The British Society for Antimicrobial Chemotherapy

SPRING MEETING 2013

Gram negative, Gram positive, fungal...and beyond.

The increasing complexities of "everyday" infections.

Thursday 14 March
Royal College of Physicians, London

Programme & abstracts

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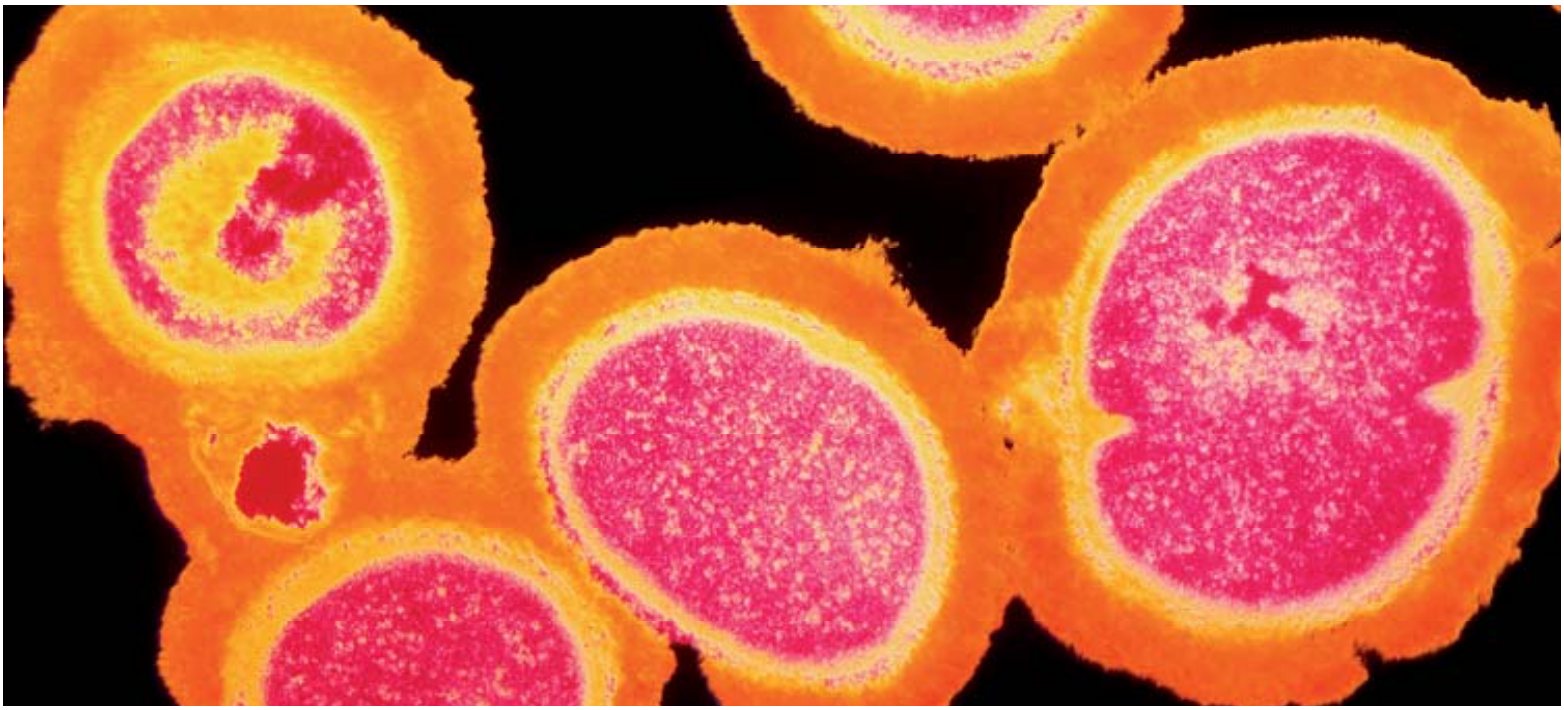

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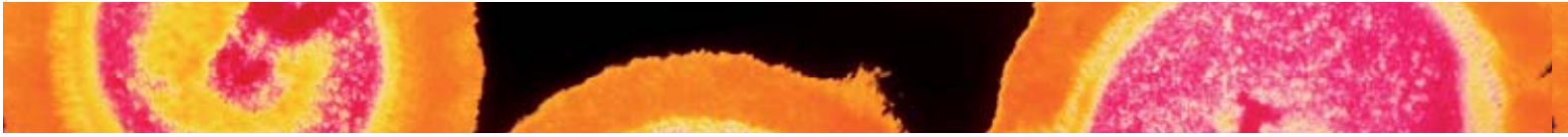

Programme

0900	**REGISTRATION & COFFEE**
0945	**Welcome & introductory remarks**

SESSION ONE
Chair: Dr Nick Brown, Cambridge

1000	**What is happening now? Epidemiology of resistance** *Professor Neil Woodford, London*
1020	**Carbapenemases in practice - lessons learnt from spread in our patch prophylaxis and first/ second line treatments** *Dr Andrew Dodgson, Manchester*
1040	**Pseudomonas in augmented care - should we worry?** *Dr Michael Kelsey, London*
1100	**COFFEE & POSTER VIEWING**

SESSION TWO
Chair: Dr Mike Cooper, Wolverhampton

1130	**Neisseria gonorrhea - the first untreatable infection?** *Professor Catherine Ison, London*
1150	**Susceptibility testing for vancomycin in staph aureus - what do we do now?** *Dr Robin Howe, Cardiff*
1210	**VRE - one difficult Gram positive after another. Treatment options for severe infections** *Dr Nick Brown, Cambridge*
1230	**BSAC AGM / LUNCH & POSTER VIEWING**

SESSION THREE: Free papers
Chair: Dr Nick Brown, Cambridge

14.00	**Increase in transrectal ultrasound guided prostate biopsy associated infection; is a change in antimicrobial prophylaxis the solution?** *Dr Cliodhna Ni Bhuachalla, Dublin*
14.10	**Antibiotic Management of Neutropenic Sepsis at The James Cook University Hospital** *Dr Katherine Watson, Middlesborough*
14.20	**Optimisation of combination therapy for treatment of Pseudomonas aeruginosa** *Dr Alexandra Cochrane, Bristol*
14.30	**Investigation of the antimicrobial activity of essential oils of culinary and medicinal herbs and spices against selected gastrointestinal pathogens** *Dr Paula Row, Swansea*
14.40	**The Perils of Medical Tourism** *Dr Theodore Gouliouris, Cambridge*
14.50	**Q&A**

SESSION FOUR
Chair: Dr Mike Cooper, Wolverhampton

1500	**Directed therapy for fungal infections - latest advances** *Professor Rosemary Barnes, Cardiff*
1530	**New uses for old agents** *Dr Kieran Hand, Southampton*
1550	**Closing remarks**

Free paper abstracts

Increase in transrectal ultrasound guided prostate biopsy associated infection; is a change in antimicrobial prophylaxis the solution?

Authors: Ni Bhuachalla C1, McNamara E2, Carroll A2, Lynch T1, Boyle B1
1. St James's Hospital, Dublin 8, Ireland.
2. Public Health Laboratory HSE, Ballyfermot, Dublin 10, Ireland.

Background: Transrectal ultrasound guided prostate biopsy (TRUS) is part of surveillance and diagnostic workup for prostate cancer. Studies report post biopsy infection rates of 0.5- 1% for bacteraemia (BSI) and 1- 3% for UTI. International guidelines recommend a fluoroquinolone (FQ) as 1st line prophylaxis pre TRUS biopsy. Approximately 600 TRUS biopsies are conducted annually in our centre. Despite antimicrobial prophylaxis with FQ and gentamicin, an increase in post biopsy infection rates was noted in 2012 which prompted a change of prophylaxis regimen.

