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Abstracts of the Eleventh Conference of the Federation of Infection Societies, 2004

*These authors have been awarded a Young Investigator Award
INVITED SPEAKERS' ABSTRACTS

S02 WHAT'S NEW RESPIRATORY VIROLOGY

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The last 5 years has seen an explosion in this field. New pathogens have been discovered, new diagnostic tests have been introduced, new vaccines are being trialed and antiviral drugs have been showing some success. The human metapneumovirus was initially thought to be as important as RSV but it is now thought to be not as common as RSV and that disease is milder. A recent observation indicates that HuMPV is usually only severe as part of a mixed infection. It is unusual in adults, though can cause outbreaks in the elderly. Coronavirus has hit the headlines in the form of SARS, but another example, NL63, was described this year. It is too early to tell if it is important, but it does account for a small proportion of previously undiagnosed respiratory tract infections. More information is becoming available on rhinoviruses; not only are they the commonest precipitating factor for asthma, but they are also found in exacerbations of COPD and are increasingly recognised as a significant cause of pneumonia. This includes the immunosuppressed. Influenza continually hits the headlines; South East Asia has had an epidemic of avian influenza which hopefully will not set up transmission chains in humans. Point mutation in influenza viruses have now been strongly associated with increased virulence in humans. On the diagnostic front, nucleic acid testing is becoming predominant and many laboratories expect to have stopped culturing respiratory viruses within 2-3 years. Nucleic acid testing is more rapid, significantly more sensitive and allows a greater number of pathogens to be detected than either culture or direct fluorescence. A full respiratory screen, including staff costs, is approximately 9 euros. Cidofovir is showing efficacy in adenovirus infections in the immunocompromised, although reducing immunosuppression is probably more efficacious. A new monoclonal antibody against RSV has its place. Vaccines are in trials for RSV and parainfluenza 3.

S04 CHANGING FACE OF EXTENDED-SPECTRUM β-LACTAMASES

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Until recently, extended-spectrum β-lactamases have largely comprised mutant TEM and SHV enzymes from nosocomial pathogens, principally Klebsiella spp. This pattern is now changing, with the rapid dissemination of CTX-M enzymes, a group of ESBLs previously prevalent only in South America. CTX-M ESBLs evolved via the escape of chromosomal β-lactamase genes from Kluyvera spp. to mobile DNA. Over 35 variants are known, split into 4 or 5 clusters. Different variants are proliferating in different parts of the world: CTX-M-2 in Argentina and Israel; CTX-M-9 in Spain, CTX-M-14 in China and CTX-M-15 in Europe. Despite this geographic variation, the consistent pattern is for Escherichia coli to be the main host and for CTX-M enzymes to occur in community as well as nosocomial isolates. Most producers are from urinary infections, but some are from bacteraemias. Prior to 2000, CTX-M producers were unrecorded from the UK but, in the past 18 months, ARARL has received over 500 referred E. coli isolates with CTX-M enzymes from over 75 UK labs. These represent only a fraction of all producers: one Trust alone has had > 350 infections due to producers. Most referred isolates have CTX-M-15 β-lactamase but a few have CTX-M-9 or other types. About 33% belong to one major strain (designated A) and a further 33% to four other strains, with all these five being of serotype 025 and maybe having a common ancestor; the remaining producers are clonally diverse. About 25% of producers are from GP patients, many of them elderly, with underlying disease and recent hospital contact. All are multi-resistant, with consistent susceptibility only to carbapenems, nitrofurantoin and fosfomycin; strain A is also susceptible to gentamicin. The spread of CTX-M enzymes has forced re-thinking of ESBL detection methods. Cefotaxime resistance -previously advocated a single indicator of likely ESBL producers- is inconsistent among CTX-M producers and it is additionally necessary to test cefotaxim. Alternatively, isolates may be screened for cefodaxime resistance. Isolates resistant to any of these cephalosporins should then have confirmatory tests performed, seeking synergy between the indicator cephalosporin and clavulanic acid. The spread of CTX-M enzymes into community E. coli means that isolates from GP samples also need screening by these methods, not just nosocomial isolates.

S05 FIVE RECENT RANDOMISED CONTROLLED TRIALS THAT HAVE CHANGED THE WAY WE MANAGE SEVERE SEPSIS

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The Surviving Sepsis Campaign represents an international collaboration of 13 critical care, infectious disease and nursing organisations. The aim of the campaign is to increase awareness and improve outcome in severe sepsis. Earlier this year, more than 50 aspects of the management of the septic patient were reviewed with the aim of providing practical guidelines. This presentation focuses on five of the guidelines that have been shown in randomised controlled trials to reduce mortality.

1. Early Goal Directed Therapy (EGDT): Earlier work showed that supra-normal haemodynamic and oxygen delivery goals applied late in the septic process had no impact on survival. Rivers and colleagues used 'normal' goals, applied for 6 h from admission to hospital. Patients with septic shock were randomised to receive either standard resuscitation end points (CVP 8-12 mmHg and MAP >65 mmHg) or standard end points in addition to the target of a mixed venous oxygen saturation of >70%. This was achieved using dobutamine + / – transfusion. The in-hospital mortality was 30.5% in the EGDT group and 46.5% in the control group.

2. Activated Protein C: The PROWESS trial was stopped after interim analysis because of the survival advantage demonstrated for drotrecogin alfa (activated). Twenty-eight day mortality was 24.7% in the group allocated to receive drotrecogin and 30.8% in the control group.

3. Ventilation with Low Tidal Volumes: The ARDS Network Trial was also stopped early as it demonstrated a lower mortality rate in those patients ventilated with tidal volumes of 6 ml/kg, compared against a more traditional 12 ml/kg (31% vs. 39.8%). Over-stretch of relatively normal alveoli is known to cause release of inflammatory cytokines and a perpetuation of the lung injury process.

4. Moderate Dose Corticosteroids: Although high doses of corticosteroids are known to increase mortality, this multi-centre RCT showed that synacthen non-responsive patients with septic shock fared better with low dose steroids compared against placebo.

5. Tight Control of Blood Sugar: This study showed a nearly 4
old. Prompt diagnosis and treatment remains the greatest influence physicians can have on the outcome of this disease and still depends on the application of simple and widely available clinical and laboratory techniques. There is now compelling evidence that adjunctive dexamethasone improves survival from tuberculous meningitis and should be given to all adults regardless of disease severity. The best treatment of HIV associated, and drug resistant tuberculous meningitis remains uncertain and studies that assess the impact and optimal timing of second-line anti-tuberculosis drugs and anti-retroviral treatment are urgently required.

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1. Thwaites GE, Chau TT, et al. Diagnosis of adult tuberculous meningitis by use of clinical and laboratory features. Lancet 2002;360(9342):1287-92.
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S06
THE 2004 BARNETT CHRISTIE LECTURE
TUBERCULOUS MENINGITIS: NEW CHALLENGES, OLD SOLUTIONS
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The diagnosis and management of tuberculous meningitis challenges physicians worldwide. It is the severest form of infection with Mycobacterium tuberculosis, causing death or severe neurological deficit in more than half affected despite treatment with anti-tuberculosis chemotherapy; but diagnostic methods have improved little since Robert Koch first stained the bacilli in 1882 and treatment has not advanced since the introduction of Mycobacterium tuberculosis to anti-tuberculosis drugs and the impact of co-infection with human immunodeficiency virus (HIV). Although older methods of diagnosis and treatment still have an important role to play in meeting these challenges, novel solutions are urgently required.

Early diagnosis and treatment has the greatest impact on outcome from tuberculous meningitis but the best diagnostic method remains uncertain. The role of clinical diagnostic algorithms,1 conventional bacteriology,2 and molecular techniques3 will be discussed, as will the impact of HIV infection and mycobacterial drug resistance on the performance of these methods (unpublished data).

Adjunctive corticosteroids have long been suggested for the treatment of tuberculous meningitis but evidence they improve outcome has been difficult to obtain and there are no data from HIV infected individuals. We recently conducted a double blind, placebo controlled trial to determine whether adjunctive dexamethasone improves survival from tuberculous meningitis, with or without HIV infection.4 The results suggest dexamethasone improves survival from tuberculous meningitis but does not prevent severe disability. The influence of HIV infection and mycobacterial drug resistance on clinical presentation, response to treatment, and outcome will be examined.

How dexamethasone improves survival is unclear and data will be presented from parallel studies that assessed serial cerebrospinal fluid and peripheral blood inflammatory response in adults with tuberculous meningitis randomised to dexamethasone or placebo.

In conclusion, mycobacterial drug resistance and HIV infection have set new challenges in the diagnosis and management of tuberculous meningitis but many of the available solutions are still dependent on the application of simple and widely available clinical and laboratory techniques. There is now compelling evidence that adjunctive dexamethasone improves survival from tuberculous meningitis and should be given to all adults regardless of disease severity. The best treatment of HIV associated, and drug resistant tuberculous meningitis remains uncertain and studies that assess the impact and optimal timing of second-line anti-tuberculosis drugs and anti-retroviral treatment are urgently required.

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1. Thwaites GE, Chau TT, et al. Diagnosis of adult tuberculous meningitis by use of clinical and laboratory features. Lancet 2002;360(9342):1287-92.
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S07
THE 2004 LOWBURY LECTURE
THE WESTERN AUSTRALIAN EXPERIENCE WITH VANCOMYCIN-RESISTANT ENTEROCOCCI—FROM DISASTER TO ONGOING CONTROL
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In July 2001, a patient in the Intensive Care Unit (ICU) developed bacteraemia caused by vancomycin-resistant Enterococcus faecium (VREF) vanB (vancomycin MIC > 256 mg/L, teicoplanin MIC 1.0 mg/L). The index patient, who had been receiving haemodialysis at RPH as an outpatient, was isolated with strict contact precautions. Screening of patients in the Dialysis Unit, Nephrology Ward & ICU approximately weekly over the next month revealed more and more carriers. Pulsed-field gel electrophoresis and plasmid analysis of the isolates demonstrated a single-strain. Despite the isolation of carriers, the VREF spread rapidly. By late September the epidemic strain had spread to 22 wards and one outpatient unit (Satellite Dialysis). 4 patients were infected and 64 were colonized. A Hospital VRE Executive Group, which included the Chief Executive and Directors of Clinical Services and Nursing, was formed to manage the outbreak directly with daily meetings. Control was handicapped by the slowness of conventional laboratory methods which took 4-5 days to identify VRE and allowed nosocomial transmission to occur before carriers were identified. A laboratory procedure to make rapid provisional identification of VREF was developed. Each rectal swab was incubated in selective enrichment broth for at least 24 h. Multiplex PCR for the vanA & vanB genes was performed directly on positive broth cultures, using novel hybridization probes which were developed to improve the specificity & sensitivity of the assay.

On average 4 rectal swabs, each collected on separate days, were needed to detect >90% of the 172 VREF carriers who were epidemiologically linked to the outbreak. Enhanced infection
control practices were used to eradicate the single-strain outbreak:
1. Cohorting of all positive & ward contact patients in separate wards with dedicated nursing staff for each cohort.
2. All inpatients (ward contacts & no known exposure) were screened during a 1-week period to identify the total reservoir of VREF carriage. 39 previously unknown carriers were found.
3. Establishment of a dedicated VRE ward cleaning service for the duration of the outbreak.
4. Environmental cultures to establish that terminal cleaning was adequate.
5. Electronic flagging of medical records of ward contacts.

During the 6-month period, July-December 2001, 118 patient carriers were detected by screening in hospital. The electronic flagging of ward contacts enabled those who had not been screened at least 4 times before discharge to be followed-up and screened. From 28 September 2001 to 30 April 2002, a total of 1,977 ward contacts were screened after discharge from hospital and 542 (2.73%) were found to be carrying VREF. The electronic labelling and active follow-up of ward contacts resulted in a significant number of carriers being detected who otherwise posed a risk of initiating further outbreaks in hospital if they were readmitted.

Ongoing control has been facilitated by targeted active surveillance cultures:
- admission to high-risk units (ICU, Burns, Nephrology, Haematology, Bone Marrow Transplant Unit)
- on transfer out of ICU
- monthly screening of patients regularly attending displays units
- opportunistic laboratory screening of inpatient faecal specimens submitted for Clostridium difficile culture

508 UNDERSTANDING HOW LISTERIA MONOCYTOGENES TARGET AND CROSS HOST BARRIERS

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Listeria monocytogenes is a foodborne pathogen responsible for listeriosis, a human infection with an overall 30% mortality rate, characterized by severe gastroenteritis, fetoplacental and central nervous system infections. This microorganism has the ability to cross three tight barriers in humans, the intestinal, the blood-brain and the fetoplacental barriers. During infection, it enters, survives and multiplies in phagocytic and non-phagocytic cells. It also spreads directly from cell to cell. These features are considered central for listeriosis pathophysiology.

The infectious process has been extensively studied in tissue-cultured cells. The series of events that occur after the initial bacterial cell contact include formation of a phagocytic vacuole, lysis of this vacuole within 30 min, intracytosolic replication, actin-based intracellular movement and cell-to-cell spreading.

L. monocytogenes entry into human epithelial cells is triggered by the interaction of a bacterial surface protein called internalin, with its host receptor, E-cadherin, a transmembrane protein critical for the formation and maintenance of adherent junctions in epithelial tissues. Internalin-E-cadherin interaction is species-specific and mouse E-cadherin, in contrast to human E-cadherin, is not a receptor for internalin. This species-specificity relies on the nature of E-cadherin 16th amino acid, which is a proline in humans and a glutamic acid in mice: replacement of this glutamic acid into a proline leads to a gain of function, establishing the critical role of this residue in E-cadherin-

L. monocytogenes strains isolated from pregnancy-related cases expressed a full-length functional internalin, as compared to only 65% of strains isolated from food products, a result in favor of a critical role for internalin in the targeting and crossing of the human maternofetal barrier. Examination of immunohistochemically labeled placental and amniotic tissue samples obtained from women with pregnancy-associated listeriosis raised the possibility that L. monocytogenes crosses the maternofetal barrier through the villous syncytiotrophoblast. Investigation of the cellular patterns of expression of its receptor E-cadherin at the maternofetal interface demonstrated that E-cadherin is expressed on the basal and apical plasma membranes of syncytiotrophoblasts. Quantitative assays of cellular invasion in trophoblastic cell lines, primary trophoblast cultures, and placental villous explants demonstrated that bacterial entry into syncytiotrophoblasts occurs via the apical membrane in an internalin-E-cadherin dependent thermal. In human placental villous explants, bacterial invasion of the syncytiotrophoblast barrier and underlying villous tissue and subsequent replication produces histopathological lesions that mimic those seen in placentas of women with listeriosis. Thus, the internalin-E-cadherin interaction that plays a key role in the crossing of the intestinal barrier is also exploited by L. monocytogenes to target and cross the human placental barrier. Current studies focus on the molecular mechanisms of L. monocytogenes crossing of the blood-brain barrier.
MOLECULAR EPIDEMIOLOGY OF TB

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The recently published Action Plan from the Chief Medical Officer, Stopping Tuberculosis in England, sets out the steps which government, the health services and local communities need to take to reverse the rise in TB. The plan includes the development and implementation of protocols for the public health use of laboratory techniques such as DNA fingerprinting of all *Mycobacterium tuberculosis* isolates, and the establishment of a central database linking fingerprinting and epidemiological data. A central system that enables early detection of outbreaks and rapidly eliminates cases from an outbreak cohort will facilitate appropriate focusing of contact tracing efforts and thus limit the spread of infection.

Application of molecular microbiological methods has improved the understanding of population structures and dynamic spread of a number of infectious agents. Some methods also allow genetic comparison of strains, facilitating the identification of the genetic basis of medically relevant microbiological traits. *M. tuberculosis* is an example of a bacterial species for which several well-standardized, powerful methods of epidemiologic characterization have been developed. Some countries have carried out longitudinal epidemiologic surveillance, allowing databases to be exchanged and compared. The techniques used most widely are IS 6110 Restriction Fragment Length Polymorphism (RFLP) and Spoligotyping and have been used successfully to investigate strains from patients with epidemiological lift and to provide information on the population genetics of *M. tuberculosis* locally and globally. Neither of these techniques is ideal for rapid, high volume, discriminatory analysis of recently isolated strains of *M. tuberculosis*, nor do they allow direct application of typing information to inform investigation and contact tracing of new cases. These characteristics are required to allow unsuspected clusters to be identified and the extent of clusters to be mapped, with the prospect of improving disease control and prevention. Rapid typing, made available during case management and treatment, will also improve the opportunities to recognize microbiological and clinical traits associated with particular typing profiles.

The Health Protection Agency has developed a National Typing Strategy for TB, and has selected the method Variable Number Tandem Repeat typing. Using 5 Exactly Tandem Repeat (ETR) loci and 12 Mycobacterial Interspersed Repetitive Unit (MIRU) loci to produce a 17 digit profile for each strain, a prospective typing service has been implemented across the Midlands from July 2003. Typing results have been reported directly to TB nurses, health protection teams and local laboratories. Typing information has focused contact tracing, and has assisted with infection control and in the management of difficult patients. TB teams have swiftly realised the benefits of the typing strategy, and have been able to limit or cancel extensive contact tracing exercises when typing has distinguished apparently clustered strains. The typing service is rolling out from Regional Centres for Mycobacteriology to the rest of England, and a national database is underdevelopment. It is anticipated that wider availability of the service will enhance the contribution to TB prevention and control.

IMMUNISATION AGAINST MENINGOCOCCAL DISEASE

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Meningococcal disease remains an important cause of morbidity and mortality worldwide. Despite decades of intensive research, *Neisseria meningitidis* which can cause both septicaemia and meningitis remains incompletely controlled by vaccination. The development of vaccines has been complicated by a number of factors of the biology of the meningococcus, including its high degree of antigenic diversity and the fact that the organism is naturally a commensal, which commonly infects humans without causing disease. Plain polysaccharide vaccines have been developed against four of the five main capsular polysaccharide types, namely A, C, Y and W-135 that commonly cause disease. But vaccines against serogroup B meningococci have proved elusive due to poor immunogenicity and concerns about cross-reactivity with human antigens. The plain polysaccharide vaccines against A, C, Y and W-135 are effective in adults and have proved to be useful in containing large-scale epidemics in, for example, Africa. However, they are ineffective in infants and do not provide long-term immunity. The development of polysaccharide conjugate vaccines has resolved many of these issues for these four serogroups as evidenced by the successful introduction of the serogroup C conjugate polysaccharide vaccine into the UK and other European countries since 1999. This vaccine has proved to be highly effective across age groups and also to induce herd immunity protecting the population at large. Efforts on developing vaccines that are comprehensive against all meningococci have concentrated on the subcapsular antigens, particularly the porin proteins. These proteins are, however, highly variable and such sub capsular antigens tend to be specific to the particular strain against which they are produced. However, molecular epidemiological studies are beginning to reveal a high degree of structuring in the antigenic variability. This structure provides clues to possible ways forwards in the development of a comprehensive meningococcal vaccine.

NATIONAL SEXUAL HEALTH AND HIV STRATEGY: UPDATE ON STIS

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The National Sexual Health and HIV strategy was published in 2001 in response to the rising incidence of teenage pregnancy and escalating rates for sexually transmitted diseases in England. Although limited additional central funding was provided, demand for specialist services has continued to increase and has far outstripped the capacity of GUM clinics. Despite record numbers of new patients being seen, the waiting times for routine appointments at many GUM clinics have become unacceptably long. Unsurprisingly, STI rates have continued to rise. Moreover, antimicrobial resistance has increased in gonorrhoea necessitating a major change to national treatment guidelines. Syphilis has re-emerged as a significant health problem in marry urban areas especially in homosexual men. Misguided advice about the safer sexual practises may have contributed to the high frequency of orogenital sexual transmission and the increasing association of syphilis and HIV infection.
The national strategy envisaged an increased role for additional providers of sexual health care, especially in general practice. Although the contribution of primary care to STI diagnosis and management has so far been limited during ongoing discussions over the new GMS contract, it is set to increase as a result of the roll-out of the national chlamydia screening programmes. This now covers 25% of England and there should be complete national coverage by 2008. Thus programme should act as a major stimulus to STI provision in primary care, will promote the replacement of less sensitive assays by nucleic acid amplification tests, and lead to increasing requests for STI and HIV diagnostic tests in microbiology laboratories. Other sources of laboratory requests may emerge. The voluntary care organisations are wishing to develop a role in testing hard-to-reach populations in non-clinical settings. New Point-of-Care tests may also permit a new self-care market and increased demands for test validation as well as training non-laboratory staff in their use.

The impending White Paper on Public Health is expected to give a raised priority for STI diagnosis and management, with the possibility of additional resources. Inevitably this will have a major impact on STI diagnostic services that will inevitably increase for the foreseeable future.

**S15 MALARIA PROPHYLAXIS: CONTINUITY AND CHANGE**

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In the last 2 years the pattern of chemoprophylaxis for malaria has stabilized. Most of the falciparum malaria in the world is now resistant to chloroquine, and this is true for most of Africa, which is the main source of imported malaria cases and fatalities in the UK. The options are now atovaquone/proguanil or mefloquine or clorocycline, except for most of the Indian Subcontinent, where the traditional proguanil plus chloroquine continues to give good protection. Changes in detailed use will be discussed, along with likely new prophylactic agents, but none are imminently available.

Attention can therefore be directed towards the most crucial problems in prophylaxis, which are about compliance; about use, rather than choice, of prophylactic measures. Epidemiological data can assist this. The evidence points to very high risk groups. People of African descent in London have a 74-fold elevated risk of contracting falciparum malaria and bear most of the burden of imported malaria in London; by contrast the case fatality rate is higher in the white population where it is heavily age dependent. Cases are highly geographically aggregated, and this can be used in targeting high risk groups. In London also, local public health groups are emerging with a focus on prevention and on increased use of protective measures. Progress has been made in paediatric preventive measures while there is a need to develop further the detail of both epidemiological and clinical surveillance, the analysis of cryptic malaria cases, and the ways in which migration is recorded and thought about. Malaria can be used as a model in developing ways to study imported diseases.
HOW TO INVESTIGATE AN INFECTIOUS DISEASE IN DIFFICULT CIRCUMSTANCES

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Outbreak investigations are an important and challenging component of public health. They serve to identify the source or means of spread of the disease and, if action is taken promptly, prevent additional cases. Even when an outbreak is over, thorough investigation can provide information that will help prevent future outbreaks.

