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Abstracts of the Tenth Conference of the Federation of Infection Societies, 2003

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Invited Speakers’ Abstracts

S01

WHAT’S NEW IN MOLECULES FOR ANTIMICROBIAL CHEMOTHERAPY?
David Payne
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The antibiotics currently in Phase I, II and III will each be reviewed with respect to their utility and spectrum of activity. Many of these are agents for the treatment of Gram positive infections and most are new derivatives from existing antibiotic classes and thus do not provide the much needed quantum jump away from established resistance mechanisms. Consequently, over the next 5-10 years few novel antibiotics with entirely new mechanisms of action are destined to reach the clinic. Bacterial genomics has been hailed as the solution to identifying new antibacterial strategies and the tremendous impact that genomics and genic based technologies has had on the discovery of new antibacterial targets will be illustrated. However, progressing from a novel genomics derived target to identifying a development candidate has proven to be an exceptionally challenging process, exemplified by the small number of novel mechanism agents currently in development. The complexities of delivering new antibiotics in the post genomic era will be illustrated along with perspective on potential solutions to some of the key research hurdles to enhance and facilitate the discovery of new class antibiotics.

S02

BEYOND THE GENOME: PRACTICAL APPLICATIONS OF MOLECULAR DIAGNOSTICS
Peter Michael Hawkey
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Despite the vast amount of press in professional and lay journals relating to molecular diagnostics the majority of work is still carried out in clinical microbiology laboratories is based upon conventional technologies. There is a steady rise in the application of molecular techniques to the diagnosis and management of infection. There has been no single massive application of molecular technology, more an accumulation of applications in various areas which are either in trial or in day to day application being either more sensitive or cost effective than other non molecular technologies. Perhaps the most striking method which is about to influence every clinical bacteriology lab is the use of molecular technology to detect MRSA. There are a plethora of PCR based techniques for the detection of the _mecA_ gene and other targets which identify _Staphylococcus aureus_ or other _staphylococcal_ species. New developments are the utilisation of the light cycler based or isothermal amplification methods. These being applied both to the characterisation of _staphylococci_ and direct detection from specimens. The theme of direct detection from specimens obviously is seductive as it offers the prospect of altering or initiating therapy much more rapidly than conventional culture methods. A notable addition is the description of a DNA probe based PCR assay for the detection of _Campylobacter spp_. in faeces. This assay utilises a variant of the reverse line blot as hybridisation assay which utilises immobilised oligonucleotide probes and hybridisation with a labelled PCR product from the specimen. This technology has recently found a number of applications. In the area of epidemiological typing a number of advances have been made with the application particularly in the typing of _Mycobacterium tuberculosis_ strains of variable number tandem repeat typing using various platforms including both DNA sequencers and DHPLC. One useful area would be the ability to use PCR typing for _MRSA_ but a recent evaluation showed that as yet PFGE is superior. Bacterial species identification is of considerable interest and recently the application _rpoB_ gene sequencing was found to be both sensitive and specific when applied to both _mycobacteria_ and _bacillus_ enabling the rapid and definitive identification of _B. anthracis_ and _M. tuberculosis_. No review would be complete without reference to SARS this year and the value and availability of rapid reverse transriptase based DNA sequencing of the _SARS_ coronavirus and the subsequent design of rapid PCR assays is undoubtedly helpful in the identification of cases, although the sensitivity of molecular methods does not approach that of retrospective sero conversion methods. Finally DNA and protein arrays are a potentially powerful tool within the study of pathogenicity and physiology of micro organisms. At the moment their complexity and expense rules them out from routine application in diagnostic laboratories, however, it will not be long before the first commercially based arrays are applied to areas of diagnosis from which the quantity and type of information cannot be gained by any other method.

S03

PLANT VACCINES
Julian Ma
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There are many potential advantages to be gained from using plants as a production system for recombinant proteins. They are higher eukaryotic organisms with an endomembrane system, they fold and assemble recombinant proteins using protein chaperones that are homologous to those in mammalian cells, and they glycosylate proteins. Moreover, they offer the potential to scale up to agricultural proportions, that offers both the possibility to produce proteins in enormous quantities, as well as the prospect of very low cost. An important application area where these benefits could be brought to bear is in the field of vaccine production, particularly in developing countries. Plant expressed IgG monoclonal antibodies were first described in 1989. Since then, transgenic plants have proven to be extremely versatile, successfully used for antibody fragments, IgG and secretory IgA antibodies, the latter already having been taken through clinical trials. A considerable amount of work has also been performed on the expression of antigens in plants, particularly with a view to oral delivery. To date, three examples have been tested in humans - _E. coli_ heat labile toxin, hepatitis B surface antigen and Norwalk virus capsid protein. Overall, proof of principle has been demonstrated for the production of recombinant pharmaceutical in plants. The next step is to progress through formal clinical trials and importantly, to commercialise the first product.

S04

INFECTION HIGHLIGHTS OF 2003—CHANGES IN PRACTICE IN RICH COUNTRIES; WHAT DO THEY MEAN FOR POOR COUNTRIES?
Bertie Squire
Liverpool School of Tropical Medicine, Liverpool, UK

Objective: To select two important areas of clinical practice that have seen significant change in the more developed countries over the course of the last year and discuss: the main reasons behind the change...
the implications of the change for clinical practice and public health in developing countries

Methods: Reflection on the literature in the light of personal experience of clinical and public health practice in UK and Africa.

Results: The last year has seen some consensus emerging, particularly in the UK and USA, in two important areas:

1. the use of cortico-steroids in the management of adults with bacterial meningitis
2. the management of drug sensitive and multi-drug resistant tuberculosis

For bacterial meningitis: the first randomised, double blind, placebo-controlled trial of adjunctive steroids (301 adults) showed a reduction in the proportion of patients who had unfavourable outcomes (15% vs 25%, \( p = 0.03 \)) and the proportion of patients who died (7% vs 15%, \( p = 0.04 \)). The benefits were most obvious in patients with pneumococcal meningitis (N Engl J Med 2002; 347:1549-1556). Adjunctive dexamethasone therapy is now recommended for most adults with suspected pneumococcal meningitis.

For tuberculosis: initial results from an important new multi-centre randomised, un-blinded trial of regimens for drug sensitive tuberculosis have been presented. This study of 1355 patients compared the ‘gold standard’ (2EHRZ+4HR) treatment with 2EHRZ+6EH and 2(EHRZ)+6EH (Study A of the International Union Against TB & Lung Disease). Rational recommendations for the management of multi-drug resistant disease have been made in new treatment guidelines from the USA even though there are no randomised controlled trials to inform practice in this area (Am J Respir Crit Care Med 2003;167:603-662).

Conclusions: Although these highlights have clear implications for clinical practice in the more developed countries, their relevance for clinical and public health practice in developing countries affected by the HIV pandemic is debated.

S06

S07

THE 2003 LOWBURY LECTURE
ATTITUDES AND BEHAVIOUR IN INFECTION CONTROL

Didier Pittet

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Microbiology and epidemiology have made significant contributions to the field of infection control. However, most healthcare-associated infections are endemic and result from cross-transmission related to inappropriate patient-care practices. To improve healthcare workers’ (HCW) compliance with practices, infection control should learn from the behavioural sciences. Infection control professionals play key roles in the identification and prevention of nosocomial infections. They act as observers, educators and, ultimately, should become change agents. Changing behaviour and shifting social norms at multiple levels through the HCW community are among the key challenges of infection control today.

Although a modification of patient-care practices is vital for infection prevention, this issue has received only little attention in the medical literature. During the latter half of the 20th century, it was suggested that social behaviour could be best understood as a function of people’s perceptions rather than as a function of real life. This assumption gave birth to several models based on social cognitive variables to improve our understanding of human behaviour. Cognitive variables used in these models include: knowledge, motivation, intention, perception of threat, outcome expectancy, perceived and actual behavioural control, and social pressure. These determinants shape behaviour; they are acquired through the socialisation process and, importantly, are susceptible to change. Some social cognitive models (Health Belief Model, Health Locus of Control, Protection Motivation Theory, Theory of Planned Behaviour and the Self-Efficacy Model) have been applied to evaluate predictors of health behaviour but, so far, none has been successfully applied to explain behaviour in the field of infection control.

Successful strategies to improve infection control practices result from their multidimensional aspect. Successful behaviour change can well be explained by applying the theory of Ecological Perspective, which is based on two key ideas: a) behaviour is viewed as being affected by and affecting multiple levels of influence; b) behaviour both influences and is influenced by the social environment. Levels of influence for health-related behaviours and conditions include intra-personal, inter-personal, institutional, and community factors, as well as administrative support. Intra-personal factors are individual characteristics that influence behaviour such as knowledge, attitudes, beliefs, and personality traits. Inter-personal factors include interpersonal processes and primary groups—family, friends, and peers—that provide social identity, support and role definition. HCWs can be influenced by or are influential in their social environments. Behaviour is often influenced by peer group pressure. Social Cognitive Theory states that people learn not only through their own experiences, but also by observing others’ actions and the results of those actions, as well as through modelling. Institutional factors to be considered to promote change include the availability and easy access to rules, policies, as well as technical and informal structures that help to promote recommended behaviours. Responsibilities for each HCW’s individual group must be clearly recognised and defined. Community factors are social networks and norms that exist either formally or informally between individuals, groups, and organisations. For example, in the hospital, the community level would be the ward. Community-level models are frameworks for understanding how social systems function and change, and how communities and organisations can be activated. The conceptual framework of community organisation models is based on social networks and support, focusing on the active participation and development of communities that can help evaluate and solve health problems. Public policy factors include local policies that regulate or support practices for disease prevention, control, and management. The institutional administration must openly support the creation of a multidisciplinary task force to address the problem of infection cross-transmission within the ward or the hospital. By this, it mandates representative members of the multidisciplinary institutional team to come together to identify the problem and to develop strategies to resolve it; it also endorses the choice and options taken and mobilizes the hospital resources needed to implement the strategies.

Based on behavioural theories and reported experiences, multimodal intervention strategies have more chance of success than single approaches or promotion programmes focusing on one or two elements only. Similarly, social models that include several levels of cognitive determinants have more chance of success to explain change in behaviour. Concrete examples applied to infection control issues will be presented. Studies are needed to assess the key determinants of infection control practices and behaviour promotion among the different populations of HCWs, to develop methods to secure senior management support, and to implement and evaluate the impact of the different components of multimodal programmes to promote optimal infection control practices.
inflammatory responses that lead to river blindness. The activation of innate inflammation by the bacteria causes the approach to the treatment of filariasis. Antibiotics have been mutualistic dependence on Wolbachia has been used in a new symbiotic relationship, could also eliminate the cause of filarial onchocerciasis and potent macrofilaricidal activity in lymphatic sustained reductions in microfilariae, long-term sterilization in doxycycline against human filariasis have been encouraging, with essential for their long-term survival. The first trials using the role of a symbiotic bacterium Wolbachia in disease blindness in onchocerciasis. Recent research has highlighted elephantiasis in lymphatic filariasis and skin disease and acute lymphangitis, chronic hydrocoele, lymphodema and.

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S10

THE 2003 JD WILLIAMS LECTURE
XENOTRANSPLANTATION: POTENTIAL INFECTION HAZARDS
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Many emerging infections such as VZV, HIV and SARS have a zoonotic origin. Therefore xenotransplantation—the grafting of animal cells, tissues or organs into immunosuppressed humans—has the potential to increase the risk of cross-species infection by microbes, especially viruses. Vertically transmitted viruses in the source animals (pigs) are difficult to eliminate and in particular genomes of porcine endogenous retrovirus (PERV) are integrated in host DNA. Pigs that are genetically modified in order to prolong xenograft survival may give rise to more readily transmissible viruses. However, analysis of exposed patients has not revealed any evidence of infection by PERV to date. The regulation of clinical xenotransplantation will be briefly reviewed.

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S12

THE 2003 BARNETT CHRISTIE LECTURE
TADPOLE TALES AND TISSUE DESTRUCTION IN TUBERCULOSIS
Nicholas M. Price
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The first matrix metalloproteinase (MMP) was found to be critical for normal tadpole tail resorption. 26 similar zinc-containing proteases have since been identified, which have central roles in physiological tissue turnover and leukocyte extravasation. 92 kDa gelatinase (MMP-9) and 52 kDa interstitial collagenase (MMP-1) are the quantitatively predominant MMPs secreted by monocytic cells, pivotal in anti-tuberculous immunity. MMP-9 degrades type IV collagen; a major component of vascular basement membrane and MMP-1 cleaves the chief structural collagens in lung tissue. Tuberculosis is characterised by a necrotising granulomatous immune response but the cause of tissue destruction is poorly understood. Since excessive MMP activity may be destructive, the hypothesis that dysregulated MMP activity causes tissue injury in TB was investigated. In vitro, human monocytic (THP-1) cells infected by live, virulent Mycobacterium tuberculosis secreted MMP-9 in a dose-dependent manner. At 24 h, MMP-9 concentrations increased 10-fold (p < 0.001 v controls) and de novo MMP-9 mRNA synthesis was detected. In contrast, upregulation of tissue inhibitor of matrix metalloproteinase (TIMP)-1 gene expression and secretion was delayed and less striking. In vivo, MMP-9 concentration per leukocyte in cerebrospinal fluid (CSF) from tuberculous
meningitis patients (n = 23) was higher than in bacterial (n = 12) or viral meningitis (n = 20) (p < 0.01). TIMP-1 concentrations were similar in tuberculous compared with bacterial meningitis or controls. Thus, a phenotype in which MMP-9 activity is relatively unrestricted by TIMP-1 developed in vitro and in vivo. In addition, MMP-9 concentrations/CSF leukocyte (but not TIMP-1 levels) was elevated in fatal tuberculous meningitis and in patients with signs of cerebral damage (unconsciousness, levels) was elevated in fatal tuberculous meningitis and in patients with signs of cerebral damage (unconsciousness, confusion, or neurological deficit; p < 0.05). However, there was no relationship with severity of systemic illness. Biopsies from patients with tuberculous lymphadenitis were next studied by immunohistochemistry. Intense MMP-9 staining was found in monocytc cells forming the center of granuloma and adjacent to necrosis. Minimal TIMP-1 expression again indicated unopposed MMP-9 activity. Since granulomas contain few mycobacteria, the existence of monocyte-monocyte cytokine networks that amplify MMP-9 secretion was investigated in vitro. Conditioned media from M. tuberculosis-infected primary human monocytes or THP-1 cells (CoMTB) stimulated MMP-9 gene expression and >10-fold increase in MMP-9 secretion by monocytes at 3–4 d (p < 0.009 vs controls). Anti-TNF-antibody (but not IL-1 receptor antagonist) pre-treatment inhibited MMP-9 secretion induced by CoMTB, or by direct infection, by 50% (p = 0.0001 and 0.0002 respectively). CoMTB and TNF-independently stimulated dose-dependent MMP-9 secretion. Pertussis toxin inhibited CoMTB-induced MMP-9 secretion and enhanced the inhibitory effect of TNF-blockade (p = 0.05), thus implicating chemokines in the network. Finally, the effects of anti-inflammatory cytokines (IL-4, IL-10 and IL-13) on M. tuberculosis-infected THP-1 cells suggested that MMP activity might be inadequately suppressed. Conversely, interferon-inhibited MMP-9 gene expression and secretion in a dose-dependent manner. In conclusion, M. tuberculosis-infected monocytc cells exhibit a matrix-degrading phenotype in vitro. A similar phenotype was observed in patients where MMP-9 activity was related to local tissue injury and found adjacent to caseous necrosis. Cytokine networks may amplify MMP-9 secretion by monocytc cells within granuloma. TNF-, critical for anti-mycobacterial granuloma formation, is a pivotal autocrine and paracrine regulator. Interferon may protect against MMP-mediated injury.

One or two-stage revision
Excision arthroplasty, arthrodesis or amputation
Studies of debridement and prosthesis retention (‘salvage’ therapy) have been limited by having small numbers and limited follow-up periods. Success rates vary from almost zero in early studies to >50% in carefully selected patients. The duration of symptoms before debridement appears to be a major factor in determining success. There are some outcome data indicating that there are differences according to infecting organism (penicillin-susceptible streptococci > coagulase negative staphylococci > S. aureus). The optimum duration for ‘antibiotic suppression’ is not clear. Zimmerli et al., using an animal model with a S. aureus device-related infection, showed that antibiotic combinations that included rifampicin have a higher rate of cure. This was subsequently supported by a randomised controlled trial.

For patients with an unstable (loose) prosthesis or other factors that make salvage impractical, a one or two-staged revision can be considered. Success rates vary from 75–90% for a one stage procedure and 70–100% in two stages. Success is most likely if all foreign and non-viable material, including cement, is removed. The timing of the two stages and route/duration of antibiotics varies between institutions and studies. Some advocate an aspiration biopsy (off antibiotics) prior to the decision to re-implant. Clearly if the joint is still clinically infected or inflammatory markers still high, a re-debridement (‘second first stage’) is needed prior to considering re-implantation. For knees, a cement spacer is inserted between the two stages. For hips, many surgeons leave the joint with no spacer. Alternatives include cement beads or PROSTALAC implants that aim to preserve function. These devices can contain antibiotics. Whether or not the joint is retained, surgery (especially with knees) may require the use of muscle flaps. Adequate soft tissue coverage (in addition to overall host status) is crucial in determining the likelihood of eradicating infection.

The use of staging systems and the development of consensus definitions may allow the eventual comparison of patient groups, and hence improve the quality of evidence to inform clinical decisions.

S13 EVIDENCE BASED PRACTICE: MANAGEMENT OF INFECTIONS INVOLVING PROSTHETIC JOINTS
Bridget Atkins
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The management of prosthetic joint infection requires a multi-disciplinary approach. Patients need to be assessed and managed jointly by orthopaedic surgeons specialised in complex revision. Tapering/pulsed vancomycin (4–6 weeks) has been used in non-comparative studies. Similarly the combination of vancomycin/rifampicin is unproven and inconsistent with susceptibility data. Saccharomyces boulardii is the best studied biotherapy for CDI, but prophylaxis and treatment efficacy data are inconsistent.
There is a risk of fungaemia, consistent with animal studies showing heterogenous virulence of *S. boullardii* strains. Biotherapy studies have usually been open and small; the true efficacy of almost all of these regimens is unknown. *Lactobacillus GG* trials in acute diarrhoea are conflicting; a recent large study showed no difference to placebo. Rectal biotherapy/infusion of faeces have been used occasionally to circumvent gastric acid degradation of probiotics. Claims of high success rates are undermined by impracticality.

A high molecular weight polymer, GT160-246, binds CD toxins A and B. It protects against death but not colitis in hamsters, and was well tolerated in Phase 1 human trials. There are case reports of CDI unresponsive to standard therapy successfully treated with iv immunoglobulin. Diarrhoea was prevented in hamsters by bovine-sourced immunoglobulin. Non-bovine derived specific anti-toxin antibodies are under investigation. A vaccine containing CD A and B toxoids was safe and immunogenic in healthy volunteers, inducing anti-toxin levels greater than those associated with protection in clinical studies.

**Workshop Abstracts**

**W01**

**ASSESSMENT OF TRAINING NEEDS IN INFECTION CONTROL: DO WE HAVE THE RIGHT APPROACH?**

A. Michael Emmerson

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Edward T. M. Smyth, Consultant Bacteriologist/ICD and Director, Northern Ireland Healthcare-Associated Infection Surveillance Centre (HISC), Kelvin Building, The Royal Hospitals, Belfast BT12 6BA, Ireland

Since the Cooke report of 1995 *Infection Control Teams (ICTs)* have been encouraged to carry out surveillance of healthcare-associated infections (HCAI). Two national prevalence surveys of HCAI have been carried out but surveillance of HCAI has been limited to alert organisms/conditions and a few surgical procedures. However, following the National Audit Office Report ‘The Management and Control of Hospital Acquired Infection in Acute NHS Trusts in England’ greater emphasis has been placed on the need for prospective surveillance of HCAI. Currently ICTs are required to report MRSA bacteraemias and the outcome of elective orthopaedic procedures. In the near future, pressure will be on the ICTs to produce surveillance data on a wider range of alert organisms/conditions and surgical site infections (SSIs) e.g. *Clostridium difficile*, glycopeptide-resistant enterococci, caesarean sections etc. However, the resources needed to carry out these additional studies are not yet in place in many parts of the UK.

This workshop will look at the staff and skills required by an ICT to carry out these mandatory surveillance tasks. As an example, the scenario of SSI surveillance will be examined in more detail. This will include the use of core and local datasets, methodologies, definitions and means of data collection. One way forward is to introduce the concept of an ‘Infection Control Surveillance Co-ordinator’ who will facilitate the whole process. Such a person may require additional training in basic data handling and analysis but these and other skills should be made available to other members of the ICT. The co-ordinator could be from the existing ICT or from others with an appropriate scientific, IT or clerical background.

Currently, the ICTs are made up of consultant microbiologists/ICD and ICNs and other support staff. The ICDs and ICNs are supported by a number of professional bodies who assist in one way or another in basic training and higher degrees. Nevertheless, the ICTs still feel that they are ill-equipped to undertake detailed surveillance of HCAI.

During the discussion a number of questions need to be answered such as who will require teaching, what need to be taught, who will teach and how the teaching will be carried out.

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**W02**

**THE EVIDENCE BASE FOR TRAVEL MEDICINE**

Ron Behrens

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Travel medicine is the rapidly expanding subspecialty of tropical medicine aimed at the prevention of morbidity in travelers. With rapid increase in travel, both regional and international and the many reasons for travel, tourism, commerce and migration the subject encompasses many aspects and specialties of medicine. When providing travelers with advice on morbidity, a risk or hazard assessment needs to be undertaken to define health risks which may be vaccine preventable or modified by behavior. Defining travelers risk requires accurate epidemiological data on morbidity in travellers. The quality of such data in widespread use and the use of endemic disease risk will be evaluated. Data available on the incidence of travel associated morbidity is very limited and of poor quality. Morbidity associated with malaria as a notifiable disease, enables the most precise risk assessment to be made, although comparatively it is a relatively infrequent health problem. Morbidity associated with pre-existing medical conditions, trauma and accidents the most important cause of severe travel morbidity are poorly defined and difficult to predict or advise on. Risk assessment is often therefore based on clinical judgments of perceived risk while efficacy of prophylactics are often based on studies undertaken on endemic native population rather than travelers. For the identified risks, the interventions available should be evidence based and the use shown to provide more benefit than harm.

Safety and toxicity data of prophylactics are often inconsistent and based on nonrepresentative groups. The effective uptake and use of evidence based interventions are poor and unpredictable. Most risk assessments made on travelers are not evidence based and the protection from prophylactic measures has not been derived from pertinent scientific investigation.

Travel medicine is currently an art form awaiting a scientific base.
W04b

SETTING NATIONAL STANDARDS: THE ROLE OF THE NATIONAL TRAVEL HEALTH NETWORK AND CENTRE (NATHNAC)

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Providers of travel medicine services in the United Kingdom vary from General Practice surgeries to specialized travel clinics. The far majority of care is rendered in the GP surgery by a practice nurse. Complex decision-making is required to advise on use of specific vaccines such as yellow fever or Japanese encephalitis, to decide on the destination-specific choice of malaria chemoprophylaxis, and to counsel travelers with special needs. It is important that practices have access to expert advice and to standardized protocols for their decision making. NaTHNaC has been funded by England’s Department of Health to contribute to this expertise with the goal of protecting British travellers. The objectives of NaTHNaC are to:

- Develop and disseminate consistent and authoritative national guidance for health professionals who advise the public traveling abroad;
- Provide a telephone advice line for health care professionals on complex situations relating to the health of travellers;
- Carry out surveillance of infectious and non-infectious hazards abroad;
- Administer Yellow Fever Vaccination Centres;
- Collaborate with health professionals in travel medicine;
- Engage the travel industry, insurance industry, and relevant government bodies in constructive dialogue towards a unified preventive approach;
- Facilitate the training of health care and other personnel in the provision of best quality travel health advice;
- Define short-term and long-term research priorities in travel medicine.

It will be important to review travel medicine practice over time to see if implementing expert advice and standards leads to more consistent advice between practices, cost-effective use of vaccines for travel, and improved health of travellers.

W04c

TRAVEL HEALTH—THE ROLE OF NURSES

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The number of travellers and thus the demand for travel health advice continues to rise, with over 59 million visits abroad made by UK residents in 2002 (Office for National Statistics, 2003). Most travel advice is delivered in the primary care setting. The far majority of care is rendered in the GP surgery by a practice nurse. Complex decision-making is required to advise on use of specific vaccines such as yellow fever or Japanese encephalitis, to decide on the destination-specific choice of malaria chemoprophylaxis, and to counsel travelers with special needs. It is important that practices have access to expert advice and to standardized protocols for their decision making. NaTHNaC has been funded by England’s Department of Health to contribute to this expertise with the goal of protecting British travellers. The objectives of NaTHNaC are to:

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- Define short-term and long-term research priorities in travel medicine.

It will be important to review travel medicine practice over time to see if implementing expert advice and standards leads to more consistent advice between practices, cost-effective use of vaccines for travel, and improved health of travellers.

W05

IMPORTED VIRAL INFECTIONS: RECOGNITION AND SAFE MANAGEMENT

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Most imported viral infections, such as Dengue virus infection, present a diagnostic challenge to clinicians unfamiliar with the disease, its course and management, and the appropriate diagnostic investigations. A few infections, however, also challenge Control of Infection and Public Health responses because of transmissibility to healthcare workers or other contacts, or because of the possibility of new pathogens becoming established in British ecosystems. Although unlikely, the importation or deliberate release of threatening viral agents has caused similar concerns.

Recent experience with SARS and concerns about West Nile virus have highlighted the need for providing information and education about such diseases, and planning for the safe care of cases, and containment of the infections. Using the longer-established examples of Viral Haemorrhagic Fevers (Lassa, Ebola, Marburg and Crimean-Congo haemorrhagic fevers), the necessary steps to recognise and manage imported viral infections will be discussed.