Objectives: To identify all patients with post TRUS biopsy infection from Jan 2010 - Nov 2012.
To review isolates and antimicrobial susceptibilities.
To review antimicrobial prophylaxis administered during this period.
To detect cases occurring after modification of prophylaxis in Dec 2012.

Methods: All TRUS biopsy cases from the study period Jan 2010 – Nov 2012 were reviewed retrospectively. Isolates were identified and antimicrobial susceptibilities performed using Vitek 2 system (Biomerieux, Marcy l'Etoile, France). Isolates were typed by DNA macrorestriction with XbaI (R6125, ProMega, USA) followed by pulsed field gel electrophoresis (PFGE). PFGE gels obtained after electrophoresis were captured in TIFF format using a GelDoc image capture system (Bio-Rad) and compared using Bionumerics software (Applied Maths NV). Data was collected prospectively following modification of antimicrobial prophylaxis to FQ and amikacin in Dec 2012.

Results: Fifteen of 1398 patients (1%) experienced microbiologically proven post TRUS biopsy infection between Jan 2010 - Nov 2012. Six patients (0.4%) developed BSI or sterile site infection (2 BSI, 3 UTI with BSI, 1 UTI with discitis) and 9 patients (0.6%) developed UTI. No infections occurred in 2010, 1 occurred in 2011 and 14 cases occurred up to and during November 2012. E. coli was recovered in all cases. 11/ 15 isolates were FQ resistant, 4/ 10 isolates tested were gentamicin resistant and 5/5 isolates tested were amikacin susceptible. PFGE of 8 available isolates from this study period (Jan 2010 – Nov 2012) demonstrated that they were distinguishable.
Prospective surveillance over 3 months following modification of prophylaxis to FQ and amikacin revealed 3 further cases of post biopsy infection, 2 BSI and 1 UTI. Both BSI isolates were FQ resistant, 1 was gentamicin resistant and both were amikacin susceptible.

Conclusion: We observed an increase in post TRUS biopsy infection in our centre between Jan 2010 and Nov 2012. Further to results of this study, review of antimicrobial resistance surveillance data and review of literature, we modified our guidelines for prophylaxis to FQ and amikacin in Dec 2012. Prospective surveillance after this modification revealed 3 cases of post biopsy infection during a 3 month period. Surveillance is ongoing and it remains to be seen whether modifying antimicrobial prophylaxis alone will impact on a potentially multifactorial increase in post TRUS biopsy infection rates.

Antibiotic Management of Neutropenic Sepsis at The James Cook University Hospital

Authors: Dr K Watson, ST1 Microbiology, Dr M Kalra, Consultant Microbiologist, The James Cook University Hospital, Middlesbrough

Introduction The National Institute for Clinical Excellence (NICE) guidelines titled Neutropenic Sepsis: Prevention and Management of Neutropenic Sepsis in Cancer Patients1 include recommendations for antibiotic therapy of suspected neutropenic sepsis. NICE recommends that all patients be offered beta lactam monotherapy with piperacillin/tazobactam as initial empiric antibiotic therapy unless there are patient specific or local microbiological contraindications. Aminoglycosides, either as mono or dual therapy are not recommended. It is also recommended that prophylaxis with fluoroquinolone antibiotics should be offered during expected periods of neutropenia to reduce the risk of patients developing neutropenic sepsis.
These recommendations differ from current antibiotic guidelines at The James Cook University Hospital (JCUH), where dual piperacillin/tazobactam and gentamicin are the first line antibiotic choice and no routine fluoroquinolone prophylaxis is used. Trust guidelines were reviewed using local data from a search of positive blood cultures taken from patients with neutropenic sepsis over the last 3 years.

Methods An APEX search of positive blood cultures for patients under the care of haematology consultants was performed. For each positive blood culture information was recorded on organism identification and antibiotic sensitivities of gram negative bacteria to piperacillin/tazobactam, meropenem, ciprofloxacin and gentamicin.

Results 512 positive blood cultures taken between February 2009 and October 2012 were identified. A total of 600 organisms were cultured: 267 gram positive bacteria (44.5%), 329 gram negative bacteria (54.8%) and 4 fungi (0.7%). Of the 329 gram negative bacteria 35 (12%) were resistant to piperacillin/tazobactam, 13 (4%) resistant to meropenem, 16

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(6%) resistant to ciprofloxacin and 15 (5%) resistant to gentamicin. 99.2% of the gram negative bacteria were sensitive to either piperacillin/tazobactam or gentamicin. In only 2 patient episodes were bacteria both piperacillin/tazobactam and gentamicin resistant.

Conclusions In accordance with NICE guidelines piperacillin/tazobactam will continue to be given as first line empirical treatment of suspected neutropenic sepsis, unless there are patient specific contraindications e.g. penicillin allergy, history of resistant organisms. However with a local piperacillin/tazobactam resistant rate of 12% amongst gram negative bacteria, it was decided that gentamicin will continue to be given for at least the first 24 hours after admission, to be reviewed with clinical response and culture results.
Trust guidance regarding the use fluoroquinolone prophylaxis was not changed. Although local bacterial resistant rates to fluoroquinolones are low, with 94% of the gram negative bacteria sensitive to ciprofloxacin, it was considered that the risk of antibiotic associated Clostridium difficile and development of antibiotic resistance was too high. Therefore routine fluoroquinolone prophylaxis for neutropenic sepsis will not be used.

References
1. National Institute for Clinical Excellence. Neutropenic Sepsis: Prevention and Management of Neutropenic Sepsis in Cancer Patients. Clinical guidelines issued: September 2012

Optimisation of combination therapy for treatment of Pseudomonas aeruginosa.
Cochrane, A1; Bowker, K2; MacGowan A1, 2.
University of Bristol1 and Bristol Centre for Antimicrobial Research and Evaluation2, Southmead Hospital, Westbury on Trym, Bristol, UK.

Objective. To define pharmacokinetic/pharmacodynamic targets for combination therapy of piperacillin/tazobactam plus gentamicin against Pseudomonas aeruginosa, and to assess dosing strategies to minimize aminoglycoside toxicity and resistance generation.

Background. The PK/PD target for optimal efficacy of beta-lactam antibiotics when used alone is time above the MIC of the organism, while the target for aminoglycosides is maximum peak concentration. However, it is not known whether these targets remain valid when the antibiotics are used in combination. In addition the effect of different dosing strategies on emergence of resistance and selection for persister phenotypes has not been fully assessed.

Method. The effect of different combinations of static concentrations of piperacillin/ tazobactam and gentamicin on killing of wild type Pseudomonas aeruginosa was assessed over 48 hours using kill curve methodology. Antibiotic concentrations from within the range that would normally be achieved in serum with standard dosing were used. The concentrations for piperacillin/tazobactam were 196 mg/l (high), 28 mg/l (intermediate) and 1mg/l (low); for gentamicin the concentrations were 15 mg/l (high), 4.5 mg/l (intermediate) and 0.5 mg/l (low). Emergence of resistance will be assessed in isolates present at 24 and 48 hours. Following these experiments an in vitro dynamic model will be used to test efficacy of various dosing strategies.

Results. A clinical isolate of Pseudomonas aeruginosa from a bacteraemic patient that was sensitive to both piperacillin/ tazobactam (MIC = 8 mg/l) and gentamicin (MIC = 2 mg/l) was chosen. Time kill results demonstrated that piperacillin/ tazobactam alone at high concentration was bacteriostatic at 24 and 48 hours (log10 kill <1 compared to time 0), while at intermediate and low concentrations there was significant growth. In contrast gentamicin alone was rapidly bacteriocidal at 1 hour with > 3 log10 kill for both high and intermediate concentrations, and this was maintained at 48 hours. Low concentration gentamicin alone had no effect on growth. Where piperacillin/tazobactam was used in combination with gentamicin, there was synergy (defined as 2 log10 greater kill in combination compared to most potent agent alone) between low dose gentamicin and both high and average dose piperacilin/tazobactam at 3 hours, and this was maintained to 24 hours with high dose piperacillin/tazobactam.

