28th ANNUAL MEETING 13 - 15TH APRIL 1992 EGHAM, SURREY

All members should by now have received their registration forms AND paper presentation forms.
Let this be a timely reminder to BOOK as soon as possible so that numbers attending AND the scientific programme can be finalized without the usual last minute rush. ACT NOW !!!

Junior members of the BSM are particularly reminded that the Society encourages the use of the Annual Meeting as a forum for fresh ideas and unpublished work.

The scientific programme will have as its core a Symposium on

DIAGNOSIS OF OPPORTUNIST FUNGAL INFECTIONS

This will start 10.30 am until 4.30 pm on Tuesday 14th April with four guest speakers:
Dr. E.G.V. Evans - Serological diagnosis of fungal infections
Professor R.Hay - Histopathological diagnosis of fungal infections
Dr. D.Coleman - Molecular techniques and their application to the diagnosis of fungal infections
The final lecture which will be published as the 15th Ian Murray memorial lecture is to be given by:
Dr. T.Walsh, National Institutes of Health, Bethesda, USA. 'An integrated approach to the diagnosis of fungal infections'
 Members and Non-members who wish to attend ONLY the Tuesday Symposium may apply to the local organizer.

Dr G.Midgley, Dept. Medical Mycology, St John’s Dermatology Centre, St Thomas’ Hospital Lambeth Palace Rd, London SE1 7EH
Registration fee: £18. (includes tea/coffee and lunch)
The deadline for booking is MARCH 1st 1992. (Delegates attending the Annual Meeting need not register separately for the Symposium).

VENUE FOR THE 1992 ANNUAL MEETING

Illustrated in the photograph is the Founders Building of Royal Holloway & Bedford New College on Egham Hill in Surrey where we have booked accommodation for the next Annual Meeting. The college is a striking example of 19th century architecture, inspired by the chateau of Chambord on the Loire, and it was opened by Queen Victoria in 1886. The whole site comprises 100 acres including some very pleasant parkland although part of this has been built on in recent years to provide extensive further academic and residential facilities, particularly since the merger of the two former independent colleges in 1982. The scientific sessions of our meeting will be held in a lecture theatre in a modern complex which is a short walk through the grounds from the Founders Building. A nearby attraction is Windsor Great Park with one of the entrances only 600 yards away from the college gates. For those who care to allow some extra time in the area it is possible to walk to Virginia Water or the Savill Garden or even as far as the Copper Horse statue which stands at the end of the Long Walk leading up to Windsor Castle itself. There will be the opportunity to see something of the history of Windsor on Monday evening when we shall have a guided tour of St. George’s Chapel followed by a buffet supper in the Guildhall. The chapel which is actually in the precincts of Windsor Castle, is one of the nation’s finest historic buildings. It was founded in 1348 by King Edward 111 but the present building dates from 1475. It has always been closely associated with the Order of the Garter and in the choir you will see the insignia (banners, sword, helm and crest) of the present Knights and also an impressive sequence of gilded stall plates, dating from the 14th century to the present time which records famous knights of the past. Among these you will find Richard 111, Wellington, Winston Churchill etc. Many of our monarchs are buried here including Henry V1, Henry V11, Charles 1 and more recently George V and George V1. The Guildhall is situated close by in the High Street. This lovely building was completed by Sir Christopher Wren three hundred years ago and contains a long series of royal portraits extending over the last 400 years.

We hope that you will take the opportunity to enjoy the venue we have chosen this year as there will be a great deal to appreciate, both at the college and in the surrounding area. We look forward very much to welcoming you next April.

ACT NOW! BOOK NOW!
SYMPOSIA & COURSES

BSM one-day Symposium on:
'Trends in the management of fungal infections'
The Symposium was held at the CPHL Colindale, Friday 25 Oct 1991. It attracted an audience of 98 (36 BSM members) and was considered by all attending to be an excellent reflection on the capacity of the Society to produce 'state of the art' Symposia. The committee extends its thanks to the local organiser Mrs Frances Knight of the Myological Reference Laboratory at Colindale for her help in its organisation. A summary of the five presentations is included for those members not able to attend the meeting.

