# BSMM News

Summer 2002

## President's Column

It is an honour for me to be elected to serve as President of the BSMM. Our Society is a small one, but its members play an important role in sustaining expertise in the field of medical mycology. Like many specialities in the medical world that depend heavily on laboratory support, medical mycology often seems to be short-changed when it comes to attracting investment and personnel. Graduates in biological subjects are seldom attracted these days to careers in routine diagnostic laboratories, and most medical graduates have lost interest in laboratory work altogether.

The activities of the BSMM have extended, over the years, far beyond the original mandate to organize regular meetings. The enormous numbers of people who seek places on its biannual Leeds course in diagnostic medical mycology are a reflection not just of the quality of the course, but of the need for mycology training that is felt throughout the hospital system. The efforts of the outgoing Executive Committee have produced the new scheme for a Diploma in Medical Mycology. The new Committee will continue to support this initiative. It is politically and administratively complex, but we hope it will lead to a higher profile for individuals who *do* seek a career in the field.

At the initiative of David Denning, we are putting together a set of guidelines on standards of care for patients with fungal diseases. This will be circulated to a group of medical learned societies for comment, and a final version will be published in a medical journal. I regard interesting and attracting the medical community to our activities by any and all means as one of the most important objectives for the BSMM.

We are in the process of expanding the scope and functionality of the BSMM website. If you feel you want to visit the site on a regular basis we will have succeeded in our objective of making it important to you. Our Secretary, Ruth Ashbee, is aiming to make our already excellent Newsletter an even livelier publication. To this end she is being ably helped by Caroline Moore and Richard Barton. We hope to make you look forward eagerly to each edition of the Newsletter: your own contributions to it will help greatly towards its success.

At next year's meeting in Manchester, we shall be welcoming members of the British Mycological Society to join us. It is curious that the fungal kingdom is big enough to sustain specialists in human diseases, plant diseases, food and drink production and cryptobotany (mushrooms and toadstools!), all of whom seem to be happy enclosed in their own separate compartment. Molecular biology has made a nonsense of those who say they don't need to be aware of the work of other groups, and our Manchester meeting is a first step in bringing together basic scientists in the mycological world with those of us who are most interested in fungi that cause human disease. We hope for a record attendance next year.

The Executive Committee has undergone a major turnover this year. We have a new Secretary, Ruth Ashbee, and three new elected members: Ken Haynes, Richard Hobson and Caroline Moore. Please join me in welcoming all these individuals. We are all keen to work hard and enthusiastically in the interests of your Society. We hope you will share our enthusiasm and give the BSMM your full support.

Frank Odds

# Members Update

Several new members have joined the Society and we look forward to seeing them at future meetings:
Dr Caroline Barelle, Dr Gwyneth Bertram, Mr Paul Dennison, Dr Huw Hughes, Miss Susan Macaskill, Miss Abigail Mavor, Miss Susan Nicholls, Mr Andrew Phillips, Dr Mark Ramsdale, Miss Claire Russell, Miss Serena Selvaggini and Dr Melissa Straffon,all from Aberdeen; Dr Annette Cashmore, Mr Marcus Marvin and Mr Robert Mason from Leicester; Dr Achyut Guleri from Glasgow; Miss Claire Price from Cardiff; and Mrs Deborah Whitehead from Leeds.
We regret to announce the death of Prof Ann Wakefield. See opposite for an obituary.

# 2003 Annual Scientific Meeting in Manchester

Mark your diaries now!

