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Infectious diseases: problems and challenges

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ABSTRACT Animals and, unfortunately, medical care are responsible for many of the problems and challenges caused by infection that we currently face. The symposium's morning session covered four zoonotic infections – Q fever, Lyme borreliosis, verotoxin-producing *Escherichia coli* and rabies – that will require improved interaction between physicians, microbiologists, veterinarians and public health agencies for their control. Representatives of each of these groups spoke, and the audience was similarly broad in its make-up. The afternoon session saw expert speakers discuss two difficult bugs – complicated *Staphylococcus aureus* bacteraemia and fungal lung infection – and the difficult clinical scenario of ensuring patients with severe sepsis receive effective initial antibiotics without fuelling antimicrobial resistance or *Clostridium difficile* disease. The wealth of information and experience provided should challenge anyone prescribing antimicrobial agents to reflect on and improve their own practice.

KEYWORDS Antibiotic resistance, antimicrobial stewardship, aspergillosis, candidaemia, *Clostridium difficile*-associated diarrhoea, endocarditis, fungal infection, haemolytic uraemic syndrome, Lyme borreliosis, methicillin-resistant *Staphylococcus aureus*, Q fever, rabies, sepsis management, *Staphylococcus aureus* bacteraemia, verotoxin-producing *Escherichia coli*, zoonoses

DECLARATION OF INTERESTS Dr Robertson was both rapporteur and speaker at this symposium and reports on his own talk. He has no other interests to declare.

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EDUCATION

SESSION 1
ZOONOSES... PROBLEMS FROM ANIMALS

Coxiella burnetii infection, or Q fever, is rare in the UK but has caused four major outbreaks since 1986. Dr Lynda Browning (Epidemiologist, Gastrointestinal Diseases and Zoonoses, Health Protection Scotland) outlined the investigation and initial management of the UK's largest occupational outbreak of Q fever with 134 serologically proven cases occurring in July 2006 at an abattoir near Stirling.[1] The source was not conclusively established, although a point source outbreak originating within the abattoir was most likely. The congregation of workers at designated smoking areas may have contributed to the size of the outbreak. Dr Paul Robertson (Specialist Registrar, Monklands District General Hospital, Airdrie) discussed the clinical features, diagnosis and management of acute and chronic Q fever, and summarised the clinical follow-up of those affected by the outbreak. Risk stratifying acute Q fever based on the presence of risk factors for the development of chronic Q fever, particularly valvular heart disease, is important as prolonged initial antimicrobial therapy to those at increased risk can prevent the development of chronic Q fever.[2]

Dr Darrell Ho-Yen (Director, National Lyme Borreliosis Testing Service, Raigmore Hospital, Inverness) spoke on the epidemiology – with particular reference to Scotland – and clinical management of Lyme borreliosis, which was recently renamed from Lyme disease to emphasise that seropositivity does not necessarily imply disease. He reinforced the importance of avoiding testing in asymptomatic individuals and making a clinical diagnosis of early localised Lyme to allow prompt treatment.

Dr Stephanie Dundas (Consultant Physician, Monklands District General Hospital, Airdrie) gave an overview of the management of acute bloody diarrhoea, before speaking specifically on verotoxin-producing *Escherichia coli* infection. Verotoxin-producing *Escherichia coli* infection is around 100 times less frequent than *Campylobacter* infection but carries a 40-fold increased risk of death with an overall mortality rate of 3.7%. Haemolytic uraemic syndrome complicates 15% of cases and should be vigorously looked for in patients presenting with acute bloody diarrhoea. Antibiotics are associated with poor outcome.[3] The use of plasma exchange in adults remains controversial but was strongly advocated by Dr Dundas following her experience of the central Scotland outbreak in 1996.[4]

