

BSMM News

AUTUMN 2003



BSMM Foundation Lecturer 2004 — Dr John E. Bennett

The Foundation Lecturer at the BSMM 2004 meeting will be Dr John E. Bennett. Jack Bennett is one of the few people who can truly be called a 'living legend' in the world of medical mycology. His contributions both as a physician and a scientist have been at the cutting edge of research and clinical care for patients with fungal diseases.

Dr Bennett has worked at the US National Institutes of Health (NIH) for most of his career. He is currently Director of the Infectious Diseases Training Program and Chief of the Clinical Mycology Section of the Laboratory of Clinical Investigation. In the 1960s he was a pioneer of serological tests for cryptococcosis, and became involved with pharmacological and clinical assessments of antifungal agents in development. His expertise spread into all areas of invasive fungal disease, and his hundreds of publications testify to his encyclopaedic knowledge of the field.

He is co-author of the *Medical Mycology* textbook first known as 'Emmons *et al*' in earlier editions and most recently written by 'Kwon-Chung and Bennett'. He is a co-author of the book *Infectious Diseases* by Mandell *et al*, which is commonly regarded as the bible for infectious disease physicians.

Jack Bennett was the President of the Infectious Diseases Society of America from 1997-98. He has been recognized with numerous awards, including the Rhoda Benham Award from the Medical Mycology Society of the Americas, but his most recent and, perhaps, most unusual honour is to have a supplement of *Clinical Infectious Diseases* published in his name. *CID* vol. 36 suppl. 3 is the Report of the John E. Bennett Forum on Deep Mycoses Study Design, and its five articles delve



Dr. J.E. Bennett

into the area that has been Dr Bennett's lifelong concern - the shortcomings of clinical trials with antifungal agents. His Foundation Lecture will explore this area, a topic that has become a virtual crusade for Dr Bennett over the years.

Dr Bennett has two outstanding professional qualities: a penetratingly sharp intellect and a remarkably broad enthusiasm for all aspects of medical mycology. He disdains studies that purport to be science but which fail to stand up to critical examination. The BSMM is greatly honoured that Jack Bennett has agreed to be our guest. We look forward to welcoming him to the Bradford meeting, and to hearing his lecture.

BSMM SUBSCRIPTIONS

The subscription fee for the BSMM increases to £20 next year. Please make sure you fill in a standing order form and return it to the Treasurer as soon as possible to ensure your continued membership.

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PRESIDENT'S COLUMN

Time to be pleased with ourselves

To judge from the activities of the BSMM, reflected in this larger-than-usual Newsletter, our Society is presently enjoying a burst of very positive activities. We should be pleased to see so many mycology events taking place under the BSMM umbrella.

Just look back over the past year. We had a very successful and enjoyable joint meeting with the British Mycological Society in Manchester. We lent our name to a well-received publication on standards of care for patients with fungal diseases, authored by David Denning, Chris Kibbler and Rosemary Barnes. We held a meeting jointly with the BMS and the Society for General Microbiology in Manchester. Our scheme for supporting members who wish to travel to mycology meetings has remained very popular; we were able to help several BSMM members to attend the ISHAM Congress in San Antonio.

Over the next year, we expect to see even more projects come to fruition. The Diploma in Medical Mycology, pioneered with the hard work of Chris Kibbler and his colleagues, is at last becoming a reality. We have received generous sponsorship from some of the pharmaceutical companies in the antifungal field, and the training videos will be made early in 2004. We are planning a one- or two-day meeting, jointly with the British Society for Haematology, to take place late in the year in 2004. The BSMM Course, which could not be held in 2002 because of departmental relocations occurring in Leeds, will be back in 2004; the course is already booking rapidly! Last, but of course not least, our annual meeting, to be held in Bradford in 2004, promises to be at least as good as those of recent years, with a real catch in the form of Dr Jack Bennett from NIH as Foundation Lecturer.

All these upcoming activities are detailed elsewhere in the Newsletter.

