Microbiology of the compromised host: an update

Dr Valerie Bevan reports on behalf of the British Society for Microbial Technology committee on the regional scientific meeting held last October in Sheffield.

Each year, the British Society for Microbial Technology (BSMT) convenes a scientific symposium at Colindale, north London, and every other year it holds a regional symposium. The following report covers the most recent regional meeting, held in Sheffield last autumn, on the 'Microbiology of the Compromised Host'.

Professor Eric Bolton chaired this excellent symposium, which attracted a smaller audience than usual – possibly because it followed on from the IBMS Biomedical Science Congress. However, the presentations stimulated wide-ranging discussion at the end of each session with input from the other speakers. The discussions and feedback on the evaluation forms highlighted how much the delegates enjoyed the talks, which are available on the BSMT website (www.bsmt.org.uk) along with the presentations from previous BSMT scientific meetings.

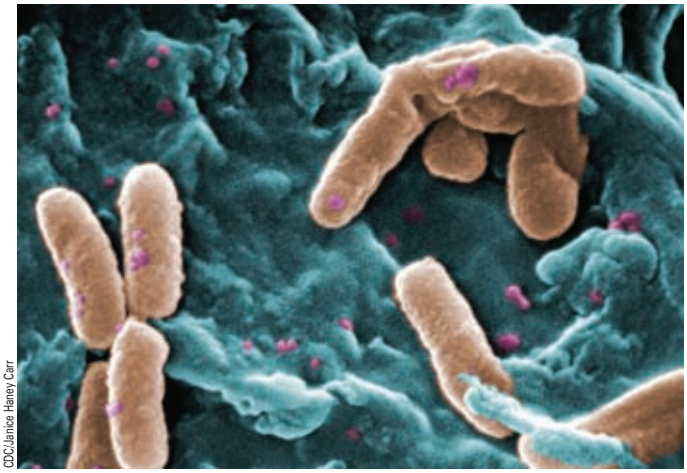
INFECTION IN THE COMPROMISED HOST

The BSMT is always grateful to the speakers who give time from their busy schedules to attend the scientific meetings. Professor Steve Green, consultant in infectious diseases, Royal Hallamshire Hospital, Sheffield, was still travelling from London at the time he was due to give the opening talk; his humorous overview was actually delivered later in the day and was no less informative for the delay. He stressed that he was not an immunologist but a consultant physician with a specialist interest in immunodeficiency, and pointed out that we never know what new diseases will appear, or when.

Illustrating his talk with images from art history, television and films, he explained that what we eat affects our immune response (we are what we eat), even leading to the extreme situation of cannibalism and the disease Kuru, which appeared in New Guinea. Professor Green showed the organs of the immune system, the role that complement plays, and what can go wrong when this complex system fails. He indicated the infections that can modify the immune system include human immunodeficiency virus (HIV) and other diseases such as diabetes, medications, malignancies, toxins, radiation and congenital problems.

Professor Green discussed what can be done to treat immunodeficiency, covering the carrying of 'splenectomy cards' and medical advances such as vaccination and the use of prophylactic antimicrobials.

Six fascinating case studies illustrated the relationship between infection and the immunocompromised host, highlighting the genetic predisposition and additional susceptibility in such patients. One poignant case study noted the sale of kidneys from live donors in Pakistan.



CDC/Janice Haney Carr

Multiresistant *Pseudomonas aeruginosa* is one organism that poses a particular problem for patients who suffer from cystic fibrosis.

SURVIVING SEPSIS

The thrust of the presentation from Dr Wigfull, consultant anaesthetist, Northern General Hospital, Sheffield, was was to emphasise the importance of time in the investigation and treatment of severe sepsis and septic shock. Prompt removal of the source of the sepsis whenever possible and the need for early broad-spectrum empirical antimicrobial therapy are crucial.

Time is of the essence and data were presented showing that survival rate when an appropriate intravenous antibiotic is administered within 30 minutes of onset of shock is 85%, which reduces to 50% if treatment is delayed by four hours. A statistical comparison with percutaneous coronary intervention (PCI) time for heart attack patients was used to demonstrate that reducing the time to antimicrobial

administration in patients with septic shock has a much greater potential for saving lives.

Dr Wigfull described the 'severe sepsis resuscitation bundle', which recommends the collection of blood cultures followed by administering broad-spectrum antimicrobials within one hour of the development of sepsis. He challenged the laboratory community to help assess and develop new technologies to provide microbiology results much earlier than traditional culture techniques, and to do so on a 24 hours a day, seven days a week basis.