A variety of circumstances can pose difficulties in outbreak investigation. Some have to do with the disease itself such as ease of diagnosis and treatment, severity of symptoms, and degree of infectivity. Others have to do with the setting. Infections may be difficult both to investigate and control if they are widely spread or in remote areas. Infections in closed communities like hospitals, nursing homes, cruise ships, military facilities, or prisons pose specific problems. More recently, the prospect of bioterrorism has added a new dimension to any investigation of an unusual incident. Most difficult of all are incidents that face vested economic or political interests, or which occur in unstable political contexts such as during war or humanitarian crisis.

We could characterise the epidemiologist’s nightmare as:

- a new disease
- whose aetiology and mode of transmission is unknown
- which has a substantial fatality rate
- but no diagnostic test, treatment or vaccine
- which has already spread rapidly in the population
- and is generating public panic, media interest, and political repercussions.

Just a little bit like SARS in fact ...

The response should always be to follow the basic principles of good outbreak investigation. The first stage is to verify the facts, to confirm the existence of an outbreak and to develop a case definition. The second stage is to gather as much information as possible about the incident including searching for undiagnosed cases, interviewing cases and analysing data by time, place and person, as well as incorporating information obtained from microbiological and environmental investigations. It is important to be clear about the purpose of the investigation, to focus on generating hypotheses about the cause of the outbreak, and to keep an open mind during these early stages. The third stage is to test hypotheses by carrying out a cohort or case-control study, to seek to draw firm conclusions from all the information gathered and to take action accordingly.

At all stages it is important to keep a log of events and key decisions, to coordinate the response through an incident team, to ensure good communication with colleagues, public, press and others, and to implement control measures as promptly as possible. Finally, a report should be written that crystallises the findings of the investigation, makes appropriate recommendations, and highlights lessons learned.

ASSESSING ENVIRONMENTAL CLEANLINESS

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A link between visible cleanliness and healthcare acquired infection has been firmly established, both politically and in the mind of the press and public, although the scientific evidence is more contentious (e.g. "A Matron’s Charter: An Action Plan for Cleaner Hospitals"). To what extent could/should Infection Control Practitioners, and others, be setting standards for environmental cleanliness?

If we should, how do we set standards, what assessment levels should be employed and of what value are the results? Is there a role/need for microbiological monitoring? Are chemical indicators that provide "instant results," more of less useful? Should we be auditing practice rather than outcomes?

I will be debating these issues in open forum with Professor Chris Griffiths of the University, of Wales Institute, Cardiff, who has been applying techniques used in the food industry to the healthcare environment.

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CLINICAL EXPERIENCE OF NASOGASTRIC TUBE ADMINISTERED FECAL TRANSPLANT FOR THE TREATMENT OF RECURRENT CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHEA

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Recolonisation of the large intestine with "normal" flora is an attractive therapeutic intervention in the treatment of clostridium difficile associated diarrhoea (CDAD) as it breaks the cycle of recurrent antibiotic administration. Recently the use of donor stool administered via a naso-gastric tube has been described as a treatment for recurrent CDAD. We describe our experiences in using this technique in six patients with recurrent CDAD.

All patients presenting to the Gartnavel Centre over a 1 year period (August 2003-August 2004) with recurrent CDAD were offered treatment with faecal transplant. Recurrent CDAD was defined as recurrence of diarrhoea, in the presence of C. difficile toxin assay positivity. This assumed initial resolution of symptoms following an appropriate course of anti clostridial treatment. Six patients had stool transplant with faeces donated by screened relatives.

Of the six patients treated, three had cure of their CDAD at follow up (41 to 12 weeks). One patient remains symptom free and awaits stool toxin assay at 3 month follow up. One patient remained C. difficile toxin positive and continued with diarrhoea following transplant. This patient did however respond to a further course of metronidazole and remained symptom free and C. difficile toxin negative at 3 months follow up. The final patient initially responded to stool transplant (no diarrhoea and toxin negative). However, she had a further episode of CDAD when subsequently treated with a course of broad spectrum antibiotics. In the cases of two patients, the relative initially screened was found to be positive for C. difficile toxin and other donors had to be identified.

Stool transplant is an effective therapy for recurrent CDAD. It is inexpensive and in our experience, not associated with any adverse effects. Patient acceptance of this treatment option was universally high despite the obvious aesthetic problems. Screening of stool donors is the most time consuming part of treatment. The identification of asymptomatic relatives with stool carriage of C. difficile is a recognised finding and underlines the need for appropriate screening of potential stool donors.

LIFE IN THE FREEZER: AN UNUSUAL ENVIRONMENTAL SOURCE OF ENTEROBACTER STERNAL WOUND INFECTION

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An outbreak of postoperative sternal wound infection is described. A rise in serious wound infections leading to dehiscence and rewiring was noted by a cardiac surgeon. The infections were predominantly with Enterobacter cloacae, and were confined to one surgical team. The principal surgeon of this team also operated in another hospital, with no recently infected patients.

**METHODS:** The outbreak was investigated by: (1) typing of the isolates by molecular and serological methods, (2) observations of surgical and anaesthetic practice, (3) Screening of the theatre environment for Enterobacter. Swabs were inoculated onto Chrom agar**, a medium generally used for the culture of urine samples, on which Enterobacter produces distinctive blue colonies.

**RESULTS:** Typing of the clinical isolates showed them to be indistinguishable from each other, and different from other isolates obtained from the same hospital. Observation of surgical practice revealed nothing untoward, and there appeared to be no significant difference between the modes of operation of the different surgical teams. Environmental screening yielded several Enterobacter isolates, but these proved to be different from the clinical isolates, except one isolate from cardiac bypass cooling water. However, this water was contained in a sealed system, and the machine was used by all surgical teams, and some of the cases had not been exposed to this particular bypass machine. Further questioning revealed one significant difference between the different surgical teams—the team with the infected patients used semi-frozen sterile Hartmann’s solution to achieve cardioplegia. This ice-slush is instilled directly into the chest cavity during surgery. The freezer used for this was swabbed, and all swabs (including swabs from the outside of the Hartmann’s bags) yielded Enterobacter cloacae, indistinguishable from the clinical isolates.

**CONCLUSIONS:** The most plausible explanation is that the freezer was recently contaminated by Enterobacter, and the bacteria then contaminated the ice-slush solution while it was being decanted, thus infecting the patients. There have been no more cases since the freezer was replaced, a rigorous cleaning schedule instituted, and steps taken to reduce the possibility of carry-over of any contaminating organisms.

**O04**

**HOSPITAL COST OF INVASIVE PNEUMOCOCCAL DISEASE IN ADULTS AND POTENTIAL FOR PREVENTION BY VACCINATION IN THE UNITED KINGDOM**

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**BACKGROUND:** Invasive pneumococcal disease (IPD) is associated with a high mortality despite antimicrobial therapy, but may be preventable by pneumococcal vaccination. A study was undertaken to establish the extent of previous exposure to pneumococcal capsular polysaccharide vaccination and economic impact of IPD in hospitalised adults.

**METHOD:** Adults with IPD admitted to either of two teaching hospitals during 1992-2000 were retrospectively identified. Receipt of pneumococcal vaccination, risk factors for IPD, death, disability and cost of treatment were determined.

**RESULTS:** 593 patients were hospitalised with IPD and 187/230 patient records from one site were reviewed. According to UK pneumococcal vaccination guidelines 58% of patients should have received the vaccine and 74% of patients if updated guidelines, which include age >65 years as an indication, are applied. In patients with known risk factors, excluding age, only 9% had been vaccinated. The modality from IPD was 21% and an additional 6% suffered major complications. The total cost of IPD was £2 511 809. Implementation of the updated vaccination policy, assuming a 30-70% efficacy, 6-year duration of effect and 90% uptake would have saved £347 846-811 641 in hospital costs at an expense of £732 117-819 577 in vaccine costs to the community.

**CONCLUSIONS:** In patients hospitalised with IPD there is a high rate of pre-existing risk factors and a low rate of administration of pneumococcal vaccination. IPD incurs significant mortality,
morbidity and economic cost and there is potential for reducing this by improved uptake of pneumococcal vaccination.

**005**

**PNEUMOCOCCAL SURFACE PROTEIN A AND PNEUMOLYSIN ACT IN SYNERGY TO PREVENT COMPLEMENT ACTIVATION BY STREPTOCOCCUS PNEUMONIAE**

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The Streptococcus pneumoniae surface protein A (PspA) and cytotoxin pneumolysin (Ply) may affect virulence by preventing complement activity. We studied the interaction of these proteins and the complement system using mice with specific deficiencies in complement components and mutant strains of bacteria deficient in PspA and/or Ply. C3 deposition on *S. pneumoniae* strains was investigated by flow cytometry. Compared to the wild-type strain, C3 deposition on the ply strain was increased in serum from wild type (WT) mice but not in C1q serum, indicating that Ply prevents classical pathway activity. In contrast, C3 deposition was increased on the pspA mutant strain in C1q serum suggesting that PspA interferes with the alternative pathway. Loss of pspA and ply was strongly synergistic, with a large increase in C3 deposition on the pspA/ply mutant strain in WT serum. We also analysed using mixed infections and wild-type or complement deficient mice whether PspA, and Ply prevent complement activity in vivo. Both pspA and ply strains were attenuated in virulence compared to the wild-type strain in WT mice, the pspA strain to a greater degree (CI = 0.025) than the ply strain (CI = 0.21). In mice deficient of all complement activity (C3−/−), the relative virulence to C39 of both the pspA− and ppsA−/ply− strains improved (CI 0.15 and 0.60 respectively), demonstrating that loss of virulence in these mutant strains is at least partially dependent on complement activity. When compared to the ply− strain the virulence of the double pspA− ply− mutant strain in WT mice was dramatically reduced (CI 0.005), but restored in C3−/− mice (CI 1.08), confirming the synergistic protective effect of Ply and PspA against complement activity in vivo. The site and timing of complement-mediated immunity during pneumonia was analysed using mixed infections comparing the pspA− ply− strain to the ply− strain in WT and C3−/− mice. Although there was some role for complement-dependent immunity at early time points within the lung, the major effect of complement was to prevent spread of *S. pneumoniae* from the lungs to the blood. Preventing the inhibition of complement-dependent immunity by *S. pneumoniae* or other primary bacterial pathogens could be a potential novel therapy for patients with septicaemia.

**006**

**DOES DETECTION OF VIRULENCE-ASSOCIATED GENES DISCRIMINATE BETWEEN INVASIVE AND COMMENSAAL STAPHYLOCOCCUS EPIDERMIDIS STRAINS ON A BONE MARROW TRANSPLANT UNIT**

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Due to their biofilm forming capacity invasive Staphylococcus epidermidis, causing the majority of nosocomial catheter-related blood stream infections (BSI), are thought to be selected at time of catheter insertion from a population of less virulent commensal strains, predicting that invasive and contaminating strains can be differentiated via detection of virulence associated genes. However, hospital environment may pave the way for catheter-related infections by promoting a shift in the commensal bacterial population towards strains with enhanced virulence. The distribution of virulence-associated genes (icaADBC, aap, atLE, bhp, fbe embp, mecA, IS256, IS257), polysaccharide intercellular adhesin (PIA) synthesis and biofilm formation was investigated in *S. epidermidis* strains from independent episodes of catheter related BSI in bone marrow transplant recipients. Results were compared with those obtained for commensal *S. epidermidis* from hospitalized patients after BMT and from healthy individuals, respectively. Clonal relation of strains was investigated by pulsed-field gel electrophoresis. IcaADBC (94% vs. 13%), mecA (88% vs. 7%), and IS256 (94% vs. 0%) were significantly more prevalent in BSI isolates than in commensal isolates from healthy individuals. However, in clonally independent, endogenous commensal strains from BMT patients the prevalence of any of the genes did not differ from invasive BSI strains. IcaADBC and meticillin resistance, factors important for establishment of catheter-related infections, already ensure survival in their physiological habitat in the hospital environment, resulting in a higher contamination probability of indwelling medical devices with virulent *S. epidermidis* strains. The dynamics of *S. epidermidis* populations reveal that detection of icaADBC and mecA is not suitable for discriminating invasive from contaminating *S. epidermidis* strains.

**007**

**THE NRAMP ORTHOLOGUE OF CRYPTOCOCCUS NEOFORMANS IS A PH-DEPENDENT TRANSPORTER OF MANGANESE, IRON, COBALT AND NICKEL**

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**BACKGROUND AND OBJECTIVES:** Cryptococcus neoformans is a facultative intracellular pathogen and one of the most important causes of opportunistic infection in immunocompromised individuals. Metal ion flux may be of critical significance in the physiology of intracellular pathogens but little is known about metal ion transport in this organism. *C. neoformans* encodes a single member of the Natural Resistance Associated Macrophage Protein (NRAMP) family of divalent transporters (CRAMP), which we sought to functionally characterise.

**METHODS:** We cloned CRAMP from *C. neoformans* cRNA, expressed it in *Xenopus laevis* cocytes and sf21 insect cells, and measured CRAMP-mediated uptake of divalent cation radio-nucleides. Transport kinetics were determined by non-linear regression modelling.

**RESULTS:** We found that CRAMP induces saturable transport of a broad range of divalent transition series cations, including Fe2+, Mn2+, Co2+ and Ni2+. Mn2+ transport is inhibited by Cd2+ and Cu2+ indicating that the substrate specificity of CRAMP may also encompass these cations. CRAMP exhibited the highest affinity for Mn2+ with a K_m of ~24 µM. Neither Zn2+ nor Pb2+ competed with Mn2+. Maximal cation transport occurs at pH 5.5-6.0, consistent with the proton gradient based energetics proposed for other NRAMP orthologues. Mn2+ transport is diminished in the presence of 140 mM Na+, compatible with a Na+ slippage.
mechanism proposed for the Saccharomyces cerevisiae NRAMP orthologue, Smf1p.

CONCLUSIONS: CRAMP is the first NRAMP orthologue from a fungal pathogen to be functionally characterised. CRAMP resembles other fungal orthologues with respect to predicted membrane topology, substrate specificity and pH dependence but differs in terms of its apparent affinity Mn$^{2+}$ and insensitivity to Zn$^{2+}$. Insights afforded by these findings will allow the formulation of new hypotheses regarding the role of metal ions in the pathophysiology of cryptococcosis.

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*008

SUPERANTIGEN RECOGNITION BY HLA CLASS II ON MONOCYTES UP-REGULATES TOLL-LIKE RECEPTOR 4 AND ENHANCES PROINFLAMMATORY RESPONSES TO ENDOTOXIN

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The devastating systemic effects of bacterial superantigens (SAGs) may be explained by powerful proinflammatory synergy with lipopolysaccharide (LPS). However, the mechanism underlying this phenomenon remains unclear and has never been investigated in humans. Specifically, there is no known link between SAG-induced immune effects and the pattern-recognition of LPS at toll-like receptor 4 (TLR4).

AIMS: To investigate whether SAGs affect expression of the LPS receptor TLR4 in monocytes; to determine the phenotype of SAG-exposed mononuclear cells with regard to LPS responsiveness; to determine whether T cell signalling or MHC class II signalling play any role in SAG-mediated interaction with the LPS recognition pathway.

METHODS: TLR4 expression on primary monocytes was determined by flow cytometry and real time PCR. TNF produced by mononuclear cells was determined by ELISA. The role of T cells was investigated by cell separation techniques and by use of SAG constructs with targeted mutations in the MHC class II and T cell receptor binding domains.

RESULTS: Staphylococcal and streptococcal SAGs induced rapid transcription and increased membrane expression of TLR4 in primary human monocytes by ligation of MHC class II. SAGs were solely responsible for monocyte TLR4 up-regulation induced by products from Streptococcus pyogenes. In parallel with enhanced TLR4 expression, priming of purified monocytes or mixed peripheral blood mononuclear cells with SAGs significantly enhanced the induction of proinflammatory cytokines by known TLR4 ligands. SAG constructs containing targeted mutations were used to demonstrate a requirement for MHC class II ligation in both TLR4 up-regulation and enhanced responses to endotoxin. In contrast to results from animal models, SAG-endotoxin interaction was not dependent on T cell receptor ligation of exotoxin or interferon gamma production.

SUMMARY: Pattern-recognition of bacterial SAGs by MHC class II receptors may exacerbate the proinflammatory response of monocytes to Gram-negative infection or endotoxin by up-regulation of TLR4.

*009

NITRIC OXIDE DEFICIENCY LEADS TO REDUCTION IN MACROPHAGE APOPTOSIS AND EARLIER BACTERAEMIA IN A MURINE MODEL OF PNEUMOCOCCAL PNEUMONIA

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BACKGROUND: Nitric oxide (NO) is involved in both antimicrobial host defense and the regulation of inflammation. We have demonstrated that macrophages when infected with Streptococcus pneumoniae (Spn) undergo apoptosis both in vitro and in vivo and inhibition of inducible nitric oxide synthase (iNOS) in vitro reduces macrophage apoptosis and decreases bacterial killing. We have now looked at the role of NO in a murine model of pneumococcal pneumonia.

METHODS: iNOS deficient mice (iNOS$^{-/-}$) or wild type C57BL6 mice received an intratracheal inoculum of 107 cfu type 2 Spn or were mock infected with PBS. At various time points post infection bronchial alveolar lavage fluid (BALF) was collected. Bacteria were quantified in blood and lungs. Neutrophils (PMN) in BALF were quantified by analysis of cytopsins. Apoptosis was determined by flow cytometry using Annexin V/TOPRO and by light microscopy of cytopsins. For survival mice were followed for 10 days.

RESULTS: The number of apoptotic cells in BALF from iNOS$^{-/-}$ mice after Spn infection was significantly less than C57BL6 mice (12 h 2.5±1.2 iNOS$^{-/-}$/ vs. 6.5±1.8% C57BL6, n=7, p<0.001; 24 h 2.3±1.2 iNOS$^{-/-}$/ vs. 5.7±0.9% C57BL6, n=8-9, p<0.001; mean±SD). Similarly, flow cytometry revealed a reduction in alveolar macrophage apoptosis. The incidence of bacteraemia at 12 h was greater in the iNOS deficient mice than wild type (86% iNOS$^{-/-}$/ vs. 29% C57BL6) but was similar between the two strains at 24 h (75% iNOS$^{-/-}$/ vs. 83% C57BL6). Clearance of bacteria was similar in the two strains at both time points. There was a significantly greater number of PMN in BALF 24 h after infection in iNOS$^{-/-}$/ compared with C57BL6 mice which resulted in significantly greater number of PMN in BALF 24 h after infection in iNOS$^{-/-}$/ compared with C57BL6 mice.

CONCLUSION: iNOS deficiency was associated with a reduction in apoptosis, earlier bacteraemia and earlier death. There was greater recruitment of PMN in the iNOS$^{-/-}$/ mice which resulted in similar bacterial clearance from the lung and no significant difference in long term survival between the two strains but at the expense of greater lung inflammation.

*010

RESPIRATORY SYNCYTIAL VIRUS INDUCED CHEMOKINE RECEPTOR EXPRESSION AND CLINICAL DISEASE SEVERITY IN INFANTS

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AIMS: Respiratory Syncytial Virus (RSV) infection is the most common cause of infant hospital admission in the UK. Serious lower respiratory tract infection is characterised by a large influx of leukocytes into the lung. This influx is regulated by chemokines, which are known to be up-regulated in RSV infection. We have shown that RSV infection of monocytes from healthy adult donors up-regulates chemokine receptor
(CCR) 1, 2 and 5 expression. Here we investigate the CCR expression on monocytes from RSV-infected infants and healthy controls.

**PATIENTS:** 34 infants, (26 admitted to intensive-care; age 120 \pm 128 days; 73.1% male), with confirmed RSV infection, were admitted to the study. 15 infants (age 218 \pm 146 days; 61.5% male) undergoing elective surgery were recruited as uninfected controls. A questionnaire including details of RSV risk factors and the course and duration of disease was completed for each patient.

**METHODS:** \sim 1 ml of blood was taken from each patient. Monocytes were isolated from this tiny amount of fresh blood using a novel density gradient and adherence method. Half the cells were infected with RSV and half treated with negative control, UV-light inactivated RSV (LN-RSV). CCIR-1 and 5 levels were determined using FACS analysis. Calcium flux measurement was by Fluo-3/Fura-Red ratio assay. Statistical tests, Wilcoxon, Mann-Whitney-U and Spearman's-rho where performed using SPSS software.

**RESULTS:** Monocytes from RSV-patients, stimulated ex vivo with virus, have significantly higher CCR1 levels than RSV stimulated monocytes from control patients (p < 0.05). Monocytes from both control and RSV-patients up-regulate CCIR-1 in response to RSV when compared to UV-RSV negative control, (p < 0.05 and p < 0.001), but the increase is greater in monocytes from RSV-patients. Therefore monocytes from RSV-infected babies appear primed to up-regulate CCR1 in response to RSV. CCR1 and CCR5 expression are co-regulated as CCR1 and 5 expression levels were correlated (r^2 = 0.7, p < 0.01). Calcium flux measurements show the up-regulated receptors to be functional. The CCR1 fold increase correlated significantly with key markers of disease severity; duration of hospital admission (p = 0.046) and duration of intensive care stay (p = 0.026).

**CONCLUSIONS:** These data show that RSV causes a functional increase in chemokine receptor expression and that this up-regulation is linked to disease severity in infants.

**O12**

**IMMUNE RESTORATION DISEASE IN SEVERELY IMMUNOSUPRESSED HIV PATIENTS: A RETROSPECTIVE STUDY OF PATIENTS WITH CD4 COUNTS OF <50 COMMENCING HIGHLY ACTIVE ANTIRETROVIRAL TREATMENT**

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**INTRODUCTION:** Immune Restoration Diseases (IRD) are a collection of inflammatory diseases seen in HIV patients after HIV viraeemia is suppressed by highly active antiretroviral therapy (HAART). IRD probably reflect dysregulated immune responses against pro-existing infections by opportunistic pathogens. It is postulated that patients with profoundly suppressed CD4 lymphocyte counts are most susceptible to IRD.

