



FUNGAL UPDATE 2015

10th Anniversary

Abstract Book & Programme

Friday, 9th January – Saturday 10th January 2015

Great Hall, St. Bartholomew's Hospital, London

Chairs: Peter Donnelly (Nijmegen, The Netherlands) and Brian Jones (Glasgow, UK)





FUNGAL UPDATE 2015
10th Anniversary

Organising Committee

Dr. S. Agrawal

Prof. R. Barnes

Dr. E. Bignell

Dr. G. Johnson

Dr. R. Manuel

Dr. M. Wilks

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FUNGAL UPDATE 2015
10th Anniversary

Welcome

Dear Colleagues,

Welcome to the 10th year of the Annual Fungal Update at Barts. To mark this anniversary, the programme has been extended, both in duration, scope and entertainment!

The topics on day one will be familiar – the ongoing challenges of antifungal management in Haemato-Oncology and ICU; but what is new: diagnostics in the clinic, future assays in development, anti-fungal stewardship and drug resistance; and do they have any impact on daily practice?

On day two we will hear the latest on cryptococcosis and pneumocystis, as well as basic mycological research and the potential for clinical translation. While keypad voting promotes participation, I would really like to encourage you to use these moments to reflect on the issues in hand and to ask questions of the speakers at Q&A time. Cases, debate and a quiz should ensure we are all entertained.

On Saturday, we have a very special tea break, with Canterbury Cathedral's Boys Choir singing for us in the Priory Church of St. Bartholomew's the Great, a beautiful and atmospheric church.

In the final analysis, to ask others to give up their time for such meetings requires one thing – an excellent programme. I hope this anniversary event achieves this.

Dr. S. G. Agrawal BSc, FRCP, FRCPath, PhD

Senior Lecturer and Honorary Consultant, Barts Health NHS Trust
& Blizard Institute, Queen Mary University of London.



Programme

Friday 9th January 2015

10:50 – 11:00	Welcome from Dr. Samir Agrawal on behalf of the Organising Committee
11:00 – 12:00	A 10 year review of IFD management in Haemato-Oncology Diagnostics in clinical practice: 10 years on, have we moved forward? <i>Prof. Rosemary Barnes, Microbiology, Cardiff University School of Medicine</i> <i>Dr. Mansour Ceesay, Haematology, King's College Hospital, London</i>
12:00 – 13:00	Improved fungal assays in our lifetime? New monoclonal antibodies <i>Dr. Chris Thornton, Biosciences, University of Exeter</i> Molecular tools for nucleic acid and protein detection <i>Dr. Gemma Johnson & Prof. Stephen Bustin, Faculty of Medical Science, Anglia Ruskin University, Chelmsford</i>
13:00 – 14:00	Lunch break; view sponsor stands
14:00 – 14:30	A 10 year review of IFD management in Haemato-Oncology (continued) Emerging antifungal resistance in <i>Aspergillus sp.</i> – a clinical issue? <i>Prof. Paul Verweij, Microbiology, Nijmegen, The Netherlands</i>
14:30 – 15:45	Candidiasis A 10 year review of antifungal management in ICU <i>Prof. Chris Kibbler, Centre for Clinical Microbiology, University College London</i> Candida (ESCMID) guidelines – where are we going? <i>Prof. Maiken Arendrup, Unit of Mycology, Statens Serum Institut, Denmark</i> Candida diagnosis – PLEX-ID in clinical practice <i>Dr. Mark Wilks, Microbiology, Barts Health NHS Trust, London</i>
15:45 – 16:00	Tea break; view sponsor stands
16:00 – 16:50	Case Presentations Cases, with interactive keypad voting, highlighting diagnostic and treatment challenges <i>Dr. Jonathan Lambourne, Infectious Diseases & Microbiology, Hospital for Tropical Diseases, London</i> <i>Dr. Subathira Dakshina, Genito-Urinary Medicine & HIV, Bart's Health NHS Trust, London</i>
16:50 – 18:00	Break – check in to hotels
18:00	Evening reception
18:00 – 18:30	Drinks reception Mycology Quiz <i>Dr. Liz Johnson, National Mycology Reference Centre, Bristol</i>



18:30 – 19:30	<p>Debate</p> <p>“This house believes that radiology and clinical acumen are sufficient to guide IFD management, without the need for biomarkers”</p> <p>Chair: <i>Prof. Peter Donnelly</i></p> <p>Proposers: <i>Drs. Keith Wilson (BMT Unit, Cardiff) & Vanya Gant (Microbiology, UCLH, London)</i></p> <p>Opposers: <i>Drs. Brian Jones (Microbiology, Glasgow) & Stephen Ellis (Imaging, Barts, London)</i></p>
19:30	Dinner

Saturday 10th January 2015

08:45 – 08:50	Introduction from the Chairs
08:50 – 09:50	<p>Fungi in the setting of HIV</p> <p>Current management and future directions in cryptococcosis <i>Prof. Tom Harrison, Infection & Immunity Research Institute, St. George's, London</i></p> <p>Current management and future directions in Pneumocystis infection <i>Prof. Rob Miller, Institute of Epidemiology and Health, University College London</i></p>
09:50 – 10:30	<p>A 10 year review: Mycological Research</p> <p>Demystification of the ‘accidental’ pathogen <i>Aspergillus fumigatus</i> <i>Dr. Elaine Bignell, Institute of Inflammation & Repair, University of Manchester</i></p>
10:30 – 11:45	<p>For attendees of this 10th anniversary meeting, the world-renowned Canterbury Cathedral Boys Choir will perform a special recital in the historic setting of St Bartholomew's The Great Church</p> <p>Tea break; view sponsor stands</p>
11:45 – 12:25	<p>A 10 year review: Mycological Research (continued)</p> <p>The role of the cell wall in determining host-fungus interactions <i>Prof. Neil Gow, Institute of Medical Sciences, University of Aberdeen</i></p>
12:25 – 13:05	<p>Host determinants of response – an emerging story of mould pathogenesis <i>Dr. Frank van de Veerdonk, Nijmegen, The Netherlands</i></p>
13:05 – 13:15	<p>Clinical research and F.A.T. <i>Dr. Samir Agrawal, Haemato-Oncology, Barts Health NHS Trust, London</i></p>
13:15 – 13:30	Summing up and close by the Chairs
13:30	Close; view sponsor stands; departures; enjoy London!



Speaker Biographies and Abstracts

Dr. Samir Agrawal



Senior Lecturer in Haematology, Queen Mary University of London and Consultant Haemato-Oncologist at Barts Health NHS Trust

Dr Agrawal qualified initially at the University of Bristol and subsequently trained at The Royal Marsden Cancer Hospital, being awarded his PhD (in Immunology) at the University of Paris. He is a fluent French speaker.