We are delighted to announce that, for the first time, our annual scientific meeting will be held jointly with the British Mycological Society, providing an exciting platform for the exchange of ideas across the full spectrum of mycology. It will be held in Manchester from Saturday 1st to Monday 3rd March 2003. Manchester, Britain's second city and home to the forthcoming Commonwealth Games, sits in a centralised spot easily accessible by air, rail or road. The local organising committee, comprising members from both societies and headed by David Denning, promise a stimulating assembly of world-renowned speakers.
All scientific sessions will take place in the prestigious neo-gothic Whitworth Hall at the very heart of The University of Manchester. The extended programme includes four symposia, with preliminary topics of (i) A debate on the roles of classical and molecular taxonomy, (ii) Antifungal agents: resistance and its implications, (iii) The impact of fungal genomics and post genomics, and (iv) Molecular biology in the clinic and the field. In addition, the meeting will provide a relaxed forum for oral and poster presentations, ideal for our newer members.
Furthermore an exciting array of social activities is planned, ensuring plenty of time to discuss those new collaborations. A welcome reception will be held on Saturday evening at The Manchester Museum. Enjoy cocktails in the fossil gallery, which houses over a quarter of a million specimens; illustrating the story of life on earth, it's origin and evolution into the variety of life on the planet today.
On Sunday evening we hope to hold our annual dinner at one of Britain's newest and most exciting venues – the dramatic Imperial War Museum North – on the banks of the Manchester Ship Canal. The museum tells the story of people – old and young – and about how their lives are shaped by war. Enjoy your meal amidst such iconic objects as a Russian T34 tank, a harrier jump jet, a Trabant estate car and the artillery piece that fired the first British shell of World War I.
For those football supporters amongst you, no visit to Manchester would be complete without seeing the Reds in action! We hope to obtain a few tickets for Manchester United v Leeds United on Saturday afternoon.
Registration details and the final programme will be included in our next newsletter. Register early – Manchester is mad for it!!

# The *Aspergillus fumigatus* genome sequencing project

In the week that the statistics (see below) were released for the whole genome shotgun phase of this project, it is an opportune moment to reflect on the sequencing of the *Aspergillus fumigatus* genome. It all seems a long way from our initial meeting just over four years ago when David Denning brought together Bart Barrell from the Sanger Institute, Philippe Glaser from the Insitut Pasteur, Celia Caulcott from the Wellcome Trust, Steve Oliver, then at UMIST, and myself. It might have taken awhile for the full impetus of the project to get going, but it looks like we will be able to deliver a fully annotated and complete genome sequence from a filamentous fungus within the next 18 months.
At the time of the first meeting (1998) whole genome shotgun sequencing was in its infancy and had been applied only to bacterial genomes. A clone-by-clone-based approach was adopted and bacterial artificial chromosome libraries constructed at the Sanger Institute and in Paris. The idea initially was to generate a physical map and to sequence a one megabase (Mb) region around the *niaD* locus. This genetic locus maps to a gene-rich region of chromosome VIII of *A. nidulans* and it was hoped that some idea of the level of conservation between the two genomes might be gleaned from this pilot project. This project funded by the Wellcome Trust and carried out at the Wellcome Trust Sanger Institute will be completed this year. Many of the loci from the appropriate region of the *A. nidulans* genetic map lie in this sequenced region, but as might be expected, the order has not always been conserved.
In the meantime, David Denning put together an international consortium to sequence the rest of the genome. The final team consists of the following centres: The Wellcome Trust Sanger Institute (UK) headed by Neil Hall with David Harris in charge of sequencing and funding from the Wellcome Trust; The Institute for Genomic Research (TIGR)(USA) headed by William Nierman (sequencing team leader Tamara Feldblyum; funding from the National Institute of Allergy and Infectious Diseases) and a Spanish consortium headed by Miguel Sánchez-Pérez from Salamanca University (other centres include Complutense University (Javier Arroyo) and the Centro de Investigaciones Biológicas (Miguel Peñalva); funding from Fondo de Investigaciones Sanitarias). A steering committee was set up to

co-ordinate this international project and as well as involving the heads of the project at each sequencing centre included *Aspergillus* biologists to act as advisors: Jean-Paul Latgé (Insitut Pasteur, France), Geoff Turner (University of Sheffield, UK) and Joan Bennett (Tulane University, USA).