**METHODS:** The Royal Perth hospital has a cohort of approximately 450 HIV-positive patients. A retrospective case note study was performed examining patients with CD4 counts of 50 cells/mm^3 or less who had commenced HAART. A total of 98 pts from June 1996 to June 2003 were identified. Patients were excluded if less than 6 months therapy had been completed or if they had been lost to follow up, if poor compliance/adherence with HAART had been identified, or it there had been no significant reduction in HIV viral load (\geq 1 log from baseline viral load) following 6 months of treatment. A total of 64 patients fulfilled the criteria. As some had been commenced on HAART more than once during the study period, more than one episode could be studied for each patient. A total of 75 such episodes were analysed. Patients clinic and ward attendances were examined and the occurrences of possible cases of IRD were noted.

**RESULTS:** Patients mean age at commencement of HAART was 43.4 years (24-66 yrs). Sex: male 80%, female 20%. Ethnicity: Caucasian 76.6%, SE Asian 10.9%, African 6.25%, Indigenous Australian 6.25%. HAART regime used: protease inhibitor based 67%, non-nucleoside reverse transcriptase inhibitor based 23%, other 11%. Mean baseline CD4 count 22 cells/mm^2 (0-49), Mean baseline HIV viral load 354.089 copies/ml (911-2,109,967).

A total of 21 cases of IRD were diagnosed (atypical mycobacterial infection 5, Kaposi sarcoma 3, VZV 3, cerebral toxoplasmosis 2, tuberculosis 1, cylomegalovirus 1, anterior uveitis 1, cryptococcosis 1, molluscum contagiosum 1, progressive multifocal leucoencephalopathy 1, disseminated HSV 1, parvovirus encephalitis 1). 8 further possible cases also occurred, as did elevations of transaminases in 5 chronic hepatitis patients (41 hepatitis C, 1 hepatitis B).

**CONCLUSIONS:** Patients with a CD4 count of <50 cells/mm^3 may be more at risk of developing IRD. We compare our data with other studies and comment on management of individual cases.

**O11**

**FOLLOW UP OF POST-TREATMENT SYPHILIS SEROLOGY AND PARTNER NOTIFICATION OF PATIENTS WITH EARLY INFECTION SYphilIS**

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**INTRODUCTION:** Recent increases in the incidence of early infectious syphilis have been particularly noted in men who have sex with men (MSM). In order to limit the spread of syphilis appropriate treatment, post-treatment serology and partner notification are important issues. British Association of Sexual Health and HIV (BASHH) post-treatment guidelines recommend a minimum follow up of three times for mono-infected or five times for HIV co-infected syphilis patients within the first year. An audit to assess adequacy of post-treatment serological follow up and partner notification was performed.

**METHODS:** Case notes of 40 consecutive patients with infectious syphilis treated at NGH in 2003 were audited. Data collected included demographic details, treatment provided, frequency of attendance for serology (VDRL) and details regarding contact tracing.

**RESULTS:** Of the 40 patients 6 were HIV co-infected. Seventeen (42.5%) failed to attend for any post treatment serological tests. Of the remaining, 17 (42.5%) attended for the first appointment and only 13 (32.5%) attended for the full 1 year follow up. The 40 patients in the study had 362 sexual contacts (59 regular and 303 casual contacts). Only 67 (18.5%) of the total contacts could be traced of which 44 (12.2%) were screened. The remaining 295 (81.5%) could not be identified for partner notification despite intensive tracking attempts.

**CONCLUSION:** This study illustrates lack of patient compliance with post-treatment serological follow up. Simplification of follow up may improve patient compliance with post-treatment serology. The low success rate of partner notification is mainly due to anonymous sex, which may be further driving the syphilis epidemic and attempts to improve this nationally should be sought.
THE IMMUNE RESPONSE TO TUBERCULOSIS IN HIV-1-
SEROPOSITIVE SUBJECTS ON HAART: PRESENT BUT NOT
FUNCTIONAL?
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OBJECTIVE: To evaluate the effector function of M. tuberculosis
purified protein derivative (PPD)-specific CD4+ T cells in HIV-1-
seropositive (HIV-1+) subjects after long term highly-active
antiretroviral therapy (HAART).
METHODS: PPD-specific CD4+ T cells were quantified by IFN-γ
Elispot in a cross-sectional study of 20 HIV-1+ subjects receiving
HAART for >12 months, with CD4 counts >300 cells/μl, and 11
age-matched low risk controls. All subjects were BCG-vaccin-
ated. Cytokine profiles of responding T cells were analysed by
intracellular staining.
RESULTS: The frequency of IFN-γ-secreting PPD-specific CD4+ T
cells was significantly lower in HIV-1+ subjects compared with
controls (medians 35 and 682 SFU/million PBMC respectively, p<
0.001), irrespective of CD4 nadir or duration of HAART. In
contrast, high frequencies of CMV-specific CD4+ T cells with IFN-
γ-secreting capacity were detected in CMV-seropositive HIV-
1+ subjects. There was no evidence of a switch to a Th2 response
as frequencies of PPD-specific CD4+ T cells with secreting IFN-γ
or IL-4 were similar among HIV-1+ subjects. PPD-specific
proliferative responses were demonstrated in a subset of HIV-
1+ subjects (n=10) and exogenous IL-12 could restore IFN-γ
secretion in response to PPD stimulation, indicating that PPD-
specific CD4+ T cells were present in these individuals.
CONCLUSION: Taken together, these data indicate a selective
loss of function in PPD-specific CD4+ T cells with secreting IFN-
γ capacity which does not appear to have been recovered after long
term HAART. As IFN-γ is a key mediator of immunity to M. tuberculosis,
our findings have implications for the risk of active
tuberculosis (TB) in HAART-treated subjects, particularly in
areas with a high TB prevalence where HAART is yet to be
implemented on a large scale.

POSTER ABSTRACTS

P01
TUBERCULOSIS CONTROL PLANNING IN HOSPITAL SETTING
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OBJECTIVES: To encourage staff involvement in policy
implementation and identify training and education needs within
individual wards and departments.
METHODS: In order to plan and progress a Tuberculosis Control
Plan within a hospital setting for the management of suspected/
actual cases of tuberculosis, key staff including modern matrons
were asked to produce a patient care pathway for their ward or
department. They were asked to include information on the roles
and responsibilities of key personnel. Respondents were also asked
whom they would inform, to provide information on patient
accommodation, the provision of advice to patients and for details
of personal protective equipment.
RESULTS: A wide range of responses was received, which
were drawn up in a variety of ways either by individuals
acting in isolation or as part of a group exercise. The most
comprehensive pathway of care was received form the care
of the elderly directorate which included action to be taken
in the community as well as within hospital setting;
reflecting the way in which healthcare delivery is organised.
One respondent indicated that they did need to have a
protocol as they only screened "well women"; this despite
the fact that multidrug resistant tuberculosis has been
identified in patients visiting the department.
CONCLUSIONS: More work needs to be done to improve staff
knowledge with regard to risk assessment as well as in the
management of suspected/know cases of tuberculosis
particularly with regard to the use of personal protective
equipment.

P02
UK EPIDEMIC MRSA 1-17: MOLECULAR TECHNIQUES FOR
IMPROVED STRAIN CHARACTERISATION
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Methicillin-resistant Staphylococcus aureus (MRSA) is a major
human pathogen both in the community and healthcare settings,
causing infections ranging from boils and cellulitis to life-
threatening disease such as osteomyelitis and bacteraemia.
The epidemic spread of MRSA is due mainly to the dissemination
of strains with enhanced capability for dispersion and transmis-
sibility. Effective control measures depend on a detailed knowl-
edge of strain characteristics and have the potential to inform
epidemiological studies and impact on infection control
strategies.
In the last two decades, 17 UK epidemic methicillin-resistant
S. aureus (EMRSA) types have been defined by phage typing.
Although phage typing and, more recently, PFGE have been
widely used studying the epidemiology of MRSA, their inter-
laboratory reproducibility is limited, which hampers strain
comparisons between centres and countries. The advent of
newer, more portable molecular typing methods offer the
promise of overcoming these limitations.
To enhance the characterisation of the 17 reference strains, we
have exploited a range of molecular techniques including DNA
sequence and PCR-based methods: Multi Locus Sequence Typing
(MLST), protein A gene (spa) sequence typing, toxin profiling,
accessory gene regulator (agr) allele determination and staphy-
lococcal cassette chromosome mec (SCCmec) typing.
The data show variable discriminatory power for the EMRSA
strains in terms of their sequence (ST), spa type, agr group
and SCC mec types, which provide valuable insights into their
phylogenetic and evolutionary relationships. For example,
EMRSA-1, 4, 7 and 11 were all ST 239, spa type t037, agr 1
and SCCmec III. They also encode a single enterotoxin, sea.
These results show that these EMRSAs were derived from a
similar genetic background. However, the most successful UK
epidemic strains, EMRSA —1, 3, 15 and 16 have MLST, spa
type, agr group and SCCmec types which differ from each
other, showing they are from distinct genetic lineages. This
suggests that other factors are important in their pathogen-
icity and epidemicity.
The discriminatory power afforded by these techniques will
augment outbreak investigations and improve our ability to map
the emergence and spread of resistant and/or virulent clones in
both community and healthcare settings.
INTRODUCTION: Cranberry juice has been given to elderly hospitalised patients in the belief that it will prevent, or treat, urinary tract infection (UTI)\(^1\). Though there is good evidence of its effect in decreasing symptomatic UTIs in younger women, whether it is effective for elderly women and men is unknown. The mechanism by which the effect of cranberry is mediated is thought to be due to the presence of "proanthocyanidins", which exhibit antiadhesion activity against both sensitive and resistant strains of P-fimbriated \textit{E. coli}, preventing adherence to uroepithelial cells lining the wall of the bladder\(^2\). Cranberry juice is an attractive therapy as it is cheap, natural and will not lead to antibiotic resistance. In this study we sought to examine its potential in preventing symptomatic UTI in elderly hospitalised patients who are at risk from adverse effects of multiple courses of antibiotics.

ABSTRACT: This was a randomised, placebo controlled, double blind trial of 376 patients aged 60 or over admitted to the Medicine for the Elderly assessment or rehabilitation units in Tayside. Participants were given either 15 Dml of cranberry juice or placebo twice daily; the juice was prescribed in the ward drug kardex. The primary outcome was time to onset of first UTI. Secondary outcomes were compliance with drinking juice, antibiotic prescriptions and bacteria isolated from UTIs. A high adherence rate to drinking the juice (around 90\%) was achieved.

A total A 21 (5.6\%) subjects developed UTI: 14/189 in the placebo group and 7/187 in the cranberry juice group. There were significantly fewer \textit{Escherichia coli} infections in the cranberry group. This is a large randomised clinical trial of cranberry juice ingestion that included males and females, but as the symptomatic infection rate was lower than anticipated the study was underpowered and thus inconclusive. Larger trials are needed to provide a definitive result; meanwhile the role of cranberry juice in the prevention of UTI in elderly hospital patients remains unproven.

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CONCLUSIONS:

COCKROACHES—BLAT ORIENTALIS

TRANSMISSION, OF BACTERIAL PATHOGENS BY DOMESTIC

quinolone use and the incidence of MRSA in hospitals.

of MRSA may partly explain the association between fluoro-

transmission than other MRSA colonised pts. Faecal overgrowth

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National Hospital has been a major problem for the last 3 years,

Havana

The outbreak of diarrhoea due to the same

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resulted in the sporadic outbreak of diarrhea due to the same

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P.G. Waiyaki

14 days. By Fisher’s exact test this was a significant association

(27.7%) control pts had received fluoroquinolones in the previous

7/11 pts. 11/11 pts (100%) with faecal overgrowth of MRSA and 5/18

growth was pure in 6/12 pts. MRSA was identified for the first time in

7/11 pts. 11/11 pts (100%) with faecal overgrowth of MRSA and 5/18

(27.7%) control pts had received fluoroquinolones in the previous

14 days. By Fisher’s exact test this was a significant association

(p < 0.001). No other causal associations were identified.

CONCLUSIONS:

Fluoroquinolone use is associated with faecal

overgrowth of MRSA. These pts excrete large quantities of MRSA

into the environment and may therefore pose a greater risk of

transmission than other MRSA colonised pts. Faecal overgrowth

of MRSA may partly explain the association between fluoro-

quinolone use and the incidence of MRSA in hospitals.

P06

TRANSMISSION, OF BACTERIAL PATHOGENS BY DOMESTIC

COCKROACHES—BLAT ORIENTALIS

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AIM: The outbreak of diarrhoea due to the same Salmonella

havana and spread of cockroaches in the Nursery Unit of Kenyatta

National Hospital has been a major problem for the last 3 years,

despite spraying cockroaches with insecticides and use of

effective antibiotics for the control and management, the

sporadic outbreak continued. The present investigation was

undertaken to find the role of cockroaches in a hospital with

sporadic nosocomial infection due to Salmonella havana and find

out how we can contain it.

METHOD: 260 cockroaches were collected from the unit and 50

of them from high-class private homes with clean environment.

Faecal pellets of cockroaches from cracks and crevices of

cupboards were swabbed. 155 cockroaches were washed in 2%

of them from high-class private homes with clean environment.

260 cockroaches were collected from the unit and 50

cupboards were swabbed. 155 cockroaches were washed in 2%

nutrient broth. Guts were removed from the other 105 and put in

similar broth. All the extract were cultured in suitable media.

Insecticide-pyrethrin was used to control cockroaches.

RESULTS:

From the gut only Serretia species were isolated.

Enteropathogenic Escherichia coli, Serretia, Salmonella, Kleb-

siella, E. coli and Proteus species were isolated from the bodies.

Also Salmonella, Serretia & EPEC were isolated from faecal pellets.

Despite spraying the cockroaches in the unit, the outbreak was not

controlled. But disinfecting the environment where enteropatho-

gens were isolated and spraying the cockroaches the sporadic

outbreak due to Salmonella havana was controlled.

CONCLUSION: Our study has shown that cockroaches do not retain

invading bacteria in the gut. The isolation of the same multiple resistant S. havana from patients and hiding places of cockroaches

show cockroaches transmitted this strain from hiding places to the

new patients and then back to the hiding places. This might have resulted in the sporadic outbreak of diarrhea due to the same S.

havana in the last 3 years. The elimination of the old cockroaches

without disinfecting the cracks and crevices could not have

controlled the outbreak of diarrhoea because the new cockroaches

would get contaminated in the cracks and crevices then pass

organisms to the new patients.

This study has shown that cockroaches can transmit pathogens

mechanically hence possible role of cockroaches in the transmission of

human pathogens should not be ignored or simply rejected.

P07

WARD CURTAINS: EFFECTIVENESS OF STEAM CLEANING

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Prevention and control of hospital acquired infection is now

given a high priority with increased attention focussed on the

maintenance of a clean hospital environment. The ward curtains

surrounding hospital beds give the patient privacy, but like other

surfaces in the ward environment, are exposed to contamination

with hospital microbial pathogens derived from patients and

staff. Consequently curtains may play a role in the spread nosocomial infections and their importance has probably been

overlooked in the past.

At the Taunton & Somerset NHS Trust curtains are laundered off

site and are often in short supply when there is a sudden

increased demand. To overcome these limitations rapid curtain
decomamination in situ using the Robby 6000 steam cleaner has
been introduced. This study was undertaken as there is little

information available on the effectiveness of steam cleaning

curtains.

A 2 m² area of curtain was sampled using a Casella slit sampler

according to a standard protocol. The areas chosen were those

identified as most likely to be contaminated by patients and

staff. The bacterial load on 13 laundered curtains in the linen

room and 20 curtains in clinical areas before and after steam

cleaning was investigated. Total colony counts (cfu) were

recorded and the data sets analysed statistically using Minitab

student-12. Steam cleaning of curtains from clinical areas

resulted in a significant reduction in colony counts (P < 0.0001).

After steam cleaning the bacterial loads on curtains from clinical

areas were comparable with those on stored, clean laundered

curtains.

Qualitative studies were carried out to identify the various

species of organisms present on laundered curtains and curtains

in clinical areas, including those surrounding the beds of patients

known to be MRSA positive. The following species were isolated:

Staphylococcus aureus, coagulase negative staphylococci,

diphtheroids, Bacillus sp., Proteus sp., Pseudomonas sp.,

Coliform sp., MRSA and unidentified Gram negative bacilli.

It was concluded that curtains in clinical areas become heavily

contaminated and are a reservoir for potentially pathogenic

organisms. Steam cleaning can reduce the bacterial load

relatively consistently by 70-80% i.e. achieving levels comparable

to those on clean laundered curtains. Steam cleaning is a

cost effective and acceptable alternative to the laundering of

visible clean unsouled curtains.

P08

A NOSOCOMIAL OUTBREAK OF PENICILLIN SENSITIVE

PNEUMOCOCCAL BACTERAEMIA (SEROTYPE 9V) ON A

REHABILITATION WARD IN A DISTRICT GENERAL HOSPITAL

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BACKGROUND: Streptococcus pneumoniae is the commonest cause of community-acquired pneumonia. Nosocomial outbreaks of infections due to penicillin-susceptible Streptococcus pneu-

moniae are now documented infrequently. We describe an

outbreak of a penicillin-susceptible isolate that caused bacter-
aemia secondary to pneumonia in three elderly rehabilitation

patients over a six-day period in July 2004.

OBJECTIVES: To describe the clinical and microbiological

features of the outbreak, its subsequent management and

infection control measures.
OUTBREAK DESCRIPTION: The index patient deteriorated rapidly with pneumonia and blood cultures grow Streptococcus pneumoniae resistant to erythromycin. Two days later a second patient, from an adjacent bed to the index case, also developed pneumonia and erythromycin-resistant Pneumococcus was again isolated from blood cultures. The infection control team were alerted and just before comprehensive investigation, a third patient, from an opposite bed to cases 1 and 2, presented with clinical sepsis and pneumococcal bacteraemia was confirmed. The Diphtheria and Streptococcal Reference Laboratory, Colindale, London performed confirmation and serotyping of isolates. The index patient deteriorated rapidly with pneumonia and blood cultures grow Streptococcus pneumoniae resistant to erythromycin. Two further patients were treated for respiratory illness on the rehabilitation ward but cultures of blood and sputum were negative. All nose-swabs from asymptomatic patients were negative for pneumococci.

CONCLUSION: Risk of nosocomial spread of Streptococcus pneumoniae should be acknowledged and isolation of infected patients considered. General outbreak measures plus removal of three ward beds resulted in control of this outbreak. Bed centres should be at least 3.6 m apart and bed groupings should be the smallest possible number. Pneumococcal serotype 9V is contained in the 23-valent vaccine and opportunistic Pneumococcal immunisation according to Department of Health guidance should be considered in a hospital setting.

*P09
AN OUTBREAK OF SALMONELLA HADAR IN A NEONATAL INTENSIVE CARE UNIT (NICU)
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OBJECTIVE: To describe the investigation of an outbreak of Salmonella hadar that occurred in the NICU of Glasgow Royal Maternity Hospital and the lessons learned from it.

METHODS: The minutes of Outbreak Committee Meetings and reports produced for the committee were reviewed retrospectively along with laboratory results for the patients involved. Members of the Outbreak Committee were interviewed.

RESULTS: Description of the outbreak
- Between 24th November 1996 and 21st February 1997, 8 babies and 4 adults were identified as infected with S. hadar.
- All adults and 5 babies were symptomatic.
- Three babies were asymptomatic; carriers detected on screening.
- Chronic carriage occurred in 3 babies.
- Transmission occurred through person-to-parson spread but was also maintained via another route.

Microbiology of the outbreak
- On the basis of plasmid digestion profiles and pulsed field gel electrophoresis performed at the Scottish Salmonella Reference Laboratory, isolates were indistinguishable and identified as S. hadar serotype 6,8,210,e,n,x.

Outbreak investigation findings
- S. hadar was probably introduced by a symptomatic mother and transmitted to her baby during delivery.
- Cross infection baby-to-baby then occurred via equipment or health care workers (HCWs).
- Baby-to-mother cross-infection then occurred by direct contact.
- Two babies identified as asymptomatic carriers were never in the same location as infected infants, suggesting a continuing environmental source or a chronic carrier among staff.
- Screening cultures from staff and equipment were unrewarding.
- Shared Yellow soft paraffin (YSP) used to lubricate rectal thermometers was proposed as a putative vehicle of transmission.

CONCLUSIONS:
- This is the first reported outbreak of S. hadar to affect neonates.
- There was a delay in halting the spread of infection as the index case did not have her diarrhoea investigated by stool culture for several days and she was not initially isolated.
- Some babies excreted and transmitted infection without ever having symptoms.
- Transmission occurred despite only very short periods in contact with a carrier.
- YSP was implicated as a candidate vehicle of transmission as the outbreak ceased when it was withdrawn and replaced by single patient use tubes although S. hadar was not cultured directly from YSP.
- Chronic carriage with S. hadar is a complication of neonatal infection.

*P10
EFFECTS OF SURVEILLANCE AND FEEDBACK ON METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) TRANSMISSION IN AN ADULT INTENSIVE CARE UNIT (AITU)
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OBJECTIVES: Firstly, to examine the dynamics of MRSA transmission in our AITU, correlating the number of patients admitted with MRSA, with the number acquiring the organism during their admission. Secondly, to determine the effects of feedback of this data on MRSA transmission rates.

METHODS: Data was prospectively collected on all patients admitted to the AITU. MRSA acquisition was defined as a patient with negative screens within 48 h of admission who grew MRSA from any subsequent specimen during their AITU stay. MRSA transmission rates were calculated as the ratio of MRSA acquisitions per MRSA colonised patient on the AITU at the time of admission (transmission ratio). The number needed to transmit (NNTT) was defined as the reciprocal of the transmission ratio. For the first 4 months of the study AITU staff were blinded to this data. In the subsequent months, a monthly report detailing MRSA transmission rates was relayed to the AITU staff. No additional MRSA control measures were undertaken during the period of the study.

RESULTS: Over a 22-month period 1569 patients were admitted, of which 1292 (82.3%) were screened within 48-hours of admission. Of these a total of 236 patients (18.3%) were found to be MRSA colonised on admission. Forty-eight MRSA acquisitions were detected over the 22-month period, with an overall mean transmission ratio of 0.24 and a NNTT of 6.5. The mean MRSA transmission ratio in the pre-feedback period was 0.51 (mean NNTT 2.2), whereas in the following 18-months it was 0.18 (mean NNTT 7.4) (unpaired Student’s t test p=0.0066).