He is Director of The Stem Cell Laboratory and Head of Diagnostic Immunophenotyping. He has designed, funded, and implemented studies on myelodysplastic syndromes, invasive aspergillosis, and chronic lymphocytic leukaemia. He is a member of the UK CLL trials committee and trustee for CLLSA (the patient-led support organisation for patients in the UK with CLL), as well as a

NICE reviewer and the Haemato-Oncology representative on the UK IVIg initiative.

His current activities in the field of invasive fungal disease are:

- an ongoing diagnostic study of high-risk haematology patients looking at early diagnosis
- developing clinical guidelines for managing IFD in the high-risk haemato-oncology setting
- promoting best practice and highlighting new developments through educational meetings and a new website for all interested in fungal disease (www.fungalcentral.com, currently in development)

Abstract: Clinical research and F.A.T.

The challenge of antifungal management in clinical practice is that of diagnosis and balancing “carpet-bombing” with antifungals and the associated toxicities and drug costs versus the fear of missing a case of invasive fungal disease (IFD). Furthermore, this area is confounded by the lack of data on actual practice in any given unit or hospital. I will present the evolution of IFD strategies in Haemato-Oncology at Barts over 15 years; the move to a diagnostic approach with TRIADx; the development of the fungal audit tool (F.A.T.), modified for stewardship (F.A.T.(s)) purposes, to provide local data and summary outputs in real-time.

Prof. Rosemary Barnes



Professor of Medical Microbiology in the Department of Medical Microbiology and Infectious Diseases within the Institute of Infection and Immunity at the School of Medicine at Cardiff University

Prof. Barnes works as an honorary consultant for Public Health Wales at the University Hospital of Wales.

Her interests include infections in immunocompromised patients and the treatment and rapid diagnosis of invasive fungal infection.

She is currently president of the British Society of Medical Mycology and previous Chair of the UK Clinical Mycology Network

She is a founding member of the European Aspergillus PCR Initiative Working Group of the International Society for Human and Animal Mycology and a board member of the

foundation European Aspergillus PCR initiative.

She is a member of the Steering Group of the NISCHR funded Microbiology and Translational Infection Research Group.



Abstract: Diagnostics in clinical practice: 10 years on, have we moved forward?

Ten years ago, despite the availability of molecular and antigen-based diagnostic tests, empirical use of antifungal agents was the accepted standard of care in a febrile neutropenic patient. Confirmed invasive fungal infection rarely occurred ante mortem, and more than 60% of patients received expensive and often harmful drugs because a diagnosis of potentially fatal fungal infection could not be excluded. The clinical utility of the diagnostic tests was largely unknown and the frequency of false positive or false negative results limited their ability to impact on patient management.

The last decade has seen standardization of molecular tests and a greater understanding of diagnostic accuracy. Studies demonstrate that both antigen and molecular assays can be used to exclude a diagnosis of invasive aspergillosis in patients not already receiving mould-active antifungal drugs but individually cannot reliably predict disease. However several recent studies have shown that combination testing with galactomannan and PCR have a good positive predictive value and can be used to rule in a diagnosis of invasive aspergillosis, often before overt disease with radiological changes has occurred. This not only reduces unnecessary empirical antifungal drug use and excess hospital costs but can also improve patient outcomes.

Combined with this, improved understanding of host factors and the immune response to fungal infection is enabling us to use our new genomic and proteomic technologies to target diagnostics at patients most at risk. This heralds a new era of personalized medicine in the field of clinical diagnostics.

Dr. Mansour Ceesay



Consultant Haematologist at Princess Royal University Hospital/King's College Hospital NHS Foundation Trust

Following basic medical training Dr Ceesay did an MSc in Communicable Disease Epidemiology at the London School of Hygiene & Tropical Medicine before pursuing general medical training and gaining Membership of the Royal College of Physicians in the UK.

He then pursued specialist training in Haematology at the London Deanery on King's rotation and became a Fellow of the Royal College of Pathologists. He recently completed a three year research programme on the diagnosis and management of

invasive fungal disease in haematology patients undergoing haematopoietic stem cell transplantation and intensive chemotherapy and was awarded MD (Res) by King's College London.

Abstract: Diagnostics in clinical practice: 10 years on, have we moved forward?

Invasive fungal diseases (IFD) continue to pose a serious threat to the immunocompromised host. The number of agents used by haematologists for the treatment of the underlying malignancy continues to increase and traditional boundaries of immunosuppression have become blurred. Progress in molecular biology is enabling identification of genetic risk factors which may amplify any acquired risk factors. While progress has been made in the diagnostics of IFD, management of patients lags behind this progress. Or is this the view of the pessimist?

In this talk we will review what progress or lack of it (in the eyes of the haematologist) has been made in the last 10 years and where this is likely to lead to in the next decade.



Dr. Chris Thornton



Associate Professor of Fungal Immunology at the University of Exeter

My research encompasses fungal biology and immunology, specialising in hybridoma technology and the use of monoclonal antibodies to track human pathogenic fungi.

My University research on point-of-care diagnostics for human mycoses has been patented and in 2012 I established a University spin-out company ISCA Diagnostics Ltd. for commercialisation of a novel lateral-flow device for diagnosis of invasive pulmonary aspergillosis in immunocompromised patients.

Abstract: New monoclonal antibodies

Fungi (yeasts and moulds) are an increasingly important group of human pathogens, causing frequently fatal opportunistic infections in immunocompromised individuals. *Aspergillus fumigatus*, the cause of invasive pulmonary aspergillosis, is the most common mould pathogen of haematological malignancy and solid organ and bone marrow transplant patients, but other fungi have emerged over recent years as pernicious pathogens causing superficial and disseminated infections in both sick and seemingly healthy individuals.

Rapid diagnosis of disseminated infections and identification of the infectious organisms are crucial for patient survival, and accurate and sensitive diagnostic procedures are urgently required to allow timely treatment with appropriate mould active drugs.

In this talk, I will present recent work on the development and clinical application of a lateral-flow device for the rapid diagnosis of IPA using serum and bronchoalveolar lavage fluids. In doing so, I will demonstrate how monoclonal antibodies specific to other mould and yeast pathogens including *Candida*, *Fusarium*, *Scedosporium*, and *Trichosporon*, could be used to track infections.

Dr. Gemma Johnson



Faculty of Medical Science, Anglia Ruskin University, Chelmsford

Gemma gained her BA and MA in Genetics from the University of Cambridge (2004). She has an established track record inventing, developing and validating molecular methods for pathogen detection at Barts Health NHS Trust (2005-2010) and Queen Mary University of London (2010-2014).

Gemma's main focus has been on fungal diagnostic research and she has published on the complexities of Aspergillosis diagnosis in the Haemato-Oncology setting.

She was awarded her PhD in diagnostic tool development for invasive fungal infections in December 2014 and is now working as a Consultant Scientist at Anglia Ruskin University and as a Healthcare Scientist for Public Health England, developing

biomarker tests for pathogen detection.