BSM Course on:
'Diagnostic Mycology'
commencing 30th March 1992 at Leeds
The course is now full, with 58 delegates booked in for a week's lectures and practicals at the Microbiology Department. Those thinking of participating will be pleased to know that the course will be a yearly feature of the BSM calendar. The course organiser Dr. Glyn Evans, Regional Mycology Lab., Microbiology Dept., University of Leeds LS29JT may be contacted for the 1993 course. Our thanks to Dr. Evans and his able assistants for running this popular course.

International Mycological Institute & Mycological Reference Laboratory training course on: 'Biology of medically important fungi' 27 April - 22 May 1992.
Specialists from both organisations will provide an extensive 4 week course on the biology and systemics of filamentous microfungi and their identification in culture; lectures and practicals. Course fee is £1200 excluding accommodation, meals and travel. Contact: Miss J. Pryse, International Mycological Institute, Kew, Surrey TW9 3AF.

TRENDS IN THE MANAGEMENT OF FUNGAL INFECTIONS

October 25 1991 at C.P.H.L.

Colindale -
Report of Talks Presented

Evaluation of antifungals in vivo and in vitro
Dr. F. Odds, Beerse, Belgium.

There are nowadays at least six groups of antifungal agents available or undergoing clinical trials. They all have different chemical properties and modes of antifungal action so it is unlikely that a single laboratory test will adequately demonstrate their potential as antifungals for human use. In vivo tests must be designed to answer specific experimental questions. The requirements for animal models to discover possible new agents in the first place are quite different from those needed to demonstrate genuine potential for human mycoses. All the major mycoses can now be modelled in small animals with and without regimes of immunosuppression. Concern with minimising the duration of experimental infections in animals means that traditional end-points for monitoring drug efficacy, particularly survival times, are being replaced with other markers such as tissue counts of fungi measured after a short period of infection. Cutaneous, intravenous, intravaginal and intratracheal infections can be achieved with different fungi simultaneously in a single animal. This approach is valuable for screening new chemicals in vivo for antifungal activity since it greatly reduces the number of animals tested. Where sophisticated monitoring of haematological or serological parameters is required, experiments with larger animals such as rabbits with implanted central venous catheters have been shown to be effective.

In vitro testing of antifungals continues to create many problems, particularly where a reliable indication of the susceptibility of a fungal isolate to an imidazole or triazole compound is needed to assist decisions in the management of individual patients. Various national groups have studied in vitro antifungal tests and have established protocols for amphotericin B and fluconazole testing that give excellent intra-laboratory reproducibility. The same is not yet true with azoles, particularly against Candida isolates.

Dose-response curves for anazole antifungal give better information about the susceptibility of a fungal strain than a single MIC can convey, because the dose-response curves indicate the extent of inhibitory action at concentrations below the MIC. Evidence was presented that spectrophotometric measurement of yeast growth relative to control growth at a single antifungal concentration can provide valuable indications of the relative susceptibility of yeast strains to a particular compound. Such tests can be performed to a high degree of reproducibility in microdilution plates with inocula standardised automatically by growth in a glucose-limiting medium. Such a test system allows tests with several strains and compounds to be set up in a single microplate; the turbidities can be read and the relative growth of the strains calculated automatically. Single concentration tests done at two temperatures, 25°C and 37°C, have shown that C. albicans isolates are notably more sensitive to amphotericin B, fluconazole and azole antifungals at the higher temperature, whereas the opposite is the case for amphotericin B. Terbinafine sensitivity was relatively little altered by incubation temperature. These results suggest that fever in an infected host may enhance the efficacy of systemic antifungal agents. Data for clinical isolates of C. albicans plotted as scattersgrams of their relative growth at 25°C and 37°C in the presence of each antifungal agent determination of the susceptibility profile of individual strains.

NEW BSM TRAINING COURSE

Many members of the Society will recall the residential courses on common fungal infections that Stephen Roberts used to run at Fitzwilliam College, Cambridge. Now, after a lapse of ten years, the Committee has agreed to support a new training scheme for clinicians and microbiologists. This will complement the established course at Leeds, with much more emphasis being placed on clinical problems and the role of the laboratory in diagnosis and management. It will be less concerned with the technical aspects of medical mycology and the identification of organisms.