Key factors in mounting an effective response are: awareness of the diseases; information on epidemiology, clinical features and key ‘warning signs’; straightforward plans for safe initial care and investigation; availability of prompt advice and assistance; reliable diagnostic tests; ready availability of operable protocols and policies for continuing care; and capability to ‘scale up’ in the event of an extending problem. It is clear that the maintenance of a body of knowledge and skills, adaptable to emerging demands, is critical to the ability to respond to these challenges.

Oral Presentations

O01

BAT RABIES IN THE UK

D. Nathwani, P. McIntyre, K. White, A. J. Shearer, N. Reynolds, D. Walker and A. R. Fooks

Infectious Diseases Service: royal Free Hospital, London NW3 2QG, UK

The United Kingdom is considered free from rabies, with the previous human death from indigenous rabies recorded in 1902. However, two cases of rabies have been confirmed in the UK in an unvaccinated volunteer bat handler and rescuer, confirmed by antemortem testing to be due to EBLV 2a infection. The UK Departments of Health have long recommended vaccination of licensed bat handlers. We report a case of rabies (CID 2003;37:598-601) acquired in the UK in an unvaccinated volunteer bat handler and rescuer. This oral presentation will outline the practical difficulties in diagnosing exotic infections and dealing with a ‘hysterical’ media and public response.
Other messages
Bites from UK bats can cause rabies in humans.
Rabies immunisation is essential for bat handlers and post-exposure treatment for rabies is essential for patients bitten by bats.
Patients with acute flaccid paralysis and presumptive viral encephalitis should be asked if they have been bitten by bats, irrespective of travel history.

Ante-mortem diagnosis of bat rabies in humans is possible using RT-PCR.

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DIENTAMOEBA FRAGILIS—A COMMON PARASITE, INFREQUENTLY REPORTED

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Dientamoeba fragilis is a neglected human parasite with a controversial history in terms of taxonomy and pathogenicity. However, there is an increasing body of medical evidence that D. fragilis can cause infection leading to acute and chronic gastrointestinal symptoms, including colitis problems and symptoms identical to irritable bowel syndrome. The parasite can also cause fatal granulomatous amoebic encephalitis (GAE) and eye keratitis. However, the pathogenesis and pathophysiology of these emerging diseases remains incompletely understood. Aims: To identify Acanthamoeba as a treatable parasite. Or would your laboratory be able to identify this treatable parasite? Or would your patients simply be labelled as having irritable bowel syndrome?

Relative utilities of urinary antigen, serology and culture for the diagnosis of infection with Legionella pneumophila in an outbreak setting

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The major outbreak of Legionella pneumophila serogroup 1 infection in Barrow in the summer of 2002 offered an opportunity to examine the relative utilities of the current diagnostic tests. Methods: Urinary antigen was screened for with the rapid immunochromatographic assay (Binax NOW), and confirmed by plate Enzyme-immunoassay (EIA) Bartels Assay. These confirmatory tests were also performed on urine from strongly suspected hospitalised cases and/or patients with positive serology who had negative urinary screening results. Serology was performed by EIA and confirmed by immunofluorescent antibody testing (IFAT) with and without campylobacter blocking fluid. A single titre of 64 or a 4-fold rise in titre to 32 was accepted as positive. Respiratory samples were cultured on blood charcoal yeast-extract agar.

Results: A total of 180 patients had infection confirmed by at least one test. Of the 45 cases in whom samples were collected for culture (16.3%) were positive. Only one patient was confirmed by culture alone. Among the 110 cases with both urine samples and adequate serological follow-up 52 (47.3%) were positive by both tests, 39 (35.5%) with positive urine failed to seroconvert and 19 (17.3%) with positive serology had negative urinary antigen assays.

Conclusions: The tests are complementary: urinary antigen allows rapid testing of many samples; serology will pick up some cases missed on urinary testing. While culture is not feasible in many cases it is important in confirming an environmental source. Continuing to accept serology as the ‘Gold Standard’ is flawed, as a substantial proportion of patients with positive urinary antigen tests (42.9%: 95 CI 32.5-53.7) will not seroconvert with the current assays even with adequate follow up. Some patients with clinically convincing evidence of Legionnaire’s disease remained negative by all tests.

Acanthamoeba induces cell cycle arrest in host cells

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Acanthamoeba is an opportunistic protozoan parasite, which can cause fatal granulomatous amoebic encephalitis (GAE) and eye keratitis. However, the pathogenesis and pathophysiology of these emerging diseases remains incompletely understood. Aims of this study were to determine the effects of Acanthamoeba on host cell cycle using human brain microvascular endothelial cells (HBMEC) and human corneal epithelial cells (HCEC). Two isolates of Acanthamoeba belonging to T1 genotype (GAE isolate) and T4 genotype (Keratitis isolate) were used and their pathogenic potential determined using HBMEC and HCEC.
for all those involved in the control of infection to understand the unique difficulties of this type of patient transport, and appreciate that even in arduous circumstances, infection control must remain a priority.

O09*

SARS—THE TORONTO EXPERIENCE FROM AN NHS PERSPECTIVE

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The world watched with morbid fascination as China, Hong Kong and Singapore were swamped by SARS in early 2003. When it became apparent that Toronto also had an epidemic, other western countries felt more vulnerable, but I think we still underestimated how easily this could happen in the UK.

I had the opportunity to spend 2 weeks in June 2003 working as an Infectious Disease physician in one of hospitals in the Greater Toronto Area. My experience there, both from the work I was able to do, plus conversations I had with people who had been there throughout the epidemic, left me with the conviction that the next ‘Toronto experience’ could very easily be in the UK.

I present a personal view of my experience working in a hospital with SARS, with thoughts on how NHS Trusts should be preparing for an epidemic of this proportion.

O10

INCREASED SKIN INFECTION BY EXFOLIATIVE STAPHYLOCOCCUS AUREUS AND HIGH USAGE OF STEROID-HEALTH PROBLEMS FOR NON-HIV/AIDS AND HIV/AIDS PEOPLE IN KENYA

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Meds: Mission of Essential Drugs

Introduction: Skin infection due to opportunistic pathogens has become a major problem to HIV/AIDS and non-HIV/AIDS people in Kenya as HIV prevalence keeps rising in the world. It represents as recurrent itchy rashes. It mimics various dermatology (e.g. cellulitis, acne etc.), allergy and asthma like conditions. This has resulted to high use of steroids, antibiotics and anti fungal without success. The immuno suppressant effect of steroids could be worsening these conditions on HIV/AIDS patients. A collaborative community based programme was initiated by Infection Control Association of Kenya (ICAK) and NGOs taking care of the sick to investigate the agents, control antibiotics and steroids/antifungal high usage, by giving health providers effective alternative.

Method: Itchy conditions were investigated (1) chlorhecidine (2) centrimide, chlorhexidine, + Centrimide, Benzalkonumechloride, providone iodine, for bacteria/fungal infections and isolates identified. Various locally available antiseptics were tried on patients with bacterial infection to eliminate the bacteria and itching and development of normal skin was monitored for three years. Steroids/antibiotics and anti fungal were withdrawn.

Results: Pure growth of exfoliative Staphylococcus aureus was isolated from 80% of recurrent itchy cases while normal skin and mixed growth of skin normal flora. This strain produces exfoliative toxins A, B and epidermolytic toxins which cause scalded skin syndrome and itching conditions. The ointment, which is composed of chlorhexidine gluconate and cetrimide, liquid paraffin and petroleum jelly is able to control itching while others did not control itching, eliminate the exfoliative staphaureus and prevent deformation of the skin. The use of
this has drastically reduced the suffering of patients and use of steroids and antibiotics.

Conclusion: The use of this very low concentration of chlorhexidine/cetrimide ointment by NGOs, (Church Health providers MSFS - Belgium - Spain - France) has drastically reduced suffering of patients, reduced use of topical steroids, antibiotics and anti fungal. For those patients who had been on steroids for a long time, their conditions looked bad and they took longer time to heal with this ointment than those who had not been on steroids. We recommend topical steroids should not be used on HIV/AIDS patients.

O11* A Q FEVER OUTBREAK IN A CARDBOARD BOX MANUFACTURING PLANT
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A large outbreak of Q fever occurred in a cardboard box manufacturing plant situated in an isolated position on Newport Dock during August and September 2002. The factory had no association with animals or animal products. Blood samples (253) were taken at the time from a total workforce of 282 employees, including a number of subcontractors, in the factory. A total of 95 cases of Q fever were confirmed by a combination of complement fixation testing and immunofluorescence. Cohort and nested case control studies were performed on staff in the factory. Questionnaires were completed by 214 individuals. Clinical and serological follow up for the period of 1 year has been completed on 66 of the 95 confirmed cases.

There were a number of individuals who were only present in the factory on certain days. These cases suggested a point source occurring around the 5-9 August 2002. The epidemic curve was consistent with this. A number of potential sources were investigated including wind borne spread from neighbouring farmland, contamination from lorries carrying hay, contaminated landfill site, feral cats and spread from an individual case in the factory. Extensive renovation work was being undertaken at the time of the outbreak and building materials were also investigated as a possible source of the outbreak.

The presentation/poster highlights a number of difficulties when investigating an outbreak of Q fever, including some of the factors of transmission. This, with the results of the modelling, provides strong evidence. Four of these provided evidence that intensive control measures including patient isolation were effective in controlling MRSA. In two others IW use failed to prevent endemic MRSA. There was no robust economic revaluation. Models showed that improving the detection rate or ensuring adequate isolation capacity reduced endemic levels, with substantial savings achievable.

Interpretation: Major methodological weaknesses and inadequate reporting in published research mean that many plausible alternative explanations for reductions in MRSA acquisition associated with interventions cannot be excluded. No well-designed studies allow the role of isolation measures alone to be assessed. Nonetheless, there is evidence that concerted efforts that include isolation can reduce MRSA even when endemic. This, with the results of the modelling, provides testable hypotheses for future research.

O13 A PROSPECTIVE COHORT STUDY OF TRANSMISSION OF NOSOCOMIAL PATHOGENS IN AN ADULT INTENSIVE CARE UNIT: RISK FACTORS AND FREQUENCY OF OCCURRENCE
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Background: Little is known about the rate of transmission of nosocomial pathogens, the risk factors involved and the relative effectiveness of infection control procedures in Adult Intensive Care Units (AICUs) under endemic conditions.

Objectives: To determine the incidence and to identify the risk factors of cross transmission of nosocomial pathogens in AICU.

Design and Setting: A prospective cohort study was conducted from January 2000 to April 2001 in a 16 bed AICU of a 1500-bed tertiary teaching hospital.

Patients and Methods: 430 patients who were admitted for >48 h to the AICU, were followed and data on exposures collected daily. Bacterial clones were identified by molecular typing. Transmission events were identified when two or more patients had indistinguishable isolates and were treated in the AICU during overlapping intervals or no more than 7 days apart. The direction of transmission could only be ascertained if the incriminated pathogen was isolated from the donor before admission of the recipient. In all other instances where the direction of transmission could not be determined, patients were regarded as potential recipients and censured for the current
analysis. Odds ratios (OR) and 95% confidence intervals (CI) for risk factors of transmission were calculated using logistic regression.

Results: Patients were followed for 3947 patient days. 275 isolates were collected and typed. In total, 40 episodes of cross-transmission were detected. Twenty-eight patients were ascertainment recipients (6.5%), giving a density (incidence rate) for the first incident of 7 per 1000 patient days and a median time to event of 5 days. Immunosuppression [OR 3.9, CI 1.2–12.5], understaffing [OR 3.3, CI 1.4–7.8], naso-gastric tubes [OR 2.9, CI 1.1–7.8], ventilation [OR 2.5, CI 1.1–6.0] and bronchoscopy [OR 5.1, CI 1.04–25] were found to be independent risk factors for cross-transmission.

Conclusion: Using the new case definitions, this study showed that endemic cross-transmission of nosocomial pathogens in AICU is infrequent compared with published studies. Risk factors for transmission were detected. Twenty-eight patients were ascertainment recipients (6.5%), giving a density (incidence rate) for the first incident of 7 per 1000 patient days and a median time to event of 5 days. Immunosuppression [OR 3.9, CI 1.2–12.5], understaffing [OR 3.3, CI 1.4–7.8], naso-gastric tubes [OR 2.9, CI 1.1–7.8], ventilation [OR 2.5, CI 1.1–6.0] and bronchoscopy [OR 5.1, CI 1.04–25] were found to be independent risk factors for cross-transmission.

The Nasal Airways: A Potential Method to Assist Adherence to Antiretroviral Medication

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Introduction: Adherence to antiretroviral medication is known to be highly important in achieving viral suppression and preventing early emergence of resistance. The complexity of regimes and tablet burden make adherence difficult and when this is combined with the chaotic nature of the lives of some HIV patients, it is not surprising that failure to adhere to regimes is common. Text messaging is cheap and accessible and automated texting to large numbers of patients has been shown to be acceptable and useful in the management of other chronic illnesses. However, it was felt that the potential stigma which still surrounds HIV would make text messaging about HIV unpopular with the majority of HIV patients.

Methods: A questionnaire, designed to look at current compliance with therapy and attitudes to text messaging, was offered to 68 HIV patients attending a clinic. Patients were asked to complete this at the time of their clinic visit and results were collected anonymously.

Results: 65/68 questionnaires (96%) were completed and returned. Mean time since diagnosis was 6.18 years (range 0–20). 55/65(85%) patients were currently on antiretroviral treatment and of those 18 found their treatment complicated. Only 13 of those on medication (24%) stated that they always took each of their medications at the right time, with the rest admitting to sometimes taking tablets late, occasionally forgetting or frequently forgetting (more than once a week) to take a
ADMINISTRATION OF VANCOMYCIN—IS WHAT YOU THINK, WHAT THE PATIENT GETS?
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Appropriate choice and use of antimicrobial therapy improves patient outcome and prevents the spread of antimicrobial resistance. Informal observations by the clinical microbiology team suggested that patients were not receiving all doses of vancomycin prescribed. Consequently, we have conducted a prospective audit of vancomycin use in our institution.

Methods: Patients receiving vancomycin therapy were identified from pharmacy and laboratory records and consultations sent to the microbiology team. A member of the clinical microbiology team reviewed patients on a daily basis. Details of patient demographics, indications for therapy, doses given and reasons for missed doses were recorded on a database. (Microsoft excel) Appropriate vancomycin therapy was defined as either treatment of a positive isolate or involvement of the clinical microbiology team in the decision to treat.

Results: Details of Vancomycin use in 33 patients have been recorded to date. Indications for vancomycin therapy are outlined in Fig. 1. Only 3/33 patients were on vancomycin inappropriately. Of 529 prescribed doses, patients received only 383 doses. 97 doses of Vancomycin were withheld for no apparent reason. Of the remaining prescriptions, doses were withheld because of either toxic drug levels (44 doses) or lack of intravenous access (5 doses).

Conclusion: Vancomycin is being used appropriately in our institution. Of the doses not given, 66% were withheld inappropriately. This study highlights the need for feedback of this audit and ongoing education of health care professionals, on administration and laboratory monitoring of Vancomycin.

![Fig. 1](image-url) Indications for Vancomycin use in 33 patients.
P04*
A CRITICAL EVALUATION OF AN ANTIMICROBIAL MANAGEMENT PROGRAMME
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At Southampton University Hospitals NHS Trust, Antimicrobial Management Teams (AMTs) comprising of a consultant microbiologist and a senior directorate-based pharmacist were established in seven directorates from September 2000. This study prospectively assessed the impact of AMT decisions on patient outcome, incidence of healthcare associated infection (HCAI) and antibiotic acquisition cost saving over a three month period in 2003.
Results: 946 patient episodes across the seven directorates of cardiology, care of the elderly, haematology, medicine, neurology, orthopaedics and surgery were analysed. 893 of 1074 (83%) AMT inputs were interventional. No significant detrimental effect on either patient mortality or length of stay as a result of stopping antibiotics was identified. In 3.1% of patient episodes the advice given by the AMT was not adopted by the attending physicians. In 55% (6/11) cases this was due to new clinical circumstances arising after the ward round. The remaining 5 episodes were rectified by the AMT the following week. The AMT ward rounds reduced use of intravenous antimicrobials by up to 48% and made direct antimicrobial cost savings on the ward round day of up to 42%. Total cost savings to the Trust ranged from £17k–£107k per annum dependent on the number of days that the antibiotic changes made by the AMT pre-empted similar decisions by the attending team. This represents up to 14% of the annual antibiotic budget for some directorates. The total cost saving to the Trust in terms of nursing time saved and prevention of health-care associated infection (HCAI) is much greater. AMTs are interventional, improve patient care and can save large sums of money.

P05*
CAN THE ANTIBIOTIC PRESSURES ON AN INTENSIVE CARE UNIT BE REDUCED?
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The increasing emergence of antibiotic resistant bacteria is of major concern for Intensive Care Unit (ICU) patients. This prospective study aimed to examine the antibiotic usage on a 9 bed adult ICU and the relationship with methicillin resistant Staphylococcus aureus (MRSA) colonisation. During an initial 8 months period all patients admitted to ICU for >24 h were included in the study; demographic and antibiotic data were collected and enhanced MRSA screening. Two hundred and fifteen patients were included, of which 26% were colonised with MRSA. Eighty eight per cent of patients received at least 1 antibiotic, with a mean of 2. Despite being used primarily as surgical prophylaxis agents, cefuroxime and metronidazole were the two most heavily prescribed antibiotics, with both being prescribed for extended periods. All evidence based guidelines for surgical prophylaxis recommend one dose on induction and we therefore implemented an educational programme involving the microbiologists, surgeons, pharmacists and anaesthetists to advocate one off surgical prophylaxis on induction. After the education programme a second period of data collection and MRSA screening took place and to date 37 patients have been included; 24% of which were colonised with MRSA and 86% have received at least 1 antibiotic. Cefuroxime and metronidazole usage has been reduced from 20.6 to 3.8 DDD/100 bed days and 33.1 to 13.8 DDD/100 bed days respectively. There has been an increased usage of tazocin, but other antibiotic usage has remained relatively constant. We have demonstrated that by using a multidisciplinary approach it is possible to reduce the post surgical prophylactic usage of antibiotics on the ICU; thereby potentially reducing the antibiotic selective pressure and in the long term the presence of multi resistant bacteria.

P06
ALTERED ANTIBIOTIC SENSITIVITY PROFILES AND CELL WALL STRUCTURE ASSOCIATED WITH A TRANSIENT CELL WALL-DEFICIENT PHENOTYPE IN STAPHYLOCOCCUS AUREUS
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Objectives: Cell wall-deficient bacteria (CWDB) have been associated with numerous disease processes, however, we still do not completely understand the factors that cause the loss of cell wall, in vivo, or the consequences of cell wall-deficiency on bacterial metabolism. Our objectives were to characterise the changes in antibiotic sensitivity and cell wall structure that occur when Staphylococcus aureus cells adopt a transient cell wall-deficient phenotype.
Methods: We induced cell wall-deficient variants of S. aureus, on media with high osmotic potential, in the presence of sub-lethal levels of penicillin. Antibiotic sensitivity profiles were determined using disc diffusion and agar dilution tests; sensitivity to cell wall active enzymes, intact cell matrix assisted laser desorption/ionisation time of flight mass spectrometry (MALDI-TOF) and high performance liquid chromatography (HPLC) methods were used to analyse cell wall structure.
Results: CWDB were resistant to b-lactams and stained gram-negative. When cells were allowed to recover their wall by passage in the absence of penicillin, they displayed stable, high level, resistance to b-lactam antibiotics and had altered sensitivities to several other classes of antibiotic. In this revertant state, the cells had decreased sensitivity to lysis by lysostaphin and an altered signature on MALDI-TOF. The revertant cells had approximately 2.5 times more mass of cell wall than wild-type cells, the peptidoglycan of which had shorter glycan chains and a greater number of pentaglycine cross-bridges.
Conclusions: Staphylococcus aureus cells which have been induced to transiently lose their cell walls, in the presence of penicillin, acquire stable, high level, resistance to b-lactams and have altered sensitivity to several other classes of antibiotics. Their cell walls are also altered and it is likely that this is partly responsible for the changed antibiotic sensitivity profile.
P07
URINE SAMPLING BEHAVIOUR IN GENERAL MEDICAL PRACTICES IN WALES
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Objectives: The aim of this study was to elucidate the factors associated with the wide variation in general practitioners (GPs) urine sampling and antibiotic prescribing behaviour for patients with suspected urinary tract infections (UTIs).

Method: A questionnaire was designed to obtain information on the management of UTIs, comprising questions on practice demographics (e.g. list size, deprivation payments), GP demographics (e.g. age, sex) and six case scenarios (requiring details of urine sampling and antibiotic prescribing behaviour). Completed questionnaires were received from 293 GPs at 103 general practices.

Preliminary Results: Twelve percent of GPs stated that they had a policy for referring samples for microbiological analysis; 28.1%—that laboratory susceptibility results always influenced the choice of agent for empirical therapy; 23.3%—would always request a further urine sample if the patient re-presented with symptoms suggestive of treatment failure; 67.8%—would always change therapy based on the laboratory susceptibility results in the case of treatment failures.

Conclusions: There is a high level of variation in urine sample submission rates throughout Wales, indicating a lack of consensus on sampling policy. The dynamics of urine sampling and antibiotic prescribing behaviour are complex. Further analysis of this data will be presented.

P08
SUCCESSFUL USE OF FEEDBACK TO REDUCE BROAD SPECTRUM, AND INCREASE NARROW SPECTRUM ANTIBIOTIC USAGE
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Background: Optimal antibiotic prescribing has become a NHS priority in a drive to reduce antimicrobial resistance and health care associated infection. (HCAI). Systematic review suggests that regular feedback is the most effective measure to alter health care workers behaviour. We examined the effect of regular feedback to doctors of antibiotic usage on antibiotic prescribing rates. The effect on rates of Clostridium difficile infection (CDI), a common form of HCAI and an unwanted side effect of antibiotic use, was also examined.

Methods: A prospective interrupted time series study, lasting 42 months (September 1999 - March 2003), with pre-defined pre- and post-intervention periods, was carried out in the acute medical wards for elderly people and included 6129 admissions. In July 2001 a new ‘narrow spectrum’ antibiotic policy was drawn up, recommending less use of Augmentin, increased use of Benzyl Penicillin, Trimethoprim and Amoxycillin and further restricting cephalosporin use. Doctors were given a laminated pocket version of the policy and received feedback, every 8 weeks, of individual antibiotic usage together with CDI rates.

Results: After introduction of the policy, the number of notional 7 day courses per 100 admissions per month fell from 13 to 2 for Cephalosporins and from 39 to 13 for Augmentin. Benzyl Penicillin use tripled and that of Trimethoprim doubled. Amoxycillin use rose by 50%. CDI rates fell from 3 to 1 per 100 admissions per month. Estimated savings of £191,000 were generated from reductions in cephalosporin use and CDI cases avoided over a 21 month period.

Conclusions: Introduction of a narrow spectrum antibiotic policy, reinforced by regular feedback, was associated with a reduction in broad spectrum antibiotic use (cephalosporins and augmentin), an increase in narrow spectrum antibiotic prescription (benzylpenicillin, trimethoprim and amoxycillin), reduction in CDI rates and considerable savings. Feedback appears to be an effective tool to optimize antibiotic use.

P09
AN OBSERVATIONAL STUDY TO DETERMINE THE ADEQUACY OF CLINICAL INFORMATION PROVISION FOR ANTIBIOTIC ASSAYS ON MICROBIOLOGY REQUEST FORMS
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Aim: To determine the level of clinical information provided for antibiotic assays on microbiology request forms.

Methods: Antibiotic assay request forms from two teaching hospitals in Leeds were collected over one month. Antibiotic dosage schedule, timing of last dose, nature of assay, sampling time and the identity of the requesting staff member (doctor/nurse) were collected on each patient.

Results: A total of 1151 request forms were analysed. Information regarding nature of assay was provided on 761 (66.1%), sampling time on 702 (61%) and antibiotic dose on 224 (19.5%). The dosage schedule was mentioned on 211 (18.3%) and timing of last dose on 105 (9.1%). Thus only 17 (1.5%) provided all the relevant clinical data.

Discussion: About two thirds of the requests had information on the assay type (peak/trough/random) and sampling time. However only a small proportion (between 9-20%) provided rest of the necessary information such as timing of last dose, dosage schedule and antibiotic dose, vital for accurate interpretation. This may result in incorrect dosage adjustment, which may potentially be detrimental to patient care and have medicolegal implications. Microbiology and clinical staff time was wasted in trying to obtain this information over the telephone.

Conclusion: The clinical information provided on microbiology request forms for antibiotic assays was inadequate. This led to modification in the request forms and an educational programme for junior medical staff was recommended.

P10
AUDIT OF OUTPATIENT AND HOME ANTIBIOTIC THERAPY (OHPAT) SERVICE: AUGUST 2001 - AUGUST 2003
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Introduction: In response to increasing bed pressures in the Medical Division at The James Cook University Hospital, an Outpatient and Home Antibiotic Therapy (OHPAT) Service was commenced in August 2002, under the auspices of an Infectious Disease Consultant (BM) and a Clinical Nurse Specialist (DB). This service would also allow patients to maintain their lifestyle, avoid hospital acquired infections as well as allowing early discharge. An audit of patients with cellulitis on the Medical Unit before the OHPAT service was commenced, found the average
stay inpatient was 9.5 days, but for those greater than 75 years old was 22 days.

The Service: Patients were mainly referred from the Medical Admissions Unit (MAU) and seen the same day by DB for suitability. Patients were administered their 1st dose of antibiotic on MAU and observed for 30 minutes before being allowed home. MAU staff arranged appropriate investigations. Patients then returned to the Infection Unit on a daily basis for parenteral antibiotics until there was satisfactory improvement. Hospital taxis were provided for those without private transport. Medical review by BM was twice weekly and management altered as thought appropriate. At discharge DB sent a discharge summary to the patient’s GP. All drug costs were incurred by the Medical Division.