Prof. Stephen Bustin



Professor of Molecular Medicine at Anglia Ruskin University, Chelmsford

Stephen Bustin obtained his PhD in Molecular Genetics from Trinity College, University of Dublin, was Professor of Molecular Science at Queen Mary University of London, Visiting Professor at the University of Middlesex and is currently Professor of Molecular Medicine at Anglia Ruskin University in the UK.

He has authored numerous papers, review articles and book chapters aimed at improving the reproducibility and robustness of real-time quantitative PCR (qPCR), including the "A-Z of quantitative PCR" (2004), "The PCR Revolution" (2011) and "PCR Technology" (2013).

He has published the first online series of qPCR-related books under the title of "Definitive qPCR" (www.qPCRexpert.com). Professor Bustin was an expert witness advising the UK High Court on qPCR technology in the Measles Mumps Rubella (MMR) vaccine - Autism class action as well as at the MMR trial in Washington DC in 2007. He led an international consortium developing the MIQE guidelines for the use and reporting of qPCR (2009) and digital PCR (2013).

His research interests include identifying prognostic biomarkers for colorectal cancer and, more recently, developing novel approaches to the early diagnosis of fungal and bacterial pathogens. Professor Bustin has extensive editorial involvements as Editor-in-Chief, Biomolecular Detection and Quantification (Elsevier), Editor-in Chief (Gene Expression), International Journal of Molecular Sciences, and as a member of the editorial boards of "Nature Scientific Reports", "Gene Regulation and Systems Biology" and "Biomarkers in Medicine".

Abstract: Molecular tools for nucleic acid and protein detection

Antibody- and real-time quantitative (qPCR)-based assays are proving useful for a more sensitive and specific identification of *Aspergillus* in clinical samples. However, both approaches have important shortcomings: the relative insensitivity of current antibody-based strategies, such as enzyme-linked immunosorbent assays and immunohistochemistry, makes them less suitable for earliest possible diagnosis, whereas the mere detection of pathogen DNA is uninformative with regards to its viability or infectivity. Hence the ultimate assay would combine the specificity of pathogen-specific antibody detection with the sensitivity of qPCR. Proximity Ligation Assay (PLA) and Proximity Extension Assay (PEA) technologies use qPCR to detect the interaction of antibodies with their specific antigens.

In this session we shall present an overview of the strengths and limitations of existing antibody- and qPCR-based assays and explore the ways in which PLA and PEA technologies could improve the sensitivity and specificity of fungal diagnostics, whilst reducing hands-on time and time to result.

Digital PCR (dPCR) promises to enhance the sensitivity of nucleic acid detection by carrying out the PCR reaction in numerous partitions and is particularly suited to the precise quantification of rare nucleic acid targets. We have substituted the qPCR-detection step of the PLA with a dPCR approach to develop a digital PLA (dPLA) assay and shall present data to demonstrate the potential for greater precision as well as sensitivity of detection of pathogen-specific proteins.



Prof. Paul Verweij



Paul Verweij is Professor of Medical Microbiology and Consultant Microbiologist at the Department of Medical Microbiology at Radboud UMC in The Netherlands

Dr Verweij's research interests include diagnosis of invasive aspergillosis, resistance in molds, and clinical studies of new antifungal agents.

He recently has published on the relationship between resistance to medical triazoles in the opportunistic fungus *Aspergillus fumigatus* and the use of azole fungicides for crop protection and material preservation.

Abstract: Emerging antifungal resistance in *Aspergillus* sp. – a clinical issue?

Itraconazole, voriconazole and posaconazole are the main azole drugs we currently use for the prevention and treatment of aspergillus diseases, including invasive aspergillosis. However, in the last decade acquired resistance of *Aspergillus fumigatus* to azoles has emerged.

Currently two routes of resistance selection are recognized: through patient therapy and through the use of azole fungicides in the environment. Resistance development during azole therapy occurs in patients that have cavitory aspergillosis, i.e. aspergilloma or chronic cavitory aspergillosis, and receive chronic azole therapy. Inside the cavity the fungus may sporulate, which is thought to enhance the risk of resistance selection. In many countries azole resistance has been reported in the environment. It is believed that the use of azole fungicides for crop protection may cause *A. fumigatus* to become resistant to these compounds. Since the molecule structure of certain azole fungicides is very similar to that of the medical triazoles, the latter will also be inactive.

Clinically, environmental resistance has major implications for patient management. There are no apparent risk factors and patients who are hospitalized with aspergillus disease may harbour an azole-resistant isolate without ever having been treated with azole drugs. The presence of these resistance mutations commonly results in a pan-azole-resistant phenotype, and animal models show that azole resistance is associated with treatment failure. Clinical cases reported in the literature indeed suggest that the probability of treatment failure is increased in patients with azole-resistant aspergillosis. Surveillance studies indicated a mortality rate of 88% in (primarily) haematology patients with azole-resistant invasive aspergillosis and a rate of 100% in ICU-patients.

In many countries the prevalence of azole-resistance in *A. fumigatus* is low, i.e. below 5%. This indicates that the probability of azole-resistant aspergillosis is still low. However, given the high mortality rates, it is important to monitor patients with invasive aspergillosis intensively, especially in areas where azole-resistant *A. fumigatus* has been recovered from the environment. Physicians are encouraged to establish a mycological diagnosis and clinical microbiology laboratories should test for azole resistance in patients where *A. fumigatus* is cultured and treatment is intended.

In cases of documented azole-resistant aspergillosis the use of azole monotherapy should be avoided, with liposomal amphotericin B or voriconazole combined with an echinocandin as preferred alternative treatment options.



Prof. Chris Kibbler



Professor of Medical Microbiology, Centre for Clinical Microbiology, University College London

He has been a member of the European Organisation for Research and Treatment of Cancer-Invasive Fungal Infections Group (EORTC-IFIG) Steering Committee and has also been Chair of the UK National Advisory Committee on Fungal Infection, Chair of the UK Clinical Mycology Network and a member of the European Conference on Infections in Leukaemia (responsible for producing the ECIL guidelines for the management of these infections).

Professor Kibbler is Past President of the British Society for Medical Mycology and Programme Director of the BSMM/UCL International MSc/Diploma in Medical Mycology.

His research interests include infections in the immunocompromised host and mycology, especially diagnostic, therapeutic, and pathogenic aspects of infections caused by *Candida* and *Aspergillus* species.

Abstract: A 10 year review of antifungal management in ICU

2004 saw the 10th anniversary of Pittet's paper on the candida colonisation index as a risk factor for invasive candidiasis¹. However, little had changed since Solomkin identified colonisation as a risk factor in 1982². Many involved in infection management on the ICU would take candida colonisation into account when making decisions about antifungal therapy, but most considered the calculation of the index too complex and of little benefit.