The new course will take place at the University of Bath from Thursday 10th to Saturday 12th September 1992. Lectures will cover a wide range of topics including the management of superficial fungal infections, the diagnosis and treatment of aspergillosis and candidosis in transplant and cancer patients, and the management of oral candidosis and cryptococcosis in AIDS patients. The role of different antifungal drugs in the management of fungal infection will be covered as will the role of the laboratory in monitoring patients on antifungal treatment. The lecturers will include Dr. Rosemary Barnes (Cardiff), Dr. David Denning (Manchester), Dr. Glyn Evans (Leeds), Professor Rod Hay (London), Dr. Malcolm Richardson (Glasgow), Dr. Tom Rogers (London), Dr. David Warnock (Bristol) and Dr. Rod Warren (Cambridge).

The course fee will be about £250. Meals and accommodation (including the cost of a special course dinner on the Friday evening) will be available at an inclusive charge of about £90.

The course will be advertised in the spring. In the meantime, any members who would like further details are invited to contact Dr. David Warnock at the Regional Mycology Laboratory, Department of Microbiology, Bristol Royal Infirmary, Bristol BS28HW.

HAVE YOU BOOKED YET?
Pharmacokinetics of new antifungal agents.
Dr. T.K. Daneshmend, Exeter.
The focus was on the three main antifungals itraconazole, fluconazole and liposomal amphotericin B; their absorption, distribution, metabolism and excretion patterns.
Itraconazole, molecular weight 706 was absorbed more readily with food eg up to 99% compared with 40% without food. This was due to a combination of factors such as gastric acid, pancreatic enzymes and bile salts aiding overall absorption. Drugs such as cimetidine or ranitidine that inhibited gastric acid production reduced itraconazole absorption and so did certain diseases eg AIDS. Itraconazole once absorbed was bound to protein (99%) with a higher concentration in certain tissues eg fat, liver, skin than in serum. The drug was metabolised via several routes mainly in the liver with active and inactive metabolites found in bile and urine <1% active drug in urine. Its half life was 20-30 hours. Fluconazole, molecular weight 305 was well absorbed orally and unaffected by AIDS or bone marrow transplant. It was poorly bound to protein and had a half life the same as itraconazole. Although it peaked 2-4 hours after ingestion it took a week to reach a steady state with daily dosage. The drug was found in the urine, mainly in its active form (80%). Liposomal amphotericin B, molecular weight 924 was an aqueous solution bound within concentric bilayers of lipid molecules. Multilayered liposomes could be used but the current drug preparation was in a bilayered carrier. This allowed it to be used as an IV infusion eg 1-3 mg/kg daily, 1-3 g over 2-4 weeks at far higher concentrations than the free drug. The drug was found in sites rich in macrophages eg liver and spleen. The reduction in toxicity could be shown by the improved stability of the RBC membrane with the liposomal form of the drug.
Dr Daneshmend’s talk also included a review of the uses of the gastroscope and several points of interest in Amsterdam.

Itraconazole in the treatment of fungal infections.
Dr. D.W. Denning, Manchester.
Studies on the effect of itraconazole in different fungal infections have shown it likely to become a drug of first choice in aspergillosis, histoplasmosis, blastomycosis, coccidioidomycosis and sporotrichosis, whereas for Zygomycetes and Pseudallescheria it was less effective.
Various studies have shown a good response in subjects with coccidioidomycosis affecting most organs (except the lungs) and for meningitis although patients had usually been on some other regime initially. In blastomycosis the skin there had been a good response in 38/49 with one failure. In histoplasmosis 31/38 responded with three failures. In histoplasmosis in AIDS an induction regime with amphotericin and itraconazole maintenance produced a response in 30/42 subjects and no failures up to one year. In sporotrichosis 7/10 responded with three failures. In candidosis the drug was successful for mucosal infection but its role in the treatment of deep lesions was questionable. Eleven of 13 with Candida oesophagitis and 7/7 with urinary candidosis responded. In cryptococcosis in AIDS it was easier to diagnose the disease by visualising the organisms using India Ink and thereby follow the effectiveness of treatment, particularly in conjunction with a fall in antigen titre - a good sign. Itraconazole was 67% effective in subjects and those who received up to 7 days amphotericin previously fared better. In some subjects the phenomenon of recrudescence ie breakthrough of disease during treatment was observed. In a review of case histories of invasive aspergillosis, predominantly pulmonary disease 55% responded to amphotericin and 75% to itraconazole. In a multicentre study of 80 patients with invasive aspergillosis, overall 70% responded to oral itraconazole including 6/7 neutropenic patients.