Conclusion. In 48 hour time kill experiments with wild type Pseudomonas aeruginosa high concentrations of gentamicin produced maximal killing, however there was synergy between piperacillin/tazobactam and sub MIC concentrations of gentamicin. This suggests that when used in combination with a beta-lactam, lower than standard doses of aminoglycosides may be adequate to provide benefit, a strategy that may reduce nephrotoxicity.

Investigation of the antimicrobial activity of essential oils of culinary and medicinal herbs and spices against selected gastrointestinal pathogens.
Chorlton, M1.; Rees, E1; Phillips, C.O2.; Claypole, T.C2.; Berry, N1 and Row, P.E3.
1 Public Health Wales Microbiology ABM, Singleton Hospital, Swansea, SA2 8QA, UK; 2 Welsh Centre for Printing and Coating, and College of Engineering, Talbot Building, Swansea University, Singleton Park, Swansea, SA2 8PP, UK; 3College of Medicine, care of Grove Reception, Swansea University, Singleton Park, Swansea, SA2 8PP, UK.

Introduction Pathogenic gut microorganisms, and dysbiosis of the gastrointestinal microbiota are a significant cause of mortality and morbidity worldwide. Moreover, alteration of the gastrointestinal microbiota has been implicated in irritable bowel syndrome, which affects 10 – 15 % of the population, and thus could potentially be targeted with antibiotics, notably rifaximin [Menees et al. (2012) Am. J. Gastroenterol. 107:28-35]. Due to increasing resistance of gastrointestinal pathogens to conventional antibiotics, and in the light of the potential treatment of large numbers of people with antibiotics to treat IBS, alternative antimicrobial agents are urgently needed. The aim of this study is to investigate whether essential oils (concentrated mixtures of aromatic compounds obtained by the distillation of plant tissues) have antimicrobial activity against selected gastrointestinal pathogens.

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Methods We have investigated the antimicrobial activity of essential oils of a wide range of culinary and medicinal herbs against type strains of selected gastrointestinal pathogens, namely Salmonella enterica, Clostridium difficile, two strains of Escherichia coli, and Candida albicans by disc diffusion assays. Grapeseed oil was the negative control.

Results Seven of the essential oils (aniseed, asafoetida, cinnamon, clove, oregano, thyme and winter savory) produced a strong and statistically significant inhibition of the growth of all five of the organisms tested whereas a further seven essential oils (coriander, garlic, lemon balm, lemon grass, May Chang, peppermint and rosemary) markedly inhibited the growth of three or four of the organisms (and these results were also statistically significant). Batch to batch variation was evident in the antimicrobial activity of some of the essential oils. This might correlate with variations in the profile of compounds present in the essential oils.

Conclusions Some of the essential oils studied might be therapeutically useful against gastrointestinal pathogens. Quality control of the oils would be necessary and further work is needed to identify the active antimicrobial compounds in the oils.

The Perils of Medical Tourism

Authors: T. Gouliouris,1,2 S.H. Aliyu,1,2 S. Ojha,2 S.J. Peacock,1,2,3 M.E. Török1,2,3

Affiliations 1. Cambridge Microbiology and Public Health Laboratory, Health Protection Agency, United Kingdom
2. Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom
3. University of Cambridge, Department of Medicine, Cambridge, United Kingdom

Introduction Medical tourism is a known risk factor for hospital-acquired infection. An estimated 5-10% of solid organ transplants worldwide are performed through transplant tourism. We present the first case of NDM-1 Klebsiella pneumoniae infection at our hospital that was acquired through renal transplantation abroad.

Case history A 55-year old man of Pakistani origin with end-stage renal disease acquired chronic hepatitis C virus infection through haemodialysis during a visit to Pakistan. On a subsequent visit he underwent a living-related renal transplant which was complicated by poor graft function, a peri-nephric haematoma, and a wound infection treated with prolonged antimicrobial therapy. He returned to the UK and presented to our hospital six months after transplantation with an infected wound. Imaging revealed peri-nephric collections, which were initially drained percutaneously but required a transplant nephrectomy. Cultures from the peri-nephric abscess grew meropenem-resistant Klebsiella pneumoniae (which was confirmed to be NDM-1 by in-house PCR and at the reference laboratory) and an amphotericin-resistant Aspergillus terreus. The patient also had norovirus diarrhoea caused by a genotype rarely encountered in the UK. The patient was treated with a prolonged course of tigecycline, amikacin and voriconazole and required multiple drainage procedures. He was discharged from hospital on day 82 post-admission.

Discussion Transplant tourism is associated with significant morbidity and mortality, particularly related to infection. Pakistan, India and China account for a large proportion of transplants performed through medical tourism. Seven case-series of transplant tourism patients published between 2001 to 2011 report one-year graft and patient survival rates of 68-100%. Bacterial wound, invasive fungal, viral and parasitic infections are common complications. The emergence and spread of multidrug-resistant (MDR) bacteria, such as NDM-1 producers, pose a significant risk to patients who travel to the Indian subcontinent for medical treatment. Such patients should be screened for MDR organisms and isolated until they are confirmed to be negative. Rapid molecular identification methods for antimicrobial resistance are crucial to confirm suspected resistance mechanisms.

Conclusions This case highlights the perils of medical tourism and illustrates the infection control and treatment challenges posed by MDR organisms in transplant recipients.

Poster abstracts

Curing: the phenotypic effects of plasmid carriage
AbuOun, M.1, Kirchner, M.1, Mafura, M.1, Thomas, C.2, Anjum, M.1.
1Department of Bacteriology & Food Safety, Animal Health and Veterinary Laboratories Agency (AHVLA) (Weybridge), Surrey, UK. 2School of Biosciences, University of Birmingham, Birmingham, UK

Plasmids are extrachromosomal double stranded circular DNA that replicate independently of their host bacterium. Plasmids can be characterised by the method of replication they possess known as replicon type. Plasmids may ensure that they are maintained within a host through a pair of genes encoding a toxin and antitoxin (known as a plasmid addiction system). Plasmids can harbour many different types of genes that offer an apparent advantage to the host such as resistance genes, toxin genes and many other genes of unknown function. To study the phenotypic effect of plasmids on their natural host, methods that generate plasmid free derivatives can be used, for example exposure to elevated temperature, ethidium bromide and other chemical curing agents. However these methods can cause unpredictable and irreversible changes to the host. pCURE2 is a directed method which uses a plasmid that interferes with the replication of the target plasmid and neutralises the effect of the addiction system by encoding antitoxin genes. Strains identified during a study to assess the influence of antibiotic treatment on the faecal flora and its antibiotic resistance were used to investigate the phenotypic effects of plasmid carriage.

The aim of our study was to determine the phenotypic effects of plasmid loss on wild type commensal strains of E. coli. Using pCURE2, which specifically targets incF plasmids, the plasmids in 4 E. coli strains were cured either by direct electroporation of pCURE2 DNA or by conjugation with S17 E. coli. The pCURE2 plasmid interferes with the replication of incF plasmids and also contains the antitoxin component of addiction systems commonly found in incF plasmids which interferes with post-segregational killing. Two strains out of six were successfully cured by electroporation of pCURE2: ARD120 (carrying IncB/O, FIB, U, FII replicons and ccdAB addiction system) and ARD289 (carrying IncFIB, FII replicons and pemK, relE, vagCD, hoksok, srnBC addition systems). Three strains: ARD289, ARD1053 (carrying IncI1, N, FIIS, FIB, R, FII replicon and pemK, vagCD and pndCA addiction system) and ARD1258 (carrying IncFIB, FIA, FIIS, FII and pemK, ccdAB, hoksok, srnBC addiction systems) were cured by conjugation of pCURE2 from the S17-1 donor and selected on M9 minimal media.