CONCLUSIONS: MRSA is endemic in many UK hospitals. Although guidelines aimed at limiting transmission of MRSA exist, it
remains a particular problem on the AITU. Feedback has been used effectively in other situations to control MRSA transmission. In this study it significantly increased awareness of infection control issues on the AITU, and was associated with a sustained reduction of MRSA transmission. Although feedback appears to have a significant effect an MRSA awareness, it is not in itself a method of MRSA control. It is a tool for facilitating other infection control measures.

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**P11**

GENOMIC DIVERSITY OF STAPHYLOCOCCUS EPIDERMIDIS ASSOCIATED WITH DEVICE-RELATED INFECTION IN THE INTENSIVE CARE UNIT

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The increasing use of indwelling medical devices has resulted in an increase in biofilm-mediated device-related infection in the Intensive Care Unit (ICU). Staphylococcus epidermidis are one of the most common organisms causing device-related infection. The staphylococcal ica operon-encoded polysaccharide intercellular adhesin is required for biofilm formation and represents an important virulence determinant. The principle objective of this study was to evaluate genomic diversity of biofilm-forming ICU S. epidermidis isolates.

31 S. epidermidis isolates, 18 of which were associated with device-related infection were screened by a PCR assay for the presence of the ica operon and typed by pulsed-field gel electrophoresis (PFGE). Biofilm-forming capacity under standard laboratory and stress inducing conditions was evaluated by a microtitre plate assay.

PFGE analysis revealed a wide genetic diversity among isolates. A total of 21 PFGE different patterns were found with two clones predominating—Clone A (seven ica positive isolates) and Clone B (four ica positive isolates). The majority of isolates belonging to the two predominant clones (10/11) were associated with device-related infection, and over half of these could be induced form biofilm. However, there was no association between clonal type and regulation of biofilm formation under the stress inducing conditions examined.

These findings suggest that no specific strains of S. epidermidis are associated with device-related infection in our ICU.

**P12**

NOSOCOMIAL RESPIRATORY SYNCYTIAL VIRUS INFECTION IN CHILDREN AT LEEDS TEACHING HOSPITALS NHS TRUST

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Nosocomial infection with respiratory syncytial virus (RSV) causes substantial morbidity and mortality in paediatric populations. A change of infection control policy was recently implemented in the trust. Previously, children were cohorted on the basis of the result of an urgent test for detection of RSV. The implemented change was to cohort children by their symptoms and to provide a timely result for investigation of respiratory viruses by direct immunofluorescence. We aimed to compare the incidence of nosocomial infections and the impact upon laboratory workload before and after the policy change.

A retrospective survey of positive diagnoses of RSV was undertaken over two 8 month periods (September–April) for the years 2000–01 and 2003–04. Appropriate respiratory samples from inpatients at the two teaching hospitals in Leeds Teaching Hospitals NHS Trust were investigated. Diagnosis of RSV infection was made by direct immunofluorescence or enzyme immunoassay. Admissions data were obtained for 2003–04; however, these data were not fully available for 2000–01 (we assumed that there was no significant difference). Infections were categorised into community acquired (diagnosis within 3 days of hospital admission) or hospital acquired infections (>3 days since admission).

For the winter of 2000–01, 650 children were investigated and 281 (43%) new diagnoses of RSV infection were made of which 112 cases (40%) were diagnosed in the emergency department. In 2003–04, 415 children were investigated; 107 (25%) diagnoses of RSV infection were made. Only one case was diagnosed in the emergency department (because of the change in testing policy). For each period studied there were 15 nosocomial RSV infections, equating to a rate of 0.5 nosocomial infections per 1000 admissions. The number of samples investigated in the laboratory fell from 886 to 570, while on-call samples fell by greater than 90%.

The change in infection control policy led to a significant reduction in ‘out of hours’ requests and a reduction in all requests for investigation for RSV. There was no significant change in the rate of nosocomial RSV infections occurring within the trust. Because of the annual variation in RSV burden longer term follow up is required to be certain of the effects of policy change on nosocomial transmission risk.

**P13**

APPLICATION OF MULTILOCUS SEQUENCE TYPING TO THE INVESTIGATION OF THE MOLECULAR EPIDEMIOLOGY OF CANDIDA ALBICANS IN THE HOSPITAL ENVIRONMENT

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BACKGROUND: Candida albicans causes infections with high attributable mortality in seriously ill hospitalised patients. A greater understanding of the epidemiology of this yeast may help to prevent infection in this vulnerable population. Various molecular techniques have been applied to the study of the molecular epidemiology of candida infections; none have been entirely satisfactory. Multilocus sequence typing (MLST) is a method that has been developed for C. albicans in recent years, and may become an attractive tool for study of the epidemiology of the organism.

METHODS: Isolates of C. albicans were collected over 6 months from patients on the General Intensive Care Unit at The General Infirmary at Leeds. A set of four pairs of isolates from a previous study, identical using karyotyping, were also analysed. Eight samples each from five of the most sampled or longest stay patients were subjected to analysis using the full set of MLST genes and using the Ca3 probe. Further samples were subjected to a truncated analytical scheme in an attempt to develop a faster and cheaper alternative to the full scheme. All samples were analysed at the two most variable loci, and samples that were indistinguishable at this stage were sequenced at further loci. Samples were considered indistinguishable if they showed the same sequence at all seven loci.
RESULTS: Initial analysis of the paired samples showed that isolates that were indistinguishable by PCR or karyotyping were almost indistinguishable by MLST. However, there appears to occasionally be a recombination event causing a heterozygous locus to become homozygous. Typing of the forty strains from the five long-stay patients revealed further examples of this occurring. Results suggest that there is a predominant strain found in each patient, and in some patients other strains are present. There is no evidence of indistinguishable strains being isolated from different patients, suggesting that nosocomial transmission is not occurring.

CONCLUSIONS: MLST is a highly reproducible technique for the study of nosocomial candida infections. A truncated variation of the scheme may provide a more affordable way of ruling out transmission of infection when clusters of cases of candida infection are seen in the hospital setting.

P14
SHOULD CLINDAMYCIN TAKE SO MUCH OF THE BLAME FOR CAUSING CLOSTRIDIUM DIFFICILE COLITIS?
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OBJECTIVE: To find out whether the use of clindamycin is associated with Clostridium difficile as frequently as was historically claimed.

DESIGN: Two-part study. To gain an impression of the problem within our department, we collected results from a retrospective audit on the management of C. difficile and performed a case note review on clindamycin usage.

SETTING: An infectious diseases unit in a tertiary hospital, South Yorkshire.

PATIENTS: Audit: In-patients with C. difficile colitis from 1 Jan 2003 to 31 Nov 2003 (23 patients). Case note review: In and outpatients who received clindamycin from July 2002 to Oct 2002 (26 patients).

METHODS: From the retrospective audit, we identified the number of patients infected with C. difficile who had received clindamycin therapy in the preceding 2 months. Vice versa, the number of patients who developed C. difficile through clindamycin therapy given by the infectious unit was noted.

RESULTS: For the audit, we had 23 patients admitted with C. difficile within the 11 months. Only one out of 23 patients (4.3%) had a history of clindamycin therapy, in topical form for her acne. From the case note review on clindamycin usage, out of 26 patients who had received clindamycin therapy, only 1 (3.8%) C. difficile case was seen.

CONCLUSION: Both the audit and case note review had the limitation of being retrospective studies. Ideally, a randomised double-blind placebo-controlled trial would be needed to adequately identify whether the association between clindamycin use and C. difficile is as strong as was historically claimed. However, through the results collected from the audit and case note review, we gained the impression that clindamycin does not increase the risk of subsequent C. difficile diarrhoea any more than other commonly used broad-spectrum antibiotics. There is a need for more research into the safety of clindamycin.

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*P15
AN OUTBREAK OF SERRATIA MARCESCENS ON THE NEONATAL UNIT: A TALE OF TWO CLONES
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BACKGROUND: Serratia marcescens, a well recognised nosocomial pathogen was isolated from several babies on a Neonatal Unit between October 2001–April 2002. We describe the outbreak and the phenotypic and genotypic characteristics of the organisms involved.

METHODS: Clinical isolates were collected from 18 patients infected or colonised with S. marcescens during the study period. These were compared to one environmental isolate and other temporally unrelated clinical isolates from patients elsewhere in the same hospital. All isolates were typed with pulsed field gel electrophoresis (PFGE) and random amplified polymorphic DNA-polymerase chain reaction (RAPD-PCR). The blactamase was characterised by isoelectric focusing.

RESULTS: In the study period 4 babies had severe invasive S. marcescens infections (meningitis and/or septicaemia), of which 2 died. A further 14 babies were colonised with the organisms or had only superficial infections. Extensive environmental and staff screening, revealed no common source. The outbreak ended following enhanced compliance with infection control measures and a change of antibiotic policy. S. marcescens continued to be isolated sporadically from various clinical sites for another 6 months.

Isoelectric focusing confirmed the presence of an inducible blactamase with a high pi, consistent with the presence of an AmpC blactamase. Both molecular typing methods revealed that two clones were present. The first, which caused invasive clinical infection in 4 babies, was afterwards replaced by a second, non-invasive clone which affected 14 babies. Phenotypically, the two strains also differed in their prodigiosin production, the first one being non-pigmented whereas the second one displayed pink-red pigmentation. The environmental isolate and clinical isolates from other wards were genetically distinct. Although S. marcescens continued to be isolated occasionally, the end of the outbreak was signalled by the replacement of the original strains with sporadic strains with other molecular typing patterns.

CONCLUSIONS: There was a clear difference in the pathogenicity of the two outbreak clones. The molecular typing methods were useful epidemiologic tools which emphasized the difference between the two outbreak strains. RAPD-PCR, although relatively easy to perform, has limited reproducibility, whereas PFGE is discriminatory and reproducible.

*P16
CLINICIANS' PERSPECTIVE: RECOGNITION, INVESTIGATION AND INITIAL MANAGEMENT OF POTENTIAL CASES WITH SEVERE ACUTE RESPIRATORY SYNDROME (SARS) OR AVIAN INFLUENZA (AI)
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In the forthcoming months people will travel to the UK from a SARS zone of potential re-emergence. We are repetitively warned of concerns over the next flu pandemic. We have an opportunity to be prepared; to contain an infection as early as possible and to prevent nosocomial amplification.
In 2004, during the SARS post-outbreak period a patient with a febrile respiratory illness was referred to North Manchester General Hospital for evaluation of possible SARS-CoV infection. The patient had recently returned to the UK from Mainland China with an illness which had started prior to departure from China. During the course of the patient’s admission several factors emerged as practical aspects of the patient’s care. We believe that there is a need for detailed step by step guidance for clinicians regarding the day to day management of such a case. As a result of our experience with this patient, we are highlighting several of these issues.

How to optimally prepare for a potential case of SARS-CoV or Avian Influenza infection may include the following:

1. Hospital plan development for dealing with such a case, with a multi disciplinary approach is crucial. The plan should provide the detail required by the various parties.
2. Assessment of which components of any plan/policy are generic with regard to other infectious diseases and build on this.
3. Practical preparedness: for example development of a 'pre-prepared kit' including all that may be required for an assessment and laminated aide memoirs on walls in isolation rooms, giving clear step by step guidance for Personal Protective Equipment (PPE) usage etc.
4. Training of staff with regular updates, which will include basic principles on how to provide safe case management. This will involve risk assessment and an adaptation of normal clinical practice.
5. Protocols regarding the use of anti-virals and data collection.
6. Optimisation of day to day infection control practices.
7. Communication plan development including who to contact, when and how.

In conclusion: we think that hospital preparedness is paramount and that generic components can be utilised for other infectious diseases.

P17
THE CLINICAL APPLICATION OF HACCP
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BACKGROUND AND OBJECTIVES: Healthcare Associated Infections (HAIs) continue to attract media and consumer attention, impact upon healthcare delivery and are a cause of morbidity and mortality. “Winning ways” (NHS action plan) has identified seven action areas, with area one recommending the use of Hazard Analysis Critical Control Points (HACCP), although little guidance on its application is provided. This study applies approaches and strategies based upon HACCP and relevant pre-requisite programmes (PRPs) to the decontamination of endoscopes.

METHODS: Observation of practices combined with examination of the documentation used by 2 endoscopy clinics was undertaken. The procedures used were compared to the 7 HACCP principles and 12 logic sequences outlined by the Codex Alimentarius Committee. Real time monitoring, as defined by Codex, was undertaken after cleaning, prior to disinfection using ATP bioluminescence, providing a measure of residual organic debris.

RESULTS: Endoscope reprocessing was conducted in accordance with the British Society of Gastroenterology guidelines. Comparison of in use “practices” with HACCP principles indicated variability between units and neither unit implemented all HACCP steps. Monitoring indicated that cleaning, an essential step prior to decontamination, was often not adequately performed. Biopsy and suction channels from endoscopes processed in both units were found to contain organic matter. The water used during decontamination was of good microbiological quality, although endoscope tips were found to be contaminated, as were environmental surfaces likely to be in contact with clean endoscopes.

CONCLUSION: The HACCP and PRP approach can be applied in healthcare environments and could help to reduce healthcare acquired infections by providing a risk based management framework.

P18
A STUDY OF DOCTORS’ AND NURSES’ KNOWLEDGE OF INFECTION CONTROL GUIDELINES IN AN IRISH UNIVERSITY HOSPITAL
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The importance of the contribution of infection control programmes to reducing patient morbidity, mortality and treatment costs incurred by hospitals has been well recognized.1 It is also acknowledged that non-compliance with standard precautions may be related to a lack of knowledge amongst healthcare workers regarding the potential risk of infection transmission both to themselves and to patients.2 The Infection control guidelines for Cork University Hospital were updated in July 2004.3 We decided, following the introduction of these guidelines, to ascertain the level of knowledge of nursing and medical staff regarding fundamental aspects of infection control practice. Prior to the introduction of the guidelines, infection control teaching had occurred on an informal basis on each ward/department but was sporadic in nature due to staff shortages.

METHODS: We designed a short, anonymous cross-sectional questionnaire. It consisted of questions based on the core elements of the first three chapters of the infection control guidelines.

RESULTS: The majority of respondents were female and members of the nursing staff. The need to place patients in a single room in order to adhere with contact, droplet or airborne precautions was underestimated. Surgical wound infection and urinary tract infection were the most commonly identified examples of hospital-acquired infection. Vancomycin was recognized twice as often as Linezolid as a possible choice of antibiotic treatment for patients with serious MRSA infection.

There was greater awareness of the risk of transmission of hepatitis C and HIV than hepatitis B in the case of a needlestick injury from an infected patient to a healthcare worker.

CONCLUSION: The study reveals a lack of knowledge amongst nurses and doctors in key areas of infection control. It may be used to guide further teaching sessions for both medical and nursing staff to reinforce the principles of infection control and optimise its practice in this hospital.

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P20
THE TRION STATEMENT: GUIDELINES FOR TRANSPARENT REPORTING OF INTERVENTION STUDIES AND OUTBREAK REPORTS OF NOSOCOMIAL INFECTION
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OBJECTIVE: Systematic review of interventions in the hospital management of methicillin resistant Staphylococcus aureus (MRSA)1 revealed major methodological weaknesses and inadequate reporting in published research. These included lack of details on study design, the timing and nature of interventions, failure to consider threats to validity of inference in the form of potential confounders and biases, and inappropriate statistical analyses. Studies were largely quasi-experimental. In order to improve standards of research and publication, enable readers to relate studies to their own situation, facilitate synthesis of evidence and improve transparency of reporting we have produced the TRION guidelines for researchers, editors, reviewers and readers.

METHOD: The CONSORT2 statement, devised to improve the quality of randomised control trial reporting, was adapted to incorporate previous guidelines3 for publication of outbreak reports and intervention studies.

RESULT: A 22 item checklist and a summary table was produced covering the title and abstract, introduction, methods, results and discussion. Particular features are statement of the objectives (for outbreak reports) or hypotheses (for intervention studies), use of appropriate statistical techniques (avoiding those that regard infection outcomes as independent events), and taking measures to record (and adjust for) confounders and avoid bias. A summary table was recommended for description of the population, clinical setting, and precise nature and timing of all interventions and outcomes, with a graphical summary of the main results. It should be clear whether the decision to intervene or report was based on any prior knowledge of outcome data. Discussion should include interpretation of results with reference to study hypotheses, threats to validity, and generalisability.

CONCLUSION: We believe that these guidelines would raise the standards of research and publication in the field of nosocomial infection generally, not just MRSA, and therefore offer them for public discussion.

References:
1. Pittet D, et al. BMJ 2000;320:1191–41.
2. Faster A, et al. J Hospital Infection 2000;45:62–4.
3. Chief Medical Officer. Winning Ways: Action Point 6. Department of Health.
4. Larson E and Kretzer EK. J Hospital Infection 1995;30:s88–106.

P21
HAND-HYGIENE BEHAVIOUR, ATTITUDES AND BELIEFS IN 1ST YEAR CLINICAL MEDICAL STUDENTS
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OBJECTIVES: The hand-hygiene compliance of doctors1 is poor. In order to guide future educational interventions, we assessed the beliefs and attitudes to hand-hygiene and the hand-hygiene behaviour of 200 medical students at an early stage of their education, their first clinical year, in the end of year Objective Structured Clinical Examination (OSCE).

METHODS: 200 first year medical students were observed, over 2 days, at one clinical station, neurological examination of the legs. Alcohol-glycerol-chlorhexidine handrub was available at all clinical stations. On both days students were observed for use of handrub at the neurological station. On Day 2, a hand washing sign was erected. A questionnaire assessing attitudes and beliefs about hand-hygiene was administered.

RESULTS: Use of handrub at the station was 9% on Day 1, and 27% on Day 2. 75% of students believed their hand-hygiene compliance was at least 60%. The three most frequently perceived barriers to hand-hygiene were lack of time (56%), lack of sinks (47%), and “nobody else does it” (25%).

CONCLUSIONS: The low compliance reported in this study of first year clinical students is similar to that of doctors1 and final year students,2 suggesting that education to remedy this should begin early. The compliance observed in this study reflects failure of current teaching processes. The results of the questionnaire suggest that future educational approaches should include bedside availability of handrub, better practice by senior doctors (role models) and feedback from teachers at the bedside.

The Department of Health is to work with the Royal Colleges to ensure hand hygiene is addressed in undergraduate curricula3 but an empirical approach is unlikely to be successful without planning implementation on the basis of psychological theory4. Further research is required to develop a theoretically grounded educational approach to the hand-hygiene behaviour of medical students.

References:
1. Pittet D, et al. Lancet 2000;356:1307–12.
2. Faster A, et al. J Hospital Infection 2000;45:62–4.
3. Chief Medical Officer. Winning Ways: Action Point 6. Department of Health.
4. Larson E and Kretzer EK. J Hospital Infection 1995;30:s88–106.

P22
AUDIT OF THE MANAGEMENT OF URINARY TRACT INFECTIONS
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OBJECTIVE: Determine the effect of Trust wide guidelines on antibiotic prescribing for urinary tract infections (UTIs) in adult medical patients.

OUTCOME MEASURES:
• Documentation of diagnostic test results
• Empirical antibiotic therapy
• Dose of antibiotics
• Duration of antibiotic therapy
• Documentation of intended treatment duration of antibiotic therapy.

Outcomes were compared with those measured in a pre-guideline audit (December 2001). Guidelines on treatment of UTI were issued in August 2002.

METHODS: All patients admitted to the medical assessment unit and six acute general medicine wards over a seven-week period in Autumn 2003 were assessed. All patients treated for UTIs were included in the study. Patients were identified in three ways:
• Microbiology records of urine samples sent for culture.
• Pharmacists identified patients suspected of having UTIs.
• Nurses’ handover sheets and ward attendance books.

A single observer collected data daily from medical and nursing notes and prescription charts.

RESULTS: 100 patients; (70 female) were identified. Sixty-four patients (34 female) had complicated UTIs. Fifty-one patients had community-acquired infection. Thirty-one patients (18 female) had catheter related UTIs.

Diagnosis: In 87 patients the result of a rapid reagent ‘ dipstick’
result was recorded (target 100). A urine sample had been sent for culture in 92 patients (target 100). Of the 92 samples sent, 54(59%) grew mixed or non-significant numbers of organisms. The MSU result was recorded in the medical notes of only 16 patients.

**Choice of empirical therapy:** Compared to the pre guideline audit, prescribing of trimethoprim fell from 37% to 2% and that of nitrofurantoin increased from 0% to 55%. Of the 64 patients with complicated UTIs, 30 were prescribed nitrofurantoin. In only 9 patients was empirical therapy modified.

**Duration of therapy:** 69% of patients with uncomplicated UTI received >3 days therapy (target 0% >3 days). 55% of patients with complicated UTI were treated for fewer than 7 days (target 0% <7-14 days). Intended duration of treatment was documented in 57 patients.

**CONCLUSIONS:** Introduction of the guidelines was associated with a fall in prescriptions of trimethoprim whilst those for nitrofurantoin increased. Nitrofurantoin was often used inappropriately, for patients with complicated UTIs. Duration of therapy was often not consistent with guidelines. Documentation of results and intended treatment duration was poor.

**P23**

**IMPROVING HAND WASHING PERFORMANCE**

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**INTRODUCTION:** We examined the effectiveness of Health Care Workers handwashing with alcohol gel and used two interventions to determine if performance improved.

**PARTICIPANTS, METHODS AND RESULTS:** All Orthopaedic staff of our hospital were asked to participate (n=92). 55 subjects in group 1 were asked to clean their hands, using 1.75 ml (one application, as suggested by manufacturer) of alcohol gel containing a clear fluorescent substance. UV light was used to identify areas which had been missed. The missed areas were recorded onto a proforma by the assessor. The subjects were shown which areas they had missed and retested in the same way 7 days later after viewing a poster showing six recommended stages of hand washing. 37 subjects in group 2 were asked to clean their hands with two applications (3.5 ml) of the same gel. Initial assessment was identical to group 1 and they were not retested. They were age (±3 years) and sex matched to 37 subjects from group 1 for comparison. 31 pairs were further matched for job description. The percentage area missed on the dorsum and palm of all hands was calculated.