Results: 282 patients have been seen, 218 (77%) having cellulitis. The mean length of iv antibiotic therapy for cellulitis was 9 days, with iv Ceftriaxone being antibiotic of choice unless there was a significant contradiction or adverse effect. Some patients were treated with prolonged courses of iv antibiotic (e.g. Malignant otitis externa for 115 days and 2 cases of MRSA spinal discitis treated for a total of 203 days). Overall 2834 patient days of iv therapy was administered. The estimated cost of an in-patient is £240/day, therefore approximately £680 160 was saved by early patient discharge. A patient satisfaction survey was organised and 51 questionnaires were distributed randomly and 33 returned. 82% of respondents were very satisfied with the service, no one was dissatisfied. 94% would have chosen the service again, if needed. 88% of patients were able to maintain their normal lifestyle

Conclusions: This service appears to have fulfilled its goal leading to early hospital discharge but maintaining good patient care. The early discharge of patients appears to save significant amounts of money, but in reality, other patients replace those discharged early. However, the ‘spill over’ of acute Medical patients into other divisions was reduced. We now intend to expand this service to other Divisions within the Trust.

P11* IN VITRO ASSESSMENT OF THE ANTIBACTERIAL ACTIVITY OF MANUKA HONEY IN THE PRESENCE AND ABSENCE OF SERUM PROTEINS

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Due to the emergence of antibiotic-resistant wound-infecting bacteria, there is a need to develop new topical antimicrobial agents. One ancient remedy currently being re-considered is honey. Broad-spectrum antimicrobial activity has been demonstrated in vitro, but if honey is to be an effective inhibitor in vivo it must retain potency in the presence of serum proteins, and this has not yet been tested. Using two wound pathogens, the aim of this investigation was to determine whether the presence of serum proteins affected the bactericidal activity of New Zealand manuka honey. Sterile manuka honey (potency equivalent to 19%w/v phenol) was used to determine Minimum Inhibitory Concentration (MIC) against methicillin-resistant Staphylococcus aureus (MRSA) NCTC 10017 and Pseudomonas aeruginosa ATCC 27853 by serial dilution in nutrient broth (Oxoid) with a microtitre plate method. Minimum Bactericidal Concentration (MBC) was determined by plating onto nutrient agar (Oxoid). To determine the effect of serum proteins on antibacterial activity, nutrient broth was replaced by 90% foetal calf serum (FCS). In the absence of FCS, MRSA was more sensitive to manuka honey than Pseud. aeruginosa with MIC values of 2.8% (w/v) and 15% (w/v) respectively. MBCs of 7% and 20.6% respectively, indicated that the mode of action was bactericidal. In the presence of FCS, MICs increased by a factor of approximately 4 and 2, respectively, and activity was bactericidal. These results suggest that although components in FCS reduce the antibacterial activity of a manuka honey in vitro, bactericidal activity against two wound pathogens was still present following dilution by a factor of at least 4. In clinical treatment, when undiluted honey is applied to wounds, exudate will be generated by osmotic effect, but this study suggests that honey will continue to retain bactericidal activity on dilution and in the presence of serum proteins when used in vivo.

P12 INFECTION DISEASES PHARMACISTS IN THE UK: PROGRESS OF A NATIONAL NETWORK 3 YEARS ON

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Background: The need for a national network for pharmacists involved with infection management was identified in 1999.1 At that time, a survey of 85 hospitals revealed that 25 (30%) had pharmacists with full-time (n = 5) or part-time (n = 20) infection management responsibilities. Our objective was to set up a network to support the activities of such pharmacists.

Methods: A national practice interest group in Infection Management was established in 2001 through an existing organisation, the United Kingdom Clinical Pharmacy Association (UKCPA). The aims of the group are to exchange information and clinical experience, evidence and best practice, to support practice research and to provide educational events. A retrospective review of the group’s activities was undertaken in Autumn 2003.

Results: There are currently over 70 members of the practice interest group. At least 50% are antibiotic pharmacists and around 33% are pharmacists responsible for working on antibiotic guidelines and audits. National study days are taking place in October 2003 and October 2004, and the UKCPA has a biannual conference providing further networking opportunities. A resource centre has been established providing material such as protocols and guidelines, and a website has been developed. An e-mail discussion group has received 37 enquiries including requests for protocols (30% of enquiries), drug administration and dosing questions (27%), clinical effectiveness issues (14%), job description requests (11%), and anti-infective supply issues (11%).

Conclusion: A practice interest group for pharmacists involved in infection management has been established in the UK and its activities are outlined. There have been at least 16 additional infection management pharmacist posts established between October 1999 and May 2003. The Department of Health1 then announced the provision of funding to facilitate the development of clinical pharmacy services to assist with antibiotic management. This practice interest group can provide professional support for the anticipated increase in pharmacists specialising in infection management.

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P13
IMPROVING THE MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA: THE IMPACT ON PROCESS AND OUTCOMES OF A MULTI-FACETED EDUCATIONAL INTERVENTION
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Background and Objective: Having previously demonstrated that community-acquired pneumonia (CAP) is sub-optimally managed in Tayside (Clin Infect Dis 2002;34:218-223), our aim was to improve the delivery and appropriateness of initial antibiotic therapy and reduce length of hospital stay.

Method: Process of care and outcomes at two Scottish hospitals were compared prospectively over two winters (November - April 2001/02 and 2002/03) before and after a planned intervention. The primary outcome was the proportion of patients receiving appropriate antibiotics (British Thoracic Society definition) within 4 hours of admission. Secondary outcomes were length of hospital stay and 30-day mortality. Pre-implementation, qualitative and quantitative methods identified potential barriers to the efficient delivery of appropriate antibiotics. This data was used to design a targeted intervention, which consisted of wall-based pathways, promotional posters, implementation packs, educational sessions and audit and feedback. Linear regression was used to calculate unadjusted and severity adjusted absolute change*.

*Absolute change = intervention hospital post - control hospital post

Results: The proportion of patients receiving appropriate antibiotics within 4 hours increased from 33% (60/181) to 56% (118/209) at the intervention hospital and 32% (19/60) to 36% (19/53) at the control hospital (Unadjusted absolute change = 20%, p < 0.01. Adjusted absolute change = 17%, p = 0.035). This was mostly due to a reduction in ‘door to antibiotic time’ rather than improved antibiotic prescribing. There were no significant differences in secondary outcomes. At the intervention hospital, the main reason for not achieving the primary outcome post-implementation was late delivery of antibiotics (71% of 91 cases of non-adherence). In the evaluation period, the maximum achievable adherence to the primary outcome was estimated to be 74%.

Conclusion: The intervention significantly increased the proportion of patients receiving appropriate antibiotics within 4 hours, although there was no evidence of a decrease in length of hospital stay or mortality.

P14
IMPROVING THE MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA: COST-EFFECTIVENESS OF A MULTI-FACETED EDUCATIONAL INTERVENTION
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Background and Objective: The aim was to calculate the cost-effectiveness of an educational intervention to improve the delivery and appropriateness of initial antibiotics in community-acquired pneumonia (CAP).

Method: Analyses were performed from the hospital’s perspective. All costs were calculated using 2002 prices. The direct costs of healthcare were divided into the costs of: 1) hospitalisation and 2) initial antibiotic therapy. Outliers (patients with a length of stay >30 days or those admitted to high dependency) were excluded. Unadjusted and adjusted differences between the mean costs pre and post-implementation were calculated using linear regression. Significantly different net costs were added to intervention costs and then linked to the primary outcome (the proportion of patients receiving appropriate antibiotics within 4 hours of admission).

Results: In the post-intervention period, 40 (95% CI, 19-63) additional patients received appropriate antibiotics within 4 hours. In the pre-intervention period, the cost of hospitalisation and initial antibiotic therapy was £1598 and £6.34 per patient, respectively. Post-intervention, these costs increased to £1601 (adjusted difference = £49, p = 0.7) and £9.01 (adjusted difference = £2.12, p < 0.001). The adjusted total net direct health care cost was £443. The total project cost (including development, implementation, evaluation and training) was £70579 (scenario A). The cost to a hospital adapting, implementing and performing a more limited evaluation was estimated to be £17810 (scenario B). The cost to a hospital adapting and implementing the intervention only was estimated to be £4841 (scenario C). Over the 6-month post-implementation evaluation period, the cost per additional patient receiving appropriate antibiotics within 4 hours with each of these scenarios was £1776 (A), £456 (B) and £132 (C).

Conclusion: The intervention resulted in improved care, but at considerable cost. Costs would decrease notably if electronic case-records were available. The cost-effectiveness ratio also becomes more favourable over time.

P15
MANAGING THE USE OF RESERVED ANTIBIOTICS—THE USE OF MANDATORY ORDER FORMS
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Background: Antibiotic resistance presents a major challenge. Local, national and international guidance suggests we should promote prudent prescribing of antibiotics, particularly for newer agents that should be used only when there are no alternatives. Linezolid, recently launched in the UK, is active against Gram positive bacteria including MRSA and vancomycin-resistant enterococci. It was approved for use in our trust, but only following microbiology or infectious diseases (ID) approval. However, by July 2002, we had treated 54 patients with linezolid in 15 months, expenditure was increasing, and we had isolated a resistant organism. Our objectives were to introduce a system to ensure that linezolid was used only where appropriate, and to assess its impact.

Methods: We removed linezolid from all wards, so it had to be obtained via pharmacy. We adapted a system of mandatory order forms for UK use; these require prescribers to complete details of patient, infection, prescriber, previous agents and microbiology/ID approval. All sections must be completed before dispensing: forms can be faxed to prescribers and back to pharmacy, or filled by pharmacists via telephone. The system also applies at evenings and weekends. We compared linezolid usage before and after its introduction.

Results: Usage decreased from an average of 3.6 patients per month in the first 15 months, to 2.8 in the next 11 months. Comparison of audit forms with pharmacy dispensing data shows that forms were completed for all 54 patients. We have complete audit data for each patient, including clinical specialties, sites of infection and organisms. There was evidence of microbiology/ID approval for 30 of the 31 patients.
Conclusion: Introduction of mandatory order forms curtailed our growth in linezolid use, and provides a system for ongoing monitoring and feedback of usage patterns. We are now extending this system to other anti-infectives.

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P16
THE EFFECT OF THE NOVEL GLYCOPEPTIDE, TD-6424, ON BIOFILMS OF SUSCEPTIBLE AND RESISTANT STAPHYLOCOCCI
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Background: Drug treatment of staphylococcal infections is complicated by the presence of biofilms that harbour populations of organisms less susceptible to antibiotic action. TD-6424 is a concentration-dependent rapidly bactericidal lipated glycopeptide.

Methods: The effects of TD-6424 and four comparator antibiotics (vancomycin, teicoplanin, linezolid and moxifloxacin) were assessed for bactericidal activity against staphylococcal biofilms. The experiments were carried out using Sorbarod biofilms. Strains tested included methicillin-susceptible and resistant strains of Staphylococcus aureus and coagulase-negative staphylococci, as well as GISA strains. Bacteria were exposed to the antibiotics at exponentially decreasing concentrations, representing parenteral administration and also at a constant concentration, representing an IV infusion. Concentrations used correspond to peak serum levels and the rates at which drug concentrations were decreased correspond to their elimination half-lives.

Results: All of the drugs tested produced a reduction in the number of cells eluted from the biofilms with both methods of exposure. Overall, the constant concentration method of antibiotic exposure was more effective than the exponentially decreasing concentration exposure in reducing the number of bacteria eluted from the staphylococcal biofilms. With both methods of exposure, TD-6424 was more effective than the established glycopeptides vancomycin and teicoplanin: 1.0–1.5 log_{10} reduction at the end of the experiment vs. 0–0.5 log_{10} reduction, respectively, in the exponentially decreasing concentration method.

Conclusions: TD-6424 was the most efficient agent among those tested against both the non-GISA and GISA strains by both methods of exposure. It can be concluded that TD-6424 appears to be a promising antibiotic for the treatment of multi-drug resistant staphylococcal biofilm associated infections.

P17
A PATIENT WITH MRSA ENDOCARDITIS RESPONDING TO LINEZOLID AND RIFAMPICIN, BUT NOT TO VANCOMYCIN
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Introduction: Linezolid is the first drug issued from the oxazolidinones, a novel class of antimicrobial agents with potent activity against gram-positive pathogens. Treatment of endocarditis caused by resistant gram-positive organisms like vancomycin-resistant enterococci (VRE), methicillin-resistant Staphylococcus aureus (MRSA) and more recently, glycopeptide-intermediate Staphylococcus aureus (GISA) is difficult. Glycopeptides are an option for MRSA and VRE endocarditis, but literature suggests that response may be suboptimal.

Case Report: We describe an 80 year old man who presented with MRSA mitral valve endocarditis. He was initially treated with IV vancomycin for 28 days, however the patient developed renal impairment during the last 10 days of treatment. 23 days later, he became pyrexial with a high C-reactive protein and blood cultures grew, again, MRSA. The renal function was still impaired and after a single dose of IV vancomycin, he was treated with oral rifampicin (300 mg BD) and linezolid (600 mg BD): the latter was given IV for the first 5 days and then orally for 23 days. Ten days after stopping linezolid, the CRP and serum creatinine came back to normal (after a transient deterioration during the last few days of the linezolid course).

Discussion and Conclusions: There are no clinical trials comparing linezolid treatment with vancomycin or other conventional agents in patients with endocarditis, only a limited number of case reports and two case series in literature. Some animal model studies have found linezolid as effective as vancomycin in treatment of experimental endocarditis. Based on this case report and the literature review, we conclude that, whilst awaiting for medical trials to be conducted, use of linezolid in resistant gram-positive endocarditis may be considered when vancomycin has failed or is contra-indicated. Use of this agent in patients with renal failure might be especially advantageous as the dose does not need to be reduced.

P18*
COMMUNITY ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS PYOMYOSITIS: IS A GLYCOPEPTIDE NECESSARY IN SOME PATIENTS?
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Pyomyositis is a subacute bacterial infection of skeletal muscle. We report a case of pyomyositis of the right thigh and iliopsoas muscle in an intravenous drug user and present a review of the literature revealing few reported cases of community acquired Methicillin-resistant Staphylococcus aureus (MRSA) pyomyositis.

The patient presented with a two week history of pain and swelling of the right thigh. Although an initial diagnosis of deep vein thrombosis was considered, laboratory and imaging studies were suggestive of right thigh and iliopsoas pyomyositis. A diagnosis of pyomyositis was confirmed at operation when incision, drainage and washout were undertaken. The patient worsened on conventional treatment with Benzylpenicillin and Flucloxacillin requiring further incision and drainage. MRSA and Streptococcus pyogenes were cultured from necrotic material excised from the thigh at the initial operation. The antibiotic regimen was converted to include a glycopeptide and following further debridement the patient slowly improved.

A review of the literature was undertaken using searches by Medline and EMBASE. The search found a number of hospital acquired cases of MRSA pyomyositis, but only three reports of community acquired MRSA pyomyositis worldwide, with no case reports in the UK until now. This case report shows that conventional antibiotics for a pyomyositis may not be effective even in patients from the community. It may be necessary to consider a glycopeptide, such as vancomycin, in the initial treatment regimen of pyomyositis in certain subsets of patients such as intravenous drug users and converting to conventional therapy only when the cultures fail to grow resistant organisms.
P19
DETECTION OF MYCOBACTERIUM TUBERCULOSIS DNA BY POLYMERASE CHAIN REACTION
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The objectives of this work were to develop a PCR for M. tuberculosis using primers to the IS6110 insertion element. Although the primers and conditions had been previously published, the PCR reaction was found to lack reproducibility, displaying a 10,000 fold variation in sensitivity. Conditions were changed and a different, thermostable Taq Polymerase was used (‘FastStart’ Taq polymerase, Roche.) Significant contamination problems occurred during optimisation but were completely controlled by use of the enzyme uracil DNA glycosylase (UNG), indicating carryover contamination rather than cross contamination. The sensitivity of the PCR reaction when used on DNA from the type strain of M. tuberculosis, H37Rv, was 5 femtograms (5 x 10^-15 g) or 15 targets. This sensitivity, as well as the specificity of the PCR reaction, was confirmed on Southern blot. From 1983, new food poisoning toxin producing agents have been identified. Application of magnetic resonance imaging for the diagnosis of discitis has led to increased awareness, and culture of disc aspirates has highlighted the bacterial aetiology. A retrospective study of the clinical presentation, investigation and antibiotic treatment of discitis was carried out between August 1996 and September 2002 by review of the clinical notes and laboratory records at the Taunton & Somerset Hospital.

P20
SEPTIC DISCITIS: AN EMERGING MICROBIOLOGICAL CONDITION
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Discitis is an inflammatory process of the intervertebral discs which usually involves the vertebral end plates and may extend into the adjacent tissues. Application of magnetic resonance imaging for the diagnosis of discitis has led to increased awareness, and culture of disc aspirates has highlighted the bacterial aetiology. A retrospective study of the clinical presentation, investigation and antibiotic treatment of discitis was carried out between August 1996 and September 2002 by review of the clinical notes and laboratory records at the Taunton & Somerset Hospital.

P21
SUB-SPECIES OF FUSOBACTERIUM NECROPHORUM IN HUMAN INFECTIONS
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Fusobacterium necrophorum is a associated with serious infections usually in previously healthy young people causing a condition known as Lemierre’s disease. It is also associated with serious infections in animals causing a condition known as necrobacillosis. This organism has been split into two sub-species known as F. necrophorum s.s. necrophorum and F. necrophorum s.s. funduliforme, sometimes referred to as biotypes A and B respectively. The literature states that biotype A is mostly associated with disease in animals and biotype B with human infection although no large-scale investigation of human isolates has been performed to substantiate this. The Anaerobe Reference Laboratory has a large collection of isolates of F. necrophorum referred for identification from cases of human infection, however sub-typing has not been routinely performed. The present paper describes subtyping investigations of 98 isolates of F. necrophorum from human infections based on chick-cell agglutination, alkaline phosphatase and some preliminary PCR-RFLP profiles that appear to differentiate between the two sub-species.

P22
A WAY OF MANAGING CHEAPLY FOOD POISONING DUE TO ENTEROTOXIGENIC E. COLI AND SHIGELLA IN COMMUNITY IN LOW-RESOURCE COUNTRIES—KENYA
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Introduction: At the present, several drug-resistant community acquired infections are causing global concern. This includes emerging enterotoxigenic and toxic E. coli and Shigella organisms transmitted by untreated water and unhygienically prepared foods. The study that has been going on for 14 years in Kenya shows the breakdown of public health facilities, use of untreated water, poverty resulting in unhygienic housing and misuse of antibiotics in trying to treat enteric pathogens thus increasing the morality and morbidity especially on HIV/AIDS people. This shows that although the current enterotoxigenic E. coli are sensitive to new introduced quinolones and cephalosporins, these drugs kill the bacteria but they are not effective on already produced toxins in patients gut. This calls for a new approach to control spread and managing toxin-producing food poisoning agents and neutralize toxins produced. Agents, which are able to neutralize toxins, should be combined with effective antibiotics.

Method: From 1983, food poisoning agents were investigated during the outbreak in Kenya. Sensitivity was done, toxin produced was investigated, and model of transmission was studied. Health providers were advised on drugs to use for management i.e. antibiotics with toxin neutralizing agents (attapulgite) and those without.

Result: From 1983, new food poisoning toxin producing agents have been discovered and added to conventional ones, thus
making management of food poisoning more expensive and difficult. These organisms continued, developing resistance to new drugs through plasmid resistant factors. Food poisoning due to toxigenic agents (E. coli) responded better with antibiotics combined with activated attapulgite (magnesium aluminum silicate). This is a chemical that has a high absorbent power to neutralize toxins produced. Those treated with antibiotics continued to have stomachache and constipation.

Recommendations: Our study shows that antibiotics with attapulgite are one of the cheapest drugs for food poisoning due to food and water borne toxin-producing agent. Eating freshly prepared food is recommended for HIV/AIDS and non-HIV/AIDS people. Raw foods (salads) are not safe in low-resource countries. Treating water at 'Point of use' using sodium hypochlorite is the best solution to controlling food poisoning diseases in low-resource countries.

P23

DIAGNOSIS OF PNEUMOCOCCAL PNEUMONIA USING POLYMERASE CHAIN REACTION ON WHOLE BLOOD

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Objectives: Despite community acquired pneumonia (CAP) being a common condition, aetiological diagnosis remains problematic. The aim of this study was to evaluate the potential role of polymerase chain reaction (PCR) on whole blood in the diagnosis of pneumococcal pneumonia in patients admitted to hospital with CAP.

Methods: A real-time PCR technique using a LightCycler™ (Idaho Technologies) was used to detect the pneumolysin gene of Streptococcus pneumoniae. DNA was extracted using the QIAamp® DNA Mini Kit. EDTA blood samples were collected from 62 adult patients with CAP. The specificity of the assay was determined by performing the test on 46 patients admitted with a diagnosis other than CAP. Results of PCR were compared with those of routine cultures. The relationship between illness severity and PCR results was also investigated.

Results: PCR was positive in 5/62 (8%) patients with CAP. Blood culture was positive in 2/62 (3%) patients. The difference was not statistically significant (p = 0.25). PCR was positive in 5/30 (17%) cases with severe pneumonia and none of the cases with non-severe pneumonia (p = 0.03). PCR was negative on all 46 control samples giving a specificity of 100%.

Conclusion: PCR on whole blood was not sensitive enough to offer any improvement in the diagnosis of pneumococcal pneumonia in this study. The small number of positive PCR or blood culture results may reflect a limited number of true cases of pneumococcal pneumonia in this study, and would have had low statistical power to detect a difference between the two diagnostic methods. PCR techniques using larger volumes of blood and different extraction techniques may improve the sensitivity. These results suggest however that there may be a role for PCR in the diagnosis of patients who are admitted with severe pneumonia or septicemia in whom a definite diagnosis is not yet established.

P24

USE OF ORAL ANTIBIOTICS IN TREATMENT OF BONE AND JOINT INFECTIONS IN THE UK

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Background and Objective: Effective treatment of adult orthopaedic infection can be difficult. Historically, 4-6 weeks parenteral therapy has been recommended. The establishment of Outpatient or Home Parenteral Antibiotic Therapy (OHPAT) schemes in USA, Europe and now the UK, facilitate delivery of prolonged intravenous (iv) therapy. We are not aware of evidence-based guidelines on the duration of iv antibiotics for bone and joint infection, but have experience in the use of initial iv followed by oral (po) antibiotics and suspect that this approach to management is used widely in the UK. Recommended use of po antibiotics by other Medical Microbiologists in this country and knowledge of treatment guidelines with respect to orthopaedic infection was investigated, to determine whether 6 weeks iv therapy is still considered standard practice for orthopaedic infection.

Method: A questionnaire about antibiotic recommendations for defined orthopaedic infections, knowledge of published guidelines and availability of local OHPAT was sent to 271 microbiologists in the British Isles and Ireland.

Results: 94 (35%) questionnaires were returned. Oral antibiotics are recommended in treatment of MSSA osteomyelitis and septic arthritis by 94% and 91% of those responding. 80% recommend iv to oral switch for MRSA osteomyelitis and 64% during 2-stage replacement of a prosthetic knee infection. 74% microbiologists responding were unaware of evidence-based guidelines on duration of iv antibiotics for orthopaedic infections. 36% had access to OHPAT locally.

Conclusions: Despite traditional use of 4-6 weeks parenteral therapy for bone and joint infection, there is a lack of evidence-base for this and oral antibiotics are commonly recommended by Medical Microbiologists in the management of these infections in this country. Early oral switch therapy may be one reason why OHPAT has not become as widely established in the UK as it is in USA.

P25

THE SEROLOGICAL DIAGNOSIS OF INFECTIVE ENDOCARDITIS

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Staphylococci, streptococci and enterococci together account for 85% of infective endocarditis (IE) cases. Diagnosis is difficult if the microorganism is not isolated, possibly due to prior antibiotic therapy. The aim of this study was to develop a panel of serological tests for the diagnosis of IE caused by Gram-positive cocci.

A panel of three antigen-based ELISAs to measure serum antibody levels to Gram-positive cocci was developed and applied to the diagnosis of IE. The assays were based on the detection of IgG specific to EfaA (enterococci), a Staphylococcus aureus whole-cell antigen preparation, and SorA (Streptococcus oralis EfaA homologue). Each component ELISA gave the following parameters:

Staphylococci Streptococci Enterococci Sensitivity 86% 91% 89% Specificity 89% 36% 89% Positive predictive value 88% 45% 59% Negative predictive value 87% 88% 98% likelihood ratio of a positive test 7.8 1.42 8.1 likelihood ratio of a negative test 6.4 4.4 8.1 Accuracy 87% 57% 89%

Serum samples were collected from 111 IE patients confirmed as ‘definite’ or ‘possible’ by the Duke criteria: 48 staphylococcal IE;
37 streptococcal IE; 17 enterococcal IE; 6 patients with IE caused by other microorganisms, and 3 polymicrobial infections. The set of three serum antibody titres for each patient were subjected to hierarchical cluster analysis using Pearson correlation (SPSS). Of the streptococcal patients 73% were located in cluster one and 83% of staphylococcal patients separated into cluster two. A diagnostic panel of ELISAs is independent of both endocardial imaging and microbial culture results. Neither is it affected by prior antibiotic therapy making it complementary to currently used investigations. This rapid and inexpensive assay may augment the Duke criteria for diagnosing Gram-positive coccal IE.