Cured strains were characterised by plasmid profile, antibiotic susceptibility by disc diffusion and PCR amplification of the replicon genes and addiction system genes. Identibact AMR08 arrays were also used to determine the presence and loss of antibiotic resistance and E. coli virulence genes. Phenotypic microarrays, concentrating on the metabolic effector panels (PM11-20), were also used to determine whether stress or other fitness responses were affected following curing of incF plasmid. Studies are currently underway to evaluate the effect of plasmid loss in vivo within a chicken host model. In two of the cured strains, ARD289 and ARD1053, 2 different curing events occurred when pCURE2 was introduced by conjugation, resulting in different plasmids being cured and different phenotypes for the cured strains. The pCURE2 system has enabled us to assess how different incF plasmids confer a selective advantage on their hosts.

RARE OCCURRENCE OF MUPIROCIN RESISTANCE AMONG CLINICAL STAPHYLOCOCCUS ISOLATES IN JORDAN
AQEL A.1, IBRAHIM A.2, SHEHABI A.3
1Faculty of Medicine, Mu'tah University, Al-Karak, Jordan
2Faculty of Allied Medical Sciences, Zarqa University, Zarqa, Jordan
3Faculty of Medicine, Jordan University, Amman, Jordan

This work was done at the laboratories of the Faculty of medicine, Mu'tah University, Alkarak Jordan.

Staphylococcal infections have high occurrence in Jordanian patients. This study was carried out to determine the rates of high- and low-level mupirocin resistance (MupH and MupL) among staphylococci with the molecular characterization. Two hundred and thirty-two non-duplicate Staphylococcus spp. isolated from different clinical specimens were tested for mupirocin susceptibility using disk diffusion method and minimum inhibitory concentration (MIC). Resistance genes and clone relatedness was studied using polymerase chain reaction (PCR) and enterobacterial repetitive intergenic consensus primers (Eric-PCR) for the latter. Plasmid curing was performed to determine the genetic location of MupA gene. Among the 232 strains, 144 (62%) were methicillin-resistant Staphylococcus aureus (MRSA), 33 (14.2%) methicillin- susceptible Staphylococcus aureus (MSSA) and 55 (23.7%) were of other coagulase- negative Staphylococcus spp. (CoNS). Of all strains tested, only 6 (2.6%) were mupirocin resistant. MecA gene was detected in both MupL and MupH strains but MupA gene was only detected in MupH. Plasmid curing improved the plasmidic location of MupA gene. Molecular typing by Eric-PCR method revealed heterogenicity of the genetic makeup of our MupL and MupH strains. Staphylococci with MupA-carrying genes are present in Jordanian hospitals, but thank to the limited use of mupirocin, they remain rare.

An audit of the diagnosis of urinary tract infections in a hospital setting to improve effectiveness and reduce antibiotic prescribing in asymptomatic bacterurias
Begley A, Maxwell S
Stockport NHS Foundation Trust, Stepping Hill Hospital, Poplar Grove, Stockport.

Background Urinary tract infections (UTIs) are very common and urine samples make up a large proportion of samples received into microbiology laboratories. It is vital laboratory processes along with clinical acumen are used to diagnose them to help reduce unnecessary sending of mid-stream urines (MSUs)and ensure patients with UTIs are correctly

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identified. However, it is well documented UTIs are over diagnosed1, and asymptomatic bacterurias are being treated especially in the elderly leading to over prescribing of antibiotics, drug side-effects, increasing risk of bacterial resistance and patients developing Clostridium difficile2. Furthermore, the dipstick of urines to perform urinalysis for leucocytes and nitrites should be carried out using point of care testing (POCT) machines were available as opposed to subjective manual dipstick testing which is prone to human error and results are often not recorded into the medical notes.

Aims and methods The aims of the audit were to improve the diagnosis of urinary tract infections. This was done by auditing consecutive MSUs requests over a week's period sent for culture and sensitivity. The results of POCT (whose results are automatically recorded onto the hospital web-based results system) and manual dipstick testing on urine samples performed on medical, surgical and gynaecological wards were audited. Additionally we assessed by reviewing the patient notes whether mid-stream urine samples were being sent on the basis of clinical symptoms suggestive of a UTI including dysuria, suprapubic pain and frequency2 with or without raised inflammatory markers.

Results The results of 53 patient samples were assessed, 63% had POCT urinalysis were facilities were available. 27 patients (51%) had urine samples sent with no symptoms suggestive of a urinary tract infection nor raised inflammatory markers. More alarmingly of these 27, 8 (30%) urine samples were culture positive indicating asymptomatic bacteruria. Overall, only 40% of positive urine cultures were from patients with symptoms suggestive of a urinary tract infection.

Conclusions POCT for initial urinalysis to detect nitrites and leucocytes which has a negative predictive value of 92%3 should be performed rather than manual dipstick testing. In this study use was suboptimal in aiding the diagnosis of UTI. Unnecessary bacterurias are being detected as a result of urine samples being sent when not clinically indicated, i.e. when there are no symptoms suggestive of a UTI which have consequences for patient care with respect to antibiotic prescribing and associated complications. Greater adherence to guidelines and more emphasis on clinical symptoms should be used in order to correctly diagnose a urinary tract infection.

1. Woodford HJ. Diagnosis and management of urinary tract infection in hospitalized older people. J Am Ger Soc 2009; 107.
2. 2. McMurdo ME. Age and Ageing 2000; 29: 297.
3. Health Protection Agency

Evaluation of the efficacy of the Vitek2 automated identification and sensitivity system & MASTDISCS ID Carbapenemase for the detection of Carbapenemase Producing Enterobacteriacae

Authors
Janet Moxham1
Phillipa J Burns1
John Moore2
Andrew Dodgson1*
1 Department of Medical Microbiology, Manchester Medical Microbiology Partnership, HPA & Central Manchester Foundation Trust, Manchester, UK
*Corresponding Author: Andrew Dodgson (Andrew.Dodgson@cmft.nhs.uk)
2 School of Biomedical Sciences, University of Ulster, Coleraine, NI

Abstract The emergence of KPC as the dominant carbapenemase within the UK poses a challenge for the diagnostic laboratory as they are not easily detected by automated susceptibility testing methods. The circulating carbapenemase producers, within our hospital trust, do not always display the high levels of carbapenem resistance associated with KPC production in other international centres.

The laboratory currently utilises the Modified Hodge Test (MHT) as a sensitive but none specific confirmatory method of carbapenemase production. The recent emergence of an NDM producing isolate, that fails to give a positive MHT result, has prompted a review of the screening method.

Many of the isolates within CMFT co-produce ESBL, AmpC and KPC which makes the recognition of the underlying resistance mechanism too complicated for the Vitek2XLs advanced expert system alone.

Objective We evaluated the performance of the MASTDISCS ID system using 100 known carbapenemase producing enterobacteriacae isolates, with various molecular mechanisms, alongside the Vitek recognition of carbapenemase production and the Modified Hodge Test.

Conclusions Confirmation of carbapenemase production can be difficult without molecular methodology; we propose a multi-step algorithm to improve the detection of CPE in the routine laboratory.

Antimicrobial Surveillance Audit: Temocillin & Colistin Susceptibility of Carbapenemase producing Enterobacteriaceae isolated from screening samples submitted to the Microbiology laboratory over a 12 month period.