Wash 1 showed a wide variation in performance (total area missed 0% to 34.7%). Females performed better that males (average area missed 6% vs 10%, p = 0.06) and Nurses better than Doctors (5.3% vs 11.6%, p = 0.013). The dorsum of the hands was missed more than the palm (13% vs 2.1% area missed, p < 0.001). In wash 2 (following education), 92% of subjects improved their performance with a mean reduction in area missed from 7.7% to 2.3% (p < 0.001).

Group 2 performed significantly better than age and sex matched Group 1 subjects before education (mean area missed 6.6% vs 1.2%; p < 0.001). Additional matching for job description did not alter this result.

There was no significant difference between Group 1 following education and Group 2 (mean area missed 2.4% vs 1.2%; p = 0.11).

**COMMENT:** This study demonstrates hand washing performance by HCWs is poor when using the volume of gel recommended by manufacturers. The improvement following education with a fluorescent gel and a UV light box demonstrates that this is an effective teaching method. However, an equivalent effect can be achieved by increasing the amount of gel used.

**P24**

**VERTEBRAL DISCITIS AND PARAVERTEBRAL ABSCESS DUE TO PASTEURELLA MULTOCIDA TREATED CONSERVATIVELY WITH CIPROFLOXACIN**

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**OBJECTIVE:** To illustrate a case of vertebral discitis and paravertebral abscess due to *P. multocida* which responded to conservative treatment with ciprofloxacin when non-surgical treatment with co-amoxiclav had failed.

**CASE REPORT:** A 29 year old man with established alcoholic liver disease presented with 2 months of back pain which intermittently radiated from his lumbar spine to his left foot. No sphincter disturbance had occurred but in the week preceding admission he had developed night sweats and became bed-bound. He recalled being scratched by his cat 2 months prior to admission but he had not required medical attention. He was febrile, tachycardic and in severe pain. Anal sphincter tone on rectal examination was intact. Straight leg raising was markedly impaired bilaterally with reduced pin-prick sensation in an L5 distribution in his left foot and reduced reflexes in his left leg.

There was an acute inflammatory response (white cell count 20.3, C-reactive protein 49 g/dL). Blood cultures grow small, Gram negative coco-bacilli which were identified as *Pasteurella multocida* on API 20NE testing (Biomerieux, France). The minimum inhibitory concentrations (MICs) for amoxicillin-clavulanic acid and ciprofloxacin were 0.094 and 0.32 by the E-test method.

Magnetic Resonance Imaging (MRI) of his lumbar spine showed an inflammatory discitis at L4/5 with an abscess extending posteriorly, impinging on the thecal sac and with marked disc space narrowing.

He was treated conservatively with intravenous amoxicillin-clavulanic acid with initial defervesence. Four days into treatment he became febrile once more with an associated rise in CRP and oral ciprofloxacin 750 mg twice daily was prescribed as adjunctive treatment and his temperature resolved. Inflammatory markers were normal after 5 weeks with complete resolution of the abscess on further MRI scanning but with marked residual destruction of both L4 and L5 vertebræ.

Ciprofloxacin was prescribed for a total of 6 weeks following which he defaulted from all further follow-up.

**CONCLUSIONS:**

- We believe this to be only the second documented case of a paravertebral abscess due to *P. multocida* and the first in which ciprofloxacin has been used.
- We suggest ciprofloxacin has a place in the treatment of deep-seated odhopaedic infections with *Pasteurella* species and its use may facilitate recovery without a requirement for surgical abscess drainage.

**P25**

**RAPID DIAGNOSIS OF INTRAPARTUM GROUP B STREPTOCOCCAL CARRIAGE BY FLUORESCENT IN SITU HYBRIDISATION**

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**BACKGROUND:** Group B streptococcus (GBS) causes considerable neonatal morbidity and mortality in the UK. A recent study indicates an incidence of early-onset (ED) sepsis exceeding 0.72/1000 live births with a modality of 9.7%, rising to 15% in premature infants. Prevention depends on identifying antenatal...
risk factors for EO GBS disease or maternal GBS carriage and the administration of antibiotic prophylaxis during labour. If swabs are taken at the onset of labour, culture-based screening methods are too slow to direct intrapartum prophylaxis. Rapid screening using fluorescent in situ hybridisation (FISH) could allow more effective delivery of prophylaxis.

METHODS: 80 intrapartum GBS screens (paired rectal and vaginal swabs) were processed in parallel by conventional culture (direct and enrichment) and GBS FISH (CreaFASTS, SeaPro thermostats). FISH slides were blinded and read independently by two investigators. Results were compared with those obtained by conventional culture.

RESULTS: 24 of 80 GBS screens were positive by culture. Using this as the standard, the sensitivity of GBS FISH was 50%, with 55% specificity. The kappa value was 0.15. The preparation, hybridisation and reading took approximately 5 h per batch of samples.

CONCLUSION: In this study, the GBS FISH technique proved to have poor sensitivity, specificity and concordance, rendering it impractical for routine clinical use. In addition, processing was lengthy, labour intensive and, in its current format, would be difficult to integrate into most diagnostic laboratories. Although the sensitivity and specificity of GBS FISH was superior to that reported for rapid immunoassays, neither is suitable to direct antibiotic prophylaxis in labour. Molecular techniques, in those laboratories able to offer a 24-h service, may prove a reliable alternative.

References:
1. Heath PT, Balfour G, Weisher AM, et al. Group B streptococcal disease in UK and Irish infants younger than 90 days. Lancet 2004;363:292-294.
2. Centres for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. MMWR 2002;51:1-18.
3. Baker CJ. Inadequacy of rapid immunoassays; for intrapartum GBS screening using fluorescent in situ hybridisation (FISH) could allow more effective delivery of prophylaxis. Molecular techniques, in those laboratories able to offer a 24-h service, may prove a reliable alternative.

*P26
THE CLINICAL RELEVANCE OF MOLECULAR DIAGNOSIS OF RESPIRATORY SYNCYTIAL VIRUS INFECTION
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INTRODUCTION: Respiratory Syncytial Virus (RSV) is the commonest cause of bronchiolitis in children. Rapid assays for the identification of RSV in those presenting with a bronchiolitis syndrome are traditionally based on immunofluorescence (IF) techniques, or enzyme immunoassorbent assays. In recent years the use of polymerase chain reaction (RT-PCR) based tests has increased, with a consequent reported increase in diagnostic sensitivity. However, there is little information on whether this increased sensitivity represents detection of truly symptomatic patients or asymptomatic carriage; the specificity of RT-PCR based assays for disease is unknown.

METHODS: We identified standard clinical markers of bronchiolitis disease severity, and conducted a retrospective case notes review of 115 children from whom we received 136 nasopharyngeal aspirates (NPA) for the diagnosis of RSV disease. Both standard IF and RT-PCR for RSV were performed on all samples, as part of a prospective study for the evaluation of novel multiplexed RT-PCR assays for the detection of 9 respiratory viruses over the winter of 2002-2003.

RESULTS: Of the 136 NPA samples, 40% were RSV positive by IF and 57% were RSV positive by RT-PCR. 46% of samples came from children meeting our case definition for clinical bronchiolitis, and of these, 52% were positive for RSV by IF, and 79% were positive by RT-PCR. The specificity of IF for the diagnosis of clinical bronchiolitis was 74%, vs a specificity of 64% for RT-PCR.

CONCLUSIONS: This RT-PCR assay is 1.5 fold more than sensitive than IF for the diagnosis of RSV associated bronchiolitis, with no significant loss of specificity for disease. A patient with an RSV negative sample by RT-PCR is more likely to have an alternative diagnosis than an IF negative patient.

Reference:
1. Dingle KE, Crook D and Jeffery K. Stable and noncompetitive RNA internal control for routine clinical diagnostic reverse transcription-PCR. J. Clin Microbiol 2004;42(3):1003-11.

*P27
AN OUTBREAK OF LISTERIA MONOCYTOGENES
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In May 2003, two immunosuppressed patients with advanced malignancy were admitted to different wards of a hospital in Cardiff with pyrexia of unknown origin. Blood cultures taken at admission from both of them grew Listeria monocytogenes. The occurrence of two cases of listeriosis in a single week was unusual; only three cases had been reported in Cardiff over the last 8 years. An outbreak management team was convened to investigate. Epidemiological investigations revealed that the two patients were day cases in the hospital on the same day, 1 week prior to becoming unwell and the only link appeared to be the fact that they had eaten commercially prepared sandwiches (with different fillings) supplied by the hospital. Further investigations were undertaken. 8 sandwiches, (with various fillings) were randomly selected from the hospital and sent for microbiological testing. Listeria monocytogenes was found in all 8 sandwiches, though the counts were within acceptable levels according to PHLS guidelines. Serotyping showed the 2 patient isolates and the sandwich isolates were indistinguishable (serogroup 1/2, AFLP type XI and phage type Y). These were the first listeria isolates of this type in the UK in 2003. The hospital sandwiches were identified as the probable source of the outbreak and immediate action was taken to prevent further cases of listeriosis.

This outbreak raises issues regarding:
1. The risk of food where widespread contamination with listeria species has occurred, although at levels in individual items that are considered acceptable;
2. Policies regarding the provision of food in hospitals from external suppliers for immunosuppressed patients.

*P28
BACTERAEMIA PREDICTION IN EMERGENCY MEDICAL ADMISSIONS: ROLE OF C-REACTIVE PROTEIN
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On admission, unwell medical patients have a variety of investigations performed. For example, blood cultures, results from which take days, are widely performed as isolation of
significant organisms may guide investigation and therapy, and defines a group of patients with severe infectious disease. Other investigations, such as C-reactive protein (CRP) and differential white count results, are available rapidly. We were interested in how the results of these rapid investigations correlate with bacteraemia, and how best to combine rapidly available results in order to detect severe community acquired illness.

To address this, we studied a cohort of 6234 patients admitted from the community, who had clinical suspected infection, as judged by the taking of blood cultures. The demographic characteristics of the Cohort and the blood culture isolates obtained have been previously described. We show the quantitative relationships between CRP concentrations added little to the information provided by neutrophil and lymphocyte counts. If one excludes cases of neutropenia (neutrophils <1 x 10^9/L), then the risk of bacteraemia rises continuously as neutrophil count rises and CRP increases: no "cut off" value is evident. Risk also increases as lymphocyte counts decline, as we have previously described. In the prediction of community acquired bacteraemic illness, in the cohort studied, CRP concentrations added little to the information provided by neutrophil and lymphocyte counts. These data should assist assessment of bacteraemia likelihood in patients admitted from the community.

Reference:
1. Wyllie DH, et al. J. Clin Path 2004;57(9):950-5.

P29 PREVALENCE OF FUSOBACTERIUM NECROPHORUM IN THROAT SWABS SUBMITTED TO A HOSPITAL LABORATORY
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OBJECTIVES: Fusobacterium necrophorum is well established as the cause of Lemierre's syndrome. However it is much less clear how commonly Fusobacterium necrophorum can be isolated in patients with symptoms of signs of throat infection. Other objectives included calculating the age and sex distribution of patients producing positive isolates and examining any epidemiological relationships to Lemierre's syndrome.

METHOD: Five hundred consecutive throat swabs were screened specifically for Fusobacterium necrophorum using Fastidious Anaerobe Agar (FAA) with vancomycin and nalidixic acid. The FAA plates were incubated in uninterrupted anaerobic conditions for 5 days. Suspicious colonies had a Gram stain performed looking for Gram-negative pleomorphic rods. These colonies were then subjected to a battery of confirmatory tests for Fusobacterium necrophorum, which included MID8 Mast Ping identification, lipase production on egg yolk agar, bile susceptibility and RAPID ANA biochemical testing. The patient characteristics of all the throat swabs tested were entered into a database.

RESULTS: In this study the prevalence of Fusobacterium necrophorum in throat swabs was 3%. (15 out of 500 patients). None of these patients went on to develop Lemierre's syndrome. Out of the 15 patients with positive throat swabs for Fusobacterium necrophorum, 14 were female. 68.9% of the total patients in the study were female. The Fusobacterium necrophorum isolates were found most commonly in teenagers and young adults. The average age of patients with positive isolates was 24.7 years compared with the average age of all patients in the study of 35.9 years. Of the 13 patients producing positive isolates for which clinical details were known, 7 had a history of recurrent sore throats.

CONCLUSIONS: Fusobacterium necrophorum was found in a small but significant proportion of patients. The age distribution of patients producing positive isolates matched what is found in Lemierre’s syndrome. However the predominance of females producing positive isolates is in marked contrast to the sex distribution in Lemierre’s syndrome where the male:female ratio is approximately 2:1. This discrepancy may be at least partly explained by socio-cultural factors such as males presenting late or not at all to their GP with sore throat thus allowing disease progression. On the basis of these prevalence results, we suggest that diagnostic laboratories should be routinely looking for Fusobacterium necrophorum in throat swabs.

P30 METRONIDAZOLE RESISTANT BACTEROIDES FRAGILIS ASSOCIATED WITH CLINICAL TREATMENT FAILURE
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Although, there have been several reports of the emergence of metronidazole resistance in anaerobes, most laboratories still use sensitivity to a metronidazole disc for preliminary identification of anaerobes in mixed culture. Metronidazole is also widely used as first line therapy in suspected or proven cases of anaerobic infections.

We describe a case of a pelvic abscess caused by a metronidazole resistant Bacteroides fragilis resulting in treatment failure. The reference lab confirmed the isolates as B. fragilis by PCR-restriction fragment length polymorphism (RFLP) and the minimum inhibitory concentration was determined to be 32 mg/L. The nimA gene, which is associated with metronidazole resistance, was identified in this strain.

We discuss the potential implication of identifying anaerobe on the basis of metronidazole sensitivity and also need to perform sensitivity studies on anaerobes.

P31 COMPARISON OF A RAPID PROTOTYPE MRSA SCREENING TEST (BACLITE™ MRSA) TO CURRENT MICROBIOLOGICAL METHODS
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BACKGROUND: The aim of this study was to compare a rapid (5 h) prototype test for the detection of methicillin resistant Staphylococcus aureus (MRSA) direct from screening swabs, to current Health Protection Agency (HPA) standard operating procedures. The prototype test uses a unique microbial marker called adenylate kinase (AK) to replace the current ‘visual’ end point detection. AK catalyses the equilibrium reaction ZADP → ATP, AMP and can be used as an ultra sensitive (<10 cells) indicator of bacterial presence by monitoring the ATP produced using firefly luciferase. This removes the need to incubate cultures for 24-48 h and allows the presence or absence of MRSA to be determined direct from a clinical sample in 5 h.

METHOD: Routine MRSA screening swabs were pre-processed using a commercial Swab Extraction Tube System (SETS, Roche Diagnostics) to obtain a standardised inoculum. Equal volumes of sample (30 ul) were analysed using the rapid prototype MRSA Screening Test (BacLite™ MRSA) currently under development at Acolyte Biomedica Ltd, and the results compared to direct culture and broth enrichment methods recommended in the HPA’s MRSA Standard Operating Procedure (BSOP 29/4.1): Direct culture: Mannitol salt agar with 2 mg/l oxacillin incubated at 37°C for 48 h. Broth enrichment: 7% salt nutrient broth incubated for 24 h and subcultured onto mannitol salt agar with 2 mg/l oxacillin incubated at 37°C for 48 h.

RESULTS: 570 swabs were processed in house using all 3 methods. There was close agreement between broth and plate
culture HPA methods. The overall sensitivity and specificity of the BacLite MRSA prototype assay (compared to both HPA methods) was 92.8% and 87.4%. A number of false positive results were attributed to luminometer 'cross talk' (where luminescence from a strong positive sample causes a 'false positive' in an adjacent well) and a quench reagent was introduced to mitigate this affect. Evaluation of a further 124 swabs in the presence of a quench reagent improved assay sensitivity and specificity to 94.7% and 91.4%, respectively.

CONCLUSIONS: The results of this study indicate that the prototype MRSA BacLite assay can accurately and rapidly identify the presence of MRSA in nose swabs. Further performance and user enhancements are now being undertaken and further evaluations, including other swabs types, are planned.

**P32**

EVALUATION OF THE USEFULNESS OF EARLY MORNING URINE EXAMINATION FOR DIAGNOSIS OF TUBERCULOSIS

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AIMS: Investigation of tuberculosis (TB) has mirrored its increasing prevalence. Three Early Morning Urine (EMUs) are a commonly collected for culture as part of the diagnostic process. This is a time consuming process, for both clinical and laboratory staff. We aimed to assess if use of this test is justified.

METHODS: We performed a database search of all EMU samples sent for mycobacterial culture between July 2003 and September 2004 by the Department of Infectious Diseases. Positive results were noted and the patients' medical notes reviewed to determine how the EMU result had altered their management.

RESULTS: During study period 485 EMUs (from 193 patients) were processed, of these only 11 (2.3%) were positive, from 9 patients.

CONCLUSIONS: The results of this study indicate that the prototype MRSA BacLite assay can accurately and rapidly identify the presence of MRSA in nose swabs. Further performance and user enhancements are now being undertaken and further evaluations, including other swabs types, are planned.

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**P33**

EVALUATION OF SYSMEX UF-100 AUTOMATED URINE ANALYSER IN A DIAGNOSTIC LABORATORY

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OBJECTIVES: To introduce automation for routine microbiological examination of urine samples, to replace manual microscopy and reduce the number of samples requiring culture.

METHODS: The Sysmex UF-100 analyser (Sysmex Corporation, Kobe, Japan) detects and enumerates white blood cells (WBC), red blood cells, epithelial cells, casts, yeasts and bacteria in urine samples using flow cytometry. The manufacturer recommends 111/μl WBC and 8000/μl bacteria as cut-off values. If samples are below both these thresholds they can be reported as urinary tract infection unlikely and culture not required. The validity of these cut-offs was tested by examining 1005 consecutive routine urine samples, comparing the UF-100 with manual microscopy followed by routine culture using CUED agar.

CONCLUSIONS: The Sysmex UF-100 automated urine analyser performed well in comparison with routine microscopy and culture. However, analyser cut-offs must be validated in the laboratory before it is introduced into routine use. In this study, cut-offs of 111/μl WBC and 8000/μl bacteria as cut-off values. If samples are below both these thresholds they can be reported as urinary tract infection unlikely and culture not required. The validity of these cut-offs was tested by examining 1005 consecutive routine urine samples, comparing the UF-100 with manual microscopy followed by routine culture using CUED agar.

**P34**

AN UNUSUAL CASE OF ACUTE TERMINAL ILEITIS CAUSED BY SALMONELLA VIRCHOW INFECTION

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BACKGROUND: Nontyphoidal Salmonella infection usually results in self-limiting acute gastroenteritis, with nausea, vomiting, diarrhea and abdominal pain. However, cases with severe complications such as acute terminal ileitis can be seen. Two case reports are presented in which patients with Salmonella virchow infection developed acute terminal ileitis.

Table 1

| Table 1 | Results (n = 1005) |
|---|---|
| | UF-100 cut-off value (number of bacteria/ml) |
| | WBC cut-off 111/μl |
| | 8000 | 6000 | 3000 | 1000 |
| Culture positive/UF-100 positive | 265 | 269 | 290 | 304 |
| Culture positive/UF-100 negative | 41 | 37 | 16 | 2 |
| Sensitivity | 87 | 88 | 95 | 99 |
| Specificity | 77 | 77 | 55 | 15 |
| PPV | 62 | 58 | 48 | 34 |
| NPV | 93 | 93 | 96 | 98 |
| NO. (%) urines flagged for culture | 427 (42%) | 467 (46%) | 606 (60%) | 895 (89%) |

Although there is a low positive yield of EMUs, it remains a useful tool in focused investigation of patients with a high clinical suspicion of intra-abdominal disease.
vomiting and diarrhoea the primary symptoms. Fevers and abdominal cramping are frequently reported and headache and myalgia may also occur.

**METHODS:** A previously healthy 18 year old was admitted with a 2 day history of fever, shivers and headache with intermittent severe central and lower abdominal pain. 3 days previously he had returned from a 4 month stay in Ghana. His bowel habit was unchanged, and he continued to pass formed stool. His temperature spiked up to 39 °C and an abdominal examination he was markedly tender in the right iliac fossa, but with no evidence of peritonism and with normal bowel sounds. He was commenced on ciprofloxacin and metronidazole whilst undergoing investigation for possible appendicitis.

**RESULTS:** Abdominal ultrasound examination demonstrated gross thickening of the distal small bowel (terminal ileitis) with proximal small bowel dilatation. A stool sample from the day of his admission cultured Salmonella virchow, which was sensitive to ciprofloxacin. Stool microscopy for ova, cysts and parasites was negative, as was acute and convalescent serology for Yersinia enterocolitica, Yersinia pseudotuberculosis and amoebae.

The patient’s condition improved over the next 5 days and he was discharged. A repeat abdominal ultrasound a month later was normal. At review 3 months following his discharge he remained well with a normal bowel habit.

**CONCLUSIONS:** This case illustrates a rare consequence of nonbubonial Salmonella infection-acute terminal ileitis with ‘pseudoappendicitis’, and the value of ultrasound examination in making this diagnosis. Infection with Yersinia enterocolitica or Yersinia pseudotuberculosis is a more commonly recognised cause of this condition.

**P35**

**ACIDOVARAX: IS IT A PATHOGEN OR A CONTAMINANT?**

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A 55-year-old man presented to his GP with increasing shortness of breath and orthopnoea for 2 weeks. He had undergone mitral and aortic valve replacement 20 years previously for rheumatic heart disease. He was taking long-term steroid therapy, (prednisolone 3 mg a day) for sarcoidosis type II diabetes mellitus, controlled by diet alone. On admission he was afebrile normal white cell count and C reactive protein (CRP). Trans-oesophageal echocardiogram showed significant paravalvular leak across the mitral valve and he was scheduled for a second mitral valve replacement. He was converted from warfarin to intravenous heparin. On day 18 of his admission he developed diarrhoea, a pyrexia of 39 °C and became hypotensive. His CRP rose to 152 g/l, and his renal function deteriorated. Repeat echocardiogram did not show any evidence of infective endocarditis. Non-lactose fermenting, oxidase negative, aerobic Gram-negative rods were isolated from four sets of blood cultures taken 2 days apart. The organism appeared susceptible to ampicillin, cefalosporins, ciprofloxacin, aminoglycosides and carbapenems by disc diffusion testing but could not be identified biochemically by routine methods.