Indeed, most progress in the intervening years had been in epidemiology. A number of studies had been published demonstrating that ICUs were the dominant source for candidaemia, but that the incidence was low and varied by country. In the UK, the incidence was 0.7% overall in a study published in 2003³, compared with higher incidences in the US and Europe. These studies also defined a number of risk factors for invasive disease, most of which included abdominal surgery and total parenteral nutrition. It was also clear that ICU candida infection carried a high mortality (> 40% 30-day all-cause mortality)⁴.

So, the stage was set for the development of antifungal strategies along the lines of those being used in haematology units. However, the difficulty has been around the low overall incidence of candida infection and the heterogeneous nature of the ICU case mix in most centres. This talk will discuss the evolution of prophylaxis, empirical therapy and risk-based clinical decision rules over the past decade and will attempt to define the optimal current management strategy.

References:

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2. Solomkin JS, Flohr A, Simmons RL. Indications for therapy for fungaemia in postoperative patients. *Arch Surg* 1982;117:1272-1275
3. Kibbler C C, Seaton S, Barnes RA, Gransden WR, Holliman RE, Johnson EM, et al, Management and outcome of bloodstream infections due to *Candida* species in England and Wales. *J Hosp Infect* 2003; 54:18-24
4. A. M. Tortorano, J. Peman, H. Bernhardt, L. Klingspor, C. C. Kibbler, O. Faure, E. Biraghi, E. Canton, K. Zimmermann, S. Seaton, R. Grillot, and the ECMM Working Group on Candidaemia. Epidemiology of Candidaemia in Europe: Results of 28-Month European Confederation of Medical Mycology (ECMM) Hospital-Based Surveillance Study. *Eur J Clin Microbiol Infect Dis* 2004; 23: 317-322



Prof. Maiken Arendrup



Unit of Mycology, Statens Serum Institut, Denmark

Dr Maiken Cavling Arendrup obtained her medical degree from Copenhagen University, Denmark, in 1988, followed by a PhD degree on neutralizing antibodies and HIV infection in 1992. In 2001, she completed further training as a specialist in clinical microbiology and in September 2013 her doctoral thesis on epidemiology and susceptibility of candidaemia was defended for the Dr. Med. Sci degree.

Currently, Dr Arendrup is Head of the Mycology Unit at Statens Serum Institut, Copenhagen, where she is responsible for the fungal laboratory, which receives 15,000 routine and reference samples per year for culture, susceptibility testing,

antigen- and antibody-detection, and PCR as well as for the semi-national surveillance of invasive fungal infections. She has also been responsible for the supervision of several PhD students.

Dr Arendrup was a founder of the Nordic Society of Medical Mycology (NSMM) and has been president since the formation of the society in 2003 until 2013. She is chair of the EUCAST Antifungal Susceptibility Testing Subcommittee Steering Committee, and head of the EUCAST Development Laboratory for fungi, a member of ESCMID Scientific Affairs Subcommittee (SAS) and an editor for Drug Resistance Updates. In 2005-9 and 2011-13 she has served as a European Confederation of Medical Mycology (ECMM) delegate on the executive organizing committee for TIMM-3 and 4 and as delegate for NSMM for the TIMM 6 in Copenhagen. She is on the international scientific committee for TIMM 7 in Lisbon, and has served as advisor for the CLSI committee for 4 years.

Dr Arendrup has authored more than 140 publications in international journals and as book chapters. She has received two research awards (Fritz Kauffman's reward in 2003 and The Danish Society for Clinical Microbiology's research award in 2010). Her main research interests include the epidemiology, susceptibility, breakpoint development, diagnostics and treatment of fungal infections.

Abstract: Candida (ESCMID) guidelines – where are we going?

Over the past decade, various organisations have prepared guidelines for the management of Candida infections. Some of these discuss the management of Candida infections from a clinical presentation point of view (e.g. treatment of Candida vaginitis) or targeting specific risk groups like the European Conference on Infections in Leukaemia (ECIL) guidelines. Others are developed with the local epidemiology and economic situation in focus (e.g. the Danish RADS guidelines on the management of invasive fungal infection) or by national infectious disease societies including the Infectious Disease Society of America (IDSA).

The ESCMID guideline for the diagnosis and management of Candida disease 2012, was coordinated by the ESCMID Fungal Infection study group (EFISG), and aimed to cover all aspects of Candida disease in four risk-subgroups of patients, namely ICU patients, paediatric, HIV/AIDS and patients with malignancies including haematopoietic stem cell transplantation. Finally, guidance for diagnostic procedures was made.

The diagnostic armamentarium for diagnosing invasive candidiasis includes direct detection by culture of blood or specimens from other normally sterile sites, and indirect detection, using Candida biomarkers (β -D-glucan, or Candida mannan antigen and antimannan antibodies) or fungal DNA by PCR. None are perfect and hence it is necessary to combine several diagnostic tests for maximal diagnostic accuracy. Susceptibility testing must be recommended for patient management for all Candida strains isolated from blood and other deep sites and is particularly important for patients exposed to antifungal agents, isolates from patients with clinical failure, and strains belonging to rare and emerging species. Importantly, interpretation of antifungal susceptibility testing results requires expertise and cautious evaluation.

Prophylactic usage of fluconazole is recommended in patients with recent abdominal surgery and recurrent gastrointestinal perforations or anastomotic leakages. For the targeted initial treatment of candidaemia and most other forms of invasive candidiasis, echinocandins are highly recommended. Exceptions are patients with meningitis, endophthalmitis, and urinary tract candidiasis, in which echinocandins are limited by their pharmacokinetics. Moreover, echinocandins should be prescribed cautiously to patients pre-exposed to echinocandins for prolonged periods of time. De-escalation to oral fluconazole was recommended after 10 days



of intravenous therapy in stable patients with susceptible *Candida* species. Earlier step down may be appropriate but lacks systematic validation.

Recommendations for the management of candidiasis in children are largely extrapolated from studies performed in adults. Main differences are related to the fact that the species distribution is different (less *C. glabrata* and more *C. parapsilosis*) and that the CNS is often involved in neonatal candidiasis where the echinocandins achieve poor concentrations.

Finally, recommendations for *Candida* disease in cancer patients were made. These are basically similar to those for the non-neutropenic population with respect to targeted treatment of documented infection. Regarding prophylaxis, recommendations were also made but in this patient population prevention of aspergillosis may be needed and thus will include specific prophylaxis of *Candida* infection.

Since the ESCMID *Candida* guidelines were finalised, the ESCMID operating procedure has been updated. The main changes are that: 1) Guidelines will be commissioned by the EC rather than by study groups; 2) There will be a core set of guidelines that are important for European practice; 3) Guidelines will be regularly revised (every 2-4 years) to ensure they are up to date; 4) There will be an emphasis on ensuring that guidelines will be used by doctors (i.e. not just an academic exercise where the main outcome is an improved H-index for the authors); 5) Ensuring a period of public consultation at the ESCMID website similar to what is current practise for EUCAST susceptibility testing and breakpoint documents; and 6) obligation to comply with the AGREE and GRADE systems and active management of conflicts of interest.

