F. Lipscomb, J.W. Murphy, M. Feldmesser

Session V:
Drugs and therapy
Lectures by S.L. Kelly, R.A. Larsen, K. Bartizal, S. Kohno, J.R. Graybill, J.E. Bennett

Session VI:
Epidemiology / Ecology / Evolution
Lectures by F. Dromer, K.J. Kwon-Chung, E. Castaneda, T. Boekhout, M. Lazera

Session VII:
Molecular biology and biochemistry II
Lectures by S.C. Chen, E.S. Jacobson, K.J. Kwon-Chung

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Trends in Invasive Fungal Infections 5

The 5th Trends in Invasive Fungal Infections, organized by J. Bille, D. Denning and B. de Pauw, will be held from 14 to 16 October 1999, in Malta.
The primary objective is to offer an educational forum for experienced clinicians from various disciplines and microbiologists who have to manage patients with fungal infections. The programme will comprise Keynote speakers, oral sessions, case presentations, poster sessions and the popular "Meet the Expert Luncheons".

Session 1:
Nosocomial Fungal Infections
Lectures by R. Wenzel, H. Richet, M.D. Richardson, A. Barnes, F. Menichetti

Session 2:
Approaches to special patient groups
Lectures by R.J. Hay, N. Singh, J. Gavaldà, H. Guiot, T. Abrahamsen

Session 3:
Antifungal resistance
Lectures by D. Sanglard, J. Bille, J.L. Rodriguez

Session 4:
Recent advances in diagnosis of fungal infections
Lectures by J. Meis, J. Oestmann, H. Hebart

Session 5:
Treatment
Lectures by G. Maschmeyer, B.J. Kullberg, G. Just-Nubling

Session 6:
New Drugs
Lectures by P. Magee, J. Edwards, B. Dupont, D. Denning

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European culture collections for pathogenic fungi

Scientific journals recommend or even require that strains referenced in papers submitted for publication are deposited in a public culture collection so that they can be made available to the scientific community for further controls or studies. Culture collections require that each deposited strain is supplied with information on its origin and methods of collection and isolation. Such collections are numerous and distributed worldwide (approximately 500 are registered at the World Data Center for Microorganisms of Riken, Japan).

Protection of an invention implying a microorganisme requires its deposit in a culture collection with the status of IDA (International Depositary Authority) according to the Budapest Treaty. This status has been recognized to 31 collections in the world among which 6 microbial collections in Europe accept filamentous fungi and yeasts implicated in human pathology. These are listed below, with an indication of the services provided.

For details refer to the paper by F. Symoens and N. Nolard, "Biodiversité des microorganismes: aspects legaux et rôle des collections", J Mycol Méd 1999, 9:49-51.

European microbial culture collections with IDA status for filamentous fungi and yeasts implicated in human pathology

Pays	*Addresses*	*Internet/E-mail addresses*	*Other services*
Belgium	**IHEM** Collection IHEM (BCCM/IHEM) Institut de Santé Publique Louis Pasteur 14, rue Juliette Wytsman B-1050 Bruxelles, Belgium	http://www.belspo.be/bccm E-mail: ihem@iph.fgov.be	Supplying of strains, identification, preservation, deposit of strains protected by a patent, deposit for preservation, training courses
Czech Republic	**CCM** Czech Collection of Microorganisms Masaryk University ul Tvrdého ç. 14 602 00 Brno, Czech Republic	E-mail: ccm@sci.muni.cz	Supplying of strains, identification, preservation, deposit of strains protected by a patent, deposit for preservation, training courses
France	**CNCM** Collection Nationale de Cultures de Microorganismes Institut Pasteur 25, rue du Dr. Roux F-75724 Paris, France		Deposit of strains protected by a patent
Germany	**DSMZ** Deutsche Sammlung von Mikrorganismen und Zelkulturen GmbH Mascheroder Weg 2b D-38124 Braunschweig, Germany	http://www.gbf.de/dsmz/dsmzhome.html E-mail: dsmz@gbf-braunschweig.de	Supplying of strains, identification, preservation, deposit of strains protected by a patent, deposit for preservation
The Netherlands	**CBS** Centraalbureau voor Schimmelcultures Oosterstraat 1 PO Box 273 3740 AG Baarn, The Netherlands	http://www.cbs.knaw.nl E-mail: info@cbs.knaw.nl	Supplying of strains, identification, preservation, deposit of strains protected by a patent, deposit for preservation, training courses
United Kingdom	**IMI** International Mycological Institute Genetic Resources Collection Bakeham Lane Egham, Surrey, TW20 9TY, United Kingdom	http://www.cabi.org.uk E-mail: d.smith@cabi.org	Supplying of strains, identification, preservation, deposit of strains protected by a patent, deposit for preservation, training courses