Phillipa J Burns 1 & Dr Ahmed Qamruddin 1 *
1 Manchester Medical Microbiology Partnership, HPA & Central Manchester Foundation Trust, Manchester , UK

Abstract: Resistance to carbapenems is rare within the UK but there has been an increase in the isolation of Carbapenemase producing Enterobacteriaceae (CPE) within the North West region. In response to the increasing numbers of CPE isolated within the Trust; the department has produced a protocol for CPE screening and detection. CPE have been monitored through rectal and faecal screening within the Trust since Oct 2009.

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Carbapenems (Ertapenem, Imipenem & Meropenem) are the only Beta-lactams reliably active against Enterobacteriaceae that produce ESBL and AmpC and are frequently used to treat serious Gram negative infections. Treatment options for Carbapenemase producing Enterobacteriaceae are limited.

Extended antibiotic susceptibility testing is performed for all screen positive isolates to monitor the antibiograms of circulating CPE.

During the 12 month surveillance period (13.01.12 – 13.01.13) a total of 9727 CPC screens were submitted from routine ward screening with an additional 134 isolates passed onto the screening bench for further work. A total of 640 isolates were considered positive for carbapenemase production utilising an established screening algorithm.

Routine laboratory susceptibility testing is performed using the Vitek2XL system (Biomerieux) with Temocillin and Colistin MICs established using Etests (Biomerieux). The MIC50, MIC90 and range of MICs were established for Temocillin & Colistin as part of an antibiotic surveillance audit.

Result Summary: Temocillin

ORGANISM	MIC 50	MIC90	RANGE
ECOLI (N=94)	8	16	0.125 - >1024
ENTE (N=47)	8	16	2-64
KOXY (N=17)	8	16	4-32
KPNE (N=470)	8	32	0.25 - >1024

Result Summary Colistin

ORGANISM	MIC 50	MIC 90	RANGE
ECOLI (N=96)	0.125	0.50	0.064 - 1
ENTE (N=49)	0.125	0.25	0.0125 - 16
KOXY (N=17)	0.125	0.25	0.125 – 0.50
KPNE (N=479)	0.125	0.50	0.064 - 64

*The MIC distributions for other less commonly encountered CPE such as Klyvera sp and Raoultella sp are discussed in full in the poster.

Conclusions Antibiotic treatment options for CPE are limited; understanding the antibiotic susceptibility profiles of circulating strains enables prudent use of antibiotics through a restricted antimicrobial policy.

Patterns of bloodstream infection and anti-microbial resistance of invasive bacterial and fungal infections in paediatric oncology patients in South West London

Calton E, Wells R, Appleby G, Le Doaré K, Sharland M, Ladhani S
Paediatric Infectious Diseases Research Group, St George's Hospital, London SW17 0JT

Aims This study describes the pathogens and anti-microbial resistance patterns of invasive bacterial and fungal infections in paediatric oncology patients across South West London during 2009-2011.

Methods A web-based questionnaire was completed for all children aged 1 month to 15 years with cancer who had a positive blood culture at any of the 5 South West London hospitals between 01 January 2009 and 31 December 2011. A significant bloodstream infection (SBI) was defined as a positive blood culture in a child who received specific antimicrobial therapy directed towards that pathogen.

Results During 2009-11, 115 children (57 female, 58 male) had 266 significant blood cultures during 149 hospital admissions (median age at admission 5.5 years). Coagulase-negative staphylococci (CoNS) accounted for almost half the pathogens isolated (n=127, 47.7%), followed by Gram-negative (n=65, 24.4%), other Gram-positive organisms (n=40, 15.0%) and fungi/yeasts (n=19, 7.1%).

Almost all admissions involved children with a central venous catheter (CVC) (144/149, 96.4%). Those with a portacath (52 admissions) were more likely to develop SBI due to CoNS (60.9% vs. 41.5%, P=0.004) and less likely to have Gram-negative SBI (10.9% vs. 28.3%, P=0.001) compared with children who had a tunnelled CVC or peripherally-inserted catheter (86 admissions).

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The pathogens causing SBI in 69 children with haematological malignancies were similar to those in 46 children with solid tumours and included CoNS (48.1% vs. 52.1%),Gram-negative (23.5% vs. 28.7%) and other Gram-positive (14.8% vs. 17.0%) pathogens. Neutropenia (<1.0 x109/L) within 48 hours of admission was present in 60 patients (40.1% of admissions) and was associated with invasive fungal infections (11.1% vs. 1.0%, P=0.001).

Empirical antimicrobial therapy was initiated during 141 (94.6%) admissions and included mainly piperacillin-tazobactam with gentamicin (Pip-Taz/G) (54 admissions, 36.2 %), or glycopeptide monotherapy (27 admissions, 18.1%). A fifth of Gram-negative pathogens (13/65,20.0%) were resistant to gentamicin, 12.3% (8/65)to piperacillin-tazobactam, and 3.1% (2/65) to carbapenems.

Empirical antimicrobial therapy was changed within 5 days in 74 admissions (49.7%), most commonly in those receiving Pip-Taz/G (66.7% changed). Reasons for antibiotic changes included addition of glycopeptides after CoNS isolation (26/74, 35.1%), suspected pathogen resistance to empirical therapy (23/74, 31.1%), and clinical deterioration (18/74, 24.3%). Overall, 33/149 (22.1%) admissions included intensive care stays. Six children died, including 3 (2.0%) attributed to infection.

Conclusions SBI continue to cause considerable morbidity and mortality in children with cancer. CoNS accounted for half the infections and were generally sensitive to glycopeptides. However, a significant proportion of Gram-negative pathogens were resistant to at least one first-line antibiotic. Further efforts to reduce central line-associated infections and limit inappropriate exposure to broad-spectrum antibiotics are needed.

Development of the TARGET antibiotics website: Treat antibiotics Responsibly, Guidance, Education, Tools

Harpal S Dhillon, Cliodna AM McNulty, Michael Moore and Christopher Gush on behalf of the ASPIC collaboration of societies and professionals (HPA, DH, BSAC, RCGP, BIA, Pharmacists, CQC, NPC, IPS and BPAIIG, RCN, HP Scotland & PH Wales and NI)
Health Protection Agency Primary Care Unit Gloucester.

Background: In the UK, eighty percent of antibiotic prescribing occurs in primary care, with over half for respiratory tract infections1. There are indications that extensive or inappropriate use of antibiotics is linked to the development of bacterial resistance2. The concept of antibiotic stewardship has been introduced in order to promote the appropriate use of antibiotics and slow the rise in antimicrobial resistance3.

The Antimicrobial Stewardship in Primary Care (ASPIC) collaboration was established in 2009 and includes the DH, RCGP, HPA, BSAC, CQC, BIA, NPC, IPS and BPAIIG, RCN, Health Protection Scotland & Public Health Wales and NI, NHS Information Centre, and interested GPs, pharmacists & microbiologists. The collaboration working closely with GPs and community medicines managers has assessed current guidelines and other materials and within a series of workshops agreed that multifaceted interventions based on the 'Why' and 'How' proposed by Butler et al should be used to improve antimicrobial stewardship in primary care. The group agreed the content of a toolkit to promote antimicrobial stewardship.

The TARGET toolkit: The web-based toolkit was developed through 2012 and launched on the Royal college of General Practitioners website www.RCGP.org.uk/TARGETantibiotics/ on European Antibiotic Awareness Day in November 2012, with much media attention. The toolkit contains a presentation template explaining 'Why' antimicrobial stewardship is so important, and 'How' the resources can be used to promote stewardship. The most popular part of the toolkit is the Patient antibiotic leaflet which contains personalised information for patients on how long their illness will last, when they should return to the doctor and information on why antibiotics were not prescribed. The leaflet aims to empower patients and give them the confidence to self care for RTIs.

The toolkit also contains the HPA antibiotic guidance template (that can be modified locally), a self assessment check list for GPs and commissioners to determine how well they are doing relative to their peers in stewardship, audit tools and links to on-line clinical modules and other useful resources.