TRANSPLANT MICROBIOLOGY

Professor Kate Gould from Public Health England (PHE) and the Newcastle Hospitals NHS Foundation Trust described the history of transplantation, where immunosuppression was more aggressive and less well controlled, and early infection was a significant cause of morbidity and mortality. Since these early days, immunosuppression has become more defined, the surgical repertoire is increasing and the recipient waiting list is lengthening.

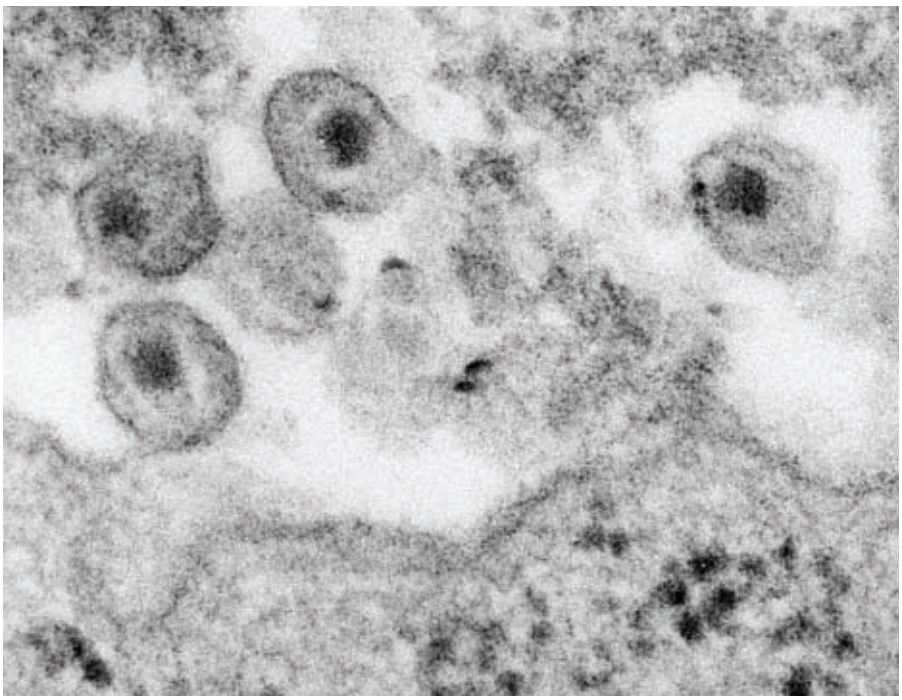
Professor Gould showed the increase in the number and survival of heart and lung transplants since the first ones were performed in the early 1980s. She reviewed the issues related to transplants (ie recipients, donors, the operation and immunosuppression) and described the bacterial infections seen in the post-transplant period where the most common is respiratory infection, followed by mediastinitis, bacteraemia and wound infection.

Professor Gould discussed the use of infected donors, commenting that common sense would suggest that organs from donors with deep-seated infection should not be used, but she questioned whether there is any science to support this. Indeed, this practice would mean fewer available donors. So, how can we minimise the risk of surgical site infection post-transplant in a patient colonised with pan-resistant microorganisms? The answer is good surgical debridement, local irrigation with disinfectant, and antibiotic prophylaxis according to results of combination testing.

HIV-RELATED INFECTIONS

Dr Cariad Evans, senior registrar in virology at the Northern General Hospital, Sheffield, gave an entertaining and interactive presentation on HIV and opportunistic infections. Her talk described the natural evolution of HIV, the multitude of opportunistic infections with which patients can present, and the burden of late HIV presenters. She also discussed two case studies to identify 'alarm bells' which should alert the clinician.

Dr Evans explained how HIV affects different parts of the body at different stages of the disease so that people present with diverse clinical conditions at each stage: the primary HIV infection, the asymptomatic stage, the early symptomatic stage, and the symptomatic (acquired immune deficiency [AIDS]-defining) stage.



CDC/A Harrison, P Feorino, E L Palmer

Human immunodeficiency virus affects different parts of the body at different stages of the disease, so patients present with diverse clinical conditions at each stage.

The opportunistic infections that may affect HIV patients were also highlighted. Dr Evans said that 50% of adults present at a late stage of HIV infection and this delayed diagnosis is accompanied by increased disability and mortality. She then discussed who should be offered HIV screening and identified conditions where HIV testing should be offered.