Chest X-ray, abdominal X-ray and ultrasound abdomen did not show any focus of infection and his peripheral intravenous catheter site was presumed to be the portal of entry for this organism. The patient was treated with ciprofloxacin for 7 days and made a good recovery. The mitral valve replacement was carried out 3 days after completing his course of ciprofloxacin. He is currently doing well 6 months post surgery. The reference laboratory identified the organism as Acidovorax species by gas chromatography of cellular fatty acids. Our case proves the pathogenic potential of this organism in a clinical setting. We grew it from four separate blood cultures taken over 2 days in a patient with clinical and biochemical evidence of sepsis. This is the first documented case of sepsis due to Acidovorax.

**P36**

**ARE LEUCOCYTE ESTERASE DIPSTICKS USEFUL IN THE DIAGNOSIS OF SPONTANEOUS BACTERIAL PERITONITIS?**

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**OBJECTIVES:** The gold standard for the diagnosis of spontaneous bacterial peritonitis (SBP) is the presence of > 250 polymorphonuclear leukocytes (PMN)/µL in ascitic fluid (1). When the diagnosis is suspected, this involves performing an urgent cell count manually, which is time consuming and laborious. SBP is a life-threatening condition which requires prompt diagnosis and treatment. A few studies have suggested the use of urine dipsticks as a suitable alternative to cell counts to diagnose SBF. We, therefore, evaluated the use of leukocyte esterase (LE) dipsticks as a rapid and effective bedside method to diagnose SBP.

**METHODS:** Ascitic fluid samples from acutely unwell patients with chronic liver disease were included in the study. Laboratory cell counts were performed using the Fast-Read counting chamber followed by routine culture. Samples with cell counts > 250 PMN/µL were also cultured in blood culture bottles. The same samples were also tested by an automated Aution analyser using Uriflet S strips. Each sample was tested for the presence of LE, blood and nitrate being read spectrophotometrically.

**RESULTS:** One hundred and thirty ascitic fluid samples from 80 patients were studied. Seven samples (from 6 patients) satisfied the criterion of SBP by cell count. Of these samples, 6 also had a positive LE test (range 25–500 leukocytes/µL). The sensitivity and specificity of this test was 85.7% and 93.5%, respectively. The positive predictive value was low (42.9%), but the test had an excellent negative predictive value of 99.1%. The detection of blood or nitrate did not assist in the diagnosis of SBR. In 7 patients ascitic fluid was culture positive (8.8%). However, in 3 patients in whom the manual cell counts were not diagnostic, the culture results may have been due to contamination.

**CONCLUSIONS:** The use of an LE dipstick in ascitic fluid samples is a rapid and reliable diagnostic method to exclude SBP. It can be used both in the laboratory and at the bedside. As majority of the ascitic fluid samples have cell counts < 250 PMN/µL, the use of LE dipsticks will reduce laboratory workload, especially out-of-hours. However, all LE positive samples need to be confirmed by traditional cell count microscopy and culture. Previous studies which used LE test in ascitic fluid using dipsticks from different manufacturers has produced similar negative predictive results.

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**P37**

**AN OUTBREAK OF STREPTOCOCCUS PYOGENES INFECTION IN SHEFFIELD**

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Over a 14-day period at the end of February 2004, 3 adults with severe, invasive group A Streptococcus (GAS) infection were
admitted to hospitals in Sheffield, UK. All were community-acquired and in non-intravenous drug users. One patient presented with necrotising fasciitis of the hand after a trivial injury, another with a short history of dry cough and malaise, the third presented to his GP with a swollen knee 2 days after a transient sore throat. The latter two patients developed septic shock and died within 24 h of admission. The cases were notable as only five adults were seen with GAS bacteraemia in Sheffield in the first 3 months of 2003.

Review of public health information and laboratory data suggested that this might be part of a more widespread problem in the community. In response, the local Consultant for Communicable Disease Control (CCDC) triggered an alert cascade. An e-mail was issued to all Sheffield General Practitioners warning them to be vigilant to the manifestations of severe streptococcal sepsis, to send bacterial throat swabs from patients with sore throats and to have a lower than usual threshold for administering antibiotics. This enhanced awareness promptly led to a noticeable rise in the total numbers of swabs received, however the percentage positivity of GAS from throat swabs was also increased, which was sustained over a 16-week period. Analysis of data from the outbreak period revealed a marked increase in the percentage positivity compared to the previous year. Isolates of those with severe disease showed a high proportion of mucoid M18 strains, however serotyping failed to identify a predominant M type amongst other strains.

We present data from the outbreak, discuss the role of the laboratory in identifying outbreaks of GAS disease and the public health response. It highlights the need for close liaison between microbiologists, infectious diseases and public health in the management of local outbreaks of infection.

P38
A COMPARISON OF POST OPERATIVE AND PRIMARY DISCITIS
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OBJECTIVES: To compare primary discitis and post-operative discitis in terms of symptoms, microbiological diagnosis, management and outcome.

METHOD: A retrospective case note analysis. Chi square test and Students t test were used in statistical analysis.

RESULTS: Overall 70 patients were identified over a period of 5 years from 1999. Primary infection accounted for 53 (76%), post-operative for 17 (24%). 51% of primary infections had premorbid factors compared to none of the post-operative patients.

| Biochemical/symptoms of infection | Post operative | Primary |
|----------------------------------|----------------|---------|
| MRI changes                      | 17 (100%)      | 53 (100%)|
| Back Pain                        | 17 (100%)      | 53 (100%)|
| Increased CRP                    | 15 (88%)       | 49 (92%)|
| Neurological symptoms            | 9 (53%)        | 34 (64%)|
| Systemic symptoms                | 3 (18%)        | 17 (32%)|
| Increased Wcc                    | 5 (29%)        | 22 (42%)|

The mean CRP at diagnosis was significantly higher in the primary infection group (107 (CI 84–130.6)) than the post op group (57.7 (CI 16.5–91.8)), \( p = 0.04 \). There was no difference in the time to resolution of CRP following treatment between the two groups. 9/17 post-op patients had biopsies for culture in the post-op group. 4 were culture positive. 8/17 had blood cultures and none were positive.

39/53 patients with primary infection had biopsies for culture, 20 were culture positive. 45/53 had blood cultures, 17 were positive. A wider variety of organisms were found. Significantly more patients with primary discitis were either blood culture or biopsy culture positive (58%) vs post op infections (24%) (\( p = 0.025 \)).

There were no significant differences in antibiotics used or length of time on antibiotics between the groups.

4/17 of the post-op patients had further surgery and 19/53 had surgery in the primary infection group.

Of those followed up there were 2 deaths in the primary group, 45% had persisting neurological symptoms and/or pain in the primary group vs 47% in the post-op group.

CONCLUSIONS: Post-op and primary discitis have similar presentations with symptoms of back pain and raised CRP in most cases. Primary discitis patients are more likely to have premorbid factors. The CRP is higher in those with primary discitis and patients were more likely to have positive cultures reflecting a greater systemic upset with more bacteraemia. A wider variety of organisms was found in primary discitis. However the treatment and outcome did not vary significantly between the two groups.

P39
OSTEOARTICULAR TUBERCULOSIS IN SHEFFIELD
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INTRODUCTION: Osteoarticular tuberculosis is uncommon, representing around 1-5% of all cases of tuberculosis. 60% of cases involve the spine, while peripheral joint infection is less common and tends to involve single or few large joints in an asymmetrical pattern. Here we present four cases of peripheral tuberculosis arthritis, three adults and one child, all of whom have presented to our service over the past year.

FINDINGS: The joints involved were elbow (two cases), ankle and shoulder. In all cases, swelling was insidious in onset, with pain in three out of four cases. All but one case had a tender effusion; the fourth had demonstrated synovial thickening without pain. All had concomitant extra-articular tuberculosis (two cases asymptomatic pulmonary, one case pulmonary and peritoneal and one case granulomatous myositis at another site), although two patients had no systemic symptoms such as weight loss, fever or sweats. Mycobacterium tuberculosis was cultured from joint fluid or synovial biopsy in three out of four cases; in the fourth, a bone biopsy showed non-specific inflammation. All four cases were from ethnic backgrounds where tuberculosis prevalence is higher than in the indigenous white population, and three had a history of tuberculosis contact. Despite this in one of the cases, the diagnosis was delayed for 5 months. All four patients received standard antituberculous therapy without surgical intervention. Three out of four patients made a full recovery in terms of joint function; one patient is currently on therapy and has had significant improvement in her joint symptoms but with mild residual limitation of range of movement.

CONCLUSIONS: Tuberculosis of peripheral joints is uncommon but should be considered in any patient with subacute joint pain and/or swelling, particularly if there is an epidemiological link. Joint symptoms may be the initial presentation of disseminated tuberculosis with the potential for transmission to others. Delayed diagnosis can lead to progressive bony destruction which may be irreversible, particularly in adults. Early treatment with antituberculous therapy alone usually leads to complete resolution and surgery is only required in severe joint deformity.
**WOUND BOTULISM IN SOUTH YORKSHIRE**

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Wound botulism in intravenous drug users (IVDUs) is an increasing phenomenon. No clinically recognised cases were reported prior to 1999. Numbers have increased year on year since, with 27 cases of suspected wound botulism being reported to the HPA in the first 8 months of 20041,2. Of these suspected cases, 25 were in England and 6 were confirmed, 3 from South Yorkshire and 3 from London.

Wound botulism is characterised by a symmetric, afebrile, descending, flaccid paralysis. Common early symptoms include blurred vision, drooping eyelids, slurred speech, difficulty in swallowing, breathlessness and muscle weakness. However, patients may present with respiratory failure due to rapid paralysis of respiratory muscles. There is no loss of sensation or of consciousness, which can lead to a 'locked in syndrome' if unrecognised. Management includes the administration of specific anti-toxin, wound debridement, antibiotic therapy and intensive respiratory support. Prognosis is good if the diagnosis is recognised and treatment commenced early, untreated the mortality is at least 25%.

**RESULTS:**
- All were male injecting drug users (IDUs). Three were "muscle poppers".
- Ages ranged from 25 to 33 years (median = 26 years).
- Visual disturbance (blurred or double vision) was an early feature in all presentations followed by dysarthria, dysphagia and progressive weakness.
- One patient complained of a "heavy head" and another was "unable to hold their head up".
- Respiratory arrest occurred in two patients (subsequent to their consideration as cases of botulism).
- Three patients required mechanical ventilation and tracheotomies.
- Of the three patients admitted to intensive care, the duration of mechanical ventilation ranged from 19 to 52 days (median = 45 days).
- All four patients had soft tissue abscesses. *Clostridium botulinum* (type A) organisms were identified in two patients from excised abscess material by FSML.
- Mouse bioassay performed at FSML identified botulinum toxin (Type A) in serum in three cases.
- Although all patients waived botulinum anti-toxin, the interval between admission and administration of antitoxin ranged from 1 to 3 days.

**CONCLUSIONS:**
- Wound botulism should be considered in any IDU presenting with neurological symptoms or signs.
- Early review by an anaesthetist is advisable and patients with suspected wound botulism who have not yet developed respiratory failure should initially be closely monitored in a high dependency unit of intensive care unit environment.
- Outcome is worse when there is delay in administering botulinum antitoxin with longer requirements for mechanical ventilation and intensive care admission.
- Protracted admissions to intensive care units are likely if mechanical ventilation is required and early tracheostomy insertion may be appropriate.
- Microbiological investigation of suspected cases should utilise the experience and facilities of a reference laboratory able to perform toxin testing in order to minimise delays in case confirmation.
We present three cases of wound botulism in IVDUs that were all managed in a central teaching hospital in June and July 2004. *Clostridium botulinum* toxin type A was confirmed in all cases. The first case, which presented to a local DGH, went unrecognized for 5 days, diagnosis being made on analysis of electromyography. The 2nd and 3rd cases were diagnosed and treated more promptly and experienced much improved outcomes.

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**P43**

**BOTULISM IN DRUG USERS: A REPORT OF A CASE COMPLICATED BY SERIOUS VENTRICULAR ARRHYTHMIAS**

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A 39-year-old intravenous drug user presented to A&E apparently very drowsy and was found to be in type II respiratory failure. He did not respond to naloxone or flumazenil and his respiratory myasthenia, but the effect was of much shorter duration than usually seen myasthenia. An atypical Guillain-Barré syndrome was considered but lumbar puncture was normal. He was found to have small lesions on his buttocks from skin-popping and the possibility of botulism was raised. He was treated presumptively for botulism and following clinical improvement, he was taken off the ventilator. He required re-intubation for hypercapnia and suffered a VF arrest, followed by an asystolic arrest as a consequence of potassium fluxes due to Suxamethonium administration in the setting of botulism. He was resuscitated successfully and went on to recover uneventfully. This case is one of several recent cases of botulism in the drug-using population in Scotland. The diagnosis should be considered in any drug user presenting with neurological problems or respiratory failure, and a Tensilon test may be falsely positive as in this case. Great care should be taken in the induction of anaesthesia due to the potential for life-threatening arrhythmias in association with suxamethonium administration in this setting.

**P44**

**AUDIT OF MEROPENEM & TAZOCIN RESISTANCE & ANTIBIOTIC USAGE IN A UK TEACHING HOSPITALS NHS TRUST**

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Broad spectrum antibiotics such as meropenem and tazocin are increasingly relied upon to treat infections caused by Gram negative bacteria. There has been much discussion locally as to which of these two drugs should be preferred. However, data on levels of antibiotic resistance and usage were lacking. To this end, an audit was undertaken of resistance to meropenem & tazocin amongst all Gram negative rods isolated from blood cultures in a 1600 bed Teaching Hospitals NHS Trust between 1998 and 2003. The usage of meropenem, tazocin, ceftriaxone, cefuroxime, gentamicin & vancomycin over the same period was also examined. Information was obtained from microbiology and pharmacy computer records. There were 3806 positive blood cultures which grew Gram negative rods during the study period. Meropenem resistance remained steady after an initial fall with overall level of 4.93% (range 2.79-9.03%). Tazocin resistance was 10.90% (range 5.99-17.36%) with significant variation throughout. There were no significant trends in these data. There were minor changes in the range of species resistant to these two antibiotics over time.

Usage of vancomycin tripled and meropenem & gentamicin more than doubled over the same period (p<0.000001) whereas cefuroxime usage remained steady and ceftriaxone usage fell (P<0.006) by around 2/3. Tazocin usage initially increased until a supply shortage in late 2001, then began to rise again towards previous levels.

In conclusion, between 1998 and 2003, in a single NHS Hospital Trust, despite significant increases in the usage of meropenem, vancomycin and gentamicin, there has been no significant increase in the levels of resistance to meropenem or tazocin among Gram negative rods isolated from blood cultures. This implies that concerns about increasing resistance to these two drugs are unfounded in our Trust and ought not to affect prescribing policy. However, continuous surveillance is required, both locally and nationally, to inform regular reviews of antibiotic prescribing policy.

**P45**

**ANTIBiotic PRESCRIBING ON GENERAL SURGICAL WARDS—CAN IT BE IMPROVED?**

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The inappropriate use of antibiotics is widespread and leads to the emergence of resistant organisms, causes unwanted adverse effects and places an extra financial cost on the health services. Attempts to improve prescribing habits of doctors have been largely unsuccessful.

This study was carried out in Beaumont Hospital, a tertiary referral teaching hospital in Dublin. Over four consecutive weeks current antibiotic prescriptions on three general surgical wards were assessed by the clinical microbiology team. Prescriptions were deemed inappropriate if they did not conform to hospital antibiotic guidelines; if duration of antibiotic treatment exceeded guidelines; if dose or dosage interval was incorrect, or if an alternative agent was indicated by available sensitivity results. In each instance of inappropriate treatment, a recommendation to change the prescription was made in the medical chart and a member of the surgical team was contacted with the advice. It was documented whether or not this advice was followed.

Treatment was felt to be inappropriate in 58% (100/171) of prescriptions studied. The two common reasons for treatment to be deemed inappropriate were prolonged administration of peri-operative prophylaxis and the co-administration of metronidazole with co-amoxiclav. Of the 100 cases in which a recommendation to change treatment was made, the advised change was implemented in A49. Trying to effect improvement in antibiotic prescribing in this manner was time-intensive (48 h over 4 weeks) and yielded only moderate results. Two specific areas of inappropriate antibiotic use were identified and further interventions to target these have been planned.
TRICLOSAN RESISTANCE IN STAPHYLOCOCCUS AUREUS
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Triclosan is a widely used broad spectrum biocide and is recommended for elimination of methicillin-resistant S. aureus (MRSA) carriage. MRSA isolates with reduced susceptibility to triclosan have been described; reduced triclosan susceptibility has been shown to occur through over-expression and or amino-acid changes in FabI. Our study was undertaken to determine the prevalence of reduced triclosan susceptibility in MRSA isolates, the role of fabI mutations in triclosan resistance, the potential transferability of triclosan resistance and its links with other antimicrobial resistance.

The susceptibility of 5243 S. aureus isolates to triclosan and a variety of other antimicrobial compounds were determined by agar dilution or disc diffusion methods. Direct nucleotide sequencing of PCR amplifiers was used to detect changes in fabI. Curing of resistance was attempted by growth at elevated temperature and conjugal transfer of resistance was carried out by mixed culture with recipient RH4220. 210 of the total number of isolates examined showed reduced triclosan susceptibility (MIC₅₀ 0.5 mg/L, MIC₉₀ 4.0 mg/L, range 0.06-4.0 mg/L). 74 of the isolates showing reduced triclosan susceptibility were found to be mupirocin resistant. 57(6.1%) of 942 non-MRSA isolates showed reduced triclosan susceptibility, compared with 3.6% of the MRSA isolates. Attempts to transfer triclosan resistance from twelve isolates were unsuccessful, neither was resistance cured by growth at 43.5 °C. fabI was amplified and sequenced from 16 isolates with triclosan MICs ranging from 0.25 mg/L to 4.0 mg/L. Eleven showed predicted FabI amino-acid changes involving positions 198, 204 and/or 208. Five did not show any fabI changes. Epidemiological investigations provided evidence that isolates with reduced triclosan resistance arose in patients both by cross-infection or through triclosan usage.

The number of isolates (3.9%) showing reduced triclosan susceptibility was found to be low despite widespread use of triclosan. No evidence was found of concomitant antimicrobial resistance associated with reduced triclosan susceptibility, including mupirocin resistance. Although the majority of isolates examined had amino-acid changes in FabI they were not essential for reduced susceptibility to triclosan suggesting other mechanisms may be involved. Attempts to transfer or cure triclosan resistance were unsuccessful, which suggests that plasmids were not involved in the resistance of our isolates.

THE CHANGING FACE OF INFECTION: A COMPARATIVE REVIEW OF ADMISSIONS TO A REGIONAL INFECTION UNIT IN THREE DECADES
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METHODS: 12 month retrospective admissions “audits” were previously carried out in 1980-81 and 1991 in the regional infection unit. Data on admissions was collected prospectively throughout 2001. All 3 studies have been compared, looking at type and number of admissions, length of stay and outcome.

RESULTS: Over the three decades, annual admissions rose from 605 to 1151. The proportion of cases with an infective primary diagnosis rose from 61% to 72% to 83%. The main diagnosis changed from gastroenteritis to cellulitis. HIV appeared after 1981, but remained at relatively low levels with only 35 admissions in 1991 and 23 in 2001. Malaria was diagnosed in 10 cases in 1981, 21 cases in 1991 and 15 cases in 2001. Length of stay decreased from a mean of 9.6 days to 7.44 days and then 5.52 days, while mean bed occupancy rose from 72% to 82% and 87% over the same timescale. Modality rates decreased from 3.1% to 0.7% overall, with rates in non-infective cases dropping from 6.4% to 6.0% to 1.4% and in infective cases the figures were largely unchanged at 1.1%, 2.0% and 0.6% respectively. Modality in HIV-related admissions was 22.8% in 1991 but 4.5% in 2001.

CONCLUSIONS: This comparison of three studies in three decades illustrates the changing nature of admissions over the three decades at a regional Infection Unit, which over time is seeing relatively more infective cases. It confirms the impression of clinicians that admissions are increasing generally but that length of stay is decreasing, while bed occupancy is increasing. HIV data parallels the situation elsewhere with inpatient admissions reduced and mortality greatly reduced. The insights gained can be put to practical use in planning future services and improving the quality and efficiency of the Unit.

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**P49**

REDUCED CIPROFLOXACIN SENSITIVITY IN A PATIENT WITH ELAPSED PARATYPHOID FEVER

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CASE HISTORY: A 55 year old UK resident presented with fever, abdominal discomfort and back pain 3 months after returning from India. *Salmonella enterica*, serovar Paratyphi A was isolated from blood cultures. Four days previously she had finished a 10 day course of ciprofloxacin 500 mg bd started when the same organism was isolated from stool in another laboratory and reported as sensitive to ciprofloxacin on disc diffusion testing. The blood isolate was found to be nalidixic acid resistant and have reduced sensitivity to ciprofloxacin (MIC = 0.125 mg/ml) which is likely to have contributed to treatment failure. In addition, there was clinical suspicion of vertebral osteomyelitis though this was not apparent on plain films, bone scan, CT of enhanced MRI. It was ultimately visualised with FDG-PET scanning which also found unexpected evidence of arteritis. CLINICAL LESSON: 1. Nalidixic acid testing should be performed before ciprofloxacin is prescribed for enteric fever. If an isolate is nalidixic acid resistant, MICs to ciprofloxacin should be measured and alternative treatments considered. 2. FDG-PET scanning can offer greater sensitivity for the detection of osteomyelitis over standard investigations and can identify unsuspected complications in enteric fever which could alter management.

**P50**

AN EVALUATION OF THE ARTUITS REALART MALARIA LC PCR KIT AND A SYBRGREEN BASED REAL TIME PCR ASSAY FOR THE DETECTION, SPECIFICATION, AND QUANTIFICATION OF MALARIA PARASITES IN HUMAN BLOOD

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Malaria is an important cause of fever in the returning traveller. It is usually diagnosed by microscopy of blood films. Microscopy requires specialised technical skill, and may not be as sensitive as PCR in laboratories where malaria is rarely seen. PCR can be time consuming and labour intensive. The development of fluorescence based “real time” PCR attempts to address this problem. The aim of this project was to evaluate a commercial kit detecting malaria parasites, but not speciating them, and to develop and evaluate a SYBRgreen based real-time PCR assay to identify the 4 *Plasmodium* species causing human malaria. The tests were evaluated using 100 consecutive specimens received for clinical investigation by the malaria reference unit at Westmead hospital, Sydney. Results were compared to expert microscopy.