Hopefully, these initiatives will facilitate continuous updates that will allow the *Candida* guidelines to incorporate the changing epidemiology and the emergence of resistance, the new diagnostic tests including PCR, MALDI-TOF identification and susceptibility tests and thereby provide better outcomes for patients with invasive candidiasis. This goal can only be achieved by early intervention strategies, based on a combination of clinical prediction rules, nonculture tests, such as biomarkers, and – ultimately – even personalized, immunogenetics-based risk profiles.

Dr. Mark Wilks



Microbiology, Barts Health NHS Trust, London

Dr Mark Wilks is Lead Clinical Scientist in Microbiology at Barts Health NHS Trust and an Honorary Senior Lecturer in Microbiology at Barts and the London School of Medicine and Dentistry, part of Queen Mary, University of London.

His interests include molecular diagnostics and the application of mass spectrometry in diagnostic microbiology.

Abstract: *Candida* diagnostics: PLEX-ID in clinical practice

The Abbot PLEX-ID/ Iridica system consisting of multiple PCRs followed by electrospray ionization mass spectrometry (PCR/ESI-MS) has the potential to detect ~800 bloodstream infection (BSI)-relevant pathogens in a single assay and in approximately 8h.

Here we describe findings from a European multicentre observational study called RADICAL (Rapid Diagnosis of Infections in the Critically Ill). The primary objective of the study was to compare results obtained from the PCR/ESI-MS technology with those obtained from standard microbiological testing as a measure of clinical performance.

The study included 543 adult patients with suspected sepsis, pneumonia, or sterile fluid or tissue infection admitted to one of nine intensive care units (ICUs) in six European countries.



Culture/PCR comparisons for BSI samples were as follows: both positive in 54 cases; culture positive/PCR negative in 13; culture negative/PCR positive in 169; and both negative in 380, with a sensitivity for PCR/ESI-MS of 81%, specificity 69%, positive predictive value (PPV) 24% and negative predictive value (NPV) of 97%.

The largest single discrepancy between the two methods by number of detections was in the identification of *E. coli*. While both culture and PCR/ESI-MS reported *E. coli* as the most abundant species, culture reported 4X fewer *E. coli* (21 vs. 89). Similarly *Candida* species, (*C. albicans*, *C. glabrata*, *C. tropicalis*) were detected by PCR/ESI-MS in 15 specimens, although on only two occasions were they confirmed by culture, both of these isolates were *C. albicans*. The significance of these results and the potential of this and other molecular technologies to change the diagnosis of fungaemia will be discussed

Dr. Jonathan Lambourne



Specialty Trainee in ID & Microbiology, Hospital for Tropical Diseases (appointed as Consultant in Infectious Diseases, Barts Health NHS Trust)

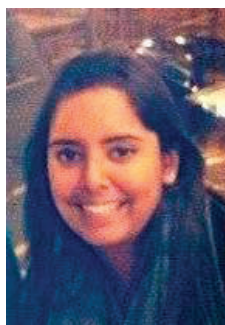
Dr Lambourne completed his PhD at St George's University of London, identifying mannose-binding lectin deficiency as a risk factor for invasive aspergillosis.

His particular interests are in infections in the immunocompromised, infections in the returning traveller and the evaluation of techniques to increase the diagnostic hit-rate in these patient groups.

Abstract: Case Presentation

I will present a case highlighting how routine diagnostic algorithms may generate misleading results, the importance of the mycology reference lab and the role of 'emerging' technologies.

Dr. Subathira Dakshina



Third year specialist registrar in Genito-Urinary Medicine and HIV at Bart's Health NHS Trust, London

She has a special interest in HIV and opportunistic infections and is currently the ward registrar at the Royal London Hospital.

In 2014 she won the BHIVA-Abbott-St Stephen's AID Trust exchange scholarship to Zimbabwe and leading on from this is about to embark on a six months out of programme experience to Zimbabwe to help aid the decentralisation of HIV care through training local healthcare professionals in the primary care setting.



Dr. Liz Johnson



Consultant Clinical Scientist in Medical Mycology, Director of the Public Health England Mycology Reference Laboratory, Bristol

Elizabeth M Johnson has been working in the field of medical mycology for more than 25 years and is the Director of the Public Health England National Mycology Reference Laboratory and curator of the National Collection of Pathogenic Fungi (Bristol, UK). Her particular interests are in the areas of antifungal drugs, and the diagnosis and identification of pathogenic fungi. In line with this she runs an annual 4-day course for 50 participants on fungal identification.

Dr Johnson has published many papers and chapters on fungal infection, antifungal susceptibility testing and resistance, and has co-authored two books which are both on their second editions. She is a former President of the British Society for Medical Mycology, a Clinical Scientist assessor for ACB, has served as an editor for the Journal of Antimicrobial Chemotherapy, an advisor for the Clinical and Laboratory Standards Institute (CLSI) and is a mycology section editor for the Manual of Clinical Microbiology.

Prof. Peter Donnelly



Radboud University Nijmegen Medical Centre and Nijmegen Institute for Infection, Nijmegen, The Netherlands

Professor Peter Donnelly is Coordinator of Studies in Supportive Care at the Department of Haematology, and is a member of the Nijmegen Institute for Infection, Inflammation and Immunity, Nijmegen, The Netherlands. He is Chair of the Infectious Disease Group of the European Organisation for Research and Treatment of Cancer (EORTC), General Secretary to the International Society for Human and Animal Mycology (ISHAM), Chair of the ISHAM Working Group – European Aspergillus PCR Initiative (EAPCRI), and a member of the European Group for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party. He is also a Fellow of the Royal College of Pathologists.

Professor Donnelly graduated with a Bachelor of Science from the University of Glasgow, UK, in 1974, earning his PhD on the topic of 'Viridans streptococci and allogeneic bone marrow transplant' in 1993. After working in Microbiology Technician posts at Gartnavel General Hospital, Glasgow, UK, and as Senior Scientific Officer at Hammersmith Hospital, London, UK, he moved to the Medical Microbiology department of the University Hospital Nijmegen, The Netherlands, in 1987 and became a staff member of the Department of Haematology.

His current research interests are the epidemiology, diagnosis and management of invasive fungal diseases, mucosal barrier injury, and infection and infectious complications of the neutropenic patient. Professor Donnelly is author of over 200 research and review papers and 15 book chapters. As of January 2015 he will be the new Editor in Chief of the Journal of Antimicrobial Chemotherapy. He also is a regular reviewer for top peer-reviewed journals including the Lancet Infectious Diseases and Clinical Infectious Diseases.