Implementation: The RCGP is now planning a marketing campaign to increase use of the website.

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Treatment of skin and soft tissue infections with daptomycin: UK Experience

Gonzalez-Ruiz A1, Seaton RA2, Hedderwick S3, Allen M4, Williams R4, Andrews C4, Jones A5 on behalf of the UK EU-CORE group
1. Darent Valley Hospital, Kent 2. Gartnavel General Hospital, Glasgow 3. Royal Victoria Hospital, Belfast 4. Novartis Pharmaceuticals Frimle, 5. Malton, N. Yorks.

Background: Daptomycin (DAP), a cyclic lipopeptide antibiotic with gram-positive activity, received marketing authorisation in Europe in Jan 2006.

Objective: To describe the UK specific clinical experience in patients (pts) with skin and soft tissue infections (SSTIs).
Methods: Data were taken retrospectively from UK institutions (13) participating in the European Cubicin® Outcomes Registry and Experience (EU-CORESM). All pts received at least one dose of DAP and 30 days follow up. Patient demographics, antibiotic usage, microbiological and clinical outcomes and adverse events from pts treated with DAP between January 2006 and June 2011 were analysed. Outcomes were assessed by investigators as cured, improved, failure and non-evaluable. All adverse events were recorded.

Results: Overall 590 pts were entered into the database of which 233 pts had SSTIs. Overall, the majority of pts (525, 89%) included in the database had underlying disease and had received prior antibiotics. Mean duration of inpatient therapy for SSTIs was 7.7 days. 46% of the 233 SSTIs were wound infections (including incisional wounds), ulcers or abscesses. 135 (58%) of SSTI pts received an initial dose of 4mg/kg. Clinical outcomes were success (defined as 'cured plus improved') 188 (81%), failure 18 (8%) and non-evaluable 27 (12%). Mean time to clinical improvement was 4 to 5 days, with 81(35%) of pts improving by day 4 or earlier. The most frequently isolated pathogen was S. aureus. In the overall DAP was generally well tolerated with adverse events (AEs) related to DAP recorded for 37 (6%) pts. Blood creatine phosphokinase increased in 6 (1%) of pts, rabdomyolysis was reported in 2 (0.3%) and myalgia in 1 (0.2%) pts.

Conclusions: Despite the number of prior antibiotic failures and multiple co-morbidities of these pts, the overall DAP clinical success in this UK population was 81%. Registries such as EU-CORE provide additional information to registration studies and an insight into real world clinical experience. These data support the place of DAP as an effective treatment option in SSTI.

Surgihoney - Biotechnological honey wound treatment: first clinical report of its use in the tropics

Heyes I1, Hughes R1, Hussein A1, Dryden A 2, Dryden MS1
1The Hampshire Hospitals, Winchester SO22 5DG, 2Peninsular College of Medicine and Dentistry, Exeter and Plymouth

The past century has seen increased use of chemical products and antimicrobials in wound dressings. Whilst this may reduce bacterial load in the wound, there has been a worrying growth in microbial resistance and some antimicrobial products may disrupt wound healing. Honey has been used as a topical agent in wound healing for millennia. A bioengineered preparation of honey enhances the antibacterial properties of honey while retaining all the natural properties of antimicrobial activity and healing.

The aim of this study was to explore the role of bioengineered natural honey in wound healing in the tropics and demonstrate its antimicrobial activity in the laboratory.

Methods: Surgihoney was used in Yei Civil Hospital, South Sudan and Vaiola Hospital, Tonga as a topical daily dressing for patients with wounds of any sort. Surgihoney was used prophylactically as well as therapeutically. The wounds included traumatic, surgical, diabetic, and chronic tropical lesions as part of a non-comparative clinical evaluation which continues to compile a substantial body of clinical experience.

Although local laboratory facilities were not available, some swabs were collected and tested in the UK. Surgihoney activity was tested by a diffusion inhibition method against the range of pathogens isolated which included Staph. aureus, Esch. coli, Pseudomonas aeruginosa, Streptococcus Group A and Group B.

Results: Surgihoney proved safe and effective as a wound dressing, providing an effective moist and protective barrier. The wounds were very varied in nature and patients had a wide range of comorbidities. The Sudan team treated 50 wounds; 12 were treated in Tonga. The wounds showed clinical improvement with no extension or development of inflammation, reduction in ulcer slough and odour and, where microbiology was carried out, a reduction in bacterial load. Surgihoney was active in vitro against all the bacterial pathogens tested with significant zones of inhibition.

Conclusions: Surgihoney may be the first biotechnology product to be used successfully in wound healing. It provides all the characteristics of an ideal wound dressing: moist barrier protection, possible local nutrition and immunomodulation, debridement of slough, and reduction of bacterial colonising load. As a wound treatment in the tropics it is an ideal low technology solution which is easily stored, applied and ought to be cost-effective.

Expanding Outpatient Parenteral Antibiotic therapy
'Is it an effective way to manage patients at home?'
Lewis A, Hodgkins P, O'Hanlon S, McGrail P
St. Helens and Knowsley Teaching Hospital NHS Trust, Whiston hospital

Halton & St Helens Community Intravenous Therapy (IV) Service was developed in 2005 by St Helens Primary Care Trust (PCT). The service aims to facilitate early discharge of patients from hospital and were possible prevent avoidable hospital admissions.

We aimed to evaluate the continued efficacy and efficaciousness for OPAT services provided through the continually expanding Halton and St. Helens OPAT service. Areas of focus included clinical outcomes, therapeutic drug monitoring, bed days saved for secondary care at the St Helens and Knowsley NHS Trust and an estimated costs saving for 2010-12

All patients referred during January 2010-2012 under OPAT program for Halton and St. Helens community IV team from the St Helens and Knowsley NHS Trust were recorded and outcome data followed up. All patient parameters where recorded included referring clinician/speciality, condition being treated, drug regime, number of bed days saved through treatment under community team and also whether appropriate drug monitoring was undertaken (both drug levels and also appropriate U&E, LFTs, FBCs etc). All outcomes for patients were determined from the patient clinical notes and classified into successful treatment or a treatment failure depending on the clinical parameters set out prior to treatment.

The service for 2010-11 saved 1,400 bed days and has grown to over 1800 bed days in 2011-12. This had an estimated saving of in excess of £420k in 2010-11 and £545k in 2011-12

Successful completion rates of therapy to the desired outcome over 2 years audit was greater than 86%. Only 3% of prescribed doses where missed under the OPAT. Less than 2% if poor patient compliance is excluded. This is considerably less than in the inpatient audits were 5-9% of prescribed doses are missed.

Greater than 84% of vancomycin levels were within the therapeutic range of 10-20 mg/l under OPAT and continues to be more accurate than in the inpatient setting.

A multidisciplinary team approach for the management of stable patients under OPAT continues provide both an efficacious and cost effective treatment option for patients needing long and short term IV antibiotics. Management of patients such as these provides diversity and complies with the department of health NHS plan vision for greater patient centred approach and care while providing potential cost saving measures.

A Shaggy Dog Story
Authors: Mahida NA1, Crusz SA1, Mistry BH1, Lemberger RJ2, Kearns AM3, Weston VC1
Address 1:Department of Clinical Microbiology,
Nottingham University Hospitals NHS Trust
Queens Medical Centre, Derby Road,
Nottingham, NH7 2UH

Address 2:Department of Urology,
Nottingham University Hospitals NHS Trust
Nottingham City Hospital,
Hucknall Road, NG5 1PB

Address 3: Antimicrobial Resistance and Healthcare Associated Infection Reference Unit
Health Protection Agency
61 Colindale Avenue
London, NW9 5EQ

Clinical History A 48 year old man with a background of renal calculi of unknown aetiology was admitted with left sided ureteric colic. Radiographic imaging demonstrated bilateral renal calculi and a left ureteric calculus causing hydronephrosis. A nephrostomy tube was inserted but during ureteric calculus removal, the patient became septic. A mid-stream urine sample cultured an organism that was reported as Staphylococcus aureus (Pasteurex slide coagulase negative [Biorad], DNAse positive) and the patient settled on empirical piperacillin/tazobactam therapy. The nephrostomy was subsequently removed having been in situ for a few weeks.