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**P26**

**MOLECULAR ANALYSIS OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS STRAINS USING PULSED-FIELD GEL ELECTROPHORESIS AND CORRELATION OF PROFILE WITH ISOLATE SOURCE**

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Methicillin-resistant Staphylococcus aureus (MRSA) is an established nosocomial pathogen with increasing reports of multiple-resistant (MR) strains and more recently observations of an emerging problem within the community. The objective of this study was to investigate whether pulsed-field gel electrophoresis (PFGE) of Smal macrofragments (considered the gold standard for typing), could be used to distinguish community-acquired (CA) MRSA strains from hospital-acquired (HA) MRSA strains. A total of 84 MRSA isolates were typed: 1 NCTC 8325 strain, 8 MR-HA-MRSA isolates (only sensitive to vancomycin, tetracycline and rifampicin), 20 CA-MRSA isolates from the West Midlands and 53 HA-MRSA isolates, including known EMRSA-15 and EMRSA-16 strains. The profiles generated were analysed using GelCompar 4.0 with the band matching coefficient of Dice and UPGMA clustering to determine profile relatedness. Analysis indicated that 15 HA-MRSA and 6 CA-MRSA strains were indistinguishable from the EMRSA-15 genotype. In addition, 12 HA-MRSA strains and 2 CA-MRSA strains shared the EMRSA-16 genotype. Interestingly, 3 HA-MRSA and 1 CA-MRSA shared the same genotype as the 8 MR-HA-MRSA strains. The remaining CAMRSA strains shared the same genotype with 1 or more of the HA-MRSA strains excluding 5 CA-MRSA strains, which had unique profiles. Overall strain relatedness was 50% but could be sub-divided into 3 distinct groups. Group 1 consisted of 16 CA-MRSA and 24 HA-MRSA; strains were 90% related. Group 2 consisted of 8 MR-HA-MRSA, 3 CA-MRSA and 21 HA-MRSA; strains were 86% related. Group 3 was a heterogeneous group consisting of 1 CA-MRSA and 11 HA-MRSA. This study suggests a correlation between the PFGE profile and isolate source which may be useful in inferring strain history.

**P27**

**THE ROLE OF ULTRASOUND-GUIDED BIOPSY IN ABDOMINAL TUBERCULOSIS**

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We present 5 cases of abdominal tuberculosis (TB) with two different means of diagnosis. Four patients were of Indian subcontinent origin and all presented with non-specific symptoms, abdominal distension and pyrexia. Two of them became very unwell and needed admission to intensive care unit. In all the cases ultrasound showed peritoneal thickening and omental cake. Two of them had chest X-ray changes in addition. Two patients had the diagnosis made on laparotomy. The first patient underwent an urgent laparotomy because of clinical deterioration. The second patient had a laparoscopy that was converted to open laparotomy. Tissue obtained from both procedures demonstrated caseating granulomas. They developed significant pain, post-surgical ileus and were starved for several days.

Three patients had their diagnosis made much more easily via an ultrasound-guided biopsy. One patient, despite absence of risk factors, grew a multidrug resistant (MDR) TB. Another who had spent considerable time caring for patients with MDR-TB, was diagnosed by histology (tubercle bacilli and caseating granulomas demonstrated). Unfortunately, in this case, cultures remained negative after 8 weeks. Both of these patients had CXR changes but were unable to produce sputum spontaneously or by induced methods.

This poster provides a pictorial review of abdominal imaging in tuberculosis and aims to demonstrate that US-guided biopsy may be the preferred option to consider in suspected cases of abdominal TB. It is minimally invasive, safe for the patient and when performed by an experienced operator has a good diagnostic yield.

**P28**

**REGIONAL SURVEY OF MRSA CONTAINMENT MEASURES ACROSS CRITICAL CARE UNITS**

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**Introduction:** Critical Care Units (CCUs) are high-risk areas for both cross-contamination and infection with MRSA. Current UK guidelines on MRSA control in hospitals were last revised in 1998. These recommend that CCUs routinely screen patients transferred from an MRSA-affected ward, undertake discharge screening and isolate known carriers if MRSA is endemic. However, in view of the increasing burden of nosocomial MRSA, these guidelines are unlikely to be fully implemented. The objective of this study was to therefore assess current MRSA control measures in CCUs to determine if present practices should influence future national recommendations.

**Methods:** A postal questionnaire was sent to 77 CCUs in the South East Thames Region. These included intensive care/high dependency units, specialist units (e.g. neurological and burns units) and coronary care/cardiac units. In addition questionnaires were sent to 44 infection control teams within the region. Of 121 questionnaires sent, 61 (50%) were returned. The majority of respondents (80%) attempted single room or cohort isolation of MRSA patients. However, only 64 CCU single rooms were identified in the survey and 72% of respondents felt that further single rooms in their unit were required. Nevertheless, only 17% of respondents would close CCU beds if cohorting MRSA patients. 51% of respondents relied on signs or tape around a bed to highlight an MRSA patient. 67% of CCUs screened all patients on admission whilst only 20% screened on discharge. 44% of CCUs preferred to use weekly surveillance methods. 40% of CCUs would only accept a known MRSA carrier if suitable isolation facilities were available. MRSA patients routinely underwent some form of skin decontamination in 67% of CCUs.

**Conclusions:** A consistent approach to MRSA containment is required across CCUs. Current national guidelines are probably unworkable due to limited single rooms and the endemic nature of MRSA in CCUs.
THE UTILITY OF FAECAL MYCOBACTERIAL CULTURE IN THE DIAGNOSIS OF PULMONARY TUBERCULOSIS

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Objective: To assess the usefulness of faecal mycobacterial culture in providing evidence of infection with Mycobacterium tuberculosis in the diagnosis of pulmonary tuberculosis.

Methods: The combined computerised database (CDS Telepath Ltd™) of processed bacteriological specimens from Glasgow Royal Infirmary and Stobhill General Hospital was analysed retrospectively for faecal and respiratory specimens which were submitted for mycobacterial culture between 1st November 1997 and 1st June 2002. Processing of specimens was performed in accordance with the laboratory standard operating procedures utilising the MB/BacT ALERT® System.

Results: The mean number of new pulmonary tuberculosis cases detected annually was 27 (S.D. = 6). In total, 206 faecal and 5222 respiratory specimens were cultured.

Of the respiratory specimens, 255 (5%) yielded M. tuberculosis from 126 patients and 54 (1%) yielded mycobacteria other than tuberculosis (MOTT). The mean age of these patients was 53 (S.D. = 19) years and 91 (72%) were male.

Faecal specimens yielded no MOTT but 13 (6%) were positive on culture for M. tuberculosis, pertaining to 12 cases of pulmonary tuberculosis of which 11 (92%) were male. The mean age of cases detected by faecal mycobacterial culture was 51 (S.D. = 12) years.

In 4 (31%) cases of tuberculosis detected by faecal culture, M. tuberculosis grew either from faeces prior to its detection in respiratory specimens or was identifiable from patients in whom it was impossible to obtain respiratory specimens.

Conclusion: Culture of faecal specimens for mycobacteria is non-invasive and can provide microbiological confirmation of infection with M. tuberculosis, an antibiotic sensitivity profile and guide decisions regarding choice and duration of therapy in patients with suspected pulmonary tuberculosis when respiratory specimens are unobtainable.

NEUROLOGICAL COMPLICATIONS OF INFECTIVE ENDOCARDITIS: RECOGNISING CLINICAL MANIFESTATIONS AND MULTIDISCIPLINARY MANAGEMENT

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Background: Infective endocarditis (I.E.) is an important cause of life-threatening infectious disease. Early diagnosis and management of I.E. and its complications can reduce morbidity and mortality. The diagnosis of I.E. may be straightforward in those who present with classical Oslerian manifestations but in those with less typical signs the diagnosis may be overlooked. Neurological complications of I.E. have been reported to occur in up to 25–30% cases. They may be the presenting feature of I.E., may occur during treatment or occur weeks to years later. These include cerebral emboli/infarction, arteritis, abscesses, mycotic aneurysms, intracerebral/subarachnoid haemorrhage, cerebritis, meningitis and encephalomalacia.

Methods: We present three cases of I.E. who presented with neurological complications to Eye casualty, the Medical Emergency Admissions unit and the Neurosurgical unit over a 3 month period. I.E. was not suspected in any of these cases until liaison with a microbiologist prompted further investigations. In one case the patient developed a second neurological complication whilst an inpatient prior to the diagnosis of I.E.

Results: All three cases had evidence of I.E. on echocardiogram. Group G Streptococcus was isolated from blood cultures in one case. In the other two cases blood cultures were taken after antibiotics had been commenced. Streptococcus milleri was isolated from pus drained from a brain abscess in one of these cases. All required multidisciplinary input to optimise management. All three cases responded to antibiotic treatment.

Conclusions: There is a need for clinicians in all disciplines to appreciate and be vigilant for the various clinical manifestations of I.E. The correct management is essential for a favourable outcome. The microbiologist can play a key role in ensuring appropriate investigations, prompt diagnosis and a multidisciplinary approach.
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Injecting drug users (IDUs) are at risk from a variety of local and systemic infective complications. Staphylococcus aureus is a common pathogen in these individuals, and causes infections which vary in severity from minor skin and soft tissue infections through to life-threatening invasive disease such as bacteraemia and endocarditis. Typically, isolates from these individuals are methicillin sensitive. However, MRSA has recently been identified causing sepsis among IDUs in the community. Sporadic and small clusters of isolates \( n = 14 \) have been received from geographically distinct areas throughout England and Wales and over a short time-frame (6 months), although one isolate (from August 2001) was identified through retrospective testing.

Detailed analysis of these MRSA isolates highlighted a number of unusual traits. Notably, these strains displayed a distinctive antibiogram (resistant to methicillin, fusidic acid and erythromycin, but susceptible to ciprofloxacin) and were lysed by a novel hemolysin. An unusual type of AmpC beta-lactamase was identified by molecular analysis. Notably, these strains displayed a distinctive genetic profile (SGM17, 100% unique for this strain).

August 2001 was identified through retrospective testing. This report highlights the importance of close liaison between infectious disease physicians, microbiologists, epidemiologists and national reference laboratories in the investigation of large outbreaks of this nature.

**P34**

MOLECULAR DIAGNOSIS OF INFECTIVE ENDOCARDITIS:
EVALUATION OF BROAD-RANGE PCR AMPLIFICATION

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Amplication of 16S rDNA by PCR has recently been applied to the diagnosis of infective endocarditis (IE). A variety of primers specific for 16S rDNA amplification have been used with varying results. In this study we assessed the sensitivity and specificity of three different 16S rDNA primer pairs for the detection of bacterial DNA in heart valve tissue. Fifty resected heart valves from 37 patients were subject to investigator-blinded 16S rDNA PCR amplification using combinations of primers that produced amplimers of 1531 bp: 690 bp and 215 bp. The causative bacterium was identified by comparison of rDNA sequence data from the 5' end of the 16S rRNA gene with sequences on the GenBank database. The results of molecular analyses were compared with clinical diagnosis and conventional microbiological analysis of heart valves and blood. According to Duke Criteria (DC), 37/50 valves tested came from 25 patients with definite (DC 1) or probable (DC 2) IE and 13 valves came from 12 patients who did not have IE. For 5/25 patients, only PCR provided a microbiological diagnosis (Staphylococcus species (4), Streptococcus species (1)). Sensitivity, specificity, PPV, and NPV values for each method are shown in the Table.

**Table**

| Test | Sensitivity compared with DC (%) | Specificity compared with DC (%) | PPV | NPV |
|------|---------------------------------|----------------------------------|-----|-----|
| PCR: 1531 bp | 30 | 100 | 1 | 0.33 |
| PCR: 690 bp | 43 | 100 | 1 | 0.38 |
| PCR: 215 bp | 16 | 100 | 1 | 0.3 |

PCRs that produced amplimers of 1531 bp and 690 bp were more sensitive than Gram stain and at least as sensitive as valve culture. All PCR tests were 100% specific. PCR provided microbiological confirmation of endocarditis when conventional methods did not and the length of the PCR product was critical for optimal test sensitivity and specificity, a 690 bp product giving the best results.

**P35**

IMPROVING THE DIAGNOSIS OF BURKHOLDERIA CEPACIA COMPLEX IN CYSTIC FIBROSIS PATIENTS IN THE DIAGNOSTIC LABORATORY

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The *Burkholderia cepacia* complex comprises nine closely-related genomvars. These bacteria can colonise the respiratory tract of patients with cystic fibrosis and cause severe respiratory disease with a poor prognosis. Time to confirmation of *Burkholderia cepacia* complex may take between 3 weeks to 3 months. In this study, we show that molecular methods can be used for routine identification of *Burkholderia cepacia* complex isolates from cystic fibrosis patients. Forty isolates were tested retrospectively: 30 were members of the *B. cepacia* complex; 10 were not members of the *B. cepacia* complex as confirmed by the HPA Reference Laboratory. To determine whether or not an isolate was a member of the *B. cepacia* complex, an area of the recA gene was amplified by PCR, as described previously by Mahenthiralingham et al., 2000, and primers specific to 16S rDNA were used to produce DNA suitable for sequence determination; resulting nucleotide sequences were compared to sequences on the Genbank database (http://www.ncbi.nlm.nih.gov/BLAST/). The sensitivity, specificity, PPV and NPV values for RecA PCR to identify members of the *B. cepacia* complex were: 96%, 100%, 1.00 and 0.94 respectively; the average time to a result was 24 hours. The sensitivity, specificity, PPV and NPV values for use of 16S rDNA PCR followed by sequence determination to identify an isolate were 92%, 100%, 1.00 and 0.88 respectively; time to complete sequence determination was between 72-96 hours. The molecular techniques assessed in this study gave accurate and reproducible results within one week. These methods can be applied in the diagnostic laboratory to improve the diagnosis and infection control of *Burkholderia cepacia* complex from cystic fibrosis patients.

### P37

**BACTERIAEMIA IN INJECTING DRUG USERS (IDUS) ADMITTED TO HOSPITAL IN NORTHEAST GLASGOW**

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**Objective:** To investigate the range of pathogens identified in blood cultures from IDUs treated as inpatients at Glasgow Royal Infirmary and Stobhill General Hospital in Northeast Glasgow during 2002 and make epidemiological observations.

**Methods:** A retrospectively review of all positive blood cultures processed between 1st January and 31st December 2002 pertaining to IDUs. Data regarding the age and sex of the patients, the identity and number of all pathogens grown was entered into a spreadsheet for processing using Microsoft Excel™.

**Results:** We identified 126 positive blood cultures from 89 IDUs of which 69 (78%) were men. This represents 5.4% of all positive blood cultures seen in our laboratory in 2002. The median age of IDU was 30 years (range 20 to 44 years). Of the 126 positive cultures, 96 (76%) grew single organisms while 30 (24%) were polymicrobial. Clinically significant isolates included *Staphylococcus aureus* (31%), *Streptococcus pyogenes* (13%), *Streptococcus agalactiae* (6%), *Candida glabrata* (3%), Methicillin Resistant *Staphylococcus aureus* (3%), *Enterococcus faecalis* (2%), *Streptococcus milleri* (1%), *Candida albicans* (1%), *Candida parapsilosis* (1%), *Escherichia coli* (1%) and *Vancomycin Resistat Enterococcus* (1%). Organisms usually considered as skin or oral commensals were also identified, particularly coagulase negative staphylococci (33%) and diphtheroid species (10%). These may reflect blood culture contamination or unhygienic injecting technique or drug use paraphernalia.

**Conclusion:** The spectrum of organisms identified in bacteraemic IDUs in Northeast Glasgow is similar to that seen in American cities. Interestingly bacteraemic IDUs are older than the general IDU population in Northeast Glasgow which suggests an association between duration of drug use and the severity of the septic complications. This increased risk of bacteraemic complications may be explained by them having to resort to skin and muscle popping as their venous access is lost.

### P36*

**PV PRODUCING STAPHYLOCCUS AUREUS INFECTION IN A GLASGOW FAMILY**

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We describe the investigation and treatment of a family in Glasgow with recurrent skin abscesses. In March 2000 the initial patient, a 15 year old girl, presented with a 4 month history of recurrent skin abscesses affecting her trunk, limbs and face. Swabs taken from these abscesses grew *S. aureus* sensitive to flucloxacillin. The patient was treated with numerous courses of antibiotics but her abscesses recur after completion of each course. At this time five other family household members were also found to have *S. aureus* associated recurrent skin abscesses.

Pulsed field gel electrophoresis (PFGE) samples of all isolates were indistinguishable and this strain was also found to contain the Panton-Valentine leukocidin (PVL) gene. All family members were treated with all over body washing (Aquasept liquid), mupirocin for nasal decolonisation and twice daily chlohexidine spray to eradicate oral colonisation. The household was also professionally cleaned using Trigene on floors, hard surfaces, toilets, window ledges and door handles. Underwear and bedding were machine washed on a daily basis. It is now over a year since this intervention and there have been no further reports of *staphylococcal* infection. Aggressive management of the patients and reduction in the environmental load of *S. aureus* did break the cycle of recurrent infection. This strain was also found to contain the PVL gene that has been associated with recurrent furunculosis in patients.

### P38

**TRENDS OF SPECTRUM AND SUSCEPTIBILITIES OF UTI PATHOGENS IN NORTH MANCHESTER: 1998 - 2002**

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Urinary tract infection (UTI) is one of the most common bacterial infections in both hospitals and communities. Antibiotic treatment for patients with suspected UTI is usually started empirically. A successful treatment depends on knowledge of local UTI pathogens and their susceptibility. The study aims to assess trends of UTI pathogens spectrum and their susceptibility in North Manchester over a period from 1998 to 2002, and to review the suitability of current recommended antibiotics for empirical UTI treatment. Over the period, UTI pathogens were isolated around 5000-6000 each year. Although more than 20 different bacterial species (or complex) were revealed, they globally belong to genera *Enterobacteriaceae, Pseudomonas, Staphylococcus and Enterococcus*. *E. coli* constituted the largest single species at any single year throughout the period, accounting from 53% to 77%. In the hospital, the places of...
Enterococcus spp and Staphylococcus aureus in the league table remains the 2nd and 5th in 1998 and 2002, but Klebsiella pneumoniae had increased its share from place 13 in 1998 to position three in 2002 (<1% vs. 6%, $P < 0.01$), and Proteus mirabilis from position eight to position four (<1% vs. 5%, $P < 0.01$). The incidence of Klebsiella pneumoniae UTI in North Manchester is 67 times higher than that in East London in year 2001. This extraordinary high prevalence can be tracked back to 1999; afterwards, it has been maintaining at a stable level in the region. The reason for this and its population dynamics and implications deserves further investigations. One interesting phenomenon noticed is that UTI pathogens in the hospital and community seems to be evolving convergently. In 1998, the top five UTI pathogens were different between the hospital and the community, but by year 2002 the top five bacterial species were the same although the orders of them were different. Antibiotic resistance of UTI pathogens had substantially increased over the period; the situation is worse in the hospital than in the community. For instance, 56 episodes of different antibiotics had been tested on the top five, 22 (39%) of them had been seen significantly increase in the hospital between 1998 and 2002, only 12 (21%) noticed in the community. Gram-negative bacilli behaved more badly than their opposites. The common oral antibiotics have been fully scrutinised to assess their suitability.

**P39**

**THERAPEUTIC SERUM TEOCPLANIN CONCENTRATION MONITORING: IS IT NECESSARY?**

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Teicoplanin, a bactericidal glycopeptide, plays an important role against Grampositive bacterial infections. Monitoring teicoplanin levels is currently not a routine practice due to a variety of reasons. The UK recommendation suggests that therapeutic monitoring may optimise dose and serum trough level should not be less than 10 mg/l. Recently several studies revealed a substantial proportion of studied populations had a concentration of less than 10 mg/l under the standard dosage, raising a concern that some of the patients may not have been properly treated. However, it can be argued that vast majority of patients had a concentration above MIC of 4 mg/l. The aim of this study was to examine the difference of clinical responses between the patients with serum trough level 4-10 mg/l and those having level of more than 10 mg/l. Clinical responses were assessed changes of body temperature, WCC and CRP. When this analysis was performed on all patients, it was found that WCC and CRP were significantly lower in those with trough level 4-10 mg/l than those with more than 10 mg/l. A significant difference was found in WCC change between the two groups, with 72.7% in group A and 22.2% in group B, showing a reduction in WCC; whereas no significant change was noticed in CRP between the groups. On the whole there was no difference of clinical response between patients with a serum level of 4-10 mg/l and those with more than 10 mg/l. The study is on going and more patients and longer observation time arrive at a conclusion.
Malignant otitis externa (MOE) is a pseudomonal infection of the retropharyngeal tissues following otitis externa and/or ENT procedures. Complications include cranial nerve palsies and osteomyelitis of the skull base. Predisposing factors including diabetes, otitis externa, ear syringing and ENT surgery are frequently present.

Methods: A prospective clinical study collected data on cases of MOE over 1 year to determine clinical features, imaging findings, microbiology, response to therapy and complications.

Results: 5 patients (4 male, 1 female) age range 61–75 years were seen. Clinical features included ear pain, cranial nerve palsies, dysphagia and meningitis. Predisposing factors including steroids, diabetes, otitis externa, ear syringing and ENT surgery were present in all cases. Inflammatory markers were raised in all patients. MRI scanning revealed inflammatory masses or abscesses. Osteomyelitis occurred in the skull base or cervical spine of 2 patients. Delays in diagnosis were common. All patients responded to a course of at least 6 weeks of dual antipseudomonal antibiotics. One patient with meningitis needed VP shunting for hydrocephalus.

Conclusions: MOE is a serious condition and delays in diagnosis and use of inadequate antibiotic therapy are common allowing the development of complications such as cranial nerve palsies or osteitis. The diagnosis should be carefully considered in patients with ear pain and raised inflammatory markers and a history of predisposing factors sought. MRI scanning and subsequent microbiological sampling of inflammatory masses should be undertaken. Treatment with at least 6 weeks of combined antipseudomonal antibiotics is required to effect a cure. Neurosurgical intervention may be required for complications.

TOXIN GENOTYPING OF GROUP A STREPTOCOCCI IN INJECTING DRUG USERS

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Background: There has been a resurgence of serious invasive group A streptococcal infections amongst injecting drug users in Brighton. Aims. This study was undertaken to see whether there was a difference in toxin genotyping of group A streptococci (GAS) blood culture isolates from injecting drug users (IDU) compared with similar blood culture isolates from the local community in Brighton.

Methods: GAS isolates were grown overnight in Todd-Hewitt broth at 37°C. The cells were spun down and genomic DNA extracted. All the isolates were toxin genotyped by PCR with specific primers. Toxin genes amplified included those encoding streptococcal superantigens streptococcal pyrogenic exotoxin A (SPEA), streptococcal pyrogenic exotoxin C (SPEC) and streptococcal mitogenic exotoxin Z (SMEZ). All isolates were also checked for the presence of the mf/Dnase B gene (also known as spef) and M serotype/emm type.

Results: 95.6% (22/23) of control GAS isolates from the community were SPEA positive compared with 30% (7/23) of IDU GAS isolates. Data for other toxin genes including SPEC and SMEZ will be presented. As expected all the GAS in both IDUs and controls possessed the mf gene.

Conclusion: GAS isolates from IDU blood cultures are distinct from those isolated from the non-IDU population. In addition to the recently reported prevalence of higher M types in IDU, carriage of the SPEA gene in the community GAS isolates is much greater than isolates from IDUs.

A CLUSTER OF COMMUNITY ACQUIRED BACTERAEMIAS IN AN INTRAVENOUS DRUG USING POPULATION DUE TO A NEW CLONAL STRAIN OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS

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Background: Staphylococcus aureus is a common cause of bacteraemia in intravenous drug users (IVDU), with about 40 admissions yearly to our hospital. Isolates from these patients are usually susceptible to methicillin (MSSA) but we noticed a recent increase in bacteraemias attributable to methicillin resistant organisms (MRSA).

Aims: To investigate the microbiology and epidemiology of a cluster of MRSA bacteraemia in IVDU population.

Methods: Sensitivity testing of S aureus isolates was performed to BSAC recommendations. MRSA isolates were typed by pulsed field gel electrophoresis (PFGE) and molecular work was carried out to determine the Staphylococcal chromosomal cassette type (SCCmec). A case note review was performed to ascertain epidemiological differences between IVDU with MRSA and those with MSSA.

Results: From Jan 2001 to Jun 2003, 21 patients had MRSA bacteraemia with a strain possessing a novel antibiogram (resistant to erythromycin and fusidic acid, susceptible to ciprofloxacin). The ‘new strain’ MRSA was clonal on PFGE and the SCCmec was typed as Group 1. In 2001, 2002 and the first half of 2003 there were 2, 8 and 11 patients respectively. 19/21 patients with ‘new strain MRSA’ were IVDU. During this period 91 other IVDU were admitted with MSSA bacteraemia. The mean age (32 years) was the same in both cohorts of IVDUs, but there were relatively more males (17/19) in the MRSA than in the MSSA cohort (73/91). The source of MRSA sepsis was often groin or lower limb infections and many of the patients were poly-drug misusers of no fixed abode.

Conclusions: MRSA bacteraemia in IVDU is a new phenomenon in Liverpool. The ‘new strain MRSA’ is clonal and distinct from nosocomial MRSA prevalent in our region. Initial review suggests epidemiological differences between IVDU with MRSA and those with MSSA and this is being investigated further.
THE USE OF ADJUNCTIVE CLOSED-DOUBBLE-LUMEN STREPTOKINASE-ANTIBIOTIC SUCTION AND IRRIGATION IN THE MANAGEMENT OF CHRONIC DIAPHYSEAL OSTEOMYELITIS AND INFECTED NON-UNION AS AN ALTERNATIVE TO ANTIBIOTIC BEADS AND MULTI-STAGE EXCISIONS

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Background: Chronic diaphyseal osteomyelitis may be difficult to treat only with systemic antibiotics and flexibility of local administration is not easily achieved with impregnated beads. We report our experience of debridement accompanied by a closed double lumen suction irrigation system, modified from that described by Lautenbach and inserted intrasosseously.