While the Society can deservedly be proud of its record of activity, the fact remains that Medical Mycology, as a career discipline, is still neglected. For many years, the majority of medical mycology posts in the NHS and academia have not been refilled with mycologists when people retire or move

elsewhere. Some institutions are actively terminating mycology posts. Let's hope the introduction of the Diploma in Medical Mycology, aimed to encourage a growth in mycology-specialized clinical scientists, will start to reverse the trend.

The saddest event of 2003 for many of us is the unexpected, premature death of Glyn Evans. I first met Glyn at a BSMM meeting in 1967; he always stood out as both a great character and a great source of support for medical mycology in all its aspects. Few people have done more for this society than Glyn. Over a long period of years he has stamped his personality and his enthusiasm on the BSMM; meetings will never seem the same again without him. In his memory, we are initiating the Glyn Evans Mycology Award, aimed to encourage inter-laboratory visits by individuals who will benefit by gaining specialist knowledge of methods and techniques in the field. You can read details about the Award on page 3. We are seeking donations to set the Award off to a good start; we hope those of you who loved and respected Glyn will contribute generously to the fund.

Frank Odds

BSMM Annual Meeting 2004 - Bradford

The 2004 BSMM Meeting will be in Bradford University, on the 18th-20th April (the weekend after Easter). The meeting will be on the University Campus, which is near the centre of Bradford, next to the Photographic Museum. On Sunday evening there will be a curry in a popular local restaurant. The Meeting will then be all day Monday and Tuesday morning, with the Dinner on Monday evening. The Foundation Lecturer will be delivered by Dr John Bennett. In addition to the usual fare, we are keen to encourage the submission of papers of clinical interest relating to the interaction between fungi and the host, and this theme is emphasised by the symposium, 'The Clinic, The Host and The Fungus', which will be in addition to a basic science symposium. There will be plenty of space for posters.

Further details of the meeting and booking forms will be circulated early next year.

Paul McWhinney

Glyn Evans Mycology Award

In memory of Glyn Evans and to acknowledge the contribution that Glyn made to the BSMM, the Committee has decided to create the "Glyn Evans Mycology Award". The Award will provide the recipient with financial support to visit another laboratory for a period of training, probably to learn a specific technique. The exact amount and frequency of the Award have not been defined, to allow flexibility to decide each Award on its merits. The Award will contribute towards the costs of travel, accommodation and directly related expenses and the deadlines for the Award will be the same as the other travel awards. Applicants should state clearly on their travel grant application form that they are applying for this Award.

The Committee would like to invite members of the Society to make contributions, in memory of Glyn, towards this Award and they should be sent to the Treasurer.

BSMM Travel Grants

At a recent meeting of the BSMM Committee, a set of criteria on which future travel grant applications would be judged were discussed and finalised. The criteria are detailed below.

Eligibility

Applicants must be fully paid-up BSMM members, normally of at least one year's standing. Preference will be given to applicants known to have made a contribution to the Society.

Types of activity funded

Any activity which is perceived to have educational merit, including attendance at training or research events will be considered for a BSMM travel grant. The grant will cover travel and registration costs (where applicable) only. Applications for laboratory visits should be made under the heading of the Glyn Evans Mycology Award.

Documentation

A copy of the registration form, or other document specifying the nature of the event which is to be funded, must be submitted with the completed application form.

Deadlines for application

There will be three application deadlines each year, published in the BSMM newsletter (see Noticeboard in this issue). Applications for events which precede the next deadline, and retrospective applications, will not be considered (i.e. the event must start after the next available application deadline). A member will not be eligible if he/she has received a previous BSMM travel grant for an event that started less than three years before the next available application deadline.

Assessment of travel grant applications

Applications will be assessed by the BSMM committee. Available travel grant funds will be distributed among applicants according to the perceived educational merit of the funded event. Criteria that will increase the likelihood of funding include junior status of applicant (e.g. PhD student or other trainee), proposed oral or poster presentation, recent active participation at a BSMM-organized meeting and application for co-sponsorship from another organization. The maximum value of a single grant will be determined by the Committee at each deadline. Funding decisions will be made within three weeks of the application deadline.