Eleven months later, a mid-stream urine sample again cultured an organism that was reported as S. aureus (this time Pasteurex and DNAse positive) with the same antibiogram as previously (resistant to Doxycycline and Trimethoprim, but susceptible to Oxacillin). The patient was admitted two weeks later with sepsis and left loin pain. Radiographic imaging showed another calculus in the left ureter and a nephrostomy tube was re-inserted. The pus drained cultured a Staphylococcus species that was initially labelled as a coagulase negative staphylococcus (Pasteurex negative, DNAse weak). However, on closer examination, the antibiogram of this organism matched the two previous urine cultures.

Using Vitek-2 (bioMérieux) the organism was identified as Staphylococcus intermedius. The ureteric calculus also cultured the same organism with a matching antibiogram. S. intermedius is known to be a coloniser and pathogen of certain animals, particularly dogs. In light of this, the patient was reviewed and questioned about animal exposure and it became apparent that he owned a large German Shepherd dog.

Screening swabs taken from the patient's nose, perineum and nephrostomy site cultured Staphylococcus hominis and Staphylococcus haemolyticus. However, swabs from the dog's ear, coat, nose and mouth cultured S. intermedius. The S.

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intermedius isolates from the dog and the patient were further compared using pulsed-field gel electrophoresis (PFGE) which showed them to be indistinguishable, representing a single strain. PCR-based analyses correctly identified the organism as Staphylococcus pseudintermedius.

Discussion and complexities
S. pseudintermedius is a recently classified species of the S. intermedius group that is the leading cause of skin infections in dogs and cats. Members of this group possess some phenotypic properties of S. aureus but also exhibit some properties of S. epidermidis, and hence can be misidentified in the routine diagnostic laboratory, as illustrated by the urine cultures.

S. pseudintermedius has zoonotic potential and human infections have been reported but this is the first case report of human urinary tract infection with associated renal calculi. Although the organism was not found to be colonising the patient, the typing is highly suggestive of it having originated from the dog and likely entered the urinary tract through the original nephrostomy. The presence of existing renal calculi may have represented a nidus for the establishment of chronic infection and this in itself, may have contributed to the ongoing stone formation. The patient made a full recovery following left ureteric stone removal.

Bacteraemia in a tertiary Intensive Care Unit in the UK
Moore LSP, Lambden S, Lambden SC, Ashworth S, Jepson A
St Mary's Hospital, Imperial College Healthcare NHS Trust, Praed Street, London. W2 1NY

Objectives: It is common practice to undertake blood culture at the time of, or shortly after, an episode of pyrexia. In the intensive care unit (ICU) there are a number of potential confounders that make the use of temperature as a guide to blood culture sampling more challenging. In a retrospective analysis covering an 18month period between 1st January 2011 and 30th June 2012 we analysed the pattern of blood culture sampling in the ICU looking at the a priori clinical indicators of fever and tachycardia in relation to positive blood cultures, and describe the trend of cultured isolates. Method: Data were triangulated from laboratory information management systems, electronic ICU physiological & clinical records, and microbiologist consult documentation.

Results: 1216 distinct episodes of blood culture were undertaken over the study period. 121 (9.95%) blood cultures were positive of which 55 (4.5%) were deemed clinically relevant. Clinically relevant bacteraemia was more likely in patients with infection diagnosed at admission (OR 2.90, p=0.002) and in patients who had undergone general (OR 2.763, p=0.045) or vascular surgery (OR 2.19, p=0.035). When compared to an age, gender, cause for admission and preceding antimicrobial use control group, there was no association between clinically relevant bacteraemia and (i) pyrexia at the time of or within two hours of sampling (p=0.847) or (ii) with a heart rate above 90 (p=0.638). To detect one clinically relevant bacteraemia the number of blood cultures that needed to be taken was 12 during days 1 to 3 of ICU stay and 28 during subsequent days. In the early period (day 1-3), Gram positive organisms played a significant role as the cause of bacteraemia (30.4% of significant positive blood cultures). In each of these cases the source of sepsis was CVC-BSI, with all patients in this category admitted either from another hospital or from another ward within the study hospital. Of the remaining early bacteraemias the Enterobacteriaciae (56.5%) are most often the causative group of organisms. After day 3 in the ICU, Gram positive organisms become increasingly common as the causative organisms, and within the Gram negative bacteraemic patients the initial frequently susceptible Enterobacteriaceae are replaced by non-fermenting organisms with more resistant antibiograms. In patients in whom a clinically relevant blood culture was obtained, 38.2% were on an appropriate antimicrobial at the time of culture, 29.1% were on no antimicrobials, and 32.7% were not on a suitably antimicrobial regime to treat the organism identified.

Conclusions: Given the challenges of detecting bacteraemia, knowledge of the pattern in the ICU can guide appropriate empiric antimicrobial therapy. Multiple blood cultures early in the ICU admission are indicated if infection is considered in the differential, even in the absence of physiological derangement. Empiric antimicrobial therapy targeted at the likely organisms with care to ensure that there is activity against Gram positive organisms and additionally after day 3 against the intrinsically more resistant non-fermenting Gram negatives is key to managing sepsis in the ICU.

The bacterial causes of meningitis in infants <3 months in the UK and the ROI: a time for change in empirical antibiotic policy?
Okike, IO1, Henderson KL2, Blackburn R2, Muller-Pebody, B2, Johnson, AP2, Heath PT1
1- Clinical Sciences and Vaccine Institute
St Georges, University of London
Cranmer Terrace
London SW17 0RE
2- Healthcare Associated Infection & Antimicrobial Resistance Department
Health Protection Services, Colindale
Health Protection Agency

OBJECTIVES: Both the National Institute for Health and Clinical Excellence (NICE) clinical guidelines on 'Feverish illness in children' (2007) and on 'Bacterial meningitis and meningococcal septicaemia' (2010) advise that the empiric antibiotic cover for infants 0-3 months of age with suspected serious bacterial infection (including meningitis) should include an aminopenicillin, in addition to a third-generation cephalosporin (3GC). This recommendation is based on the fact that Listeria monocytogenes (LM) is an important cause of serious bacterial infection in young infants and that LM is not susceptible to 3GCs. A neonatal meningitis study in England and Wales in the 1990s which defined the aetiology of

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bacterial meningitis reported that Group B streptococcus (GBS) was by far the leading cause and that LM was implicated in 5% of the cases. We therefore set out to define the current causes and examine the relevance of LM as clinicians hold divided opinion about it.

METHODS: We undertook a comprehensive surveillance for meningitis over a 13 month period (1 July 2010-31 July 2011) and used multiple sources of data. This included paediatricians (and neonatologists) via the BPSU, microbiologists via national reference laboratories, parents of cases and parent support charities.

RESULTS: In 298/365 (82%) cases a causative bacteria was defined. GBS and E. coli together constituted almost two thirds of the isolated bacteria (GBS: n=150, 50%) and (E. coli: n=40, 13%). Others were Streptococcus pneumoniae (Spn) 28 (9%), Neisseria meningitidis (NM) 23 (8%), LM 11 (4%), other Gram-positive bacteria 24 (8%) and other Gram-negative bacteria 25 (8%). During the neonatal period (first 28 days) GBS 111 (58%), E. coli 28 (15%), Spn 11 (6%), LM 10 (5%), NM 3 (2%), other Gram positive 14 (7%) and other Gram negative bacteria 14 (7%) were the causes identified. Between 1 and 3 months, NM and Spn became more common (20/105; 19% and 17/105; 16% respectively), although GBS 39 (37%) still remained predominant. There was only one case of LM meningitis in a 29 day-old. However, between 2 and 3 months, Spn 13 (29%), NM 11 (24%) and GBS 11 (24%) were the leading causes.