Methods: We treated 35 consecutive patients with a diagnosis of chronic diaphyseal osteomyelitis: 20 secondary and seven primary. Nine other patients had infected non-unions, five with bacteriological confirmation of infection at operation. Patients had been treated surgically on average five times previously (Range 1 to 13) for their infections for an average of 10 years (Range 0.5 to 49). A regimen of 4-hourly drainage and local antibiotic instillation, usually with teicoplanin, was used over a three-week period. Streptokinase instilled into the central lumen overcame system blockage in all cases. Systemic antibiotics were also given as indicated by operative and subsequent drainage cultures and usually for a period of 6 weeks after discharge from hospital.

Results: At follow up of a mean 44 months (range 2 to 73) the mean C-Reactive Protein (CRP) level had reduced to 6 (Range 1 to 25) from 74 (Range 5 to 158) at initial presentation. This was achieved with an average of 1.3 procedures (range 1 to 3), with 77% of patients considered as successful outcomes with no subsequent surgery required. Cultures of antibiotic-free irrigant fluid improved microbiological monitoring of continuing/super infection. Emergence of Gram negative superinfection lead to adoption of a standard teicoplanin-gentamicin mixture in the irrigant.

Conclusions: Debridement, local teicoplanin and streptokinase can reduce the number of operations and increase flexibility of chemotherapy in chronic osteomyelitis.

A CULTURAL AND MOLECULAR ANALYSIS OF BACTERIA ASSOCIATED WITH ORAL SQUAMOUS CELL CARCINOMA

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Introduction: Interest in the possible relationships between bacteria and the different stages of cancer development has been rising since the classification by the W.H.O. of Helicobacter pylori as a definite (class 1) carcinogen. The association of bacteria with oral squamous cell carcinoma (OSCC) has yet to be adequately examined.

Objectives: The primary aim of the current study was to identify any bacterial species detected within OSCC tumour tissue by a combination of cultural and molecular techniques.

Methods: At the time of surgery 1 cm³ specimens were collected by aseptic technique from deep within the tumour. Surface decontamination of tissue specimens was performed by immersion in Betadine. Specimens were subsequently bisected: Half of each was aseptically macerated, resuspended in PBS and cultured under aerobic and anaerobic conditions on non-selective media. The remainder of each specimen was digested with proteinase K, subjected to DNA extraction, and analysed by a nested PCR-DGGE technique using universal primers. Bacteria detected by both methods were identified by 16s rDNA sequence analysis.

Results: A diversity of bacterial species including gram positive and negative, facultative and anaerobic species were isolated and identified using both methods. The PCR-DGGE approach detected the presence of additional species over and above those isolated by culture. Negative results from cultural and PCR analysis of washes of the tumour specimens signified that surface decontamination was successful and that the bacteria detected were from within the tumour tissue.

Conclusions: A diversity of bacterial groups has been isolated from within the tissue of oral squamous carcinoma by culture and molecular means. The significance of these bacteria within the tumour tissue warrants further study.
P49
THE CASE FOR 'TRAVEL' HISTORY IN THE EPIDEMIOLOGY OF OUTBREAK
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Isolates of Escherichia coli producing extended-spectrum-lactamase were identified from clinical samples of three patients resident in a surgical ward. A fourth isolate was obtained from another patient in the ITU, on a different floor of the hospital. Serotyping, antibiogram and pulse-field gel electrophoresis, following digestion with restriction endonucleases XbaI, were performed. The isolates were indistinguishable by all three typing techniques.

Initially, there appeared to be no connection between the three patients on the surgical ward and the fourth who had never been admitted there. However, a detailed review of all four patients revealed that patient 2 had been briefly in the adjacent bed to patient 4 whilst on the ITU for post-operative care. The spread of multi-resistant organisms is facilitated by the practice of patient movement from ward to ward. It is essential to limit the unnecessary movement of patients who are colonized or infected with multi-resistant bacteria in order to effectively control nosocomial transmission.

P50
DETECTION OF EXTENDED-SPECTRUM BETA-LACTAMASES IN ENTEROBACTERIACEAE FROM BLOOD CULTURES
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The production of Extended-Spectrum Beta-lactamases (ESBLs) by Enterobacteriaceae poses a therapeutic problem, as these organisms can be associated with severe illness, such as pneumonia and meningitis. This compromises the use of third generation cephalosporins as empirical first line therapy in these conditions. The aim of this study was to evaluate how well routine sensitivity tests predict ESBL production.

50 E. coli and 50 Klebsiella spp. from blood cultures were tested for ESBL production using double disc synergy tests and combination disk tests. Routine sensitivity testing in the clinical laboratory was by a breakpoint method, which included ceftazidime as the representative third generation cephalosporin.

Overall, the proportions of ESBL-producing E. coli and Klebsiella spp. were 2% and 20% respectively. Routine testing detected 10/11 ESBL-producing Enterobacteriaceae (sensitivity 91%, specificity 99%). While only 18% of the total isolates were taken from medically intensive environments, 45% of ESBL-positive isolates came from such an environment.

ESBL-producing pathogens may appear to be susceptible to third generation cephalosporins in vitro, whilst being resistant in vivo. Our results confirm that organisms resistant to the screening cephalosporin should be assumed to be ESBL-producers and confirmatory tests undertaken. ESBL detection from high-risk patients and locations must be actively sought and not opportunistically gleaned. This may involve including two screening two different third generation cephalosporins in routine sensitivity testing, or testing specifically for ESBLs for isolates from high-risk units/patients.

P51
THE COMMUNITY PREVALENCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN OLDER PEOPLE LIVING IN THEIR OWN HOMES: IMPLICATIONS FOR TREATMENT, SCREENING AND SURVEILLANCE
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Background: There is concern about the appearance of methicillin Resistant Staphylococcus aureus (MRSA) in the community. MRSA is predominantly nosocomial, occurring mainly in people aged 65 or older. The prevalence of MRSA in older people in care homes can be high but little is known of its prevalence and risk factors in those living at home.

Methods: We studied the prevalence in one London general practice, screening 258 older people living in their own home. Information on potential risk factors was gathered at interview and from the practice database and local hospitals’ MRSA
AN OUTBREAK OF GASTROENTERITIS AMONGST BRITISH TROOPS DURING MILITARY OPERATIONS IN IRAQ
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Objectives: A British military field hospital was deployed in southern Iraq during Operation Telic in 2003. An outbreak of gastroenteritis affected many British units in the area including the staff of the field hospital. We undertook a basic epidemiological analysis of the outbreak using patients from local units.

Methods: Data on patient admissions were collected from hospital computer records and infectious disease notification forms. In the early stages of the outbreak, patients were asked about exposure to specific risk factors.

Results: Over a one month period there were 2065 hospital presentations, of which 1466 (71%) were referred to physicians, of which 1340 (91%) were due to gastroenteritis, of which 975 (73%) required hospital admission. Rates of admission for gastroenteritis were initially high at 92%, but reduced with time to 13%. Average length of stay for gastroenteritis patients was 1.65 days, which led to 1605 bed-days being occupied and bed occupancy rates in the hospital reached > 90%. Hospital staff accounted for 36% of all gastroenteritis cases.

The epidemic curve of all gastroenteritis cases showed a rapid increase followed by a biphasic reduction, whereas that for hospital staff cases showed a more rapid decrease. 43% of cases amongst non-hospital staff came from just 3 local units. Risk factors for gastroenteritis amongst these patients included having affected colleagues (83%), eating fresh fruit (52%), using centralised catering (47%), poor hand-washing facilities (45%) and eating pasteurised yoghurt (43%). Units with the most cases had higher than average exposure to these risk factors. Stool investigations revealed the presence of caliciviruses only.

Conclusions: Gastroenteritis was a major cause of morbidity during this operation and may have had an impact on the operational effectiveness of those units affected. Further studies and changes to working practices have been initiated to prevent and control similar outbreaks in the future.
measures of factors relevant to the occurrence of antibiotic resistant infections. Much of this data could be extracted economically with IT automation.

P55
MLST ANALYSIS OF SCOTTISH PNEUMOCOCCAL ISOLATES AND THEIR RELATIONSHIP TO MAJOR ANTIMICROBIAL-RESISTANT CLONES
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We examined 250 pneumococcal isolates submitted to the Scottish Menincoccal and Pneumococcal Reference Laboratory by multilocus sequenced typing (MLST) and compared them to the globally significant antimicrobial resistant clones identified by the Pneumococcal Molecular Epidemiology Network (PMEN clones) (McGee et al. J Clin Micro 2001; 39:2565-2571).

Antimicrobial susceptibility in the Scottish isolates was determined by Etest methodology. A Burst analysis was performed of the Scottish MLST data alongside the MLSTs of the PMEN clones. The 250 isolates contained over 30 different serogroups. 91 Sequence types (ST’s) were assigned to the Scottish isolates; of which 41 were new to the MLST database. Three of the 25 STs of the PMEN clones were present in the Scottish collection, these were ST156, (7 isolates) ST9 (6 isolates) and ST377 (1 isolate). With the exception of one Scottish ST156 isolate (erythromycin MIC 2.0 mg/L) all Scottish isolates related to the PMEN clones had lower penicillin and erythromycin values than those described for the corresponding type strain. Although the number of PMEN STs in our collection is low, there are a number of single(SLV) and double locus variants (DLV) of these STs present. These include a SLV clonal group that are related to ST 81 (PMEN 1 Spain\textsuperscript{218}). A second group containing SLV and DLV related to ST 156 (PMEN 3 Spain\textsuperscript{219}). The third PMEN-related group present in the Scottish collection, consists of DLV’s related to ST 37 (PMEN 4 Tenessee\textsuperscript{220}). The highest level of resistance to penicillin, ciprofloxacin and erythromycin was found in two serotype 19 (ST 320) isolates. This ST is not one of the previously recognised PMEN clones. These results provide a snapshot of resistance levels and the genotypic background of Scottish pneumococcal isolates.

P56
VALUE OF MRSA BACTERAEMIA SURVEILLANCE IN A TERTIARY REFERRAL CENTRE
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In 2001 the Department of Health introduced mandatory surveillance of MRSA bacteraemia in England and Wales. Since 1998 Freeman Hospital, part of a tertiary referral teaching Trust has performed surveillance of MRSA bacteraemia, the results of which were fed back to clinical units via an annual report.

Results: Over a 5 year period between 1998 and 2002 the percentage of Staphylococcus aureus bacteraemia caused by MRSA has increased from 32% to 46%.

Striking differences between the relative incidences in the various clinical units within the hospital were noticed. Surpris-ingly, the renal unit, who had the greatest overall incidence of S. aureus bacteraemia, maintained a rate of MRSA below 30%. For General surgery, which includes a regional vascular unit, MRSA bacteraemia has nearly always accounted for more than two thirds of all bacteraemias.

Conclusions: National data collection for MRSA bacteraemia may not provide useful information for individual hospitals, as the relative incidences of MRSA from clinical units within hospitals can vary widely.

P57
PROGRAMME FOR THE MAINTENANCE OF A RISK FREE WATER SCULPTURE—SOME ISSUES AND EXPERIENCES
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A water sculpture, designed by internationally recognised sculptor William Pye, was installed at the main entrance of the newly built PFI initiative, Queen Elizabeth Hospital, Woolwich in May 2003. It was funded as part of the King’s Fund ‘Enhancing the Healing Environment ’ scheme. The sculpture has been very popular with staff and is soothing for patients and relatives who relax within its environment.

Liaison with the Infection Control Team and the facilities company, Skanska, was continuous from the inception of the project, ensuring appropriate microbiological and environmental safety standards. A daily maintenance programme of water testing and water top up, was organised, and in addition to a monthly drainage and cleaning programme, carried out by the sculptor’s professional team.

Early liaison with Dr John Lee of WEMRU, at the Health Protection Agency, Colindale was helpful in reassuring microbiologists that bromine was an appropriate & safe disinfecting agent. The stainless steel fabrication of the sculpture prevented the use of chlorine. Bromine is useful in situations where there is to be organic contamination and as the sculpture is situated on a ground level concrete plinth in the middle of a flowerbed, bromine was the agent of choice.

The practical infection control issues and details of the maintenance programme are elaborated in the poster.

P58
STENOTROPHOMONAS MALTophilia BACTERAEMIA:
ENGLAND, WALES AND NORTHERN IRELAND 2002
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The majority of microbiology laboratories in England, Wales and Northern Ireland routinely send voluntary, anonymised, reports of clinically significant infections to the Communicable Disease Surveillance Centre (CDSC) via regional units.

This report details Stenotrophomonas maltophilia bacteraeas reported to CDSC London from 1 January to 31 December 2002. Data was analysed using LabBase2 and Microsoft Excel. Bacteria were isolated from blood by laboratories across England, Wales and Northern Ireland. No information is available on the source of infection and it is not possible to identify nosocomial infections. A total of 606 reports of S. maltophilia bacteraeas were received. The number of S. maltophilia bacteraeas reports from England and Wales increased by 18% compared with 2001. Reported susceptibility results are shown in Table 1. Sixty per cent of reports included susceptibility information for at least one antimicrobial, a marked decrease compared to 2001 (72%). Two isolates were reported with a multiple resistance
pattern including ciprofloxacin, gentamicin, imipenem, ceftazi-dime and piperacillin/tazobactam.

The high percentage (89%) of *S. maltophilia* bacteraemias resistant to imipenem, is not surprising, given that this organism has a carbapenemase conferring inherent resistance to this antimicrobial.

Eight per cent of reports included susceptibility to co-trimox-azole, the main agent for the treatment of *S. maltophilia* bacteraemia, an increase from 3% in 2001. However, this compares poorly with the reporting of other, less relevant antimicrobials.

*A full data set for January to December 2001 is not available for Northern Ireland.*

* As a % of reports with susceptibility data

### Table 1 Antimicrobial resistance in *S. maltophilia* bacteraemia reports (n = 606) from England, Wales and Northern Ireland 2002

| Antimicrobial          | Resistant | % | Sensitive | No Information |
|------------------------|-----------|---|-----------|----------------|
| Gentamicin             | 167       | 46| 198       | 241            |
| Ciprofloxacin          | 225       | 62| 136       | 245            |
| Imipenem               | 193       | 89| 25        | 388            |
| Ceftazidime            | 33        | 11| 273       | 300            |
| Meropenem              | 61        | 59| 43        | 502            |
| Piperacillin/tazobactam| 18        | 10| 160       | 428            |
| Co-Trimoxazole         | 2         | 4 | 48        | 556            |

healthcare associated infections, including the implementation of a national surveillance scheme for GRE bacteraemias, *C. difficile* infections and serious untoward incident reports, and the strategy for analysis and feedback of local and regional reports for the new mandatory orthopaedic surveillance programme.

#### P59

**SURVEILLANCE PROGRAMMES FOR HEALTHCARE-ASSOCIATED INFECTION IN ENGLISH HOSPITALS: PRESENT AND FUTURE PROPOSALS**

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National surveillance schemes are the cornerstone of healthcare epidemiology. There have been considerable advances in voluntary and mandatory surveillance schemes in the UK and several key schemes are in development at present.

**Surgical site infection (SSI).** The present surveillance system for SSI has evolved from the Nosocomial Infection National Surveillance Service (NINSS) and now receives reports from over 200 hospitals in England. The scope and use of this national surveillance information resource can be illustrated by reference to analyses on the variation of rates between and within hospitals for five of the twelve categories of ongoing surveillance. Figure one summarises the distribution of the incidence of surgical site infection for each hospital by category of surgical procedure for the strategy for analysis and feedback of local and regional

**Hospital-acquired Bacteraemia (HAB).** Between May 1997 and March 2001 HAB reports were received from 81 hospitals. A wide variation in rates of HAB between specialities and a considerable variation in specialty-specific rates between hospitals, particularly for intensive care units was identified by this surveillance. In 2001, mandatory MRSA bacteraemia surveillance was implemented and the interpretation of these data will be informed by the lessons learned from the predecessor of this programme.

**New surveillance programmes.** At present there are a number of proposed changes to the English surveillance programme for

#### P60

**MICROBIOLOGY OF SPUTUM CULTURES FROM PATIENTS ATTENDING THE NATIONAL ADULT CYSTIC FIBROSIS UNIT, ST. VINCENT’S UNIVERSITY HOSPITAL DUBLIN, JANUARY 2002- JUNE 2003**

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This study describes the epidemiology of laboratory confirmed lower respiratory tract infection in patients attending the National Adult Cystic Fibrosis Unit (NACFU) at St. Vincent’s University Hospital. Using WHONET, a software epidemiology package we looked retrospectively at sputum culture results from January 2002 to June 2003 and combined this information with the Cystic Fibrosis patient database to describe the following:

1. The number of patients with sputum culture positive for *Pseudomonas aeruginosa*, and with aminoglycoside resistant strains by disc diffusion (British Society for Antimicrobial Chemotherapy BSAC) method.
2. The incidence of *Burkholderia cepacia* complex (BCC) infection.
3. The number of patients with *Staphylococcus aureus* and methicillin resistant *S. aureus* (MRSA) infection.
4. The number of patients culture positive for *Stenotrophomonas maltophilia*, *Alcaligenes* species and also the number of patients with atypical mycobacterial infection.

Two hundred and eighty-three patients (2003 figures) attend the NACFU. (159 (56%) were male) and during the study period four patients underwent lung transplantation. Between January 2002 and June 2003 200 patients sampled were culture positive for *P. aeruginosa* giving an estimated incidence of 71% for *P. aeruginosa* infection, however samples were not sent on all patients. *P. aeruginosa* with combined gentamicin, tobramycin and amikacin resistance was found on two or more occasions in 31/200 (16%) patients, and colomycin resistance on two or more occasions in 18/200 (9%) of patients. We plan to examine these strains in more detail soon, measuring minimum inhibitory concentrations, and undertaking molecular typing.
One hundred and twenty-six patients had S. aureus infection, and of these 26 patients (21%) were MRSA sputum culture positive. S. aureus remains an important pathogen in our patient population, and in our experience MRSA infection may be transient in cystic fibrosis patients.  

Twelve patients, 12/283 (4.2%) were infected with B. cepacia complex, of these eight were BCC genovar II, one genovar IIIb and one genovar IV and in two the type was unknown. Twenty-seven patients (27/283, 10%) had Stenotrophomonas maltophilia, and 13 patients (13/283, 5%) had Alcaligenes spp. isolated from sputum respectively, figures compatible with a breaks, and the development and use of reliable, reproducible molecular epidemiological typing to detect and control out-organism emphasise the importance of surveillance, access to antibiotic resistance, and outbreaks of infection 4,5,6 with this leading pathogens in cystic fibrosis and problems with emerging P. aeruginosa fibrosis patients is essential.

Ongoing surveillance of lower respiratory tract infection in cystic Scedosporium apiospermum, an unusual fungal isolate which is cellulare Mycobacterium abscessus, and the other with M. avium intracellularare, however the number of patients for whom mycobacterial sputum culture was performed is unknown. Scedosporium apiospermum, an unusual fungal isolate which is amphotericin resistant has been isolated in two patients. This organism may have implications for lung transplantation. Ongoing surveillance of lower respiratory tract infection in cystic fibrosis patients is essential. P. aeruginosa remains one of the leading pathogens in cystic fibrosis and problems with emerging antibiotic resistance, and outbreaks of infection 4,5,6 with this organism emphasise the importance of surveillance, access to molecular epidemiological typing to detect and control outbreaks, and the development and use of reliable, reproducible sensitivity testing methods (including synergy testing) to guide treatment.

"The definition used was 'two or more resistant strains' to allow for possibility of fault disc or transcription error."

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P62
INTERFERENCE BETWEEN MSSA AND MRSA IN THE ANTERIOR NARES: IMPLICATIONS FOR MRSA EPIDEMIOLOGY

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Introduction: Colonisation of the anterior nares with Staphylococcus aureus may be a risk factor for infection, so there has been an increasing emphasis on the eradication of S. aureus from the anterior nares of patients with an increased risk of S. aureus infection. Also many hospital procedures, such as use of prophylactic antibiotics might be expected to alter microbial colonisation in the anterior nares. One of the mechanisms by which antibiotics select for colonization with Methicillin-resistant S. aureus (MRSA) may be through damage to the commensal flora including MSSA.

The purpose of this study was to estimate the extent to which Methicillin-sensitive S. aureus (MSSA) inhibits colonisation with MRSA.

Methods: MRSA and MSSA were isolated from 753 routine
screening nasal swabs collected over a six months period and identified using standard laboratory methods. The difference in the observed number of patient swabs with co-colonisation was compared with that expected assuming no interference between MSSA and MRSA.

**Results:** Results from 680 routine patient screening swabs were available for analysis. There was a significant trend for carriage of MRSA with increasing age, and in males compared with females. One hundred and fifteen patient swabs were colonized with MSSA alone, and 56 with MRSA alone. Both MRSA and MSSA were isolated from only four nasal swabs which was significantly less than expected ($p = 0.021$). The potential impact of different rates of colonisation with MSSA on the epidemiology of MRSA is illustrated using mathematical modelling.

**Conclusions:** Those interventions which modify the microbiota of the anterior nares have the potential to facilitate MRSA colonization. An understanding of the ecology of the anterior nares has the potential to inform the development of new strategies for the control of MRSA.

**P63**

**SURFACE CHARACTERISTICS, BIOMATERIAL ADHERENCE AND BIOFILM FORMATION OF *S. EPIDERMIDIS* ISOLATES ASSOCIATED WITH NEUROSURGICAL DEVICE-RELATED INFECTION**

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Adherence of *Staphylococcus epidermidis* to biomaterials and biofilm formation is an important virulence determinant in the pathogenesis of prosthetic device-related infections. The relative hydrophobicity and surface charge of the bacterium and the prevailing environmental milieu influences adherence while biofilm formation is largely dependent on the ica operon-encoded polysaccharide intercellular adhesin.

**Aim:** To conduct an analysis of adherence and biofilm forming capacity of five *S. epidermidis* isolates associated with neurosurgical device-related infection.

**Methods:** Isolates were screened for the presence of the ica operon with a PCR assay. Using a microtitre plate assay, biofilm-forming capacity was evaluated under standard laboratory and stress-inducing conditions (growth at 42°C, in 4% NaCl and 4%EtOH) Cell surface hydrophobicity, zeta potential and adherence of isolates to silicone discs during both logaritmetic and stationary phase was measured under the above conditions.

**Results:** Three isolates contained the ica operon. Two isolates (one ica positive) remained biofilm-negative under all conditions. Of the remaining three isolates, one was weakly biofilm forming under standard laboratory conditions and all could be induced to form strong biofilm under stress-inducing conditions. Induction of biofilm under stress-inducing conditions was associated with increased cell surface hydrophobicity. The surface charge of individual isolates under standard and stress-inducing conditions did not correspond to specific adherence or biofilm-forming characteristics. Isolates containing the ica operon showed a tenfold increase in adherence to silicone discs but variations in adherence under stress-inducing conditions did not necessarily correlate with biofilm formation under the same conditions.

**Conclusion:** The presence of the ica operon was associated with increased adherence to biomaterials but was not necessarily sufficient for biofilm formation. Cell surface hydrophobicity may play a role in initial adherence. Understanding the surface properties and adherence characteristics of *staphylococci* may assist in the development of biomaterials that are more resistant to bacterial adhesion.

**P64**

**DIAGNOSING CENTRAL VENOUS CATHETER RELATED BLOODSTREAM INFECTION: HOW CAN WE PROVIDE ACCURATE DATA?**

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Catheter related bloodstream infection (CRBSI) remains an important cause of morbidity and mortality in patients in intensive care units (ICU). Guidelines for the prevention of such infections are available and it is important for units to undertake ongoing surveillance of CRBSI to assess the adequacy of their procedures. However, for surveillance to be meaningful we require accurate and reliable methods of diagnosis, which do not involve significant additional resources for either clinicians or the laboratory. We have prospectively studied the use of paired central and peripheral blood cultures, differential time to positivity (DTP), catheter tip culture, and clinical features, to make the diagnosis of infection, and have compared catheter days and patient days as denominators for calculating rates of infection.

Over a nine month period in an eight-bedded ICU 26 patients were investigated for suspected CRBSI, and had one or more positive blood cultures. Of the 14 where both central and peripheral cultures were received simultaneously and were positive, 9 had DTP >2 hours and in a further 3 DTP was >1 hour. In two of these, however, an alternative source for the bacteraemia could be found, and in one the bacteraemia persisted following line removal. Over a three month period we calculated the number of patient catheter days and the number of patient days. Although catheter days was consistently lower than patient days, there was a linear relationship between the two.

These data suggest that paired central and peripheral cultures with assessment of DTP may be helpful in the diagnosis of CRBSI in the ICU setting, although they do not always exclude other sources. For the calculation of infection rates, catheter days provides the most accurate denominator, but patient days may be an acceptable and simpler alternative.

**P65**

**REAL-TIME PCR-BASED DETECTION OF METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) IN BLOOD CULTURES**

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MRSA is an important cause of bacteraemia. Recent surveillance data in England has shown that over 40% of *Staphylococcus aureus* (SA) bacteraemias are caused by MRSA. This has major implications for the choice of antibiotic therapy, but results of identification and susceptibility testing of blood cultures can take two days or more.

We have looked at the use of a rapid method of detecting MRSA in blood cultures at the time of detection of positivity of the culture, using an automated blood culture detection system and at the impact that this might have on choice of antibiotic therapy.

In a retrospective study, 108 positive blood cultures were used to evaluate the Roche Light cycler mecA and staphylococcal PCR.
Blood cultures previously demonstrated to be positive were re-
cultured and, in addition, an aliquot of culture broth was
extracted using the MagNaPure kit and the PCR reaction
performed.
Of 74 samples containing coagulase negative staphylococci (CNS)
alone, 60 gave a compatible PCR result while 14 were either
negative or showed some inhibition. Of 10 samples containing
MRSA alone, 10 gave a compatible PCR result. In 2 cases where
the culture was mixed MRSA and CNS, one gave an equivocal
result and one was positive only for CNS (meC A positive).
Overall, sensitivity and specificity for detection of MRSA were
83% and 99%.
In a retrospective analysis of 50 staphylococcal bacteraemias,
details were collected about clinical advice given at the time of
initial culture positivity and compared with appropriate advice in
the light of the identification and sensitivity results. In 24 (48%),
the correct management was advised at the time of initial
positivity. In 17 (34%), an unnecessary antibiotic was rec-
ommended and in 9 cases (18%), the appropriate antibiotic was
not recommended.
Using this method of rapid detection is sensitive and specific and
can give a result within 5 hours. This could significantly impact on
clinical practice, guiding appropriate management. It could also
decrease laboratory workload by identifying insignificant isolates
before further culture occurs.