Dr. Keith Wilson

Senior Lecturer/Honorary Consultant Haematologist, Programme Director for South Wales Blood and Marrow Transplant Programme

Dr. Vanya Gant



Consultant in Microbiology and Infectious Diseases, and Divisional Clinical Director at University College London Hospitals NHS Foundation Trust

Statement

I have been practising ward-based infectious diseases medicine and microbiology for over 20 years. My main interest at work is diagnosing and treating fever in patients with immune deficiencies, mostly due to cancer, treatment for leukaemia or bone marrow transplantation. I am also interested in the emerging evidence that probiotics can and sometimes do work for restoring and maintaining health, and I strongly believe that antibiotics are used far too freely and unnecessarily, sometimes with adverse effects.

Medical training

Dr Vanya Gant studied medicine at the Middlesex Hospital in London and qualified in 1980. He then gained a decade of clinical experience in general hospital medicine, treating patients across several medical specialities. He studied for and gained a PhD in cellular immunology and has since then focused his clinical work within the field of microbiology and infectious diseases.

He has held the following posts:

- Senior Lecturer in Microbiology at Guy's and St Thomas' Hospitals: Dr Gant held this post for five years, during which time he established a specialist clinical infection service, delivered at the bedside of patients in intensive care and in HIV inpatient units.
- As Clinical Director at the University College London Hospitals NHS Foundation Trust he formed the Division of Infection.

Current appointment

Dr Vanya Gant is Consultant in Microbiology and Infectious Diseases and Divisional Clinical Director at University College London Hospitals NHS Trust where he has responsibility for an inpatient infectious diseases ward, which also houses the UK's World-renowned Hospital for Tropical Diseases. He also has specific responsibility for matters of Infection Control in the Trust's large haematology inpatient Unit. He is also responsible for London's Tuberculosis Find and Treat Service, a unique London-based organisation which diagnoses TB and ensures treatment completion in the hard-to-access homeless, who often have several other problems, such as Hepatitis C as well as drug and alcohol dependency.

Dr Gant continues to be research-active and is currently Clinical Principal Investigator for an EU-funded £5 million rapid Diagnostics Grant and has published over 70 papers relating to infection.



Dr. Brian Jones



Consultant Microbiologist & Head of Service, NHS GGC, Glasgow

Dr. Jones trained in Immunology and Medicine at the University of Glasgow. He completed his postgraduate training in Medical Microbiology in Edinburgh, Glasgow and Cambridge, taking up his current appointment in 1996.

In addition to his role as Head of Service, Dr. Jones is the Medical Director of the Scottish Parasite Diagnostic and Reference Laboratory, Director of the Scottish Haemophilus, Legionella, Meningococcus, Pneumococcus and Streptococcus Reference Laboratories and Lead Microbiologist for the Beatson West of Scotland Cancer Centre, the Princess Royal Maternity Hospital and the Antimicrobial Management Team for NHS GGC. He is also the designated microbiologist for the stem cell transplant programme at the WoSCC.

Dr. Jones is the lead for infection teaching in the undergraduate medical school curriculum and holds an honorary post as Clinical Associate Professor in the College of Medical, Veterinary and Life Sciences at the University of Glasgow. He is also an examiner for the Royal College of Pathologists and a clinical expert advisor to the Scottish Medicines Consortium.

He has developed an amateur interest in fungal diagnostics and is a member of the Clinical Working Party of EAPCRI.

Abstract: Debate

Dr Jones will use skills honed in the white heat of the recent Scottish referendum debate to convince the audience that biomarkers do indeed have an important role to play in the management of invasive fungal disease.

Dr. Stephen Ellis



Imaging, Barts and the London NHS Trust, London

Dr Ellis qualified from Cambridge in 1991 and has been the lead Consultant Thoracic Radiology consultant at Barts and the London NHS Trust since 2002. He trained in radiology at Kings College Hospital followed by a 2 year fellowship in thoracic radiology at the Royal Brompton Hospital. He has given numerous lectures both nationally and internationally and he is the author of the "WHO manual of diagnostic imaging, radiographic anatomy and interpretation of the chest and the pulmonary system" and more recently the book "Interpreting Chest X-Rays (SCION Publishing)". He was recently appointed as the Clinical Lead for the Royal College of Radiologists e-learning project - RITI.

Abstract: Debate

The utility of imaging in the diagnostic pathway is well established and in the face of normal CXR in an immunocompromised patient, with symptoms of infection, a CT chest is part of standard management. CT findings form part of the EORTC criteria for diagnosis of fungal infection. The CT performed should be a volume scan without IV contrast and the negative predictive value is quite high. Where imaging falls down is in the characterisation of infection. The EORTC criteria reflect this considering a new infiltrate as a major finding, which could be anything from a small nodule to extensive cavitating consolidation. Even the famous halo sign is only included as a +/- feature. In the context of suspect infection in an immunocompromised patient the decision to treat may be aided by imaging but the decision of how to treat requires more data.



Prof. Tom Harrison



Tom Harrison is Professor of Infectious Diseases and Medicine, and Deputy Director of the Institute for Infection and Immunity, at St Georges University of London, and Honorary Consultant at St Georges Hospital, London

Prof. Harrison trained in Infectious Diseases in London and Boston, USA. His initial research training was in Boston, where he worked on immune responses to *Cryptococcus neoformans*. He leads a clinical research programme on cryptococcal meningitis, developed first in Thailand, and subsequently across sites in Sub-Saharan Africa. He is also involved in phase II and III clinical trials on the chemotherapy of tuberculosis. He has served on the cryptococcal guidelines panels of the IDSA, The Southern African HIV Clinicians Society, and WHO.

Abstract: Current management and future directions in cryptococcosis

Deaths related to HIV-associated cryptococcal meningitis remain unacceptably high, probably between 100,000 and 300,000 per annum, with the burden particularly high in Southern and East Africa, and no significant decrease in cases in recent years. The high burden is driven in large part by the high associated mortality rate for cryptococcal meningitis in Sub-Saharan Africa, estimated at 70% at 90 days. The challenge remains of translating progress in diagnostics, antifungal therapy, and management and prevention of complications, into routine practice reductions in cryptococcal specific mortality.

The case for screening HIV-seropositive patients presenting for ART with a low CD4 cell count, and pre-emptive fluconazole for cryptococcal antigen positive individuals is strong and prospective programmes and studies are ongoing, enabled by the new point-of-care cryptococcal antigen test. We should be realistic, however, about expected outcomes. While screening should prevent unmasking cryptococcal IRIS cases, most ART-experienced patients now presenting with cryptococcal meningitis are not unmasking IRIS but simply ART failure due to non-adherence and ART resistance.

Earlier diagnosis of symptomatic cases is essential and may be an equally important use of the point-of-care diagnostic test - if the test could be made widely available. Antifungal regimens that can clear infection more rapidly than fluconazole at up to 1200 mg /d, but that are more readily and safely sustainable in resource-limited settings than 2 weeks of amphotericin B-based induction, are being tested in a phase III trial: fluconazole plus flucytosine, and short course (1 week) amphotericin B induction. Intermittent high dose Ambisome also holds promise for rapid and safe induction that could be practical in all settings. Management of raised CSF pressure through careful therapeutic lumbar puncture and timely initiation of ART, probably at around 4 weeks into antifungal therapy, are also vital.