In 2000, Celera published the whole genome shotgun (WGS) sequence of *Drosophila melanogaster* and the processing power at TIGR and the Sanger Institute had increased sufficiently for this approach to be adopted for *A. fumigatus*. The WGS phase was started in April 2001 and completed in June 2002. Just over 500,000 reads (~ 10 x genome coverage) have been generated which have been assembled into 971 contigs. One hundred and forty one contigs are > 10 kb with the largest at 1,796,676 bp; these >10 kb contigs contain 97 % of the sequence. The total assembly length is approximately 29 Mb which fits nicely with our previous estimates (28 to 30 Mb). *Aspergillus fumigatus* contains the standard telomeric repeat (TTAGGG), which has already been found in *A. nidulans*. It might however be harder to define the centromeres, as there is no genetic map to help us locate them. On the basis of what has been found in *A. nidulans* and *Neurospora crassa*, we will have to look for a highly repetitive A+T-rich region. One of the major hurdles in defining the centromeres might be that they have not been cloned in the first place in any of the constructed libraries. In addition, even if they have been sequenced, they have probably not been assembled correctly because of all the repetitive sequence. As we enter the finishing stage of the project which involves closing sequencing and physical gaps, checking the compiled sequence and sorting out repetitive sequences, problematic regions, like the centromeres, telomeres (not all of them have been identified) and ribosomal DNA repeat, will have to be dealt with. This job is going to be undertaken by the two main sequencing centres (the Sanger and TIGR), though I will be involved in sizing the ribosomal DNA repeat using pulsed-field gel electrophoresis.

In October 2001, a Wellcome Trust-funded project was initiated to set up a database for *Aspergillus* genomic data. We are currently building this database (Central *Aspergillus* Data REpository (C*A*DRE)) and our plan is to be ready to host the pilot project sequence by the end of this year. We will then host and curate the complete annotated sequence as provided by the Sanger Institute and TIGR when they deliver it to us next year. An exciting aspect of the curatorship of the sequence will be the involvement of experts from the research community, whom we hope to recruit and who will add their comments about the function of various protein families. In the future, it is our intention that we will host other *Aspergillus* genomes and other types of genomic data, such as that from micro-arrays.

Finally I wish to end on a personal note that it has been a privilege to be involved in this project, which I believe, will play a major role in the years to come in stimulating basic and applied *Aspergillus* re search. I get the impression that even the 6 x WGS assembly that was released by TIGR in November last year has been immensely useful (it certainly has for our research here in Manchester). Who knows what insights will arise from whole genome analyses, combined with comparisons with other genomes and other datasets? I am certainly looking forward to finding out.

For further details about the *Aspergillus fumigatus* genome sequencing project, visit The *Aspergillus* Website (www.aspergillus.man.ac.uk). For a personal view about the biological and medical benefits that will come out of this sequence, see Denning *et al.*, Lancet Infect Dis 2002; 2:251-253.

Michael J Anderson

## Obituary: Prof Ann Wakefield

Professor Ann Wakefield died at home in Charlbury Oxfordshire on 1st May 2002, of recurrent pulmonary metastases from an osteosarcoma. Over the last 4 years, despite chemotherapy and several operations, she continued to write grants, supervise students, give lectures, carry out bench work and publish papers.

For 16 years Ann's research focussed on *Pneumocystis carinii* infection and was based in the Department of Paediatrics in the Weatherall Institute of Molecular Medicine in Oxford. Her interest in the organism began at a time when it was still considered to be a protozoan. An early break through came with the design of the primers pAZ102-H and pAZ102-E, by which DNA from *Pneumocystis carinii* could reliably be amplified. These primers are known eponymously as "Wakefield primers" (and were named after her father Albert Zaudy).

Ann's own research group alone, or in collaboration with other groups in N and S America and Europe were able to refute many conventionally held views about *Pneumocystis carinii* infection. Her research showed *Pneumocystis* is a fungus, infection is host species –specific and that infection in man is not always clonal. She was also able to show that *Pneumocystis carinii* pneumonia in man arises by exogenous reinfection, rather than by reactivation of latent infection. Recently her group reported the first convincing evidence of human person-to-person transmission of pneumocystis.

Meeting Ann for the first time was always an experience. Her intellectual ability to reduce a scientific question down to its basics was combined with an enormous nervous energy and an infectious laugh. What also shone through was her tremendous humility and an ability to talk to anyone, from peers in the scientific community – research students – to laboratory technical staff. Her advice, not just on research problems, but also on personal issues was also thoughtful and always from the heart.

From 1989 to 1993 Ann was Royal Society Research Fellow and from 1993 to 1997 she was University Lecturer. She was promoted Reader in 1997 and became Professor of Infectious Diseases in 1999.