P66* CENTRAL VENOUS CATHETER ASSOCIATED BACTERAEMIA IN A
TERTIARY REFERRAL CENTRE IDENTIFIED USING A
COMPUTERIZED CODING SYSTEM
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Bacteraemia in patients with non-tunnelled central venous
catheters (CVC) was measured using a denominator of patient
and catheter days. A computerized coding system was used to
identify catheterised patients.
Methods: A computerized procedure coding system identified
patients who had CVC inserted over a six month period. Patient’s
notes were reviewed and those with bacteraemia identified from
the laboratory database. CVCs in use for less than 48 hours were
not included when measuring the rate of infection.
Results: 191 CVCs were inserted of which 96 (50.3%) were placed
as emergencies. Over half of the lines were in place for fewer
than 7 days, mean duration was 6.9 days. 79 (41.4%) CVCs were
inserted in critical areas, 86 (45%) were inserted on general
wards and 26 (13.6%) in Theatres. Of the 106 lines where reasons
for removal was documented 20 (19%) were removed due to
infection. The sum life span of the CVCs was 1241 days. Ten
episodes of bacteraemia were identified. The overall CVC
associated bacteraemia rate was 8.1 catheter days. In each
episode the same organism was also grown from the line tip. 60
(31%) line tips were submitted for culture. 34 yielded a
significant growth of bacteria.
Conclusions: The rate of bacteraemia was higher than many
published surveillance systems. UK data of hospital acquired
bacteraemia exists, but does not record rates per catheter days.
The method used here allows the calculations of this more useful
rate as opposed to numbers of catheters infected. The rate
measured total bacteraemias, not just primary line associated
infections. The computerized coding system failed to record all
the lines inserted; missing many critical care episodes. Retro-
spective review was time consuming but is likely to result in
accurate bacteraemia rates. The measured rate suggests that
locally antimicrobial impregnated lines would be cost effective.

P67 THE ENVIRONMENT AS A FACTOR CONTRIBUTING TO ENDEMIC
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS
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Objectives: The control and prevention of methicillin-resistant
Staphylococcus aureus (MRSA) in hospitals, where it is endemic,
remains a challenge. Failure to eradicate from environmental
sources in clinical areas is recognized as contributing to
persistence and continued spread. We investigated environmen-
tal sites positive for MRSA in the rooms of patients in isolation
to determine which aspects of routine cleaning and decontamina-
tion should be enhanced.
Methods: Horizontal surfaces were sampled with contact plates,
and air was sampled with a Surface Air Sampler (SAS) and settle
plates, twice a week for up to four weeks in the rooms of patients
isolated for MRSA in a hospital where MRSA is endemic. All plates
were incubated for 48 hours and isolates were identified and
antibiotic susceptibility testing performed using standards
methods.
Results: The environment of 25 patients (13 males, 12 females)
was sampled; 64% of patients were colonized and 36% were
infected. A total of 1003 samples were obtained; 502 from
horizontal surfaces and 501 air samples (settle plates, 251; SAS,
250). 54% of horizontal surfaces (contact plates) were positive,
e.g. 55% of samples from chairs. 34% of air samples were
positive; 28% of SAS and 40% of settle plates.
Conclusions: A high proportion of environmental samples taken
from rooms occupied by patients with MRSA were positive,
representing a continuing source of endemic MRSA. Enhanced
environmental cleaning and decontamination, especially of
horizontal surfaces is required, and will reduce airborne spread
as part of an effective programme of MRSA control.
of the hand-wash basin drains. All clinical and environmental isolates collected were indistinguishable by PFGE. Review of ward practices revealed that respiratory equipment, including tracheostomy tubing, was routinely rinsed at the bedside hand-wash basins. Five patients had acquired the organism without overlap with other known cases suggesting an environmental reservoir. The case (n=9) control (n=48) study identified a number of significant risk factors such as: length of stay, presence of tracheostomy, ventilation >24 hours, and prior anti-pseudomonal therapy. After multivariate analysis however, only presence of a tracheostomy remained significant (p = 0.04). This is consistent with the theory that transmission of multi-resistant P. aeruginosa from the environment to the patients occurred during tracheostomy care.

A number of control measures were employed to control the outbreak with some success. These included enhanced hand hygiene using alcohol gel, regular disinfection of sinks with hypochlorite and a change in practice of tracheostomy care. A prospective study was carried out over a nine month period from 1/08/02 to 30/04/03 and information obtained on all episodes of IVD related Staphylococcus aureus bacteraemia in SEHB, Ireland incorporating one regional and three general hospitals over a nine month period.

Method: A prospective study was carried out over a nine month period from 1/08/02 to 30/04/03 and information obtained on all episodes of IVD related Staphylococcus aureus bacteraemias.

Results: There were 42 episodes of IVD related Staphylococcus aureus bacteraemia over the nine month period with peripheral venous device as the source in 12 episodes, central venous device as the source in 14 episodes and permcath device as the source in 16 episodes. Metastatic complications occurred in 4 patients and death directly related to the Staphylococcus aureus bacteraemia occurred in 5 patients.

Conclusion: This prospective study led to a three month programme focusing on the revision and implementation of guidelines for insertion and management of intravascular devices with subsequent surveillance currently ongoing.

P70
THE CHANGING PATTERN OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) ANTIBIOTIC SENSITIVITIES
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Aim: To review changes in susceptibility patterns of hospital acquired MRSA within the three constituent hospitals of UHL NHS Trust over the period of July 1998 to June 2003, inclusive.

Methods: All microbiology specimens from UHL patients yielding MRSA were selected from the pathology computerised database. Susceptibility pattern over time, specimen site and hospital site were analysed. Macrolide prescribing information was obtained from the pharmacy department.

Results: A total of 5934 patients had MRSA during this period. The proportion of MRSA sensitive to erythromycin (ES strains) in hospital A increased from 17% to 43%, in hospital B from 0 to 17% and at hospital C from 4% to 29%. Over all the three hospitals the change was an increase from 6% to 26%. The proportion of ES strains isolated from sterile sites (blood cultures, CSF etc) increased from 4% to 17%. Susceptibility testing methods have remained unchanged over this period. Total macrolide usage has increased over this period. A limited number of ES strains were phage typed. All were EMRSA 15. The annual number of new MRSA positive patients increased slightly from 1056 in 1998/99 to 1295 in 2002/3.

Conclusion: Surprisingly, an increasing proportion of MRSA isolates in our Trust are susceptible to macrolides. Paradoxically, increases in erythromycin susceptibility occurred at the same time as an increase in macrolide prescribing. The increase in the proportion of invasive MRSA susceptible to erythromycin was similar to the overall change in erythromycin susceptibility. Thus there was no evidence to support a claim of increased invasive potential of ES strains as an explanation for the change in resistance.

P71
A REVIEW OF A WEST LONDON TRUST’S RESPONSE TO SEVERE ACUTE RESPIRATORY SYNDROME (SARS)
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Objective: In March 2003, SARS was found to spread readily in the healthcare setting. We review a West London’s NHS Trust response to SARS and the lessons learnt.

Methods: A retrospective review of actions taken in response to SARS at a multi-site 1300 bedded Trust with over 5000 employees and an evaluation of outcomes and effectiveness.

Results: 5 patients fulfilling diagnostic criteria for SARS were admitted over a 3-week period. No cases were subsequently confirmed. Many more worried patients and staff were dealt with in A&E or by telephone consultation. The Infectious Diseases (ID) team admitted the first case to the ID unit on 30/3/03. A SARS policy was written by the Infection Control Team (ICT) recommending the initial management giving clear instructions about referral/admission pathways, infection control precautions and Occupational Health advice for staff. Information was reviewed daily and the policy was redrafted as necessary. There was close liaison between Occupational Health, ID, Infection Control, Microbiology, and Human Resources. Educational sessions were arranged for staff. Planned recruitment of nurses from Singapore was postponed. The Infection Control Doctor participated in a web-based chat on the hospital’s Intranet site, which allowed open discussion and alleviated fears. An Occupational Health hotline was set up for staff at the Trust with any work related or travel query.

Conclusions: Implementation and rapid distribution of a SARS policy was effective at keeping staff informed and provided guidance on management of suspected SARS patients. The majority of contact was with the worried well, in particular employees, and involved advice and reinforcement of infection control measures. Lessons learnt included 1. Importance of close collaboration between clinical leaders and infection control 2. Inadequacy of isolation facilities. 3. Staffing implications are significant and must be addressed early. 4. Need for effective communication. 5. Rapid response depends on the ICT being flexible and multi-disciplinary.
P72 DOIS CHARACTERISATION OF COAGULASE NEGATIVE STAPHYLOCOCCI BY ROUTINE MICROBIOLOGICAL TECHNIQUES MISLEAD THE DIAGNOSIS OF CATHETER RELATED BLOODSTREAM INFECTION?

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The microbiological diagnosis of catheter-related bloodstream infection (CR-BSI) is primarily based on the recovery of identical microorganisms from the catheter tip and blood culture (based on species and antibiogram). The major cause of CRBSI are the coagulase negative staphylococci (CoNS) and confirmation of their identity is commonly based on biochemical profiles and antibiogram. The aim of this study was to determine if these laboratory methods for identifying CoNS are sufficiently discriminative to facilitate the diagnosis of CR-BSI. Eight bone marrow transplant patients with a clinical diagnosis of CR-BSI were recruited into the study. Patients had routine blood and catheter tip cultures performed, all of which yielded CoNS. For each patient, 8 representative colonial types of CoNS (3 from blood culture and 5 from the catheter tip) were characterised phenotypically by antibiogram and biotype (API ID 32 STAPH) and by Smal chromosome macrorestriction profiles using pulsed-field gel electrophoresis (PFGE). Analysis of all isolates studied demonstrated that PFGE distinguished more strains of CoNS compared to biotyping or antibiograms (20, 16 and 14 respectively). Phenotypic and genotypic characteristics of multiple strains of CoNS correlated in only 5 out of 8 patients. Four out of 5 of these patients had identical microorganisms from both blood culture and catheter tip and thus supporting the clinical diagnosis of CR-BSI. Genotypic and phenotypic characteristics of CoNS recovered from the remaining 3 patients did not correlate. Characterisation of multiple colonies of CoNS recovered from blood and catheter tip cultures revealed that strains were heterogenous in 4 out of 8 patients which did not support the clinical diagnosis of CR-BSI. Characterisation of CoNS based on biotype and antibiogram lacks discriminatory power. In addition, selection of multiple colonies of CoNS for characterisation should be routinely undertaken for facilitating the diagnosis of CR-BSI as identification of a single colony may lead to misinterpretation.

Results: Four phenotypes, based on ESBL testing and antibiograms were demonstrated among the 36 test bacteria. A dominant clone was demonstrated by PFGE with 34 out of 36 test strains belonging to a single genotype (type A). The remaining two isolates had only 1 and 2 band differences from genotype A on PFGE and were designated as subtypes of genotype A (Types A1 and A2).

All test strains demonstrated the presence of ESIsLs by the Mast DD system. A representative sample from each phenotype was subjected to bla SHV PCR using SHV-FOR and SHV-REV primers and all four strains were positive for the bla SHV gene, indicating production of SHV-type enzymes. Restriction endonuclease analysis with Nhe I enzyme on the above amplicons confirmed a point mutation in the SHV structural gene at position 238 (glycine to serine switch) indicating presence of an extended-spectrum SHV-type β-lactamase.

Conclusions: This study demonstrates that molecular fingerprinting by PFGE is a useful and reliable epidemiological tool for investigation of outbreaks caused by multi-resistant E. cloacae. It also highlights that acquisition of ESIsLs may be one of the alternate mechanisms of multi-antibiotic resistance in E. cloacae strains in addition to chromosomally encoded cephalosporinases.

P74 PERCUTANEOUS BIOPSY FOR DIAGNOSING PROSTHETIC JOINT INFECTION—IT’S NOT WHAT YOU DO, IT’S THE WAY THAT YOU DO IT

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Aim: To investigate the sensitivity and specificity of radiologically-guided joint biopsy for the diagnosis of prosthetic joint infection (PJI).

Methods: Retrospective analysis of presumptively infected prosthetic joints undergoing radiological biopsy to aid diagnosis in patients managed in a specialist musculoskeletal infection unit. Data were obtained by cross-referencing the Microbiology and Histopathology databases. Histology was used as the criterion standard for diagnosing infection.

Results: Seventy-nine patients underwent biopsy between February 2000 and June 2003. Of these, 54 (68.4%) were culture-negative and 25 (31.6%) positive. Of 29 isolated organisms, 21 (72.4%) were Staphylococci, 19 of these being coagulase-negative. Knees represented 57.0% and hips 40.5% of biopsied joints. The likelihood of achieving a positive culture was related to the number of samples, being 21.4%, 37.9% and 50% for one, two and three samples received, respectively. Only 20.7% of samples cultured for 3 days were positive compared with 38% positive with a 7-day ‘sterile site’ culture protocol. The Bonnopy biopsy technique resulted in the most positive cultures (36.4%); for aspiration, the likelihood of a positive result was 34.4%. Against histology, culture is 67% sensitive and 76% specific.

Conclusions: Prosthetic joint biopsy is more specific than sensitive for the diagnosis of PJI. Taking multiple samples, and using prolonged culture techniques may improve sensitivity, as the sensitivity of an individual sample is only approximately 20%. We advocate taking at least two biopsy samples for culture, using prolonged incubation, and sending material for histology. The study also highlights difficulties in evaluating diagnostic tests when robust consensus definitions of infection are lacking.
**P76**

**RISK FACTORS FOR SURGICAL SITE INFECTION IN HIP ARTHROPLASTY SURGERY: ANALYSIS OF DATA FROM THE NOSOCOMIAL INFECTION NATIONAL SURVEILLANCE SERVICE**

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Data collected on 24 808 hip arthroplasties from 102 hospitals in England between 1997 and 2001 were analysed to estimate the incidence of surgical site infection (SSI) and strength of association with major risk factors. Demographic, operative and infection data on in-patients was collected prospectively over a four-year period by hospitals participating in the Nosocomial Infection National Surveillance Service (NINSS). Generalised linear models were used to estimate the associations between potential risk factors and SSI after allowing for confounding.

The incidence of SSI was 2.2% in primary total hip arthroplasties, 5% in primary hemiarthoplasties, and 3.7% and 7.6% in revision total hip arthroplasties and revision hemiarthroplasties respectively. Staphylococcus aureus was identified in 50% of SSI; 59% of these were methicillin resistant (MRSA). In hemiarthroplasties, MRSA was a causative pathogen in 40% of SSI. Most SSI were superficial (75%), but 9% involved bone or joint. The multivariable regression analysis identified age group, trauma, duration of operation and ASA score as significant independent risk factors for SSI. When these factors were taken into account, type of arthroplasty was not a significant predictor of risk of SSI. After allowing for these factors there was still significant interhospital variation in rates of SSI, which was still evident when the length of post-operative stay was taken into account. Patients undergoing hemiarthroplasty are older, have higher ASA scores and are more likely to have surgery as a result of trauma. The variation in incidence of SSI following hip arthroplasty is more likely to be explained by these characteristics than the type of procedure. The variation in incidence of SSI between hospitals is not fully explained by case-mix, but comparisons of rates should take into account significant risk factors. Methicillin resistant *Staphylococcus aureus* is an important pathogen in SSI of hip arthroplasty, especially in patients undergoing hemiarthroplasty.

**P77**

**DENTAL INSPECTION IS IMPORTANT BEFORE JOINT REPLACEMENT: VIRIDANS STREPTOCOCCAL INFECTION OF JOINT PROSTHESSES**

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**Background:** The issue of antibiotic prophylaxis for dental work in the presence of a joint prosthesis is controversial. However, advanced dental sepsis requires detection and treatment prior to joint replacement.

**Methods:** Patients from whom non B-haemolytic streptococcal infection were recovered from revisions of prosthetic joints over the period 1993-2003 were retrospectively reviewed for predisposing factors.

**Results:** 9 patients had viridans streptococcal infection detected and confirmed by histology and culture at excision arthroplasty. 9 additional patients were excluded—4 because there was no historical proof of infection and 5 because only a single isolate was made from the infected joint (Oxford Criteria). Five patients had continuing dental sepsis which antedated the last joint replacement: one had pre-existing radiation proctitis. One other patient had mixed coagulase negative staphylococcal and viridans streptococcal infection without evidence of dental sepsis. No patient had endocarditis. Two of the dental patients had had multiple revisions. Mean interval in these patients since last surgery was 7.6 years. All dental patients required multiple dental extractions in the interval between excision and revision arthroplasty. One patient had a broken tooth reported at the time of his last surgery and had received reassurance, one an overt dental abscess 15 years, one an occult dental abscess revealed on radiology. Two others had extensive dental caries with blackened stumps as teeth. Follow-up after antibiotic treatment and revision arthroplasty is limited in these cases but results appear satisfactory.

**Conclusion:** Looking in the mouth is now a routine part of assessment prior to primary joint replacement in Oswestry as it would be in a cardiac surgery unit. Patients referred from other centres for revision arthroplasty receive a dental examination if excision arthroplasty cultures yield viridans streptococci.

**P75**

**A PILOT STUDY TO DETERMINE THE INCIDENCE OF STERNAL WOUND INFECTIONS USING A MODIFIED WOUND SCORING SYSTEM IN PATIENTS FOLLOWING CARDIO-THORACIC SURGERY**

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**Objectives:** Post operative wound infections are a significant cause of morbidity, mortality and an increased financial burden. This study was carried out to determine accurately the incidence of sternal wound infections and permit their early diagnosis in patients following cardiothoracic surgery.

**Methods:** A prospective observational study involving assessment of sternal wounds following cardiothoracic surgery for a three-month period was carried out. Wound assessment was based upon a wound scoring system modified from the original scoring system devised by Wilson et al., which included erythema, pain/tenderness, serous discharge, purulent discharge, wound dehiscence and positive microbiology as wound infection criteria. Each criterion was given a score of 5 except purulent discharge and positive microbiology from deep swabs or fluid/tissue, which carried a score of 10. Patients were assessed until they developed wound infection or were discharged from hospital. Risk factors were not investigated because this study was to determine the crude wound infection rate.

**Results:** 186 patients had cardiothoracic surgery during the above period. 148 had Coronary Artery Bypass Graft operation (CABG) and 27 patients had aortic or mitral valve replacement. One patient had ventricular septal defect closure and one had aortic root replacement. The remaining patients had a combination of procedures. Nine patients were found to have wound infection giving a crude infection rate of 4.8%. The average stay in hospital following surgery was 10 days while mean duration of stay in those who developed wound infection was 32 days. The mean time to diagnose wound infection was 11 days. The microorganisms isolated were methicillin sensitive *Staphylococcus aureus*, methicillin resistant *S. aureus* (MRSA), coagulase negative staphylococci and Enterococcus spp.

**Conclusion:** The crude infection rate in sternal wounds was 4.8%. The modified wound scoring protocol was easy to use and a simple method for detection of wound infection at an early stage.
P78
SHORT COURSE VANCOMYCIN THERAPY IN 2 STAGE REVISION KNEE REPLACEMENT: SUSPECTED INFECTED PATIENTS FOLLOWED FOR A MINIMUM OF 1 YEAR
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Objective: A regimen of 2 weeks vancomycin therapy after excision arthroplasty for suspected infection was initiated in 1998. Follow-up was for 1 year, minimum.

Methods: 32 patients were initially assessed with aspiration of the prosthetic joint for culture, histology, and measurement of inflammatory markers. 22 patients were infected on the basis of neutrophil infiltration at excision arthroplasty with one patient unassessable because of inflammatory joint disease and one because histology was omitted.

Results: 13 of these 22 had microbiologically confirmed infection on aspiration or operative microbiology. 4/6 initial aspirates yielding coagulase-negative staphylococci proved to be false positives as judged by operative histology and culture. Initial aspirates yielded false negative results as assessed by operative culture in 1 patient. 4 Staphylococcus aureus or haemolytic streptococcus recoveries from aspirates were always predictive of histological infection but cultures were often negative due to antibiotics. Mean interval between excision and revision arthroplasty was 100 days. 5 patients grew coagulase-negative staphylococci at the 2nd stage from multiple samples. Three had had negative and one enterococcal infection at excision: one had had previous coagulase-negative staphylococcal infection. Only one with previous negative excision cultures but positive aspiration developed infection in the subsequent revision. Five further patients developed signs of infection at follow-up having had negative operative cultures at first and second stage revision. 25 patients had at least 24 month follow up and for the total group follow-up was 12–46 months. Only one patient has had evidence of recurrence of the organism recovered at initial aspiration or excision arthroplasty and overall a satisfactory outcome was achieved in 78% overall and 90% who had only had a single revision arthroplasty.

Conclusion: Vancomycin therapy after excision arthroplasty may be restricted in duration. Bacteriology from aspirates and second stage arthroplasty is a poor guide to definitive aetiology and outcome respectively.

P79*
PRESENTATION OF NEW HIV POSITIVE PATIENTS IN BIRMINGHAM, UK
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Introduction: National statistics show annual rises in the number of people infected with HIV. Estimates suggest one third of those infected are diagnosed. Those who present late with symptomatic disease and low CD4 counts have a poorer prognosis and respond less well to anti-retroviral therapy. This study aimed to review the mode of presentation of patients with HIV infection and to determine whether earlier diagnosis was possible.

Methods: Case notes were reviewed for all those newly diagnosed with HIV infection during 2001 to 2002. The patient’s age, sex, ethnicity, country of birth, risk group and CD4 count at diagnosis were recorded. Their mode of presentation was reviewed and any delay in diagnosis noted.

Results: 53 new diagnoses were made and 42 sets of notes reviewed. 48% were Caucasian and 43% were black African. The major risk factors for HIV acquisition were homosexual sex and heterosexually acquired infection abroad. 50% of patients were diagnosed with symptomatic disease, including tuberculosis, PCP, cryptococcal meningitis and oesophageal candida. Seven patients were identified with a delay in diagnosis. All were Caucasian and had CD4 counts of less than 100. 5 of the 7 acquired HIV heterosexually. Of the 21 who acquired HIV heterosexually abroad, 2 were identified following asymptomatic screening, 7 at antenatal screening, 2 following contact tracing and 10 because of ill health.

Conclusion: Heterosexual Caucasians do not perceive themselves as being at risk of HIV and are not considered at risk by medical staff. In contrast, there was no evidence of delayed diagnoses in black Africans, but this group did not access screening and presented late with symptomatic disease and low CD4 counts. Work needs to be done to remind medical staff to consider HIV infection in those not considered as at risk and to work with the African community to encourage earlier testing.
P81* AN AUDIT OF OUTPATIENT MANAGEMENT AND SCREENING INVESTIGATIONS OF PATIENTS INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS (HIV): A COMPARISON OF PRACTICE BETWEEN A GENITOURINARY MEDICINE (GUM) DEPARTMENT AND AN INFECTIOUS DISEASES (ID) UNIT

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Background: Outpatient management of HIV infected patients allows for screening of infections and malignancies as well as monitoring disease progression and adherence to treatment. We conducted an audit to review these aspects of care.

Method: A retrospective case note review of a random selection of HIV patients was conducted. 143 notes were reviewed: 80 GUM and 63 ID, covering the period 2001 to 2002 inclusive.

Results: Patients in GUM were reviewed more frequently (mean interval 1.7 months, median 1 visits) than ID patients (mean interval 2.4 months, median 8 visits). This did not greatly effect the mean interval at which CD4 counts and viral loads were performed (GUM 3.2 months; ID 3.8 months). Only 52% of ID patients and 56% of GUM patients had repeat syphilis serology documented in the last 2 years. 52% of ID patients and 68% of GUM patients had repeat hepatitis B serology documented. These tests were done on average every year. Only 36% of ID women had a repeat cervical smear recorded, compared to 66% in GUM. Repeat smears were performed on average every 12 months in GUM and every 16.6 months in ID. In their last 3 outpatient visits only 25% of ID patients and 16% of GUM patients were asked a repeat sexual history. Of all patients taking highly active antiretroviral treatment only 44% of ID patients and 32% of GUM patients were asked about adherence.

Conclusions: Substantial differences exist in the approaches to outpatient management and screening between the two departments. Both departments are poor at repeating screening investigations, assessing the risk for sexually transmitted infections and adherence with medications. A ‘reminder’ proforma will be introduced in both clinics and the outcomes audited again (against the new draft guidelines produced by the British HIV association).

P82 MODULATION OF INTRACELLULAR SAQUINAVIR ACCUMULATION-POTENTIAL FOR AUGMENTING ANTI-HIV EFFECT

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Background: Drugs targeting HIV replication need to penetrate inside cells to exert antiviral effect. Drug efflux transporters such as P-glycoprotein (P-gp) may have a key role in determining intracellular drug concentrations. We have previously reported differences in intracellular accumulation of HIV protease inhibitors (PI) in vitro and in vivo, but failed to observe boosting of intracellular saquinavir (SQV) or indanavir in vivo by ritonavir. In this study we sought to examine the effect of the antimalarial drugs mefloquine (MQ), chloroquine (CQ), halofantrin (HF), mepacrine (MC) and amodiaquine (AQ) as well as the P-gp inhibitor XR9576 on HIV replication, and on the intracellular accumulation of SQV.