In addition, more work is needed to understand protective host immune responses, the evolution and virulence of the organism, and the pathophysiology of infection in all patient groups. Studies rooted in the clinic hold out the promise of advances in our understanding of both host and pathogen that may ultimately translate into novel preventative and therapeutic strategies.



Prof. Rob Miller



Institute of Epidemiology and Healthcare, University College London

Professor Rob Miller is Reader in Clinical Infection at University College London, and Honorary Consultant Physician at Camden Provider Services, CNWL, NHS Foundation Trust, and at University College London Hospitals NHS Foundation Trust. Since 1987 he has worked clinically in the field of HIV care, being based on the inpatient unit (originally at the Middlesex hospital, now at UCL Hospitals).

His research focuses on the respiratory complications of HIV infection, specifically *Pneumocystis jirovecii* pneumonia and tuberculosis, ICU outcomes for HIV-infected patients and infectious and malignant pleural disease among the general population. Rob is Editor in Chief of British Journal of Hospital Medicine, and was previously co-

Editor of Sexually Transmitted Infections. He has co-edited four books on aspects of HIV/AIDS and additionally has over 500 publications, including peer review articles, reviews, case reports, and book chapters.

Abstract: Current management and future directions in *Pneumocystis* infection

The opportunistic fungus *Pneumocystis jirovecii* is the cause of pneumonia (PCP) in HIV-infected and other immunocompromised patients. While there has been a reduction in HIV-associated PCP, it is increasingly recognised among those who are medically-immunosuppressed.

This presentation will focus on:

- 1) Identifying HIV-infected and non-HIV infected immunosuppressed patients at risk of developing PCP.
- 2) Diagnostic tests - and their pitfalls - specifically molecular detection and serological assays (including LDH, AdoMet and beta-glucan).
- 3) Treatment of PCP - and troubleshooting when things go wrong.
- 4) Novel treatment regimens.
- 5) New disease associations.

Dr. Elaine Bignell



Institute of Inflammation and Repair, University of Manchester

Elaine Bignell is a Reader in Applied Mycology at the University of Manchester and Deputy Director of the Manchester Fungal Infection Group (MFIG). Elaine has more than 20 years of experience in molecular genetic manipulation of model and pathogenic fungi and has worked extensively on transcriptional and post-translational regulation of fungal pH signalling.

Since 2000, initially funded as an MRC New Investigator, Elaine has developed murine models of invasive fungal infections and used them to identify fungal processes critical to mammalian infection, including the first and only in-host transcriptomic profiles of *Aspergillus fumigatus* pathogenic activities.

Current research programmes include mechanistic aspects of calcium-mediated signalling in *A. fumigatus* and structure-function analysis of a pH-responsive molecular switch required for fungal virulence. Elaine is a member of the BBSRC Pool of experts, and a member of the Fungal Education and Outreach, and Fungal Biology and Research, Committees of the British Mycological Society.

Abstract: Demystification of the 'accidental' pathogen *Aspergillus fumigatus*

Many fungi propagate and disseminate via release of airborne spores, but none surpass the capacity of *Aspergillus fumigatus* to cause human disease. *A. fumigatus* is a filamentous mould which is capable of



saprophytic growth in the natural environment and parasitic growth in susceptible human and animal hosts. How does the transition from saprophytic soil-dweller to life-threatening pathogen come about? As the quest for *A. fumigatus* virulence factors continues apace, our understanding of the pathogenic qualities expressed by this 'accidental pathogen' has reached a new, higher order appreciation of the host-pathogen interaction and how this fragile inter-relationship might be tipped towards or against initiation or resolution of disease.

Prof. Neil Gow



Institute of Medical Sciences, University of Aberdeen

Professor Gow graduated with a B.Sc. from Edinburgh University in 1979 and a Ph.D. from Aberdeen University. He was a research fellow in Denver, before returning to Aberdeen as a faculty member in 1984. He is a founding member of the Aberdeen Fungal Group and contributed to building this group to its current status as one of the largest centres of excellence for medical mycology.

Professor Gow currently holds the post of Director of Research and Commercialisation for the College of Life Sciences and Medicine. Under his direction this group has recently been awarded a Wellcome Trust Strategic to coordinate research and training activity and build capacity in the field of medical mycology and fungal immunology across the UK and in developing countries.

He is a fellow of Institute of Biology, the Royal Society of Edinburgh and the American Academy of Microbiologists and is a former President of the British Mycological Society and current President of ISHAM (the International Society for Human and Animal Mycology). He has in recent years helped coordinate the SGM Eukaryotic Division and was a past member of Council and editor of the SGM's journal Microbiology. He was a recent Editor in Chief of Fungal Genetics and Biology and helped establish the new SIHAM journal Medical Mycology Case Reports.

Abstract: The role of the cell wall in determining host-fungus interactions

Fungal dermatophytic infection is listed as the third most common ailment by the WHO and systemic fungal infections kill more people worldwide than malaria and twice as many hospital patients as MRSA [1]. Despite these grim statistics investment in medical mycology has lacked behind that in other infectious disease disciplines and has not been properly incorporated into worldwide imperatives for example to understand and devise new strategies to offset the potentially cataclysmic rise of microbial antibiotic resistance.

International societies and national research councils must help to promote a world-wide awareness campaign to promote the importance of medical mycology alongside research into viral, bacterial and parasitic diseases.

My own group's work has focused on the fungal cell wall as an opportunity to address the urgent need for better antifungal therapeutics and diagnostics and to investigate drug resistance mechanisms of antibiotics that target fungal cell wall biosynthesis. The fungal cell wall defines the perimeter of its own self and a boundary of communication with other organisms with which it interacts. For a fungal pathogen, every component and layer of the cell wall plays a specific role in its interactions with cells of the human host. We have tried to unpeel the functions of cell wall components by combining genetics, biochemistry and immunology to understand how the wall is assembled and how its constituents are recognized by the human immune system. This work has shown how the polysaccharides of the cell wall activate both the inflammatory and anti-inflammatory responses of the innate immune system.

Most recently we have focused on the role of chitin in immune responses to fungi. Chitin is an essential polysaccharide of the walls of all fungal pathogens and the exoskeleton and eggs of invertebrate parasites. We identified NOD2, TLR9 and the mannose receptor as three essential fungal chitin-recognition receptors of innate immune cells and showed that the activation of NOD2/TLR9 receptors by low concentrations of small chitin particles, generated via the action of human chitinases, leads to selective secretion of the anti-inflammatory cytokine IL-10. In contrast, higher concentrations of chitin particles promoted a pro-inflammatory response via

dectin-1-TLR2 signalling. NOD2 and TLR9 polymorphisms are associated with susceptibility to inflammatory conditions such as Crohn's disease, allergy and asthma. Chitin therefore promotes size-dependent anti- and pro-inflammatory immune responses that are critical for immune homeostasis, but can also promote the development of asthma and allergy.