The Artus RealArt™ Malaria LC PCR kit was shown to be sensitive and specific (97.1%, and 90.6%, respectively). Clinically useful objective estimation of the parasite load is achievable using this kit. Dissociation curve analysis can differentiate *P. falciparum*, from the other pathogenic species. The SYBRgreen based real time PCR assay had an overall specificity of 100%, and a sensitivity of 82%. Eighty of 100 evaluation specimens were correctly reported, the other 20 being false negative (twelve) or incorrectly speciated (Eight, five of which indicated possible mixed infections undetected by microscopy). Further improvement is needed before this assay could be used for reliable diagnosis of malaria.

**P51**

RESPONSE TO GENHEVAC B® IMMUNISATION, A HEPATITIS B VACCINE CONTAINING PRE-S2 ANTIGEN, IN NON-RESPONDERS TO CURRENTLY AVAILABLE UK LICENSED VACCINES

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BACKGROUND: In the UK, healthcare workers who undertake exposure-prone procedures are required to demonstrate immunity to hepatitis B virus. If they are unable to acquire immunity then the scope of their work may be limited. Antibody to hepatitis B surface antigen (anti-HBs) at a level of greater than 100 mIU/ml is considered a protective response to vaccination. Two vaccines for hepatitis B are currently licensed for use in the UK: Engerix B® (GSK) and HBvaxPRO® (Aventis Pasteur). Both are recombinant, yeast-derived vaccines and contain S protein as their antigen. GenHevac B® (Aventis Pasteur) is a cell-derived vaccine and contains both pre-S2 and S antigens. It is widely used in France, and is available in the UK on a named-patient basis.

METHODS: A retrospective case note and database review of patients prescribed GenHevac B® within our unit. All patients had previously failed to show adequate immunological response to both UK licensed vaccines, and had no serological evidence of current or previous hepatitis B infection. The vaccination regime consisted of 20 mcg doses given intramuscularly at 0, 1 and 2 months with anti-HBs titres rechecked after approximately a further 3 months.

RESULTS: 31 patients had received GenHevac B®, and all had completed a 3-close course. 3 (10%) were lost to follow-up prior to having their anti-HBs levels rechecked. Of the remaining 28 patients 16 (57%) showed a detectable increase in anti-HBs, and 10 (36%) developed anti-HBs titres of greater than 100 mIU/ml, indicating protective immunity.

CONCLUSIONS: Non-responders to immunisation against Hepatitis B with Engerix B® and HBvaxPRO® may show a useful response to GenHevac B®, a pre-S2 antigen containing vaccine available in the UK on a named-patient basis.

**P52**

CHARACTERISATION OF MENINGOCOCCAL INTERACTIONS WITH MACROPHAGES USING A DIFFERENTIATED TRANSFORMED CELL LINE

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BACKGROUND: Investigation of bacterial interactions with macrophages is limited by the lack of readily available differentiated cell lines. In an effort to limit the requirement for using primary cells such as monocyte-derived macrophages (MDM) we have used a recently described protocol to differentiate U937 cells and studied the interaction of these cells with meningococci.

METHODS: U937 were differentiated using PMA (dU937) and results compared to those obtained with MDM. Cells were
infected with *Neisseria meningitidis* type B. Internalisation of bacteria was assessed by immunohistochemistry, intracellular viability determined by antibiotic protected killing assay, and apoptosis determined by DAPI staining for nuclear fragmentation. Mitochondrial membrane permeabilisation (MMP) was measured by JC-1 staining and flow cytometry.

**RESULTS:** In comparison to untreated U937, dU937 developed a differentiated adherent phenotype with increased nuclear to cytoplasmic ratio. dU937 phagocytosed meningococci with similar efficacy to MDM: adherent bacteria per cell, dU937 vs. MDM (7.4 ± 6.25 vs. 20.3 ± 17.87, p > 0.05, mean ± SD), internalised bacteria per cell (2.9 ± 4.817 vs. 10.9 ± 14.33, p < 0.05). dU937 were also able to kill internalised bacteria: during a 20 h incubation there was a 99.3% decrease in bacterial viability. dU937 demonstrated low levels of constitutive apoptosis, as do MDM. Following infection With meningococci there was no evidence of host-mediated macrophage apoptosis in either dU937 or MDM and MMP was not apparent. However, despite lack of p53, dU937 did demonstrate inducible apoptosis when exposed to positive controls or to meningococci mutants known to induce macrophage apoptosis: % apoptosis, wild-type vs. mutant: dU937 vs. MDM (1.1 ± 1 vs. 8.4 ± 2.1, p = 0.02).

**CONCLUSION:** dU937 are a useful model with which to study host pathogen interactions involving macrophages. Initial studies demonstrate these cells are able to phagocytose and kill meningococci. Despite altered expression of certain apoptosis regulatory proteins they are susceptible to apoptosis during host defence responses.

**P54**

**EPIDEMIOLOGY AND SENSITIVITY PROFILES OF CANDIDAEMIA IN NORTH MANCHESTER GENERAL HOSPITAL OVER A 5 YEAR PERIOD**

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**INTRODUCTION:** With increasing use of broad-spectrum antibiotics in hospital practice, the incidence of candidaemia has been rising over time. We reviewed all cases of candidaemia in our institute from 1999 to 2003 looking at changes in incidence, modality and antifungal sensitivity.

**MATERIALS AND METHODS:** Cases were identified from the microbiology laboratory database. We reviewed all patient hospital records and calculated the annual incidence and mortality rate. We compared the antifungal sensitivity and patient outcome in each candida subspecies.

**RESULTS:** A total of 73 cases of candidaemia were identified during this 5 years period. The median patient age was 66 years (range 16 to 89). There were 32 male and 41 female patients. *Candida albicans* was identified in 34 cases (47%), followed by *C. tropicalis* in 16 (21%), *C. glabrata* in 12 (16%), and *C. parapsilosis* in 5 (7%). *C. lusitaniae* in 3 (4%) and *C. guilliermondii* in 1 (1%).

Remaining two cases were non-*C. albicans* species but were not further categorised. The annual incidence rate has doubled from 28.4 /100,000 admissions in 1999 to 55.5 /100,000 admissions in 2003. Between 2000 and 2001 *C. albicans* was more prevalent, however in 1999, 2002 and 2003 non-*C. albicans* was more prevalent. The overall modality rate for candidaemia was 48% (35/73). All the *C. albicans* were sensitive to amphotericin B and 93.9% to fluconazole. On the other hand, non-*C. albicans* were 94.6% sensitive to amphotericin B but only 51.4% to fluconazole.

**CONCLUSIONS:** The incidence rate of candidaemia has increased over time. Given that non-*C. albicans* were more common and highly resistant to fluconazole in our hospital, we are more inclined to use amphotericin B as the empirical therapy for candidaemia in particular very ill patients until definite antifungal sensitivities are available.

**P55**

**PERSISTENT TRICHOSPORON ASAHII BLOOD-STREAM INFECTION IN A NON-CANCER PATIENT RECEIVING COMBINATION ANTIFUNGAL THERAPY.**

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**CASE HISTORY:** Invasive infection with *Trichosporon* species is unusual in patients without malignant disease. We report persistent bloodstream infection, despite removal of probable sources of infection, in a trauma patient. A 71 year old man with a history of non-insulin dependent diabetes mellitus sustained crush injuries to his abdomen, pelvis and lower limbs in a farming accident. Following surgery, he
rapidly developed metabolic acidosis, coagulopathy and acute renal failure requiring haemodialysis.

On hospital day 4, blood cultures grew Enterobacter cloacae. He was commenced on ciprofloxacin and gentamicin to which meropenem was later added. In response to continued pyrexia despite maximal antibacterial therapy, liposomal amphotericin B 500 mg daily was added on day 16 of his admission. Blood taken for culture on the fourth day of amphotericin B therapy became positive after 72 h of incubation with a germ-tube negative yeast, later identified as Trichosporon asahii.

The patient had received 7 days treatment with liposomal amphotericin B, to which the echinocandin caspofungin was then added. Ten days after the first isolation, on the 14th day of antifungal therapy, a second blood culture yielded Trichosporon asahii. Central venous catheters were exchanged regularly; notably all had been exchanged concurrently on days 6 and 21 in response to persistent pyrexia and blood culture isolates.

Thirty-two days following admission the patient died as a result of severe systemic inflammatory response syndrome and multi-organ failure. At autopsy there were no findings supportive of invasive fungal disease.

**CLINICAL LESSON:** We believe this is the first report of Trichosporon asahii blood-stream infection in a critically ill, non cancer patient in the UK. Our patient had persistent bloodstream infection, despite removal of probable sources of infection and combined antifungal therapy.

In view of this, we contend that amphotericin B cannot be considered suitable first line therapy in the treatment of invasive trichosporonosis and, consistent with available in vitro data, there is no place for caspofungin in therapy for this infection. Azole antifungals are probably the drugs of choice for Trichosporon infections. Of these, voriconazole may come to be the preferred agent although its delivery in the ICU may be limited by patients’ unreliable intestinal function and the frequent use of haemodialysis.

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**AN INVESTIGATION OF RECURRENT LABORATORY PSEUDO-OUTBREAKS OF MYCOBACTERIUM INTRACELLULARE**

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**OBJECTIVE:** To investigate an increased incidence of M. intracellulare isolates cultured at Glasgow Royal Infirmary Medical Microbiology Laboratory (GRIMML).

**METHODS:** Isolates of M. intracellulare cultured at GRIMML were identified by the Scottish Mycobacteria Reference Laboratory (SMRL) using a Polymerase Chain Reaction restriction assay, which involves PCR amplification of a 439 base pair sequence of the gene encoding the 65 kDa mycobacterial heat shock protein (hsp65) followed by restriction digestion of the PCR product using Bse11 and Hae111. Antibiotic sensitivities were determined using a semi-automated BacTec™ 460TB System. Isolates were reviewed for date of receipt, specimen type, date and order of processing and patient location. Data was assessed for epidemiological links using Microsoft Excel™ software. GRIMML standard operating procedures were reviewed for potential points when cross-contamination of specimens could occur.

**RESULTS:** Twenty-four isolates of M. intracellulare were cultured between 31st March 2002 and 31st March 2003 and 16 had an identical antibiogram. Of these, 12 had been processed on either 29/04/02, 16/09/02 or 23/09/02, suggesting laboratory pseudo-outbreaks of M. intracellulare at GRIMML. There were no other epidemiological links. Multi-use beakers of sulphuric acid and water (used during specimen decontamination) were identified as a putative source of reagent contamination. After introducing single-use aliquots of sulphuric acid and water, no further clusters of M. intracellulare with the pseudo-outbreak antibiogram, were identified.

**CONCLUSIONS:** The increased incidence of a strain of M. intracellulare resulted from contamination of mycobacterial cultures. An epidemiological investigation suggested at least three laboratory pseudo-outbreaks had occurred and a review of laboratory standard operating procedures suggested multi-use beakers of sulphuric acid or water as a possible source of reagent contamination. Contaminated sulphuric acid has not previously been implicated in pseudo-outbreaks with mycobacterial species. The assistance of a reference facility able to speciate mycobacteria and perform antibiotic sensitivity testing enabled identification and resolution of the pseudo-outbreaks.

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**FACTORS ASSOCIATED WITH MORTALITY IN A COHORT OF HCV PATIENTS**

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**BACKGROUND:** Hepatitis C infection results in long-term severe outcomes such as liver cancer and death. The exact burden of mortality has not been well researched. Most existing studies are either retrospective involving patients with liver disease resulting in biased severe outcomes or prospective with short periods of follow-up, therefore not reflecting the true severity of the infection. The pattern of mortality will also affect the treatment requirements of these patients.

**AIM:** To determine the pattern of and risk factors for mortality in a cohort of hepatitis C patients.

**SUBJECTS:** 2000 patients with hepatitis C registered in the Trent Hepatitis C study group cohort.

**METHOD:** Cox regression models (survival analyses) were used to describe and identify risk factors for mortality in the cohort.

**MAIN OUTCOME MEASURE:** Adjusted hazard ratios with 95% confidence intervals. (AHR).

**RESULTS:** 10 year survival of the cohort was 89%. HCV was responsible for 40% of all deaths lifestyle (particularly overdose) accounted for a further 22%. Causes unrelated to HCV or route of infection accounted for the remaining 38% of deaths. Predictors of mortality during follow up were increasing age AHR 17.6 (95%CI 1.9-167) for age >51 compared to those <30; severe fibrosis or cirrhosis AHR 7.5 (1.4-40) compared to no fibrosis; average ALT >100, AHR 3.2 (1.5-16.9) compared to normal ALT; past heavy drinking AHR 2.9 (0.9-9.6) compared to never heavy drinking and drug use compared to no known risk factor AHR 10.4 (1.3-84).

**CONCLUSIONS:** Many younger HCV infected patients die from their drug related problems but those who get past this phase in their life may die from their HCV infection. This supports the national strategy of case finding unrecongnised infected individuals.

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**THE EARLY-PHASE EPIDEMIOLOGY OF CTX-M TYPE EXTENDED SPECTRUM BETA-LACTAMASE-PRODUCING ESCHERICHIA COLI IN BELFAST**

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OBJECTIVES: To describe the demographics, recognised risk factors and outcomes among the first adult hospitalised patients who had infection and colonisation with ESBL-producing E. coli in a university hospital in Belfast.

METHODS: Retrospective casenote review of patients who were culture-positive between 1st January 2004 and 30th April 2004.

RESULTS: Of 44 patients identified, only 29 casenotes were available for review. The mean age was 74.6 years (range 51–94) and 72.4% of patients were female. Most (59%) patients were in a medicine or elderly care unit at the time of the positive culture. Many (48.3%) had an indwelling urinary catheter. The mean number of antibiotic-days prior to first isolation of the organism was 11.5 (range 0–28) days. Fluoroquinolones were the most commonly prescribed class of antibiotic. Half of patients had an isolate from urine only; 20% had positive blood cultures and in 10% (he isolate was recovered from an alternative sterile site. 58.6% of isolates were associated with a clinical infection; 65.5% of this group appeared to acquire that infection while in hospital. In these patients, the median duration of inpatient stay prior to onset of infection was 24 days (range 4–240). Of patients receiving antimicrobial therapy, a successful clinical outcome was achieved in 63.2% of instances. The crude 30-day mortality among patients with clinical infection was 27.6%; the attributable mortality was estimated at 20.7%. Of those patients who appeared to die as a result of the infection, the mean time from onset to death was 13 days.

CONCLUSIONS: The demographics of patients colonised and infected with this organism appears to be similar to groups associated with other multiresistant pathogens, although the proportion of patients admitted to hospital with community-acquired infections is surprisingly high. Recent antibiotic consumption was an almost universal finding, and urinary catheterisation was very common; whether these directly influence risk or are simply markers of severe illness remains to be determined.

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A RAPID DNA EXTRACTION AND RANDOM AMPLIFICATION OF POLYMORPHIC DNA METHOD FOR THE MOLECULAR TYPING OF MULTIPLE-RESISTANT METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

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Methicillin-resistant Staphylococcus aureus (MRSA) is a significant cause of nosocomial infection and an emerging problem within the community. Many MRSA isolates are multiple-resistant (MR) and the need to characterise strains rapidly to inform infection control management has become extremely important. This study investigated whether it was possible to take colonies of MRSA directly from solid media and generate a discriminatory genomic profile that could distinguish MR-MRSA within a single working day. A total of 100 MRSA isolates were typed: sixty-nine were from blood cultures collected within the University Hospital Birmingham, UK (UHB) and designated hospital-acquired (HA) MRSA. Thirty-one were samples from non-hospitalised patients sent to the UHB by general practitioners from the Birmingham area and designated community-acquired (CA) MRSA. Twenty-eight of the isolates were designated MR as a result of their sensitivity only to tetracycline, rifampicin and vancomycin. Bacterial cells were taken directly from Brain Head Infusion agar plates, washed, suspended in water and heated to 94°C for 12 min to release chromosomal DNA. This rapid method was compared to a standard phenol extraction and alcohol precipitation. The extracted DNA was subjected to random amplification of polymorphic DNA typing (RAPID) to characterise the isolates. The RAPID consisted of two separate reactions in which two arbitrary 10mer primers were used. The RAPD was optimised and tested for reproducibility, typability and discrimination. The generated profiles were analysed using GelGompel II with the band matching coefficient of Dice and UPGMA clustering to determine profile relatedness.

Ten different RAPID types were generated from the 100 isolates investigated. All 28 MR-MRSA were the same RAPD genotype. Thirty-five HA-MRSA and 29 CA-MRSA were indistinguishable, sharing the same genotype. In addition, five HA-MRSA and two CA-MRSA had unique profiles. The discriminatory capacity of the RAPID was 58% as determined by Simpson’s Index of Diversity. This study demonstrates the power of RAPID to discriminate rapidly between strains in an epidemiological setting. The method provided results within 8 h and the information obtained within such a short time frame is useful in directing adequate infection control. This could prove especially important in the control of MR-MRSA transmission in hospitals.

P60
THE PREVALENCE OF HIV-1, HEPATITIS B (HBV) AND HEPATITIS C (HCV) AMONG MEDICAL IN-PATIENTS AT QUEEN ELIZABETH CENTRAL HOSPITAL, BLANTYRE, MALAWI

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BACKGROUND: Little data are available on hepatitis B and C prevalence and co-infection with HIV-1 in Malawi. Evidence suggests co-infection with hepatitis B or C virus and HIV-1 can accelerate both diseases. In addition, this is of concern as highly active anti-retroviral therapy (HAART) is becoming widely available. The HAART combination used in the Global Fund programme is a fixed combination of 3 drugs called Triomune®. It contains nevirapine, (associated with hepatotoxicity) and lamivudine which can treat chronic hepatitis B, but can also lead to “flares” without good adherence. High prevalence of infection may necessitate prior testing for HBV and HCV, consideration of universal HIV vaccination, and re-assessment of Triomune® usage.

AIMS AND METHODS: A prospective study was conducted. Consentng adults were recruited 1 day per week over 3 months and tested for HIV-1, HBV (HBsAg) and HCV antibody. Abdominal ultrasound was undertaken if liver disease stigmata or hepatitis B infection was suspected. Results were noted to have liver disease signs and symptoms; of these, 226 patients (39% male) were enrolled with median age 35 years (range 14–80). HIV-1 prevalence was 76%, HBsAg was found in 37% and HCV antibody in 4%. Co-infection with HIV-1 and HBsAg was found in 69% (32%) while HIV-1 and HCV co-infection occurred in 5% (2%). HEIV and HCV co-infection was noted in 4% (2%), while triple infection was found in 3% (1%) patients. 38 (17%) patients were noted to have liver disease signs and symptoms; of these, 20 (53%) were HBsAg positive and 3% (8%) HCV positive. Of 53 HBsAg positive patients, 10 (19%) had evidence for parenchymal disease or cirrhosis; hepatocellular carcinoma was diagnosed in one. Two patients with HCV had evidence for parenchymal disease.

CONCLUSIONS: High HIV-1 prevalence is consistent with previous studies, but rates of HBsAg positivity and co-infection with HIV-1 are of concern. Further studies are now required to assess their
implications in the light of the Global Fund un-rolling of HAART in sub-Saharan Africa.

**P61**
FOR YEAR EPIDEMIOLOGICAL ANALYSIS OF EXTENDED SPECTRUM BETA-LACTAMASE-PRODUCING ISOLATES IN NORTH MANCHESTER GENERAL HOSPITAL

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INTRODUCTION: Extended-spectrum beta-lactamase (ESBL) producing organisms with their limited options in treatment are fast becoming a worrying issue for clinicians. We investigated the changes of epidemiology and antibiotic sensitivity profiles to ESBL organisms over 4 years period.

MATERIALS AND METHODS: We reviewed all hospital and community records in our laboratory database for ESBL-producing organisms from 2000 to 2003. ESBL-producers of *E. coli* and *Klebsiella* sp. were identified by VITEK 2 automated machine. Statistical analysis was carried out using SPSS software version 11.0.

RESULTS: A total of 632 cases of ESBL organisms were identified over this 4 years period. The mean patient age was 67.3 years (range 5 to 101). The number of ESBL organisms had increased significantly from 95 (2.0%) of 4788 isolates in 2000 to 238 (3.6%) of 6542 isolates in 2003 ($X^2$, $p<0.0001$). The commonest organism isolated by frequency was *Escherichia coli* (53.0%), followed by *Klebsiella pneumoniae* (30.9%) and *Klebsiella oxytoca* (16.1%). Specimen distribution according to sites were urine (65.3%), sputum (10.9%), wound swabs (10.3%), blood culture (5.5%) and others. *E. coli* was isolated more frequently in urine but *Klebsiella* sp. were more common in sputum and wound swabs. Blood culture ($n=5$) yielded 15 *E. coli* isolates, 15 *K. pneumoniae* and 5 *K. oxytoca*. The overall mortality rate for patients with ESBL septicaemia was 37.1% (13/35). Antibiotics susceptibility patterns for all ESBL organisms were 99.5% to meropenem, 90.9% to nitrofurantoin, 67.9% to ciprofloxacin, 58.5% to piperacillin/tazobactam, 56.4% to gentamicin and 33.8% to trimethoprim. Over the 4 years, ESBL *E. coli* demonstrated an increasing trend of resistance to ciprofloxacin, gentamicin and trimethoprim ($p<0.0001$). A total of 46 very closely-related isolates that produced a CTX-M type were differentiated by pulsed-field gel electrophoresis (PFGE). Eight of these gave an atypically large (1900 bp) promoter region PCR product (suggesting the presence of IS26) but not to nitrofurantoin, piperacillin/tazobactam and meropenem. However there were no statistically significant changes in susceptibility patterns in ESBL *Klebsiella* sp.

CONCLUSIONS: There is a steady increase of ESBL organisms in our hospital over the years. We found there were increasing resistance patterns of ESBL *E. coli* to ciprofloxacin, gentamicin and trimethoprim over time but not for *Klebsiella* sp.