Methods & Results: The antiviral activity of SQV, MQ, CQ, HF, MC, AQ and XR9576 was tested on HIV-1 infected U937 cells. Neither the antimalarials nor XR9576 exhibited significant anti-HIV activity compared with SQV (selectivity index 2.5 vs 2716). MQ, but not CQ was able to significantly increase intracellular 3H-SQV at concentrations 300 M (p = 0.02) in infected U937 cells. Isobolograms constructed across a range of concentrations revealed antiviral synergy between SQV and MQ (but not SQV and CQ). Finally, the effect of XR9576 on the intracellular accumulation of 3H-SQV was evaluated. XR9576 had no effect upon intracellular SQV concentrations in CEM cells. However, in CEM/35/100 cells (overexpressing P-gp) where the intracellular SQC concentration was diminished, XR9576 was able to almost completely restore intracellular SQV accumulation.

Conclusion: The ability to modulate intracellular concentration of HIV drugs suggests that this may be a means of enhancing antiviral activity. Moreover, P-gp inhibition may allow increased penetration of drugs into other sanctuary sites such as the CNS and male genital tract. Further studies are required to characterise the unbound fraction of intracellular drug, and to relate intracellular drug accumulation with virological suppression in vivo.

P83 IMPACT OF CLINICAL NURSE SPECIALISTS ON ADHERENCE WITH HAART

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Purpose of the study: Good adherence with HAART (highly active antiretroviral therapy) is an important determinant of virological suppression. Our unit has two clinical nurse specialists who have been trained on all aspects of HIV management including HAART and adverse effects. They instruct and closely follow all patients commencing HAART. Patients on therapy have ready access to nurses and are encouraged to contact nurses with any issues. This study looks at the impact of nurse education and their monitoring of patients on adherence.

Methods: A retrospective chart review was undertaken on all patients on HAART and details such as initial and current viral load measurements and CD4 counts, duration of undetectable viral loads, any viral breakthrough, treatment regimens and drug toxicities were entered into a database maintained by the nurses. All patient encounters by nurses were documented.

Results: We have 60 patients currently on HAART, and of these, 53 (88.3%) have a viral load < 50 copies/ml (18/18 women and 35/42 men). The median duration between the initial undetectable and current viral load is 31 months (range 1 - 61 months) with 25 patients having had transient episodes of viral breakthrough. The initial median CD4 count was 188 cells/mm³ (range 12 - 981 cells/mm³). The current median CD4 count is 484 cells/mm³ (range 42 - 1630 cells/mm³). 70% are on a NNRTI/NRTI combination. Most patients attended clinic every 3 months and were in contact with nurse on one occasion for test results.

Conclusion: Clinical nurse specialists have an important role in promoting patient compliance with HAART. They provide ongoing information and support, and patients are encouraged to discuss any difficulties with their medications.

P84 AN AFRICAN HIV COHORT IN A NORTH EAST OF ENGLAND HIV UNIT

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Background and Objectives: HIV originating from areas of high prevalence has been increasing in the UK. The UK dispersal...
program for asylum seekers has increased our number of HIV patients of African origin. We evaluated our cohort looking at demographics, immigration status, HIV status at presentation, psychosocial issues and adherence.

**Methods:** Retrospective case cohort study using local data base and case notes.

**Results:** 26% (87/330) of our HIV cohort are of African origin of these 73 had their case notes reviewed. 55 (76%) are from sub-Saharan Africa. 70% of these are from Zimbabwe. 54 (72%) are female. 32 (44%) are current asylum seekers, 20 (27%) have refugee status. 15 (73), 20.5% were diagnosed during hospitalisation, 13% newly diagnosed during antenatal care. 36% had known diagnosis of HIV. Physical and mental trauma included sexual or physical abuse, history of killed relatives and abandoning immediate family. 12 (16%) are lone parents and 5 have known HIV positive children in the UK. 7 (9.5%) needed interpreters with six different languages spoken the commonest being English, French and Portuguese. Proportion of CDC stages in the cohort were AIDS (26%), symptomatic (26%) and asymptomatic (48%). Active tuberculosis and hepatitis B infections are common. Cultural, psychosocial and language difficulties have a major impact on patient care. Resources needed to improve multidisciplinary HIV care.

**P85**

**Virologic response in patients on Tenofovir**

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**Introduction & Objectives:** Tenofovir was launched as an antiretroviral with an appealing side effect profile, minimal drug-drug interactions and once daily dosing. Recent data has suggested that the combination of once daily tri-nucleoside + abacavir + lamivudine (TDF, ABC, 3TC) is suboptimal with evidence of early virological non-response (VNR) i.e. < 2-log decrease from baseline within 8 weeks or > 1 log increase above nadir at any subsequent visit. The aim of this study was to gauge the virological response in patients switched/started on TDF as part of anti-retroviral therapy (ART) within our cohort.

**Method:** Retrospective case note study of patients prescribed TDF.

**Results:** 52 of 230 patients on ART had been prescribed TDF. 4 were ARV naive when commenced on TDF, 48 were switched onto TDF because of virological failure (42%); lipodystrophy (24%); peripheral neuropathy (16%) or side effects with other drugs (16%). 18(35%) had VNR; 27(52%) patients had successful virological suppression. 10(37%) of these were on triple nucleoside/tide regimes compared with 9(36%) with VNR. All but 1 patient with VNR had been pre-treated with 3 previous ARV regimens. In those responding to nucleoside/tide ART, 2 had M184V mutation and 1 had K65R mutation; 2 of those with VNR had M184V mutation. No patients were on once daily TDF + ABC + 3TC.

**Conclusions:** Current advice includes avoiding TDF + ABC + 3TC in naive patients and monitoring CD4 counts and viral loads in those already on this regimen. This data suggests that careful monitoring is required with triple nucleoside/tide regimes containing TDF as early VNR may occur. Whether drug interactions, reverse transcriptase mutations or other reasons are the cause requires further investigation and evaluation.

**P86**

**IT’S THE STRAW THAT BREAKS THE CAMEL’S BACK: BARRIERS TO CHLAMYDIA TESTING WITHIN PRIMARY CARE**

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**Chlamydia trachomatis** screening has commenced within 10 sites in England. But this has not extended into general practice because of ‘logistical issues.’ We undertook focus groups to determine the barriers to opportunistic testing.

**Methods:** Focus groups were held with randomly selected high and low testing general practices in Herefordshire, Gloucestershire and Avon. Open questions were asked about the management of genitourinary symptoms, and opportunistic testing for chlamydia. Data were collected and analysed concurrently until saturation occurred.

**Results:** The greatest barriers to opportunistic chlamydia testing were lack of knowledge of benefits, when and how to take specimens, lack of time, worries about discussing sexual health and lack of guidance.

I would want to see clear evidence that it is justified, bearing in mind the overall cost restraints to the NHS.

It’s time, I mean we don’t have [the staff] you can’t get locums, even locum nurses anymore are harder [to find],... and it takes a long time, not only [to test] but you have to talk about what you are doing.

I think we are just lucky to get some people to come for their smears without going further down the road.

Health care staff stated that any increased testing should be accompanied by clear, concise PCT guidance on when and how to test, including how to obtain informed consent and perform contact tracing. Staff felt that testing could be undertaken at family planning clinics or with cervical smears if patients received information before the consultation. Alternatively, in larger practices specific chlamydia clinics could be held.

**Conclusion:** Efforts to increase chlamydia screening in this setting should be accompanied by clear guidance, education and have appropriate financial and staff resources. GUM clinics, or level three practices with GUM expertise, will need to be increased to provide appropriate contact tracing and follow-up.

**P87**

**Self-collection KITS for the Diagnosis of Genital Herpes Simplex—the Way Forward?**

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**Introduction:** Diagnosis of genital herpes is difficult without taking viral swabs at the onset of symptoms. To make this more practical, kits for the self-collection of viral swabs were given to selected patients.

**Method:** Kits including a sterile swab and viral medium were
distributed to individuals attending a genitourinary medicine clinic with a history suggestive of genital herpes, but in whom diagnosis was proving difficult. Kits were posted to the virus laboratory for analysis by polymerase chain reaction (PCR). By case note review of these 71 patients, information about their characteristics, nature and duration of symptoms, clinical findings on history and examination, and the results of diagnostic tests were analysed using Microsoft excel and SPSS software.

Results: 21/71 patients were diagnosed with HSV type 2 and 7 with HSV type 1. This diagnosis was made by self-collection kit in 20 and by clinic swab in 8. Of these 8, a greater proportion had been symptomatic at the time of first attendance at the clinic (6/8, versus 10/20) and they had been attending longer with their symptoms before being issued with a kit (mean 33.75 versus mean 15.3 weeks). It took longer to reach a diagnosis (mean 10.13 versus mean 7.5 months), with more consultations at the clinic (mean 3.75 versus mean 2.9), but none of these differences were statistically significant. In 158 patients alternative diagnoses were made.

Conclusions: This study illustrates the difficulties in reaching a diagnosis of genital herpes. Innovative use of diagnostic techniques could improve the management of this debilitating infection. Further work is warranted to investigate the cost effectiveness and acceptability of self-collection kits for diagnosis of HSV. This method is a useful adjunct to testing in the conventional setting and may provide a swifter, more flexible route to diagnosis and management of genital herpes for some individuals.

P88
YOUNG ATTENDEES AT A SEXUALLY TRANSMITTED DISEASES (STD) CLINIC IN IRELAND
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Background: Attendance at STD clinics in Ireland has increased dramatically in recent years. An increase in the incidence of STDs has paralleled this. Attendees aged twenty and under comprise a significant proportion of new infections.

Methods: Between January 1999 and December 2002, all attendees at an STD clinic aged less than twenty were followed, and data recorded on demographics, reasons for attending diagnosed, and risk behaviour for STDs.

Results: 1170 people in this age group attended over the period. Female patients exceeded males each year (mean 69%). Most 1170 people in this age group attended over the period.

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- 21/71 patients were diagnosed with HSV type 2 and 7 with HSV type 1. This diagnosis was made by self-collection kit in 20 and by clinic swab in 8. Of these 8, a greater proportion had been symptomatic at the time of first attendance at the clinic (6/8, versus 10/20) and they had been attending longer with their symptoms before being issued with a kit (mean 33.75 versus mean 15.3 weeks). It took longer to reach a diagnosis (mean 10.13 versus mean 7.5 months), with more consultations at the clinic (mean 3.75 versus mean 2.9), but none of these differences were statistically significant. In 158 patients alternative diagnoses were made.

Conclusions: This study illustrates the difficulties in reaching a diagnosis of genital herpes. Innovative use of diagnostic techniques could improve the management of this debilitating infection. Further work is warranted to investigate the cost effectiveness and acceptability of self-collection kits for diagnosis of HSV. This method is a useful adjunct to testing in the conventional setting and may provide a swifter, more flexible route to diagnosis and management of genital herpes for some individuals.

P89
MOTHER-TO-CHILD TRANSMISSION OF HUMAN HERPESVIRUS 8 IN SOUTH AFRICA
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Background: The modes of transmission of human herpesvirus 8 (HHV8) in Africa are unclear.

Methods: To investigate mother-to-child transmission of HHV8 in South Africa, 2546 mother-child pairs were recruited from rural vaccination clinics and tested for antibodies against lytic (K8.1) HHV8 antigens. HHV8 DNA copy number in saliva and breast milk was determined for a sample of mothers by competitive quantitative PCR. Findings. In children over 1 year (who are unlikely to have maternal antibodies), the prevalence of antibodies was 9% (54/579) if the mother was HHV8 seronegative and 25% (103/413) if she was seropositive (odds ratio [OR] 3.2, 95% confidence intervals [CI] 2.2-4.7) and increased with increasing maternal antibody titre (x^2 = 48, p < 0.001). 15% (145/978) of mothers had detectable HHV8 DNA in saliva (mean viral copy number 488,450 copies/ml, range 1550-660,000); the prevalence was 10% (51/532) in HHV8 seronegative women and 33% (71/216) in women with the highest antibody titres (OR = 4.6, 95% CI 3.0-6.9). The prevalence of anti-HHV8 antibodies in children was 15% (109/735) if the mother had no detectable HHV8 in saliva and 28% (12/43) if the mother had a high HHV8 copy number (>50,000) in saliva (OR = 2.2, 95% CI 1.1-4.5). Among 43 women with high anti-HHV8 antibody titres, 12 had detectable HHV8 DNA in breast milk, but at lower levels than in saliva (mean viral copy number 5800 copies/ml, range 1550-12,540).

Interpretation: We provide evidence of mother-to-child transmission of HHV8 and that maternal saliva is a likely route.

P90*
HYPOGLYCAEMIA IN HERPES SIMPLEX ENCEPHALITIS
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Commonly, the cerebrospinal fluid (CSF) from patients with herpes simplex (HSV) encephalitis/ meningitis show normal glucose levels. A case of herpes simplex encephalitis with unusually low CSF glucose is presented. We also reviewed 21 previous glucose measurements from 29 HSV PCR positive CSF samples taken between 1996 and 2003. The CSF glucose range was <1 to 12 mmol/L, with a mean of 3.6, SD 2.5. The ratio of CSF: serum glucose ranged from 0.07 to 0.64 with a mean of 0.46, SD 0.17. One other patient had a CSF glucose of <1 associated with HSV meningitis. With the advent of molecular diagnostics a wider spectrum of HSV encephalitis/meningitis is now being recognised, and our series suggests that a low CSF glucose value does not rule out this diagnosis.
P91*
AN OUTBREAK OF MEASLES IN STRATHCLYDE UNIVERSITY—THE CASE FOR MMR?
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Background: Adult measles is generally an imported infection in the UK. Outbreaks of measles are becoming of increasing concern with reduced uptake of MMR.

Case Report: A 26 year old Indian man was referred to an infection unit with a one week history of fever, cough, diarrhoea and rash. He had returned from India two weeks previously. On admission he was noted to have an erythematous throat, cervical lymphadenopathy, fever and a widespread maculopapular rash on his face, arms, trunk and legs. The rash had initially appeared on his face 24 hours prior to admission. Investigations showed abnormal liver function, a CRP of 59 mg/L, a normal chest X-ray and negative malaria films. There was spontaneous resolution of fever and rash over the next 4 days. Serology for measles showed a positive measles IgM and negative measles IgG and PCR was positive for measles. Convalescent serum showed positive measles IgM and IgG.

Nine days after discharge, and prior to the serological diagnosis of the initial patient, his flatmate was admitted with a similar history and clinical findings. Measles was diagnosed serologically. Both patients were students staying in halls of residence. Although a program of screening and vaccination with MMR was employed by public health one further student was admitted with serologically diagnosed measles.

Conclusion: The diagnosis of measles should be considered in patients with maculopapular rashes. There is increased risk with foreign travel to countries with a high incidence of measles and patients with maculopapular rashes. There is increased risk with foreign travel to countries with a high incidence of measles and patients with maculopapular rashes. This may become an increasing diagnosis in the UK given the recent controversies over the MMR vaccination program.

P92*
DIAGNOSIS OF NOROVIRUS INFECTIONS BY EIA: IMPACT ON P92*
in patients with no clear history of vaccination. This may become
foreign travel to countries with a high incidence of measles and
patients with maculopapular rashes. There is increased risk with

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an increasing diagnosis in the UK given the recent controversies
over the MMR vaccination program.

P93
STEATOSIS IN CHRONIC HEPATITIS C: RELATIVE CONTRIBUTIONS OF VIRUS AND HOST FACTORS
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Background & Objectives: Steatosis is common in patients with chronic hepatitis C virus (HCV) infection and is thought to accelerate disease progression. Viral and host factors reported to influence the formation of steatosis include obesity, age, alcohol consumption and HCV genotype.1–3 To address the relative contributions of the virus and host factors we studied 221 patients, 107 of whom were infected with genotype 3, with liver biopsy proven chronic HCV in whom data on all 4 variables was available.

Methods: Retrospective analysis of patients attending the regional Hepatitis C service.

Results: Steatosis was found in 47% of liver biopsies (54% of patients with genotype 3, 40% of patients with genotype 1). In univariate analysis, steatosis correlated with clinical obesity (BMI 30) (p < 0.01), but not with age, alcohol consumption or HCV genotype. On repeat analysis of patients with BMI < 30 (n = 192), steatosis was significantly associated with genotype 3 (p < 0.02).

Conclusion: In this large cohort of patients (including 107 patients with genotype 3 infection) steatosis is strongly associated with the host factor of obesity, rather than alcohol consumption. Genotype 3 infection may influence steatosis in individuals who are not clinically obese. Our data indicates that risk factors for nonalcoholic fatty liver disease (NAFLD) need to be addressed in all patients with chronic HCV.

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P94*
TRAVEL IN THE HEPATITIS C POSITIVE PATIENT
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Introduction & Objectives: Since 1986 the global travel industry has almost doubled in size and Hepatitis C (HCV) is a
recently emerging disease affecting almost 200 million people world-wide, yet knowledge about previous travel, health, drug adherence, alcohol intake and risk behaviour in the HCV positive (HCV+) traveller is limited.

**Methods:** Prospective questionnaire-based study of patients attending the Joint Hepatitis C Services at Newcastle Hospitals NHS Trust over five week period addressing issues of travel, HCV and risk behaviour (Special Study Module which was limited in time and patient numbers).

**Results:** 47 patients eligible completed the questionnaire. Patients diagnosed with HCV for less than one year were excluded. Of the cohort, 32 patients had liver disease, 7 had cirrhosis and 1 patient had hepatocellular carcinoma. 38 patients (80.9%) had travelled, 68.4% within Europe, 31.6% beyond Europe. 24 patients (63.2%) received no advice before travelling. 20 (52.3%) obtained travel insurance, but only 3 were specific for HCV + travellers. 18 patients were vaccinated against hepatitis A virus, and 16 against hepatitis B virus. 38.3% (18) carried a first aid kit and 23.4% (11) were ill whilst travelling; 4 required medical attention. 31.6% of patients (12) have travelled whilst on HCV medication; 1 admitted to non-adherence. 3 patients travelled to malarial endemic countries: 3/3 obtained malaria prophylaxis, and 2/3 adhered. 47.4% (18) consumed alcohol whilst travelling. 57.9% (22) were sexually active whilst travelling and 2 of these admitted to having unsafe sex with a new sexual partner. 5 patients (12.2%) used intravenous recreational drugs whilst travelling and 2 shared equipment.

**Conclusion:** HCV + patients are a travelling population, but are often ill prepared. High-risk behaviour including unsafe sex and drug use occurs whilst travelling. To improve the care of HCV + travellers in the future, pre-travel advice specific to the HCV + patient should be promoted.

**P96**

HEPATITIS A TESTING AND SEROPOSITIVITY AMONGST HEPATITIS C POSITIVE INJECTING DRUG USERS IN MERSEYSIDE

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**Background:** Hepatitis A (HAV) outbreaks in the UK in the last 2 years have frequently involved injecting drug users (IDU) and active immunization of all IDU has been proposed to protect the general public health. Hepatitis A (HAV) poses extra risks when it causes superinfection in chronic hepatitis C (HCV) carriers. In Merseyside, where IDU is a common problem, HCV prevalence has been found to be as high as 67%. However little was known about HAV, making it difficult to plan vaccination guidelines for the region.

**Aim:** To assess the rates of HAV screening in IDU in hospital based services. To document rates of natural immunity to HAV.

**Method:** A retrospective review of laboratory databases of IDU seen in our services with positive HCV antibody tests between 1996 - 2003. Tabulation of HAV, Hepatitis B (HBV), and HCV was undertaken.

**Results:** HAV serology was only performed in 381 of 2235 (17%) HCV positive IDU overall. However, the population tested rose to 112 out of 155 (72%) in those screened since 2001, when a screening policy was adopted. HAV IgG serology was positive in 219 of 381 (57.5%). Hepatitis B surface antigen was positive in 40 of 315 (13%) of those tested for both HAV and HCV.

**Conclusions:** Hepatitis A screening rates were low before 2001 and still need to be improved. Over half of HCV positive IDU already have immunity to HAV, and this might affect cost calculations for immunization programmes that include pre-vaccination screening. Although these results are subject to ascertainment bias, the overall conclusion is likely to be similar in a prospective study.

**P97**

EPIDEMIOLOGY OF HUMAN ROTAVIRUS IN IRANIAN CHILDREN

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Diarrhoea is the most common infection in children resulting in the death of up to 6 million children every year. Human Rotavirus (HRV) is responsible for between 20% to 25% of these deaths. Diarrhoea is one of the main health problems in Iran, although there is no information on the pathogens involved. This study describes the aetiology of viral diarrhoea and the characteristics of HRV in Shahrekord, Iran.

259 Children < 5 ys admitted to Hajar Hospital, 245 attending primary health centres in Shahrekord, with acute diarrhoea and 114 children hospitalised for elective surgery were selected from
October 2001 to August 2002. Stool samples were collected for ELISA, EM, RT-PCR and electrophoretotyping. 186 viruses were identified of which 146 were HRV. Ten (6.4%) HRV were identified in children without diarrhoea. The second most frequent virus was coronavirus with 16 cases, followed by calicivirus (9). Other viruses included adenovirus (8), astrovirus (6) and parvovirus (1). HRV was more frequently identified in children <2 years old. The RT-PCR successfully typed 139 of the 146 (95%) HRV G types and 124 (85%) P types. The most frequent P type was P[8], 61 (42%) samples, P[8] in 48 (33%), P[4] in 16 (11%) and was non-P-typeable in 22 (15%). Among the G types, G1 was identified in 78 (53%), G1* in 42 (29%), G2 in 19 (13%) and was non-G-typeable in 7 (5%). HRV is the most important pathogen causing severe diarrhoea in Shahrekord and has a marked seasonal variation, being most frequently isolated from November to February (50% of HRV recovered). These results are in agreement with studies reporting a peak of HRV in the winter months (Maltezou HC et al. 2001; Grimprel E et al 2001; Caeiro JP et al. 1999).

P98* THE DIAGNOSIS OF ACUTE HEPATITIS C VIRUS INFECTION DURING SEROCONVERSION
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A 29 year-old asymptomatic male intravenous drug user of six years was under the ongoing care of an addiction team when routine screening tests revealed significant elevation of liver transaminases; alanine aminotransferase (ALT) was particularly elevated. Despite no known exposure to a definite HCV positive contact, there was a high index of suspicion for acute hepatitis C virus (HCV) infection. Additional risk factors were recent tattooing and recent episodes of unprotected sexual intercourse.

Upon admission to hospital, hepatitis C virus (HCV) screening IgG antibody was non-reactive. However, a specimen taken on day 11 was weakly reactive, although a supplementary assay, the recombinant immunoblot assay-3 (RIBA-3), was negative. By day 15 both IgG and the RIBA-3 had become positive.

Retrospective real-time, quantitative, polymerase chain reaction (PCR) amplification of RNA extracted from all of the specimens referred to above was carried out. PCR positivity 10 days prior to seroconversion was observed in this case. The patient was followed up at an outpatient clinic and after 8 weeks of remaining HCV RNA positive it was decided that he should receive combination antiviral therapy with pegylated interferon and ribavirin.

This case raises several interesting issues:
Seroconversion including viral load kinetics in HCV infection is rarely observed. The diagnostically confounding seroconversion window is important to remember
• In the setting of a seronegative result from a high risk patient, discussion with the virology lab may be useful
• Molecular diagnostic methods and the opportunity for diagnosing acute disease raises an important possibility for public health intervention measures among ivdu contacts.
• Molecular methods with quantitation also raise questions about a period of watchful waiting to avoid toxic, expensive, treatment of patients who may spontaneously clear virus.

P99 SENSITIVITY OF SACCHAROMYCES CEREVISIAE TO FLUCONAZOLE, ITRACONAZOLE AND VORICONAZOLE
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Objectives: Saccharomyces cerevisiae is a yeast found in many foodstuffs. It occasionally causes opportunistic infection especially in immunosuppressed patients. There is limited information on sensitivity of clinical isolates of Saccharomyces cerevisiae to azoles especially the newer agents. We tested the sensitivity of Saccharomyces cerevisiae to fluconazole, itraconazole and voriconazole and performed DNA fingerprinting to distinguish between strains.

Methods: 17 clinical isolates of S. cerevisiae predominantly from surveillance cultures from immunosuppressed patients were collected from April 2002 to August 2003 and tested for sensitivity to fluconazole, itraconazole, voriconazole using E-test strips. Germ-tube negative isolates were identified using API 20C AUX. Sensitivity tests on RPMI media with 2% glucose and yeast suspensions adjusted to a turbidity of a 0.5 McFarland standard, at 35 °C was read after 48 hours. DNA fingerprinting was performed to exclude the possibility of an outbreak strain as 10/17 isolates were from the same Unit. Results The MIC to fluconazole ranged from 0.5–24 g/ml. 16/17 isolates were sensitive to fluconazole. 1 strain showed reduced sensitivity (MIC 24 g/ml). The MIC to itraconazole ranged from 0.19 to >32 g/ml. 12 strains showed resistance (MIC >0.5) and 5 reduced sensitivity MIC 0.19–0.5 g/ml.

The MIC to voriconazole ranged from 0.006–0.125 g/ml indicating that all isolates would be sensitive to voriconazole (using the criteria, sensitive as ≤1 g/ml).

DNA fingerprinting on 14 isolates identified 11 different strains.

Conclusion: Most strains appeared to be sensitive to fluconazole but showed reduced sensitivity or resistance to itraconazole. Itraconazole prophylaxis is commonly used for prophylaxis on our Haematology Unit which may explain the high number of resistant strains. All isolates however appeared to have low MICs to voriconazole suggesting that it may be a therapeutic option for serious Saccharomyces cerevisiae infections. DNA fingerprinting is useful in distinguishing between strains.

P100 IN VITRO SUSCEPTIBILITY OF VORICONAZOLE AGAINST CANDIDA SPECIES WITH REDUCED SENSITIVITY TO FLUCONAZOLE AND ITRACONAZOLE
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Objectives: We tested Candida isolates with reduced susceptibility to fluconazole and itraconazole, mainly from surveillance specimens from immunocompromised patients, for voriconazole sensitivity, a new potent triazole, to assess the potential for its use against resistant strains in our hospital.