Fluconazole in the treatment of systemic fungal disease.
Dr. S. Shaunak, London.
Increasing numbers of HIV infected individuals worldwide has resulted in a major epidemic of tuberculosis in sub-Saharan Africa as well as an increase in the number of cases of cryptococcal meningitis. It is becoming increasingly clear that trials of new antifungal agents will be undertaken in patients with AIDS if we are to obtain answers from controlled clinical trials within a short period of time. The concept of induction therapy as well as maintenance therapy (which is familiar in oncology) is now being adopted for the management of opportunistic infection in patients with AIDS because control of the disease rather than the cure is the only realistic end point.
Fluconazole has the advantage of being remarkably non-toxic in relation to its therapeutic efficacy. Its interaction with tolbutamide, warfarin, rifampicin, cyclosporin and phenoxin have now been well defined and can be monitored during long term therapy. Fluconazole may have a role to play in the management of hepatosplenic candidosis (chronic disseminated candidosis) Two recent studies suggest that it may be of value, but controlled clinical trials have yet to be performed. In the case of Cryptococcus neoformans meningitis, two ACTG studies have provided some controlled data. Protocol 0106 was a maintenance protocol which compared fluconazole 200 mg/day with amphotericin B at 1mg/kg/week in patients whose CSF cultures had become negative after induction therapy. Of 183 patients entered into these studies, 2/106 relapsed in the fluconazole group compared with 13/77 in the amphotericin B group. The trial was stopped prematurely.
The second protocol (protocol 059) is an induction protocol with fluconazole (200 mg/day increased to 400 mg/day if there had been no response within two weeks), with amphotericin B (0.3 mg/kg given three times a week) with or without fluconazole. In the interim analysis of 99 patients the response rate was 53% for fluconazole compared with 49% for amphotericin B. Mortality was 23% in both groups. It is worth noting that the time to sterilise the CSF was shorter in the amphotericin B group than in the fluconazole group. The final results of this study are awaited with considerable interest.
In the light of these studies most authorities would currently recommend induction therapy with amphotericin B with or without fluconazole for 2-4 weeks in patients with Cryptococcus meningitis. Ideally, the CSF Cryptococcus antigen titre should have fallen to less than 32 before the decision to change to oral fluconazole is made. Patients with high CSF antigen titres and continuing clinical evidence of disease who cannot tolerate amphotericin B should be treated with fluconazole, 400-600 mg/day as induction therapy, and a subsequent maintenance dose of 200 mg/day. The length of therapy should be determined by the overall response of the patient. A period of 10 weeks of induction therapy would not be unreasonable.

Liposomal amphotericin B in the treatment of fungal infections.
Professor R. Hay, London.
Liposomal amphotericin B (Ambisome) is a true liposome, an amphotericin/lipid complex with much reduced toxicity. The rationale behind the complexing is that there is a higher concentration of drug at the site of infection. Previous considerations for the need for granulocytes do not seem valid as enough drug is released from the liposome to be effective.
In studies Ambisome was effective against Aspergillus, 13/18 cured or improved; with Candida 39/41 cured or improved and for Cryptococcus 3/3 cured or improved. Less adverse reactions were observed in these patients and overall it was felt to be an encouraging drug, effective in both systemic candidosis and aspergillosis.
In transplant patients it proved effective in Candida infection. It had still to be shown to be effective in meningitis and its long term toxicity had not been resolved.