Claiming the award

Receipts should be sent to the Treasurer to claim the award and this may be done before the meeting has taken place.

Requirements of travel grant recipient

The recipient must produce evidence of attendance at the meeting and a report of the activity attended, within 3 weeks of its completion. The report should be approximately 500 words in length, and may be published in the BSMM newsletter.

BSMM 2004: Bradford, April 18th-20th

Report from Travel Grant recipients

International Conference on Molecular Mechanisms of Fungal Cell Wall Biogenesis

The "II International Conference on Molecular Mechanisms of Fungal Cell Wall Biogenesis" in Salamanca, Spain was a very interesting and informative meeting. The main focus of the meeting was on *Saccharomyces cerevisiae*, but many fungal pathogenic species including *Candida albicans*, *Aspergillus fumigatus* and *Cryptococcus neoformans* were also represented.

I was able to get a very good overview of the regulation of *C. albicans* cell wall synthesis and important insights that are emerging in studies of other fungi such as *Aspergillus niger*, *Schizosaccharomyces pombe*, and *Candida glabrata*. Many experts presented very interesting work on septum formation in yeast. Enrico Cabib described the septation apparatus, involved in septum formation and cell separation. He showed that Cla4p a protein kinase of the p21 activated kinase type is involved in anchoring septins to the mother-daughter neck, which is responsible for maintaining the integrity of the mother-daughter neck along with chitin synthase 3. If one of these fails the mother-daughter neck remains the correct width, however if both fail the neck expands and septation does not occur. Peter Lipke presented exciting new evidence that expression of Als5p cell wall protein of *C. albicans* in *S. cerevisiae* mediates adherence of *S. cerevisiae* to extracellular matrix proteins and human buccal epithelial cells. Als5p mediates adhesion of fungal cells to each other and this cellular aggregation has properties characteristic of unrelated amyloid proteins such as β -Amyloid. This mechanism may be employed by *C. albicans* to colonize its host.

This meeting was very interesting and very beneficial for me as I am studying chitin biosynthesis of *C. albicans* for my PhD. I was given the opportunity to present my results as a poster and to meet experts and other students working in the field of the cell wall. I have received a lot of important

feedback that has been incorporated into the experiment plan for my final year. I also met many people who may be important in my career development in the future. Many thanks for the support provided by the BSMM, which is appreciated and valued.

Rhian Whitton

Chicago ICAAC 2003

The 43rd ICAAC conference was held in the windy city during September. Despite the meetings broad "infectious disease" spectrum, there was plenty for us mycologists to get our teeth into.

I work in a regional antifungal laboratory and so have a particular interest in diagnostic techniques. Raoul Herbrecht outlined the current options with *Aspergillus* in his "Early Diagnosis: CT, Antigen or PCR" presentation. It seems likely that all of these technologies have a place in management strategies, particularly in view of the problems with diagnosis. A number of speakers stressed the need for more standardised PCR methods, as there are too many varying in-house methods. PCR indeed has the potential to revolutionise identifications, with results in hours rather than days or even weeks.

Another hot topic this year was the use of prophylaxis. There was a particularly interesting meet-the-experts session, with Bart-Jan Kullberg and Thierry Calandra, on this very subject in ICU candidiasis cases. Questions raised were not only which drugs should we be using, but whether we should be using prophylaxis at all. As there is no clear-cut answer, opinions were varied. Prophylaxis may reduce treatment costs, but mortality rate is not often shown to be reduced. However, the overall feeling was that it is useful in specific high-risk patients. Many highlighted that "blanket" use was unnecessary, a drain on already tight finances, and may actually be unfavourable by potentially selecting for resistant species, increased toxicity and drug interactions. Studies looking into this vary so much in design, it is often hard to compare results. The timing of intervention is also important (prophylaxis, empiric or pre-emptive).