Methods: 54 clinical Candida isolates including C. glabrata (40), C. krusei (7), C. albicans (3), C. guilliermondii (3), C. dubliniensis (1) which showed reduced susceptibility to either fluconazole or itraconazole were tested for voriconazole MIC by E test. After identifying germ tube negative candida isolates by API 20 C AUX, sensitivity testing was performed on RPMI media with 2% glucose with yeast suspensions adjusted to a turbidity of a 0.5 McFarland standard. Plates were incubated at 35 °C for 48 hours.

Results: Overall 51/54 (92.6%) isolates had voriconazole MIC <2 μg/ml (MIC 90:0.5 μg/ml).

For C. glabrata, 24/40 (60%) isolates were fluconazole sensitive but of decreased sensitivity to itraconazole, the voriconazole MIC range was 0.004–0.125 μg/ml. 12/40 (30%) had reduced sensitivity to both fluconazole and itraconazole and voriconazole
MIC range was higher at 0.125–8.0 μg/ml. 3 out of these 12 (25%) had MIC >2 μg/ml. 4/20 (20%) in spite of high fluconazole and itraconazole MICs had low voriconazole MIC range of 0.023–0.094 μg/ml.

For the other Candida isolates, voriconazole MIC ranged from 0.024–0.25 μg/ml for C. krueri, C. albicans 0.024–0.094 μg/ml, C. guillermondii 0.032–0.047 μg/ml and C. dubliniensis 0.032 μg/ml.

Conclusions: There are no established breakpoints for voriconazole in literature, so based on putative breakpoints of MIC <1 μg/ml as sensitive and ≥2 μg/ml as resistant, our data suggests that voriconazole may be very useful for treating serious candida infections in our group of patients. However, it is essential to perform sensitivity testing as occasional strains e.g. C. glabrata may be resistant to voriconazole and this may not be evident by fluconazole and itraconazole sensitivity tests.

P101 TARGETING HIGH RISK PATIENTS BY ANTIFungal PROPHYLAXIS COULD PREVENT FUNGAL INFECTIONS AFTER LIVER TRANSPLANTATION IN CHILDREN

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Background: Fungal infection (FI) causes significant morbidity and mortality after liver transplantation (LTx) in children. The aims of this study were to establish the incidence of, and risk factors for, FI, and the value of antifungal prophylaxis in high risk patients.

Patients, methods & results: Initially, 79 children (0-16y) undergoing LTx between 1997-98 (group I) were studied. The incidence of FI was 40% (32/79): half of these were invasive. Candida spp. were recovered in 73% of patients; 55% were Candida albicans. The following were risk factors for FI: pre LTx colonisation with fungus; ICU stay >2w; antibacterials for >3w within 2 months of LTx; steroids; retransplantation, and hepatic artery thrombosis. In this group, 48% (38/79) children were colonised by fungus pre-LTx: C. albicans in 71.5%, and Aspergillus spp. in 3%. Post-LTx the same number were colonised, but C. albicans and Aspergillus spp. were more frequent. An antifungal prophylaxis protocol was introduced between 1999 and 2000 for 93 children (group II). Fluconazole was given immediately after and for 2w post-LTx to those with risk factors (see above; 27 patients), or amphotericin B to those also colonised by Aspergillus spp. or non-C. albicans yeasts (20 patients). During this period 44% (41/93) were colonised pre-LTx: 68% by C. albicans and 5% by Aspergillus spp.; post-LTx the incidence of detectable colonisation was 16% (15/93). The incidence of FI and invasive FI in group II was 10% and 2%, respectively.

Conclusions: Although this is not a controlled study, this targeted approach to antifungal prophylaxis appears to have been effective in reducing the incidence of both non-invasive and invasive FIs in children after LTx. However, the influence of changes in antibacterial policy-that may have affected both fungal colonisation and FI-are acknowledged and will be discussed.

P102 A FATAL CASE OF DISSEMINATED ZYGOMYCOSIS DUE TO CUNNINGHAMELLA BERTHOLLETIAE IN A PATIENT WITH DIABETES MELLITUS USING BLOOD GLUCOSE MONITORING EQUIPMENT

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Background: Zygomycoses are rare, angioinvasive fungal infections caused by various zygomycetes including Cunninghamella bertholletiae. They are usually opportunists with low pathogenic potential. Known risk factors for invasive disease include: immunocompromise, diabetes mellitus (D.M.) and desferrioxamine therapy. The incidence of zygomycoses is rising due to an increase in the number of susceptible patients. Disease can be rhinocerebral, pulmonary, cutaneoarticular or disseminated. Rapidly overwhelming sepsis with a high mortality rate is usual. Survival is associated with early diagnosis, aggressive surgical debridement, high dose Amphotericin B and immunostimulation.

Methods: A 68 year old man with type II D.M. and myelodysplastic syndrome (M.D.S.), requiring regular blood transfusions and regular desferrioxamine infusions, was admitted with a five-day history of a painful swollen left index finger- the site used for blood glucose monitoring. Pus from the finger was sent to microbiology. Over the course of 48 hours the patient deteriorated rapidly and died despite antimicrobial therapy. A post-mortem was performed.

Results: Postmortem findings showed evidence of fungal septicaemia. There were infarcts in the kidney, spleen and brain, severe pericarditis, necrotising areas in the myocardium and severe meningitis. Thrombi in the coronary arteries contained numerous fungi. The morphology of the fungi on histological staining suggested a zygomycete. The pus from the patient’s finger yielded C. bertholletiae, but this result was only available post mortem.

Conclusions: This case highlights the rapidity at which invasive zygomycosis can progress. Two cases of cutaneous zygomycosis acquired by inoculation due to C. bertholletiae have been reported previously, raising the possibility that the infection may have been introduced by home blood glucose monitoring in this case. Patients in whom such procedures are required, particularly those with other risk factors, may be at increased risk of infection.

P103 NASAL CARRIAGE OF STAPHYLOCOCCUS AUREUS BY DIABETIC FOOT ULCER PATIENTS—POTENTIAL FOR HEALTH PROTECTION

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Infection of diabetic foot ulcers (DFU) by Staphylococcus aureus is common and associated with increased mortality, due to compromised co-morbidities. Whilst elimination of nasal carriage of S. aureus is known to be a useful health protection measure in some patient groups, its status and role in diabetes mellitus is controversial and unknown in DFU patients. We therefore sampled the anterior nares and ulcers of 98 DFU outpatients to isolate S. aureus. Macrorestriction with Smal was used to distinguish or match ulcer and nasal isolates from individual patients. As a control, 111 healthy individuals (medical students) at the same institution had nasal swabs taken for culture to determine a baseline carriage rate. Of the 98 DFU patients, 38 (38.7%) were nasal carriers of S. aureus. All but one patient had S. aureus isolated from their ulcers. This was significantly different from the controls, 28 (25.2%) of whom were carriers (P < 0.05). 78.9% of DFU isolates were penicillin-
resistant, compared to only 12.3% of \textit{S. aureus} in baseline controls. Macrorestriction determined that 35 (92.1%) of the 38 DFU patients with nasal carriage had the same strain of \textit{S. aureus} in their ulcer \((P < 0.001)\). The positive and negative predictive values of a nose swab as a simple measure to determine whether a DFU is likely to be infected or not, were 85.0% and 92.1%, respectively. Nasal carriage of \textit{S. aureus} is therefore linked to infection of DFU and protocols for its eradication are required to protect these patients against infection.

P104
CMV PCR SURVEILLANCE IN RENAL TRANSPLANT PATIENTS
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Purpose: To assess the impact of routine CMV PCR surveillance on the incidence of CMV infection/disease and the efficacy of aciclovir prophylaxis in the high risk CMV mismatch (Donor +, Recipient -) renal transplant patients in Freeman Hospital Newcastle-upon-Tyne.

Methods: Retrospective analysis of case notes of high-risk CMV mismatched renal transplant patients who had CMV PCR surveillance between January 2000 - March 2002.

Results: 249 renal transplants were performed between January 2000 - March 2002. 40 patients were in the high-risk (D +, R -) group. 34 of these were available for surveillance out of which only 2 patients had full surveillance, 4 had partial surveillance and 28 had significant gaps in surveillance. 20 of the 34 patients were CMV PCR positive. Out of the 20 who were PCR positive, 14 had CMV disease and 6 had infection (of which 4 received pre-emptive treatment). 24 of the 34 patients under PCR surveillance received aciclovir prophylaxis however 10 of these patients developed CMV disease. The mean interval between transplant and CMV PCR positivity was 77 days in the aciclovir group and 44.6 days in the patients who did not receive prophylaxis. The cost of managing patients with CMV according to current protocol was £46,884 as compared to £51,015 if all the high-risk patients were to receive ganciclovir prophylaxis with the caveat that 15% of these patients will still end up with CMV disease. Conclusions: No significant difference was noted between the cost of managing high-risk patients as per the current protocol and if all these patients were to receive ganciclovir prophylaxis instead. Prophylactic aciclovir does not prevent CMV disease/infection but may delay it. Incidence of CMV infection/disease and rate of adverse outcome was higher than expected in the study group.

P105
CMV SURVEILLANCE AND MANAGEMENT IN LIVER TRANSPLANT PATIENTS: A TWO YEAR AUDIT
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Objectives: To evaluate our protocol of CMV surveillance and pre-emptive treatment with oral ganciclovir in CMV mismatched liver transplants. Protocol compliance was in doubt and there was no consensus on whether pre-emptive therapy or universal prophylaxis is the optimal approach against CMV infection.

Methods: Retrospective database analysis and casenote review of liver transplants (January 2000-December 2002) was performed. Management of CMV-mismatched patients (D + R -) was assessed against the agreed protocol. This comprised regular CMV-QPCR monitoring for three months, twice-weekly for in-patients then weekly following discharge. 14 days pre-emptive oral ganciclovir was to be given in the event of a single high viral load (VL) \((10^5 \text{ copies/ml})\) or a VL increasing by 0.5 log in sequential samples. Therapeutic intravenous ganciclovir was indicated if there was evidence of CMV disease.

Results: 100 liver transplants were performed. Of 15 CMV mismatches, 14 survived and were evaluated. In 3/14 (21.4%), CMV-QPCR remained negative. 11/14 (78.5%) developed positive titres \((10^5-10^6 \text{ copies/ml})\). 3 out of the 11 (27.2%) with positive titre had evidence of CMV disease at time of first positive VL and were successfully treated with intravenous ganciclovir. 8/11 (72.7%) had no evidence of CMV disease initially; 3/8 received neither pre-emptive nor therapeutic ganciclovir, 4/8 were given intravenous then oral ganciclovir and all 7 remained well. 1/8 developed serious CMV disease after delayed pre-emptive treatment and required intravenous ganciclovir.

Conclusion: Of 14 evaluable CMV mismatches, agreed protocol was strictly followed in only 6/14 (42.8%) cases. In the remaining 8 (57.1%), 50% were given unnecessary oral or IV ganciclovir. Compliance with the protocol was poor. After discharge, follow-up in out-patients or in distant referring centres lead to delays in CMV surveillance. Lack of confidence in the protocol may have resulted in some unnecessary use of intravenous ganciclovir. Following review, we have now introduced prophylaxis with oral ganciclovir (90 days) for all CMV-mismatched liver transplants.

P106
RHINOVIRAL INFECTIONS IN ADULT BONE MARROW/PERIPHERAL STEM-CELL TRANSPLANT RECIPIENTS
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Objective: To study the role-played by rhinovirus infections in transplant-associated morbidity and mortality (1996/7-2000/1). Methods: Computer records of patients with features satisfying the published criteria for respiratory tract infection in BMT recipients were reviewed retrospectively over five winter seasons (1996/7-2000/1), from the Christie Hospital, Manchester, UK.

A standard pro-forma was used to collect patient data including age, sex, primary diagnosis, type of transplant, immunosuppressive therapy, respiratory symptoms, specimens collected, laboratory diagnosis, antimicrobial agents used (antiviral, anti-bacterial etc) and outcome of these infections. The \(2 \times 2\) chi square test was used for statistical calculations.

Results: The 5-year data collected showed a total of 626 adult patients who underwent transplants. This unit accepts patients over the age of 18 years. 11 patients had infection with rhinoviruses accounting for 40% of viral diagnosis. Other viruses present include, respiratory syncytial virus (RSV) (22.2%).
influenza A (18.5%), Para influenza (PIV) (14.8%) and enteroviruses (7.4%). Herpes simplex and CMV infections were excluded from the study and no adenovirus infections were found. Only patients with rhino viral infections will be further discussed in this report. The frequency of infection due to rhinoviruses was 1.8%. The prevalence being higher in allogeneic compared with autologous recipients. 2 out of a total of 4 deaths were directly attributable to a rhinovirus respiratory infection.

Conclusions: Respiratory viral infection is increasingly reported as an important cause of morbidity and mortality in bone marrow transplant (BMT) recipients. In the recent past, considerable experience has been gained regarding the role of viruses including RSV, influenza A, PIV and adenoviruses, there is however relatively little data describing the role of rhinovirus infections in these patients. This report highlights the increasing importance of rhinovirus chest infection in causing morbidity and mortality in BMT patients.

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P108* EXTRACELLULAR PROTEASES OF PATHOGENIC ACANTHAMOEBA CONTRIBUTE TO INCREASED PERMEABILITY OF THE BLOOD-BRAIN BARRIER

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Granulomatous amoebic encephalitis is a serious human infection that almost always leads to death, however the pathogenic mechanisms associated with this disease remain unclear. Several lines of evidence suggest that haematogenous spread is a prerequisite for Acanthamoeba encephalitis but it is not clear how circulating amoebeae cross the blood-brain barrier to gain entry into the central nervous system. We have recently developed an in vitro blood-brain barrier model using human brain microvascular endothelial cells. Using this model, we determined the effects of Acanthamoeba (encephalitis isolate belonging to T1 genotype) on blood-brain barrier permeability and factors responsible for these changes. We observed that Acanthamoeba produced more than 60% increase in the blood-brain barrier permeability. To determine whether Acanthamoeba mediated increased permeability is contact-independent, Acanthamoeba conditioned media were produced and incubated with the blood-brain barrier. A timedependent increase in permeability was observed with more than 60% permeability within 5 h of incubation. Prior treatment of conditioned media with PMSF (a serine protease inhibitor), abolished permeability changes indicating the role of serine proteases. Of interest, alpha-mannose inhibited Acanthamoeba binding to human brain microvascular endothelial cells but increased the blood-brain barrier permeability. Zymography assays revealed that Acanthamoeba produces three distinct proteases, two of which were inhibited by PMSF. In conclusion, we have, for the first time, shown that Acanthamoeba produces blood-brain barrier permeability which can be blocked by PMSF, indicating the potential role of serine proteases. Further understanding of the mechanisms associated with Acanthamoeba encephalitis will allow us to develop novel strategies to prevent this serious infection.

P109 MGRA, ACTS AS A TRANSCRIPTIONAL REPRESSOR OF THE GENES WITHIN THE RLR PATHOGENICITY ISLET IN STREPTOCOCCUS PNEUMONIAE ALTERING BACTERIAL ADHESION TO EPITHELIAL CELLS

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Streptococcus pneumoniae normally resides in the human nasopharynx in a nondisease state. In response to yet unknown triggers it can invade mucosal surfaces and enter the bloodstream causing disease. Regulation and activation of virulence genes play essential roles in this process of disease development. Characterization of S. pneumoniae regulatory networks has been a recent area of interest but despite inroads there is little known about regulation of virulence genes in this pathogen. A putative transcriptional regulator in S. pneumoniae, Mgra, with homology to a virulence gene activator, mga, of Group A streptococcus (GAS) was identified as being required for development of pneumonia in a murine model. In this work we confirm that mgaR is required for both nasopharyngeal carriage and pneumonia. Transcriptional profiling by microarray technology shows that mgaR acts as a repressor of genes in the rlrA pathogenicity island that mediate adherence to respiratory epithelial cells in vitro. A second regulator within the island, rlrA, activates transcription of the same genes. Interplay between these two regulators may control expression of these adhesins in response to changing host environments hence altering the invasive and/or adhesive properties of the bacteria.

P110* CASPASE ACTIVATION ENHANCES PNEUMOCOCCAL INNATE IMMUNE DEFENSE

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Background: Caspases are cysteine aspartate-specific proteases that regulate cell functions including programmed cell death, cytokine processing and cytoskeletal homeostasis. Caspase activation contributes to poor outcomes in models of sepsis.

Methods: Human monocyte-derived macrophages (MDM) or murine bone marrow-derived macrophages (BMDM) were infected with type 1 pneumococci (Spn) in vitro. A resolving model of pneumococcal infection in C57BL6 mice was established, in which apoptosis was quantified by morphologic analysis of lung sections. Results: Caspase activation was a feature of phagocytosis of Spn by MDM. Inhibition of caspase activation decreased MDM apoptosis after infection. NMDA receptors in MDM and BMDM were greater following treatment with zVAD than in control cultures. MDA: 1.5 x 10^-4 cfu (1.3 x 10^2–9 x 10^3) vs. 0 cfu (0–1.2 x 10^3). BMDM: 222 cfu (28–500) vs. 0 cfu (0–233), p < 0.05 (median: 25–75 percentile). In vivo rates of alveolar macrophage (AM) apoptosis were enhanced by infection of Spn. AM apoptosis was 3.7% (2.4–9.3) vs. 1.8% (0.8–2.5). Caspase inhibition resulted in a decrease in AM apoptosis (1.5% (0.7–2.4)).
however bacterial internalisation in vitro and inflammatory cell recruitment in vivo were not altered. Bacterial clearance was $1.2 \times 10^5$ cfu/lung (0.35 – 103) after zVAD vs.0 cfu/lung (0–38.3 \times 10^5) in controls and a greater number of mice were bacteriæmic (6/13 vs.0/8, $p < 0.05$). Caspase 1 deficient mice showed no alteration in AM apoptosis or in bacterial clearance as compared to wild type.

Conclusions: Caspase activation is associated with macrophage apoptosis induction and bacterial killing in a resolving model of pneumococcal infection. Apoptosis induction contributes to bacterial clearance.

P111
GENETIC ANALYSIS OF GASTROINTESTINAL COLONISATION BY SHIGELLA FLEXNERI
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Members of the genus Shigella are pathogens of the gastrointestinal (GI) tract of humans, causing severe and sometimes fatal bacillary dysentery responsible for approximately one million deaths annually. Shigella spp. can invade the mucosal surface of the gastrointestinal tract and initiate an acute and intense inflammatory reaction that leads to the destruction of epithelium and breakdown of the intestinal barrier. However, far less is known about how the bacterium survives within the hostile environment of the gastrointestinal (GI) tract; Shigella spp. must be extremely adept at this critical initial phase of pathogenesis as only 1–10 microorganisms given orally are sufficient to cause diarrhoea in healthy volunteers.

We have begun to investigate the factors that S. flexneri requires during colonisation of the GI tract. Through analysis of a library of transposon mutants, we have identified mutants of the bacterium that are unable to cause sustained infection of rabbit ileal loops, the most validated non-primate model of intestinal shigellosis. Several mutants that are defective in lipopolysaccharide (LPS) biogenesis were identified. We have shown that strains with marked truncation of their LPS structure are unable to withstand the bactericidal effects of an anti-microbial peptide, cecropin, or complement (which is secreted into the GI lumen during acute infection). Even mutants with minor changes in LPS, such as those which are unable to glycosylate the O antigen repeating subunit (gtr mutants), were also defective for colonisation; this effect is dependent upon the invasive capacity of the bacterium. Glycosylation and acetylation of the O antigen is the basis for the multiple serotypes of Shigella spp.

Expression of LPS is essential for survival in the GI tract and different serotypes of Shigella spp. may inherently different fitness for survival in the host.

P112
NOVEL NEISSERIA MENINGITIDIS FACTORS REQUIRED FOR SURVIVAL IN THE NASOPHARYNX AND ADHESION TO EPITHELIAL CELLS
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Neisseria meningitidis is the leading cause of bacterial meningitis in the UK, and an important cause of septic shock. The bacterium is present as a component of the normal flora of the upper respiratory tract of between 10–20% of healthy adults. The step of successful colonisation is a necessary step in the pathogenesis of infection, and for subsequent spread of the bacterium to susceptible individuals. Analysis of the interaction of the bacterium with isolated immortalised epithelial cells has identified a number of bacterial adhesions such as pili, and the opacity proteins Opa and Opc. However, during infection of the upper respiratory tract, the bacterium is also associated non-epithelial cells in the nasopharyngeal mucosa.

Therefore, to gain a full appreciation of the molecular mechanisms that the bacterium has evolved to successfully inhabit its niche in the host, we have examined the behaviour of N. meningitidis in human tissue explants. Nasal turbinates were infected with N. meningitidis and bacteria failing to penetrate through the epithelial layer were identified. We isolated mutants that were unable to successfully colonise the upper airway tissue, including two that do not express pili, a characterised adhesin for meningococcal interactions with epithelial cells. We also recovered colonisation defective mutants with insertions novel genes of unknown function. We have begun to analyse the function of these genes by expressing them as a recombinant proteins in E. coli, and determining whether the heterologous proteins mediate binding of E. coli to host cells.

Studying the interaction between pathogenic bacteria and host tissue should reveal further mechanisms underlying colonization and pathogenesis than using models relying solely on immortalised cells.

P113*
INFLUENCE OF STREPTOCOCCAL EXOTOXINS ON INTERNALIZATION BY EPITHELIAL CELLS
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Introduction: Internalization of Streptococcus pyogenes by human gingival epithelial and skin epithelial cells may contribute to its pathogenesis, especially recurrent throat infections.

Aim: To characterize the internalization process of an M89 clinical isolate and isogenic strains with mutations in the superantigen genes smeZ (streptococcal mitogenic exotoxin Z) and mfs (mitogenic factor)–additional isolates with mutations in speB, ska, slo, and slo were also used.

Methods: Internalization assays used human epithelial cell lines (A549 and SVK14) for an in vitro model in which extracellular bacteria were removed by washing or killed by antibiotics. The internalization mechanism was further investigated by using an actin cytoskeleton inhibitor and $\beta 1$ integrin subunit blocking antibodies. To measure cytotoxicity to epithelial cells, culture media was removed after infection and LDH measured by an enzymatic assay. For analysis of transcripts, bacterial RNA was extracted at desired growth phases, transferred to nitrocellulose, and probed with DIG labelled PCR products.

Results: The M89 strain exhibited inoculum dependent internalization. Internalization was dependent on actin cytoskeleton rearrangement and the $\beta 1$ integrin subunit. Interestingly, TNF$\beta$ and IL-1$\beta$ inhibited internalization. Loss of a functional smez gene increased the isolates internalization and also increased the LDH release by epithelial cells. The smez mutant had marked enhancement of slo transcription. Paradoxically, in an M49 strain, slo was associated with a decrease in internalization and an increase in cytotoxicity.

Conclusion: Contrary to published results, this data indicates that in some serotypes slo may not be a key factor in determining
internalization. Furthermore, other factors such as fibronectin binding proteins may be downregulated by smeZ or adjacent regulatory factors. This is a rigorous system for investigating GAS internalization in epithelial cells offering a platform with capacity for screening of a genome-wide mutant pool.

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abstract withdrawn

P115
HERD IMMUNITY FROM 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (7-PCV) IN THE UK
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Background: Recent evidence has documented the significant decline in adult invasive pneumococcal disease (IPD) in the US in parallel with the increasing use of 7-PCV in infants and young children, presumably due to herd immunity.1 Rates in adults 20–39 years, 40–64 years and 65+ years fell 32%, 8% and 18% respectively, from 1998/99 to 2000/01. We have recently published the first UK pharmacoeconomic (PE) analysis of the prevention of paediatric pneumococcal infection in the UK.2

Objectives: To apply the US observed decline in disease to both IPD and pneumococcal pneumonia in the UK, to calculate the number of cases and deaths indirectly preventable and to re-analyse the cost per life year gained (CLYG) accordingly.

Methods: Hospital Episode Statistics and Office for National Statistics 1999 data were used for calculating adult cases and deaths respectively. The proportions of adult 'unspecified' meningitis, septicaemia and pneumonia attributable to pneumococcal infection were, respectively, 56%, 1.1% and 32%. Infants and young children (but not adults) would be vaccinated according to the SmPC for their age group.

Results: For the age groups 20–39/40–64/65+ years, for pneumococcal meningitis, septicaemia and pneumonia, there are estimated to be 177/251/162, 52/156/306 and 17466/44201/39797 cases and 8/28/31, 4/11/25 and 81/671/10090 deaths respectively, reducible by 32%/8%/18%. Using either a 6% all-cause pneumonia efficacy or a 20.5% pneumococcal pneumonia efficacy, an IPD efficacy of 97.4% and a paediatric otitis media efficacy of 7%, the CLYG is £2500.

Conclusions: Universal paediatric use of 7-PCV in the UK would prevent 1957 deaths at a CLYG of £2500. This is highly cost effective.
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P116
BARRIERS TO INFLUENZA IMMUNISATION IN OLDER PEOPLE
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Influenza in older people is a major cause of hospitalisation and mortality during winter months. In spite of studies which show that influenza is both safe and effective, vaccine uptake in older people still remains sub-optimal. This study aims to examine why older people often miss out on the jab.

A qualitative study using in-depth interviewing with approximately 50 people aged 65 years and over was carried out in South Wales. The sample consisted of those people who regularly have the jab, those who refuse to have the jab, those who have stopped having the jab and those who have had the jab for the first time in 2001/02.

Initial analysis identified three main themes. Firstly, the majority of those people interviewed did not feel at risk from flu. Secondly, potential and actual side effects of the flu jab were reasons for many patients either refusing to have a flu jab or deciding not to have it again. Thirdly, a tentative association was found between the level of patient contact with health professionals and their decision to have the jab.

Clear communication of the risks of flu, particularly to healthy older people, may be an important determinant of flu vaccine uptake. Health professionals can promote immunisation both by personalising the risk of catching flu and by tackling misconceptions about side effects.