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5. Wagener, J. et al (2014). Fungal chitin dampens inflammation through NOD2 and TLR9 activation. *PLoS Pathogens* 10(4): e1004050. doi:10.1371

Dr. Frank van de Veerdonk

Nijmegen, The Netherlands



The research of Frank van de Veerdonk over the last five years has focussed on the primary immunodeficiencies (PIDs) chronic mucocutaneous candidiasis (CMC), hyper IgE Syndrome (HIES) and chronic granulomatous disease (CGD). These PIDs are all associated with fungal infections, and studying the antifungal host defence in these diseases has elucidated several new insights in immunology.

He has unravelled the causative mutation in CMC in 2011 (STAT1 mutation, *NEJM* 2011) via functional and focussed genetic approach, and is involved in collaborations on developing new treatment strategies in CMC and HIES.

He discovered that CGD has an autoinflammatory component caused by a deficiency in LC3-associated phagocytosis (LAP) that is amendable to IL-1 targeted treatment, which was also effective in clearing fungal infection in CGD mice (*PNAS* 2014). He has identified novel roles of the new IL-1 family members IL-36 and IL-37 in fungal host defence and Th17 (*J. immunology* 2013, *PLoS Pathogens*), the function of IL-36Ra and IL-38, and the identification of the receptor of IL-38 and its role in modulating fungal-induced Th17 responses (*PNAS* 2012).

Furthermore, he discovered that a fungal component named galactosaminogalactan (GAG) can induce IL-1Ra in the host and in this way can suppress IL-1 induced host defence (*Plos Pathogens* 2014). Since GAG can induce IL-1Ra, he is currently investigating in collaboration with Prof. Jean-Paul Latge (Institute Pasteur, Paris) GAG as a new treatment compound for IL-1-associated diseases such as gout.

Abstract: Host determinants of response – an emerging story of fungal pathogenesis

A balanced immune response is crucial to fight invading fungi. On the one hand the host defence needs to be vigorous and quick, on the other hand it needs to be tightly controlled in order to prevent collateral damage and even autoimmunity. It has become apparent over the last decade that cytokines of the IL-1 family and mechanisms that regulate the IL-1 family of cytokines, such as inflammasome activation and autophagy, play a critical role in a balanced immune response against fungi. I will discuss the crucial components of the host defence against fungal infection and the translation of the research of fungal immunology into clinical practice, with emphasis on the role of the IL-1 family of cytokines in antifungal host defence.



FUNGAL UPDATE 2015
10th Anniversary

Special 10th Anniversary Event

Recital by the Canterbury Cathedral Boys Choir – Saturday 10th January



(Photographs L to R): Canterbury Boys Choir 2014, photograph courtesy of Debbie Patterson; St Bartholomew the Great Church, London

It is a great privilege that attendees of this 10th Anniversary Fungal Update Meeting will have the opportunity to experience a special recital by the world-renowned Canterbury Cathedral Boys Choir in the historic setting of St Bartholomew's The Great Church.

This performance is conducted on a voluntary basis by the choir and we hope that you will show your appreciation by considering a donation to Child Bereavement UK.



Child Bereavement UK supports families and educates professionals when a baby or child of any age dies or is dying, or when a child is facing bereavement. Their vision is for all families to have the support they need to rebuild their lives.

As a national charity, their ability to help grieving families and the professionals who care for them depends on the generosity and support of concerned individuals. Please visit the website below to learn more about the important work of the charity and make a donation:

www.childbereavementuk.org/get-involved/donate

Thank you in advance for your kind support.



David Flood



Director of Music, Canterbury Cathedral, Master of the Cathedral choristers and the Cathedral organist

Having begun musical studies at an early age, David held his first parish church organist post at 15 and has been deeply involved with church music ever since. He became Organ Exhibitioner of St John's College, Oxford and spent a further postgraduate year in at Clare College, Cambridge. In 1978 he was appointed Assistant Organist at Canterbury Cathedral, a post he held for eight years. During this time he was involved in many national and international occasions, such as the enthronement of Archbishop Runcie and the visit of Pope John Paul II. He has made several recordings and has appeared on radio and television as well as performances in Cathedrals, churches and concert halls. He has given organ recitals in France, Germany, Holland, Australia, New Zealand and USA. He has studied with Gillian Weir and Jean Langlais.

In 1986 he was appointed Organist and Master of the Choristers at Lincoln Cathedral and, after two enjoyable years, returned to Canterbury in 1988 as Organist and Master of the Choristers. He has been responsible for the music at all the special occasions, in particular the Enthronements of Archbishops Carey, Williams and Welby, and the 1998 and 2008 Lambeth Conferences. The Cathedral choir under his direction has regularly toured in Europe and North America, most recently in April 2012. All the Canterbury Choir recordings (15 in the last 22 years) have been greeted with considerable acclaim.

He was invited by the Riga Dom Boys Choir and the Latvian Ministry of Culture to direct a week of workshops and lectures on the training of boys' voices in March 1997. Annually since August 1997 he has hosted an American Children's Choir Festival with up to 400 children. In 1999, he visited Australia and New Zealand to direct residential choir courses and give recitals and made his first appearance as conductor at the Berkshire Choral Festival in Massachusetts, USA. He is much in demand in the USA to direct choral festivals and workshops, currently travelling two or three times every year. In 2008 he made his first appearance as director of the Washington All-State Symphonic Choir. In July 2002 he was awarded the honorary degree of Doctor of Music by the University of Kent and in 2008 an Honorary Fellowship of Canterbury Christ Church University, where he has recently been appointed a Visiting Professor in Church Music. David is also a Visiting Fellow of St John's College, Durham.

The responsibility of daily sung services is naturally the most important part of his work and performing exciting music for the millions of visitors and pilgrims to the Cathedral each year is a great joy.

The Choir of Canterbury Cathedral sings at the daily services in the Cathedral, providing music which enchants and delights the many thousands of visitors and pilgrims as well as the regular congregation.

The boys performing are aged between 9 and 13 and attend St Edmund's School, Canterbury. Each chorister learns to play at least two instruments as well as the very special training for his singing. Choir practice takes place every day, early in the morning before school and again before Evensong, and they perform music from the widest repertoire: medieval to modern.

In recent years the choir has toured in Malta, France, Italy, Holland, Canada and the USA. The choir made their first tour to Norway in April 2014 and a tour in April 2015 will spend two weeks in southern USA, giving eight concerts. These trips, together with concert, television and radio appearances and the making of CDs, are some of the many exciting bonuses which come during a boy's time as a chorister. It is a time which lives with them for ever and a training which is envied all over the world.