Naturally there was great interest in the "new" antifungals, very few mycology presentations

went by without the mention of voriconazole and caspofungin, amongst others. To hear of their further successful clinical use was encouraging, especially in the non-trial setting. With more treatment options than ever before, and new/improved diagnostic techniques, it certainly is an exciting time for the mycology world.

With parallel sessions running from 7.15am, often into the evening, it was certainly a busy 5 days. It gave me the opportunity to meet many mycologists whom I had only previously heard of and read papers by. Thank you for the opportunity to attend such an interesting and enjoyable meeting.

Susan J Howard

Joint Symposium

SGM Eukaryotic Microbiology Group, British Mycology Society and BSMM

This two day symposium presented by many internationally renowned experts covered many aspects of post genomic research in a wide variety of eukaryotic microorganisms. Included were the green alga *Chlamydomonas reinhardtii*, African trypanosome *Trypanosoma brucei*, the malaria parasite *Plasmodium falciparum*, *Dictyostelium* and fungal species we are more familiar with, the model organisms *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Ashbya gossypii*, the human pathogens *Candida glabrata*, *Candida albicans* and the plant pathogens *Phytophthora infestans* and *Magnaporthe grisea*. The symposia highlighted the powerful tools available to dissect important biological questions in a post-genomics age.

Especially interesting to the medical mycologist was the talk by Mike Lorenz, University of Texas Medical School, who used DNA microarray technology to analyse the gene expression profile of *C. albicans* upon interaction with macrophages. Mike had already published data on the importance of the glyoxylate cycle in survival of *C. albicans* in the phagolysosome. Genes of the glyoxylate cycle were up-regulated when *C. albicans* was phagocytosed. The expression pattern

following phagocytosis resembled that of *S. cerevisiae* after starvation. Genes were identified that were regulated during *in vitro* starvation and filtered out of the cohort of genes induced in macrophages to obtain macrophage-specific genes. A group of genes, 191 in total were identified that were expressed 4-fold higher or lower in contact with macrophages. A staggering 55 % of these were of unknown function and will make interesting candidates for further analysis. Among the genes of known function was *FOX2* gene, which encodes a protein required for β -oxidation. Deletion of this gene generated a mutant that could grow as well as wild type cells on glucose but was unable to grow on medium with oleate as the carbon source. The *fox2 Δ* mutant was avirulent in a mouse model of systemic candidiasis validating this approach to identify genes important for survival in the host.

Malcolm Whiteway, National Research Council of Canada, highlighted the key role the cAMP signalling pathway plays in the yeast to hyphal morphogenetic switch of *C. albicans*. He focused on two components of this pathway the adenylyl cyclase Cdc35 and Ras1 thought to be involved in regulating Cdc35 activity. He demonstrated that the adenylyl cyclase *cdc35 Δ* mutant and the *ras1 Δ* mutant were killed more readily by macrophages than wild type cells and showed the analysis of the transcriptional profiles of these mutants.

Christophe D'Enfert of the Pasteur Institute presented his work on biofilm formation in *C. albicans*. A DNA microarray comparison of the genes expressed during planktonic growth with those expressed during growth in a biofilm identified up-regulation of the sulphur amino acid biosynthesis pathway. In addition two cell wall proteins were up-regulated in biofilm formation Pga59 and Pga62, both were confirmed to be cell wall localised by GFP-tagging. Deletion of *PGA62* gene resulted in a biofilm formation defect.

Turning to *C. glabrata* Ken Haynes, Imperial College, described his work on the *ace2 Δ* mutant; ACE2 encodes a transcription factor. Cells of the *ace2 Δ* mutant don't separate due to defective expression of chitinase. Treating *ace2 Δ* with chitinase separated the cells. This mutant is hyper-virulent in an immunocompromised mouse systemic model

and an *ace2Δ* infection resulted in high tissue burden and a massive increase in cytokine levels. A proteomics approach was taken to analyse differences between *ace2Δ* and wild type cells utilising the COGEME proteomics facility at University of Aberdeen. This identified changes in protein folding and regulation, cytoskeletal assembly, cell polarity and cell wall remodelling.