BSM Membership as of 15 Jan 1992
We are pleased to welcome new members to the Society
Miss Alison Cady, Dept. Biochemistry, University of Wales, Cardiff
Dr N.J. Russell, Dept. Biochemistry, University of Wales, Cardiff
Miss Tanya Sims, Sandoz Pharmaceuticals, Frimley
Dr C. Tang, Dept. Bacteriology, Hammersmith Hospital, London
Dr A. Walker, Bristol-Myers Squibb Pharmaceuticals, Hounslow
Membership applications pending - 4 Total membership now stands at 205
AS I RECALL - a series of articles by senior members of the BSM recalling the early days of the Society. The first article in the series is by Dr. R.R. Davies DSc, past Secretary, President and a Founder Member of the BSM.

After a year as demonstrator in biology at University College, Swansea, I had the good fortune to be appointed junior lecturer in the Department of Biology at St Thomas’s Medical School in Nov 1952. Research with the late Professor Ivor Isaac on strains of the plant pathogen Verticillium from trees needed to be completed. However, a Medical School on the embankment seemed an unpromising environment for forestry pathology. It was then decided to look into the possibility of research into some aspect of Medical Mycology that would lead to a PhD. In 1952, "Medical Mycology - An Introduction to its Problems" by G.C.Ainsworth was published by Sir Isaac Pitman & Sons Ltd, price 15 shillings. At that time Dr Ainsworth was Reader in Mycology at the University College of the S. W. of England, Exeter. Although I had never met Geoffrey Ainsworth I wrote to him. I said I had read his book with great interest and was considering the possibility of a research topic in Medical Mycology. I wondered if on some occasion he was in London and had a little time to spare he might come and have lunch with me at St Thomas’s. He replied he would be in London to attend a meeting of the Medical Research Council’s Medical Mycology Committee and that he would come to lunch with me at St Thomas’s House. After lunch we continued our discussions on a walk through the Pathology Museum and dissecting room. He did not advise anybody to take up Medical Mycology, but as I already had a teaching job in the Medical School it was probably suitable for me. He was Secretary of the MRC’s Medical Mycology Committee and was organizing a meeting for paper reading in Medical Mycology at Exeter in the Spring. "You can come. I will invite you as a student observer" he said.

The invitation came and I attended my first residential meeting for Medical Mycology at Hope Hall, now at the University of Exeter. As I recall those attending included Alec Barlow, Frank Chattaway, Jimmy Gentles, Bill Frankland, Kate Maunsell, Howard Whittle, John Wilkinson, Charlie La Touche, Jim Hirst, Phillip Gregory, Harold White, D.A. Williams (DA to his friends), Mervyn Richards, Peter Austwick, Phyllis Stockdale, a refugee orthodontist E.C. Fox, Professor Ingram, Drs Holmes and Everall and a Mrs Carlier who had conducted a ringworm survey in Birmingham. An Exeter physician named Fuller spoke on Farmer’s lung. I recall he had collected X-rays of farmers with this disease then thought to be caused by fungi, but had lost his collection of films in the Exeter Blitz.

The topics of the meeting were Dermatomycoses and aerobiology. Ainsworth and his young assistant Austwick had been engaged in a survey of animal mycoses. They provided a demonstration of the fungi recovered and techniques used. This was before chloramphenicol was incorporated into Sabouraud’sagar. Gentles and Holmes reported on their survey on Tinea pedis in coal miners using pit-head baths. Harold Hyde, Mervyn Richards, D.A. Williams, Jim Hirst and Phillip Gregory all reported studies on the fungal content of the air. These workers together with Bill Frankland and Kate Maunsell were very much concerned with fungal allergens. Kate Maunsell appealed to the meeting for a mycologist who could collaborate with her. I was introduced to Kate and began studies on moulds and allergens in house dust and in the air. When I began this research I had about 30 glass Petri dishes, some with aluminium lids and access to a small autoclave and a hot air oven. I made extracts of house dust and fungal that Kate used to skin test and challenge her patients, activities which now seem prohibited by the Medicines Act and the Safety of Medicines Committee.