**P62**
CAPSULE SWITCHING IN PNEUMOCOCCI

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The aim of this study was to assess the level of genetic diversity and investigate the relationships between capsular type and genotype in diverse disease-causing pneumococci. The isolates included a wide range of serotypes (not preselected for antibiotic resistance, disease type or patient age) submitted to a National Reference Laboratory (SMRPL). Isolates were analysed by MLST using a semi-automated protocol to determine the sequence type (ST). We analysed 252 isolates (190 blood isolates, 8 CSF isolates, 22 eye isolates, 9 ear isolates, 7 sputum isolates and 16 isolates from miscellaneous sources). These were selected initially on the basis of serogroup to include at least 5 members where available. The collection includes pneumococci from 37 serotypes submitted over the period 1996-2003. The 252 isolates contained 109 STs, 41 of these STs were new to the MLST database. Analysis of the relationships between capsular type and genotype show that whilst MLST correlates with serotyping, isolates within a serotype can belong to a number of individual clonal complexes or sequence types. We also show that isolates of the same ST can express different capsular polysaccharides i.e. display capsular switch, and that this phenomenon is observed both for capsular types commonly isolated from invasive disease and for serogroups less commonly isolated from invasive disease but which may commonly be carried asymptotically in the human nasopharynx. In conclusion, our results suggest that levels of capsular switch may be higher than previously reported. We believe this to be a reflection of the wide-range of serotypes included in our collection, which includes rare capsule types. This could have important implications for vaccine strategies.

**P63**
MOLECULAR CHARACTERISATION OF EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING ESCHERICHIA COLI FROM AN OUTBREAK IN HAMPSHIRE

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BACKGROUND: Since Autumn 2003, isolates of *E. coli* producing extended-spectrum beta-lactamases (ESBLs) have been detected from over 500 patients at the Health Protection Agency (HPA) South East Southampton Laboratory. Analysis by the HPA’s Antibiotic Resistance Monitoring and Reference Laboratory previously identified a prevalent strain that produced a CTX-M group 1 ESBL, CTX-M-15. This ‘outbreak’ CTX-M-15-producing strain contains an insertion sequence (IS26) within the beta-lactamase promoter region.

METHODS: *E. coli* isolates expressing ESBLs were identified by E-tests and antibiotic sensitivities (antibiograms) determined by the breakpoint method. Strains were genotyped by pulsed-field gel electrophoresis (PFGE) of Xbal-digested genomic DNA. ESBL production was investigated using generic PCRs for genes encoding CTX-M, SHV and TEM enzymes. Primers specific for genes encoding CTX-M enzymes of groups 1, 2 and 9 were also designed. A PCR specific for IS26 upstream of the CTX-M-15 beta-lactamase (*blaCTX-M-15*) gene was evaluated for detection of isolates belonging to the outbreak strain.

RESULTS: Sixty-five ESBL-producing isolates (cefotaxime-resistant, with or without ceftazidime resistance) were examined. *blaCTX-M* genes were detected in 58 isolates; 56 (97%) produced group 1 enzymes and two (3%) group 9 enzymes. PFGE identified 46 very closely-related isolates that produced a CTX-M group 1 ESBL. These gave an atypically large (1900 bp) beta-lactamase promoter region PCR product (suggesting the presence of IS26) and were confirmed as belonging to the outbreak strain by PCR for IS26-*blaCTX-M-15*. Non-outbreak CTX-M group 1-producing isolates yielded a typical (900 bp) beta-lactamase promoter region PCR product ($n=10$), were relatively heterogeneous by PFGE (differing from outbreak strains by at least seven bands) and yielded no product by PCR for IS26-*blaCTX-M-15*. Strains harbouring SHV ($n=3$) and TEM ($n=2$) ESBLs were also identified, together with two potential SHV/TEM co-producers.

CONCLUSIONS: An outbreak strain of *E. coli*, which produces a CTX-M-15 ESBL, is prevalent in Hampshire and isolates are
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USING A MAPPING TOOL TO INVESTIGATE THE GEOGRAPHICAL DISTRIBUTION OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN BELFAST

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OBJECTIVES: This presentation aims to use a commercially available mapping tool to investigate the distribution of MRSA isolates received from General Practitioners (GP’s) in Belfast.

MATERIALS/METHODS: We retrospectively examined clinical specimens received in Belfast Link Laboratories (two teaching hospital bacteriology laboratories) from GP’s between January 2002 and May 2004. For isolates of Staphylococcus aureus, duplicates were removed and only first episodes from individual patients were considered. MRSA samples were mapped with Microsoft® Mappoint software using GP postcodes and those of individual patients, when these were available. For those practices that generated substantial Staphylococcus aureus isolates (≥40), MRSA positivity was expressed as a percentage of total Staphylococcus aureus. We summated and charted the monthly totals of MRSA over the period of the study.

RESULTS: 6536 specimens received from non-hospital sources were included in the study. A total of 2717 Staphylococcus aureus cultures were identified once duplicates had been removed. Of these 596 were found to be methicillin resistant (21.9%). Although we received MRSA samples from almost every GP in the Belfast area, it was not surprising that the greatest concentration of isolates came from a number of large multi-doctor or multi-practice health centres. MRSA positivity for practices that generated ≥40 Staphylococcus aureus isolates ranged from 8.86% to 38.78% (mean: 21.04%). There was no significant change in our monthly totals of MRSA over this time period.

CONCLUSIONS: Mapping software can be a useful means of visually presenting microbial epidemiological data, such as antibiotic resistance, to inform public health debate and direct educational and surveillance activities in the non-hospital setting. Microsoft® Mappoint is limited by its coverage (19% for Northern Ireland, but 100% in Great Britain) and postcodes themselves may have slight inaccuracies. Our ability to accurately map MRSA is limited by incomplete patient postcode data (17% of patients in this study). Similarly, knowledge of hospital contact or recent antibiotic use might facilitate more pertinent analysis of antibiotic resistance in the community. We would recommend this technique for pathogens such as Clostridium difficile and other resistance phenotypes (penicillin resistant pneumococci, extended spectrum β-lactamases) where there is a paucity of epidemiological data in non-hospital settings.

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PENICILLUS MARNEFFEI AND HIV CO-INFECTION IN CHINA: REVIEW THE PUBLISHED LITERATURES AND REPORT A NEW CASE

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Penicilliosis marneffei is a life threatening invasive fungal infection caused by Penicillius marneffei, which has been reported predominantly from Southeast Asia and southern China. Though Penicilliosis was discovered in China very early, the disease associated with HIV infection was confirmed lately in 1999 in China. Since then, 17 cases with disseminated penicilliosis marneffei and AIDS were reported in China. The 17 cases included 13 male and 4 male with an age range from 25 to 50. The patients acquired HIV infection due to heterosexual contact and/or injecting drug using. Fever, cough, and anemia were seen in all cases. Rash and lymphadenopathy were found in 12 cases. Splenomegaly and hepatomegaly were presented in 10 and 8 cases, respectively. Oral candidiasis was the commonest complication associated with the co-infection. P. marneffei yielded from the cultures of blood, bone marrow, secretion of skin lesions, pleural fluid, and pericardial fluid. The fungus was also found in the smears of bone marrow and biopsy of lymph nodes and skin lesions. 13 cases received anti-fungal therapy using amphotericin B and/or one azole (fluconazole or itraconazole). Interestingly, fluconazole alone made two patients’ condition obviously relieve, though P. marneffei was usually resistant to the agent. Of the 17 cases, 3 was cured, 5 improved, 6 died, and 3 lost. In conclusion, unlike in Southeast Asia, penicilliosis marneffei remains a very rare opportunistic infection associated with HIV infection and is more frequently seen in HIV negative individuals in China. The disease is primarily found in Guano province, southern China. However, the disease has spread to other parts of China including Beijing, Guangdong, Yunnan, and Sichuan. Fever, cough, anemia, rash, lymphadenopathy, and hepatosplenomegaly are the common manifestations of P. marneffei and HIV co-infection. Penicilliosis is a fatal opportunistic infection in AIDS patients.

A NEW CASE: A 26-year-old policeman who resided in Guangxi Province for 3 years presented to his county hospital with a 2-month history of high fever and cough. A provisional diagnosis of pulmonary tuberculosis was made and he received anti-tuberculosis chemotherapy for 1 month but without a clinical improvement. Following admission to West China Hospital, blood and bone marrow cultures as well as bronchoscopy biopsy were positive for P. marneffei. Confirmatory serologic testing for HIV was positive. Combination therapy with amphotericin B and itraconazole was instituted and the patient made a good clinical response. Endobronchial involvement caused by this emerging fungal microorganism has rarely been described previously. Clinicians need to be aware that HIV positive patients with a history of residence in or travel to southern China and a clinical presentation suggestive of tuberculosis but responding poorly to anti-tuberculosis treatment may have penicilliosis marneffei infection.

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THE ROLE OF A RECOMBINANT ANTIGEN BASED ELISA FOR THE SERODIAGNOSIS OF ONCHOCERCA VOLVULUS

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OBJECTIVES: 18 million people worldwide are known to be infected with the filarial nematode Onchocerca volvulus, the causative agent of onchocerciasis. The usual method of diagnosis, acquisition of skin snips and microscopy for presence of typical microfilariae (mf) is invasive for patients and lacks sensitivity, especially in early infection. A sensitive and specific onchocerciasis ELISA based on the recombinant antigen OvH3 has previously been developed and tested on known mf positive patients on a research level only. In this study we used the OvH3 ELISA on clinical samples and we also examined the performance of an OvH3 ELISA implemented on a commercial analyzer.
antigen to set up and validate an onchocerciasis assay for use in a diagnostic tertiary referral laboratory.

MATERIALS AND METHODS: OvH3 antigen was produced and incorporated into an indirect non-competitive ELISA and tested against sera from recently untreated mf positive individuals from Cameroon and Guatemala. The assay was also tested against a set of definite and probable onchocerciasis patients from our hospital. To determine specificity, the assay was tested against sera from patients with Loa loa, Wuchereria bancrofti and Mansonella perstans as well as with sera from patients with intestinal nematodes and other helminth infections. Sera from travellers and expatriates who had no evidence of helminth infection were used as controls. An additional IgG4 step was performed on 35 sera from patients with confirmed onchocerciasis from Cameroon and our hospital was 78.8%, 89.4% and 75.7% respectively. The addition of an IgG4 step did not improve the performance characteristics of the assay.

DISCUSSION: We have developed a sensitive and specific onchocerciasis assay based on the recombinant antigen OvH3 which has excellent results when tested both on sera from previously untreated patients and onchocerciasis patients diagnosed in our hospital, most of which had received some ivermectin treatment prior to serological testing. These results show an improvement on our current filaria ELISA which has high sensitivity for the diagnosis of onchocerciasis but which has a high false positive rate, especially with patients infected with Strongyloides stercoralis.

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ANTI-BODY RESISTANCE OF COMMUNITY-ASSOCIATED STAPHYLOCOCCUS AUREUS AND MOLECULAR CHARACTERIZATION OF COMMUNITY-ASSOCIATED METHERCILLIN-RESISTANT S. AUREUS FROM SEOUL, KOREA

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An epidemiologic investigation was performed to analyze profiles of resistance of community-associated Staphylococcus aureus to antibiotics, and to assess spread and genotype of community-associated methicillin-resistant S. aureus (CA-MRSA). S. aureus strains were isolated from nasal swab of 3096 healthy volunteers from January 2003 to December 2003 in Seoul, Korea, and their susceptibilities to anti-staphylococcal drugs were studied by the antibiogram method. The evolutionary relationship between CA-MRSA and hospital-acquired MRSA (HA-MRSA) was elucidated by pulsed-field gel electrophoresis (PFGE) analysis of Smal macrofragments as well as staphylococcal cassette chromosome mec typing by PCR analysis. The resistance rates of the 781 isolates to penicillin, erythromycin, gentamicin, tetracycline, cephalothin, oxacillin (MRSA) were 91.8%, 14.2%, 9.3%, 8.2%, 4.0%, and 3.8%, respectively. Also the resistance rates to clindamycin, ciprofloxacin, and sulfamethoxazole/trimethoprim were 2.6%, 0.8%, and 0.6%, respectively. However, none of the isolates was resistant to rifampin, nitrofurantoin, ticlopinin, and vancomycin. PCR analysis exhibited that all 30 MRSA isolates contained a macA specific gene and many of them contained pB110 sequence. In contrast to the results of similar studies, PFGE revealed that most of the CA-MRSA isolates did not show a common pulsed field type observed in HA-MRSA infections in Korea, and harbored several variants of staphylococcal cassette chromosome mec type I, II, and IV suggesting that the strains were not closely linked to the previously known isolates.

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CHYLOUS ASCITES COMPLICATING INTRA-ABDOMINAL TUBERCULOSIS IN A PATIENT WITH HIV/AIDS

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A 42 year old female woman of South African origin is described, who originally presented with fever, weight loss, anaemia and vomiting. Imaging studies revealed marked intra-abdominal lymphadenopathy, a pancreatic cyst, peri-pancreatic inflammation, hypodense lesions in liver and spleen, and bowel wall thickening. She was found to be HIV-1 positive (CD4 count 49 × 10^9/L, HIV VIL 5.27 log copies/ml). Lymph node biopsy was not possible for technical reasons. Empirical anti-tuberculous chemotherapy was commenced for suspected intra-abdominal tuberculosis. Mycobacterium tuberculosis was subsequently isolated (from urine sample).

After a stormy course, including persistent upper small bowel obstruction (managed conservatively), pancreatitis, severe nutritional impairment and secondary fungal peritonitis, she eventually improved and was discharged from hospital after an 8-month admission. However, 2 weeks later she re-presented with marked abdominal distension. Paracentesis revealed milky white fluid consistent with chylous ascites, which has been recurrent despite regular drainage and other therapeutic interventions. Chylous ascites in an unusual condition, most commonly associated with intra-abdominal malignancies and after surgical intervention. Various infections, including tuberculosis, have occasionally been reported as the cause. There are very few reports of chylous ascites in patients with AIDS, but rare cases related to lymphoma, MAC disease, KS and tuberculosis have been described. The prognosis appears to be poor and optimal management is unclear at present. The potential management options, including a medium chain triglyceride diet and the synthetic somatostatin analogue octreotide, will be discussed further in this presentation. Our patient’s response to these measures will also be described.

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POST-EXPOSURE PROPHYLAXIS FOR HIV, SUPPLY AND USAGE IN MEDICAL STUDENTS GOING ON ELECTIVE PLACEMENTS

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The majority of medical students undertake a period of elective study abroad. A significant proportion of students choose electives in developing countries where the prevalence of HIV
is considerably higher than in the UK; often in exposure prone specialties such as surgery, trauma and obstetrics and gynaecology.

AIMS: To assess the current information that is available to Manchester University medical students regarding their elective, focussing particularly an HIV post-exposure prophylaxis (PEP).

METHODS: A questionnaire was distributed to medical students who attended a pre-elective seminar at North Manchester General Hospital (NNMGH) over a 2 year period from July 2002 to July 2004. This was completed immediately after the lecture. Students who took a supply of PEP on their elective were asked to complete a further questionnaire on their return. PEP was available to students who attended the seminar and were planning an elective to a country with an HIV prevalence of >5%.

RESULTS: 79 students completed the pre-travel and 32 students the post-travel questionnaires. The majority were planning an elective in Sub-Saharan Africa 53/77 (69%); of this group 21 had chosen exposure prone specialties. Only 16/72 (22%) of students reported receiving advice on what country and 47/69 (68%) on what speciality to choose. Health advice pre-elective was obtained from a variety of sources most commonly their General Practitioner. Following the pre-elective seminar at NNMGH 68% were aware of the 1 in 300 risk of catching HIV from a needlestick and 92% of the 1 in 1000 risk from a mucosal splash injury. All understood there was a greater than 70% risk reduction when PEP was taken.

Of the post travel respondents one student received a needle-stick injury from an HIV positive patient and two students a mucosal splash injury from HIV negative patients. Only the student receiving the needle-stick injury took PEP.

CONCLUSION: From the questionnaires returned, 3 students from Manchester Medical School had exposure incidents in the last 2 years; the true figure is likely to be much higher. Medical schools have a duty of care to ensure that students are aware of the potential health risks on their elective. We recommend all medical schools adopt a policy of educating students about their risk of catching HIV and ensuring PEP is available to them.

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OUTCOME OF ACUTE HEPATITIS C IN HIV POSITIVE MEN

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BACKGROUND: In London increasing numbers of HIV positive individuals are presented with acute hepatitis C (HCV). We describe the presenting characteristics and virological outcomes of consecutive patients attending a central LONDON HIV treatment centre. Some were treated during the acute phase following published reports showing high clearance rates in HIV negative patients treated with interferon alone (Jaeeckel et al. N Engl J Med. 2001;345:1452-7).

METHODS: Acute hepatitis C was defined as positive HCV RNA by PCR with either a) seroconversion from negative to positive HCV antibody within 1 year, b) an indeterminate HCV antibody, or c) elevated ALT > ×20 ULN with no evidence of hepatitis from other causes e.g. drugs, other hepatitis viruses. Retrospective testing of stored samples was undertaken in some cases. From 2001, patients were offered treatment with pegylated interferon for 24 weeks: non-responders (HCV RNA positive) at 12 weeks also received ribavirin.

RESULTS: Patient characteristics: Between Jan 1999 and May 2004, 55 individuals were identified; three were excluded from analysis (two with HCV antibody seroconversion outside 1 year, one newly diagnosed with follow up data <4 weeks). All were homosexual, HIV-infected males. At diagnosis of acute HCV: age mean 38 years, duration of HIV infection mean 7.3 years, CD4 count mean 464 cells/ml. 30 (58%) were on HAART. HCV genotype: type 1: 35 (67%), type 4: 8 (15%), type 2/3: 4 (8%), untypable: 5 (10%). Presentation: Investigation of abnormal LFTs performed as part of routine HIV care: 32 (61%); symptoms: 9 (17%). Outcome: 39 were not treated in the acute phase, of whom 5 (13%) spontaneously lost detectable HCV RNA over the period of follow up. Of 13 patients treated during the acute phase 9 completed treatment, 4 (31%) were responders at end of treatment (w24): 3 of 12 (25%) at w48, but 2 of the 3 relapsed after w48 (at w63 and w111).

CONCLUSIONS: There is ongoing transmission of HCV among HIV-infected, homosexual men. Most cases of acute HCV were identified through routine monitoring of LFTs during HIV care. Few patients cleared HCV RNA spontaneously, and among those treated the virological response was poor. RCTs of longer treatment with combination therapy are needed.

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SURVEILLANCE OF CHLAMYDIA TRACHOMATIS INFECTION AT THE REGIONAL GENITOURINARY MEDICAL CLINIC IN NORTHERN IRELAND

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Genital chlamydia is the most common bacterial sexually transmitted disease (STD) in the United Kingdom. This infection is often asymptomatic in female patients. The aim of the study was to a) describe the number of tests for Chlamydia trachomatis sent to a Belfast laboratory over a 3 year period (2001-2003) according to the referring source and b) carry out a descriptive epidemiology study on all patients with laboratory confirmed C. trachomatis diagnosed at the regional genitourinary medical (GUM) clinic over a 4 week period. An enhanced surveillance questionnaire was used to collect demographic data and risk factor information.

The positivity rate was 9.8% of patients tested for chlamydia infection from 2001-2003, the majority (76% of positives) were patients who attended the GUM clinic. In the four-week survey, a total of 90 patients were involved with a sex ratio of 1.3:1 males to females. The mean age range for both sexes was 25 years (range 16-45 years). Females were mostly in the 16-25 age bracket and male patients in the 18-30 years of age. Male patients were more likely to be symptomatic than females (p = 0.0007). Most patients were heterosexual (96.7%). The average number of sexual partners was 2 in the previous 3 months (median of 1) and 4 in the previous 12 months (median of 2). Barrier protection was used by 41.4% of patients and 14.9% used the oral contraceptive pill alone. Concomitant STIs were uncommon (16.9%) with warts occurring most frequently. This study highlights the need for a chlamydia screening programme in Northern Ireland especially for young female patients who are likely to be asymptomatic and sexual health education with regards to usage of barrier methods for prevention of STD.

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SARS CORONA-VIRUS: THIN-SECTION ELECTRON MICROSCOPY

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In early 2003, the first pandemic of the 21st century emerged in southern China. Within 3 months more than 8000 cases of Severe Acute Respiratory Syndrome (SARS) had been recognised in 32 countries. Unprecedented international scientific collaboration led to rapid identification of the previously unknown pathogen, named SARS-associated corona virus (SARS Co-V), with development of diagnostic tests within weeks of the outbreak being declared. We present pictures of thin-section Electron Microscopy of the SARS virus, with a brief discussion of the similarity and differences to other coronaviridae.

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AN INFECTIVE CAUSE OF BLINDNESS REQUIRING IMMUNOMODULATORY TREATMENT
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In the summer of 2004 the Department of Infectious diseases in Sheffield was involved in the care of two cases of acute retinal necrosis (ARN). This is a condition associated with reactivation of infection with members of the herpes family of viruses and frequently has a poor prognosis in terms of visual recovery. This rare condition accounts for 1.5-5.5% of all cases of uveitis, and is complicated by retinal detachment in 60-70% of cases. Both cases were diagnosed speedily, upon recognition of the typical eye findings of a hazy cornea with multiple keratic precipitates, numerous cells in the anterior chamber, occlusive retinal vasculitis and areas of peripheral retinal necrosis.

Treatment was begun with intravenous aciclovir and topical atropine and steroid drops. High doses of oral steroid, and aspirin were commenced on day 3 as per accepted guidelines, but, in both cases clinical improvement did not begin until the dose of steroids was significantly increased.

Both cases were secondary to Varicella zoster reactivation as proven by positive PCR of anterior chamber fluid, in the context of being otherwise healthy individuals with a history of childhood chickenpox and IgG positive, IgM negative serum. Neither had dermatological manifestations of shingles. Both cases were HIV negative and were otherwise immunocompetent.

The first case went on to develop involvement of her other eye 3 weeks after discharge, and subsequently has developed the well-recognised complication of retinal detachment. The second has made a good recovery to date...

LEARNING POINTS: These cases illustrate the immune-mediated nature of this very disabling and frustrating condition and the important role of immunomodulatory drugs in its treatment. The use of methyl prednisolone in the treatment of this condition has not been documented previously, and it would seem that the dose of steroid was critical in effecting clinical improvement in the acute context.