Overall the symposium was very stimulating and it was of interest to learn about the progress that has been made in other eukaryotic organisms some that were more challenging to culture in the laboratory than the fungi we work with! The application of these post-genomics approaches to your favourite organism can provide a wealth of information on a global scale and will continue to revolutionise the way we do our science.

Carol Munro

Obituary

Professor E. Glyn V. Evans

1941-2003



The unexpected loss of a person who commanded so much affection and respect throughout the world of medical mycology is a shock that is hard to bear. Glyn Evans died on August 4th 2003 after several recent episodes of pneumonia. His achievements and contributions to our work in combating fungal disease live on. We can temper our sorrow at losing Glyn with the fond recollection of the ways he touched the lives of so many of us, professionally and personally. A former

Secretary then President of the BSMM, Glyn Evans is someone who impressed all who knew him with the strength of his personality, his sense of humour and his obvious professionalism.

Glyn entered the world of medical mycology via his PhD research on *Cryptococcus neoformans* at the University of Glasgow. He was a favourite protégé of his supervisor, Jimmy Gentles, a founding father of British medical mycology. In 1970 Glyn moved to Leeds University to take up post as a lecturer. He soon expanded his activities from teaching and running a routine mycology diagnostic service in the Dermatology Department into scientific and clinical research. Glyn collaborated actively with his colleagues in medical and surgical departments and undertook many joint projects on the epidemiology, serodiagnosis, pathogenesis and treatment of mycoses.

As his career evolved, Glyn became renowned internationally as a world-class authority on superficial mycoses, and many of his more than 100 publications concern the diagnosis and treatment of fungal infections of skin nails and mucosae. He provided the laboratory support for more than 20 clinical trials of antifungal agents in dermatology. During the 31 years Glyn worked at Leeds (and moved steadily up the ranks to Senior Lecturer then Professor) his diagnostic service expanded into a fully accredited reference laboratory, ultimately becoming one of the two UK PHLS Mycology Reference Laboratories, with Glyn as its Head. He co-authored seven books on medical mycology and microbiology and lectured on fungal disease at venues all round the globe.

This rather formal account of his professional achievements does no justice to Glyn Evans' constant hard work as an initiator of projects that create and sustain awareness of mycology and its contribution to medicine. Examples of his advocacy of our field are many and varied. Glyn set up this Society's working party on fungal serodiagnosis, an activity that resulted in the "little black book" that was reprinted several times into the late 1980s. He initiated the BSMM course in diagnostic

mycology that we now all know as “the Leeds course” and which has become the standard for training medical laboratory personnel in the art of fungal culture and identification.

He set up a one-year course at Leeds that turned out MSc graduates in medical mycology. This course attracted many participants from countries outside the UK, particularly from the Far East, and led to Glyn’s widespread international links for teaching abroad. His networks included institutions in India, China and South America, and he was rewarded with an honorary professorship from the University of Beijing in 1999. His international participation also included seven years as Chief Editor of what is now called *Medical Mycology* – the journal of the International Society for Human and Animal Mycology (ISHAM). He moved on to become Secretary, then President of ISHAM, and was accorded honorary membership of ISHAM in recognition of his many years of devoted service to that society.

Devoted service is the hallmark that characterizes Glyn Evans’ life. Few people are willing to take on the burdens of administration and organization that Glyn always seemed to tackle with enthusiasm. He enjoyed creating and managing projects that provided frameworks from which others could benefit. This is self-evident from the courses he instituted and the scientific meetings he organized. But even at the local level, he spent several years as adviser to undergraduate students who lived in University accommodation.

Many of those who worked for or with Glyn at an early stage chose to remain in the medical mycology arena for the rest of their careers: the hallmark of an inspirational leader. The list of individuals who owe Glyn such a debt of gratitude includes David Warnock, Malcolm Richardson, Peter Donnelly, Valerie Hopwood and the present writer.