The first meeting at Exeter was not all work. There was no bar at Hope Hall, but on the second night, quite by accident I walked into a pub near the Hall where Jimmy Gentles, and Jim Hirst were already installed.

The third meeting organized by the MRC Mycology Committee for paper reading was held at Alexander Hall Cardiff. This reflected on the preeminence of D.A. Williams, Hyde and Richards into research on mould fungi as allergens at that time. At this meeting my brother, a lecturer at the Royal Veterinary College attended and shortly after the last morning session, we found ourselves with Jimmy Gentles, Paddy Meenan and John Curry enjoying a drink at The Angel Hotel.

The bars were all closed but someone was a resident! The pattern of paper reading and socializing was beginning. Residential meetings in University accommodation were cheaper for young people than hotels however, bars in Halls of Residence although now the norm were uncommon at first. In 1962 when the Meeting was jointly organised by Geoffrey Ainsworth at the Commonwealth Institute and by Peter Austwick of the Central Veterinary Laboratory, residence was at the Star and Garter Hotel. The Oxford boat race eight were also staying at the Star and Garter at that time and the papers were read at the hotel and also at Weybridge. I recall that when Charlie La Touche was Secretary of the MRC Mycology Committee he would only send details of the programme to persons who had booked for the meeting. Abstracts and what took place at the Meeting were confidential - part of the Minutes of the Meeting and not available to anyone who had not attended. Members of the MRC Committee travelled first class with their expenses paid for by the MRC. After 11 paper reading sessions the MRC felt that support for the Committee had been adequate and that it was time Mycology was able to stand on its own feet. Thus under the auspices of the MRC the British Society for Mycopathology was formed at a meeting in Newcastle - built on the pattern established at the MRC Committee.

At the first of the BSM Meetings, kindly organized by Dr Stephen Roberts in Cambridge, the bar was overcrowded, so under the leadership of the then Secretary, a group took their drinks into the lecture room. The lecture room had a raised stage at one end and there was an old upright piano on it. In response to the Secretary’s appeal Seamus O’Sullivan played and there was an enjoyable sing-song around the piano until midnight when one of the Proctors ordered us to quit and go to bed!

The following year in Woolton Hall Manchester, after the Annual Dinner we adjourned to a common room and there just happened to be a piano. Seamus again performed and the choir was ably led by Jimmy Gentles. Since this was so much enjoyed, colleagues who were organizing the next Meeting in Bristol were asked that a piano should be made available for after the Society Dinner. With the agreement of the President, Dr Ainsworth I wrote the resolution that “Dr Seamus O’Sullivan be the Society’s Honorary Director of Music”. The resolution was accepted nem con with acclaim.

When the Meeting was in Cambridge, Geoffrey Ainsworth was in his second year as President. Harold Whittle had been a regular attendee and valued friend of the Society. Since Cambridge was his academic home, where he had been consultant dermatologist for many years we took, the unprecedented step (not provided for in the Constitution) of having the AGM declare him President Elect - to succeed when Geoffrey Ainsworth’s Presidency ended. We thought a kind thing to do.

We have evolved in ways that some might think surprising, and I should be astonished if any other Society in the calender of Biological Societies has an Honorary Director of Music. Although we have not been a computer dating agency it was at one of our Meetings that Peter Austwick met Joan Longbottom and now they are man and wife.

The BSM has come to mean so much to so many. We have a tradition of encouraging young people to read reports of work in progress for higher degrees. This goes back to the time when we were a self help group and the constructive comments of the more experienced members were welcomed. For this reason the proceedings of the Meetings have always been confidential.

The second time I read a paper it was at a meeting of the BSM and I was nervous but the sympathy showed by the members to a young person reading a paper, for the first time in their midst, helped in no small way to put me at my ease.

In those days we never had papers on Monday morning. We worked on Saturday mornings, Sunday was a day apart, and whenever possible we travelled to Meetings on the Monday morning.

We are now a little less tolerant than we were. At almost every AGM there seems to some member who wants something different. However since 1953, we, in the BSM have developed traditions of our own, which I hope, the members will value and continue.