Rob Miller

# Noticeboard

Got something you want to tell BSMM members? Why not contribute to the Newsletter? There will be three issues a year and members are welcome to send in information for inclusion. The next Newsletter will be Autumn 2002 and contributions should be submitted to the Secretary (Ruth Ashbee, email h.r.ashbee@leeds.ac.uk) by September 15th

Travel grants will now be awarded three times a year. The deadlines for submission are 15th October 2002 and 15th January 2003. Application forms are available from the BSMM website (www.bsmm.org)

# Report from BSMM Annual meeting in Aberdeen

This year the annual conference was hosted by the Aberdeen Fungal Group. Delegates were greeted with a welcome pack containing the conference timetable and, to the delight of many, a free sample of single malt from one of the conference sponsors (Glenmorangie PLC).

In a courageous break from tradition the poster session was held on the first evening, as was the infamous Traditional Mycological Sing-Song. All present were in fine voice, and the rendition of Bohemian Rhapsody was truly memorable!

The first full day of the conference was devoted to Advances in Molecular Mycology. Invited speakers included June Kwon-Chung speaking about *Cryptococcus neoformans*, Dominique Sanglard speaking about the molecular mechanisms of drug tolerance in *Candida albicans* and Frank Odds asking us "How does molecular biology benefit the patient?". Offered papers covered a wide range of topics about many different fungi, from genetic variation via genetic characterisation to signalling, from *Candida* via *Aspergillus* to *Trichophyton*.

Pete Magee gave the Foundation Lecture on the subject of "Genomic variation via chromosome rearrangement and mating in *Candida albicans*". He spoke about the population shift seen when a commensal becomes pathogenic, and how this may arise by silent mutations becoming homozygous. He went on to increased rate of genetic change *in vivo* compared to *in vitro*.

The Annual Dinner was held that evening, which was followed by a whisky tasting session, and some traditional Scottish Ceilidh dancing. A very Scottish affair, with many of the men dressed accordingly.

The following day was dedicated to Medical Mycology. Invited lectures were given on oral mycology (Jeremy Bagg), non-invasive methods for diagnosis (Holger Hebart), developments in superficial mycoses (Glyn Evans), "Non-molecular mycology methods: evolving or decaying?" (Gillian Shankland) and current clinical challenges (Tom Rogers). Offered papers covered subjects including antifungal activity of epithelial cells, murine models of *Candida* infection and the role of mitochondria in the pathogenicity of *Candida albicans*.

The conference was both informative and enjoyable. Thanks go to the Aberdeen Fungal Group for taking on the organisation of the meeting.

Penny Cliff

# Book review

**Identification of Common *Aspergillus* Species**

MAREN A. KLICH. 2002.

ISBN 90-70351-46-3.

Centraalbureau voor Schimmelcultures. Pp. 116.

€28,00

This first edition is aimed at providing a morphologically based system for the identification of *Aspergillus* species.

The introduction has a good overview of the genus and also reminds us of the positive medical and economic importance of *Asp*. spp., as well as the negative pathogenic aspects. Included is a practical "how to" guide and identification key.

In all 45 species are detailed in full, from *Asp*. *alliaceus* to *wentii*. Each includes colony morphology, microscopic characteristics, distinguishing features, habitats and taxonomic references. The content and text arrangement may lend itself more as a reference book, rather than a quick bench guide. Incorporation of medical importance of each species would be of great value to clinical microbiologists.

Ideally colony photographs for each species would have all been in colour, understandably the publishing cost presumably restricted this possibility. There are some beautiful pictures of conidial heads, in some instances it may have been advantageous to show a diagram in addition to these for clarity. A good example would be in the case of *Asp. nidulans*, where it may be useful to see conidiophores, conidia and Hülle cells in the same frame. A standardised sizing scale for easy comparison could be another option. It was interesting to observe scanning electron micrographs (SEMs) of conidia, although not for use as a routine identification tool.

Overall it is a comprehensive, detailed and helpful text, which also covers species that are not commonly encountered in the medical laboratory. It is a useful reference book for specialised mycology labs or those with an interest in *Aspergillus* identification.

Susan Howard