Travel abroad was, to Glyn, both an immense pleasure and a health hazard: the latter because his lungs often reacted badly to long-distance flights. He never complained; he always arrived on time to give presentations and chair meetings, even when he was unwell. He was a true

professional, who refused to let his lifelong medical problem interfere with his work.

He moved from Leeds to Cardiff in 2001. This completed a kind of cycle, since the University of Cardiff was Glyn’s *alma mater*. His intention in Cardiff was to “slow down a bit” - reduce his working hours and commitments and plan for retirement - and he set about slowing down in his characteristic way. He had always had a passion to be an entrepreneur, so in addition to his contractual obligations to a diagnostic mycology service for the Cardiff area, he founded a company that provided commercial mycology laboratory services for clinical trials. Glyn was an unstoppable enthusiast for his mycology work; true retirement would not have come easily to him.

Glyn was a wonderful person to count as a close personal friend. I can now no longer pick up a telephone and seek his friendly advice, or comment, or the wit that was invariably a tonic when feelings had run low. Glyn and I shared a sense of humour that some find extreme; but without a healthy conviction that every human activity has a comic side, one can too easily become depressed at the state of the world we live in. Glyn’s smile could warm a room; his laughter infected many people. “At least you know you’re alive!” he would exclaim when events prodded one or both of us into some new activity we may not have sought and did not necessarily relish having to do.

Now he is gone. His widow, Rosalind, and his two sons, Alun and Hywel, to whom he was very close, grieve for him.

The news of his death caused a large and spontaneous outpouring of tributes to his family, who had truly not previously appreciated the extent to which his colleagues held him in esteem. He lived life both for its own enjoyment and to help and support those who could benefit from it. None of us who knew Glyn Evans can ever possibly forget him.

Frank Odds

The family of the late Professor Emlyn Glyn Vaughan Evans would like to express their heartfelt thanks for all the kind expressions of sympathy received during their recent sad loss.

NOTICEBOARD

BSMM Course in Diagnostic Medical Mycology 2004

The next BSMM course will take place between March 29th - April 2nd. The course, which takes place in Leeds, is aimed at Biomedical Scientists, Clinical Scientists and Specialist Registrars in Microbiology or Infectious Diseases. The course is always over-subscribed and it is advisable to book your place early. Places can only be reserved on payment of the course fee. To register your interest, please email the course organiser, Ruth Ashbee (h.r.ashbee@leeds.ac.uk).

BSMM Committee Vacancies

The five-year term of office of the current Treasurer, Dr Gillian Shankland will come to an end next year. Gillian has served two terms of office and after 10 years service as Treasurer would like to have a well-earned rest! The committee would like to invite nominations for this post. Nominations may be made by the Committee or by any two BSMM members, and should be sent, together with the written consent of the nominee, to the Secretary as soon as possible. In the event of more than one nomination being received, an election will be held.

The current President, Frank Odds will also finish his two-year term of office next year, but is eligible for, and willing to stand for re-election. Other nomination should be supported by two members of the Society, as above.

BSMM Travel Grants

BSMM Travel grants are awarded three times each year. The deadlines for submission of applications next year are January 15th, June 15th and October 15th. Application forms are available from the BSMM website (www.bsmm.org). See also the article in this issue on the Glyn Evans Mycology Award.

Forthcoming meetings

Federation of Infection Societies (FIS)

The 10th meeting of FIS will take place between 19-21st November in Cardiff. Further information about the meeting can be obtained from the website (www.fisconferences.com)

Second Russian Congress of Medical Mycology

The 2nd Russian congress will take place in Moscow on March 24-25th, 2004. Sessions include fungal infections in haematology units, empirical therapy in cancer patients, mycoses in ophthalmology and ENT and onychomycosis. Further information can be obtained from the website (www.mycology.ru/congress/en).

Contributions for the next issue of the Newsletter should be submitted to the General Secretary (Ruth Ashbee, e-mail h.r.ashbee@leeds.ac.uk).

BSMM Autumn 2003 Newsletter compiled by Ruth Ashbee (h.r.ashbee@leeds.ac.uk)