SESSION 2
ZOONOSES... MORE PROBLEMS FROM ANIMALS

Prof. Anthony Fooks (Rabies and Wildlife Zoonoses Group, Veterinary Laboratories Agency, Weybridge) outlined the changing European and global epidemiology of rabies, emphasising the spread of infection into new animal species and new geographical areas. Although dogs are responsible for more than 99% of human

cases,[5] bat lyssavirus represents a more imminent threat in the UK, with eight cases of bat rabies and one fatal human case[6] in the past 30 years. Dr Mary Worrall (Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford) summarised the clinical features of human rabies infection. Rabies is a nearly universally fatal disease that is entirely preventable if judicial pre-exposure prophylaxis and urgent post-exposure prophylaxis are implemented. Dr Worrall recommended pre-exposure prophylaxis to those travelling to areas where rabies is endemic, and to those with significant bat exposures in the UK. Both presenters commented on the global under-recognition of rabies, referring to a study where 11% of Malawian children dying of suspected cerebral malaria were found to have rabies encephalitis.[7] To achieve global control, an integrated veterinary and medical response at national and international levels is required.

SESSION 3 DIFFICULT BUGS

The Stanley Davidson Lecture was given by Dr Vance G Fowler Jr (Duke University Medical Center, Durham, USA) who entertainingly summarised the increasing frequency and complexity of *Staphylococcus aureus* bacteraemia (SAB), with *Staphylococcus aureus* now the leading cause of both native[8] and prosthetic valve[9] endocarditis. Dr Fowler argued that the increased frequency of SAB was due to increased nosocomial infection, particularly from vascular access devices, and that the growing use of prosthetic devices was responsible for the increased complexity of SAB. Sadly, therapy remains suboptimal with a 27% 12-week mortality rate in SAB associated with a prosthetic device.[10] No antibiotic has yet been shown to be superior to anti-staphylococcal penicillins and vancomycin in the treatment of methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia respectively. Roles for the other effective antibiotics (linezolid,[11] daptomycin[12] and tigecycline) were described. The worrying rise of community-acquired MRSA, genetically and clinically distinct from hospital-acquired infection, was also outlined.

Prof. David Denning (University Hospital of South Manchester) untangled the often challenging issue of therapy for fungal lung disease, which remains difficult to diagnose ante mortem. Delay of effective therapy is strongly associated with poor outcome.[13] Specifically requesting fungal culture from respiratory samples, as well as making use of new molecular tests, can increase the speed and accuracy of diagnosis. The cornerstones of managing invasive aspergillus infection are prompt administration of voriconazole,[14] ensuring therapeutic levels are achieved, surgery for localised disease, and reversal of immunosuppression where feasible. Chronic pulmonary aspergillosis was also discussed.

SESSION 4 DIFFICULT CLINICAL SCENARIOS

Dr Ian Gould (Aberdeen Royal Infirmary) described the European epidemiology of resistant Gram-negative organisms and MRSA, and the worrying lack of new antimicrobials in development, particularly with activity against Gram-negative organisms. The choice of empirical antimicrobial therapy for severe sepsis should take into account the likelihood of resistant organisms. Empirical therapy will usually involve broad-spectrum agents, but should be rationalised based on subsequent microbiological test results. Prof. Dilip Nathwani (Ninewells Hospital and Medical School, Dundee) gave an overview of sepsis management and selecting appropriate empirical antimicrobial therapy. The high mortality of severe sepsis requires early recognition and appreciation of severity, followed by timely effective antimicrobial and physiological intervention.[15,16] Execution of these ideals in a real-world setting is likely to require a 'bundle'-based approach – several simple interventions that must all be applied for optimal outcome.

Dr Andrew Seaton (Brownlee Centre, Gartnavel General Hospital, Glasgow) discussed the clinical conundrum of using antibiotics that can be simultaneously life-saving and the cause of potentially life-threatening complications such as *Clostridium difficile*-associated diarrhoea (CDAD). Using recent experience from his own trust, he provided evidence that adherence to an antibiotic policy restricting the use of third-generation cephalosporins and co-amoxiclav, in combination with infection control measures, can reverse increasing CDAD rates. He emphasised the importance of multidisciplinary antibiotic management teams as part of the solution to antimicrobial resistance and CDAD.

The day ended with five interactive cases covering topics discussed during the day.

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