In conclusion, Dr Evans noted that, at the end of 2011, an estimated 96,600 people were living with HIV in the UK, with approximately a quarter (22,600, 24%) undiagnosed and unaware. Finally, she stressed that identification and recognition of opportunistic infections is paramount in the diagnosis of HIV.

WHAT AN ORTHOPAEDIC SURGEON WANTS

Mr Simon Royston, consultant orthopaedic surgeon at the Northern General Hospital, Sheffield, gave an entertaining talk specifying his needs from the microbiology laboratory. He began by covering some basic science related to bones, their structure and composition, and reminded delegates that bacteria predate humans and will survive us.

The first process at the injured site is debridement of the damaged tissue. Every time a bone is damaged, its internal structure becomes compromised, particularly when metal structures are inserted during reconstruction procedures. Mr Royston described the Lautenbach system of irrigation and drainage whereby antimicrobial agents, along with varidase, are instilled at the infected site. The instillate is sampled, together with any infectious materials and inflammatory mediators present, and sent to the laboratory for culture once or twice a week, and antimicrobial treatment is changed according to the culture results.

Although oral antimicrobials have a role, high-dose gentamicin is the main antimicrobial treatment at the infected site as there is no systemic absorption of the agent and it can penetrate the biofilms. Sampling of the instillate is continued until three clear samples are achieved. Pinsite swabs are not needed. Mr Royston concluded that his main need from the laboratory is to provide timely culture and sensitivity test results from the instillate, and he stressed the need for good communication.

NEUTROPENIC SEPSIS IN CANCER PATIENTS

Professor Barry Hancock OBE, Emeritus Professor of Oncology, retired in 2009 after 35 years' service to the University of Sheffield. The OBE is just one of the awards Professor Hancock has received in recognition of his contribution to medicine and his subject.

Professor Hancock differentiated between neutropenic sepsis, which is a significant inflammatory response to a presumed bacterial infection in a person with or without fever, and febrile neutropenia in which fever develops in a patient with neutropenia, often with other signs of infection. Some 85% of infections are bacterial. Previously, Gram-negative infections predominated but this has now changed to Gram-positive organisms. Classical signs and symptoms may be absent and there is often no laboratory evidence, and he stressed how important it is to assess the whole patient. As always, communication is key.

Delegates were told that neutropenic sepsis is a life-threatening complication of anticancer treatment. It can occur anywhere in the body, with the most common sites being the mouth and throat, skin, intestine, lungs, kidneys and bladder, especially associated with a urinary catheter, and at the site of a drip or central line. Professor Hancock's presentation then focused on the published 2012 National Institute for Health and Care Excellence (NICE) clinical guideline 151 on the prevention and management of neutropenic sepsis in cancer patients.

The guideline provides a definition of neutropenic sepsis and describes the information, support and training required in the management of patients, and the preventative treatment, identification and assessment, and initial and subsequent treatment needed. Again, the importance of good communication with patients and carers from well-trained healthcare workers was stressed.

WHAT A CYSTIC FIBROSIS PHYSICIAN WANTS

The final talk of the day was given by Dr Frank Edenborough, consultant respiratory physician, Northern General Hospital, Sheffield, who discussed what a cystic fibrosis (CF) physician wants from a microbiologist. He first described the disease, which is the most common autosomal recessive genetic disorder in Caucasians and was probably recognised in the 16th century, although not formally described until the 1930s. It results from abnormalities of chloride transport in many exocrine glands, resulting in a condition dominated by maldigestion, malabsorption and progressive lung damage. Dr Edenborough described the aetiology of CF and noted that it is related to many other conditions including diabetes, liver disease, infertility, rhinosinusitis and polyps, electrolyte abnormalities, osteoporosis and consequent fractures.

Initial treatment includes daily airway clearance techniques to remove infected mucus that causes airway obstruction, and encouraging exercise to strengthen the muscles and improve posture. Inhaled drugs including antibiotics, mucolytic agents, DNase and bronchodilators and oral and intravenous antibiotics, anti-inflammatories and steroids are the mainstay of pharmacological treatment for the chest.

The microbiology of infection varies according to the stage of the disease and age of the patient, with *Escherichia coli*, *Haemophilus* and *Staphylococcus* being isolated in the young, and *Pseudomonas*, *Stenotrophomonas* and *Serratia* being isolated as CF patients get older. *Burkholderia, Pandorea* and *Achromobacter* appear later, with occasional infections due to acid/alcohol-fast bacilli (AAFB; *Mycobacterium abscessus*), fungi including *Aspergillus*, *Scedosporium* and *Exophiala dermatiditis*, and viruses.

Specialised CF centres house expert, experienced multidisciplinary teams. Treatment has now improved with a strategy for lung disease including screening sputa at every clinic, segregation of patients depending on their microbiology, improved hand and equipment hygiene, vaccination and prophylaxis for some organisms. In some cases, organisms can be suppressed or even eradicated using aggressive treatment regimes of high doses for a considerable time in combination therapy. Survival rates have improved and now over 60% of adults survive to 40 years old. Double lung transplantation, another treatment option, now has a survival rate of 60% after 10 years.

Dr Edenborough discussed two particular organisms known to represent a particular problem, and these are multiresistant *Pseudomonas aeruginosa* – he commented that *in vitro* testing of *Pseudomonas* is pointless – and *Burkholderia cepacia* complex, which are associated with poor prognosis; however, new organisms are appearing. He then discussed dilemmas for the physician, including the difficulty of differentiating colonisation from chronic infections, and the complexity of treatment options, particularly when opting for toxic treatments that impair other organs.

Dr Edenborough concluded that he valued interested microbiologists who helped educate young doctors. He also valued flexibility from the laboratory and, again, stressed that good communication is vital.

ANTIMICROBIAL RESISTANCE: A BITTER PILL TO SWALLOW

The next scientific symposium, scheduled for 16 May, is entitled 'Antimicrobial Resistance: A Bitter Pill to Swallow', and is a response to the publicity on television and in the popular press raised by Professor Dame Sally Davies, the Chief Medical Officer for England, who has suggested that the spread of antimicrobial resistance is potentially as bad a threat to humanity as global warming and terrorism. Dame Sally has also made the point that development of new antimicrobials has slowed and that no new class of antimicrobial agent has been launched since the 1980s.

Professor John Watson, Deputy Chief Medical Officer for England, will be opening the symposium to set the scene. Professor Peter Borriello, Chief Executive, Veterinary Medicines Directorate, will follow and provide a veterinary perspective on the use of antimicrobial agents.

Professor Gunnar Kahlmeter, president of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) and former chairman of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), will discuss antimicrobial resistance from a European perspective. He will also review the initiatives that ESCMID and EUCAST are implementing and will cover recommendations that EUCAST is making for the laboratory detection of resistance mechanisms.

The third speaker will be Professor David McDowell from Northern Ireland who will discuss the relationship between antimicrobial resistance and the food chain. Problems faced by the pharmaceutical industry in bringing new antimicrobials to the market will be discussed by Dr Ian Morrissey, from International Health Management Associates (IHMA) Europe. He will also review the new agents that are expected to become available and how they fit into the current armoury in the battle against developing antimicrobial resistance.

Dr Ian Laurenson, Director of the Scottish Mycobacteria Reference Laboratory, will bring the meeting up to date with resistance in TB and how laboratories should be responding. Dr Nicola Williams, from Wirral, will then talk about the transmission from animals to humans of extended-spectrum β-lactamases (ESBLs) – enzymes produced by these bacteria which make them resistant to the cephalosporins. The last speaker of the day will be Professor Neil Woodford, PHE Colindale, who will present on the dilemmas of detecting carbapenemase-producing Enterobacteriaceae. More details may be found on the BSMT website (www.bsmt.org.uk). ■

The BSMT is grateful for the support in Sheffield given by Alpha Laboratories, Bruker UK, BD Diagnostics, BioConnections, bioMérieux UK, Grifols, Launch Diagnostics UK, Mast Group, MWE (Medical Wire), Oxoid (Thermo Scientific) and Pro-Lab Diagnostics. Such support allows the BSMT scientific meetings to continue.

Dr Valerie Bevan CSci FIBMS is the London region representative on the IBMS Council and chair of the BSMT. Valerie chaired the working group that developed UK Standards for Microbiology Investigations for Clinical Bacteriology (previously National Standard Methods) for 18 years. She has written several reports and articles for *The Biomedical Scientist*, including those concerning the position of women in healthcare science.

The BSMT is a not-for-profit organisation composed of microbiologists working as biomedical scientists, other healthcare scientists and medical microbiologists mainly in the NHS and PHE. The society's aim is to promote an exchange of information on laboratory practices in clinical microbiology and is particularly aimed at bench microbiologists. If you would like to become more involved with the BSMT committee, please contact Dr Bevan or any committee member – email addresses may be found on the website (www.bsmt.org.uk).