CONCLUSION: This study shows that GBS is still by far the leading cause of bacterial meningitis in infants < 3 months of age. The proportion caused by GBS declines with age as SPN and NM becomes the leading causes after the first two months of life. There was only 1 case of LM beyond the first 28 days. Although there are no available data on the number of children for whom amoxicillin/ampicillin has been prescribed for empiric therapy of presumed LM meningitis; the number is likely to be large. Given the evidence from our study, we do not believe that amoxicllin/ampicillin is a necessary part of empiric antibiotic therapy for bacterial meningitis beyond the first month of life. This study provides a platform to start this debate.

This study was collaboration between St George's, University of London, the BPSU and the Health Protection Agency. Funding was by the Meningitis Research Foundation.

Disseminated fungal infection caused by Exophiala following Transarterial aortic Valve insertion.

Authors: Raviprakash. V, Budai I, Garbutt.P.
Place: James Cook University Hospital, Marton road, Middlesbrough, TS43BW.

Abstract: Tran arterial aortic valve insertion represents an endovascular alternative to conventional open heart surgery without the need for sternotomy, aortotomy or cardiopulmonary bypass patients with severe aortic stenosis. It is considered as an alternative to surgery in patients with severe aortic stenosis, who are considered at too high a risk for surgical replacement. There are not many cases of postoperative infection by a TAVI device reported in literature. We report a case of disseminated fungal infection caused Exophiala following a TAVI procedure. This was an 81 yr old patient who was admitted to the stroke ward with history of left sided weakness and decreased GCS and was found to be pyrexial on admission. CT scan done on admission showed multiple emboli and thought to be from Cardiopulmonary source .The patient continued to deteriote clinically and died of overwhelming sepsis. Multiple blood cultures and also the post mortem specimens from heart, kidney, and brain spleen grew Exophila species which was identified as Exophiala dermatitidis at the reference lab. Although few cases of endocarditis caused by fungi has been reported, this is the first case of disseminated fungal infection following TAVI.

Clostridium difficile a pathogen still in need of new therapeutic options, introducing SMT 19969.

R Vickers, G Tillotson, R Echols.
Summit plc, Abingdon, Oxon.

Objective: to describe the continuing need for and emerging novel therapies for Clostridium difficile infection(CDI).

Introduction: CD continues to cause significant morbidity and mortality, largely due to the spread of more virulent, epidemic strains e.g. 027 (USA) & 001(UK). Stringent infection control efforts in the UK, USA and some European nations have decreased the incidence locally; the epidemic continues to grow globally. Clinical recurrences remain common particularly with the epidemic strains. Fidaxomicin, the first new treatment for CDI in 25 years appears to have a lower recurrence rate for non-epidemic strains. New therapeutic approaches are in development including anti-toxin antibodies, vaccines, biopharmaceuticals and probiotics. Restoration of the normal microbiota appears to reduce multiple recurrences. We will describe the developmental agents with a focus on a novel antimicrobial agent, SMT 19969, with highly selective activity against C difficile.(CD)

Methods: Standard minimum inhibitory concentration, resistance selection, post-antibiotic effect, kill curve and hamster studies data were all conducted with SMT 19969.

Results: SMT 19969 showed an MIC90 to CD of 0.12ug/ml, no spontaneously resistant CD mutants to SMT 19969 were observed despite 14 serial passages, a PAE of 6 hours was noted with a 5xMIC while a 2 hr post-antibiotic effect was noted at 2x MIC and a bactericidal effect was observed after 24hr. Studies in the hamster model showed SMT to be superior to vancomycin , 100% survival vs 40% survival in VAN group. Interestingly in the human gut model miminal disruption of the normal micorbiota was noted as well as the levels of toxin were below the levels of detection with no SMT resistance detected.

Conclusions: Promising advances in CDI therapeutics, including multiple modalities is encouraging. Novel agents such as SMT 19969, by minimizing disruption of the normal microbiota could be a valuable addition to our treatment options.

MULTIPLE LIFE-THREATENING INFECTIONS IN A 7 YEAR OLD WITH AUTOSOMAL RECESSIVE CHRONIC GRANULOMATOUS DISEASE

.C Waruiru1, F Shackley1, P Fenton1, R Primhak1, A Ragavan1, D Barge3, Claire Nash1 T Flood2
1 Sheffield Children's Hospital NHS Foundation Trust, Sheffield
2. Great North Children's Hospital, The Newcastle upon Tyne Hospital NHS Trust
3. Dept Immunology, Newcastle upon Tyne Hospitals

Introduction This case illustrates the fulminant presentation, with multiple isolated infective organisms and the complexity of safe antimicrobial use in a young girl newly diagnosed with Autosomal Recessive Chronic Granulomatous Disease.

Case A previously well 7 year old girl, whose sibling had died a year before with Fanconi's anaemia travelled to Pakistan. Within a week of return, she presented with recent rash, left cervical adenopathy, scabbed haemorrhagic rhinitis, an infected toe, chest pain and persistent fever. Chest X-ray on admission was unremarkable.
She deteriorated with rampant progression of necrotising pneumonia, requiring intensive care. Figure (i) CXR – intubated, (ii) Chest CT – LLL abscess.
Inflammatory complications of limb musculature affected her mobility for months. Figure (iii). MRI -Pelvis.
Work-up including a percutaneous lung aspiration showed multiple causative organisms:- see table below

An abnormal DHR confirmed neutrophil dysfunction, with a diagnosis of AR CGD.

Microbiology

	Specimen	Microbiology	Sensitivities
16.5.11	Faeces	Adenovirus DNA	N/A . Blood = not detected
16.5.11	Right Toe Swab	***Staph aureus***	Penicillin – R only
19.5.11	Mouth swab	***Measles virus RNA***	N/A
24.5.11	**BAL**	***Aspergillus flavus***	Fully sensitive
2.6.11	**Left lung aspirate**	***1. Nocardia farcinica***	Cotrimoxazole-S, Imipenem -S, Amikacin -S
		2. M tuberculosis	Fully sensitive
3.6.11	ET secretions	***1. Nocardia farcinica***	As above
		2. Aspergillus terreus	**Ambisome-R,**
23.6.11	Sputum	***E coli ESBL***	Ciprofloxacin –R Gentamicin -S

Conclusions Challenges in her management that exemplify the increasing complexities of infections included:
- Huge number of antimicrobials, with many not licensed for children
- Dosing issues
- Route of delivery with poor absorption
- Drug interactions
- Adverse effects
- Duration of treatment

***Pseudomonas aeruginosa* infection of the central nervous system: negotiating the obstacles of a complex infection caused by an ubiquitous organism**

Wheldon, GK and Yiannakis, EP; White, B; Weston, VC
Department of Clinical Microbiology
Queen's Medical Centre
Nottingham University Hospitals NHS Trust
NG7 2UH

Background: Pseudomonas aeruginosa is an opportunistic pathogen that is a well recognised cause of nosocomial infection, including post-neurosurgical meningitis. Treatment of P. aeruginosa infection of the central nervous system (CNS) can be complicated by drug resistance, limited penetration of antibiotics into the CNS and drug allergies.

Case History: Our case regards a 55 year old lady with a background of an intradural and intra-medullary ependymoma. In 2005, she underwent debulking on two occasions followed by radiotherapy at another centre. Unfortunately she relapsed and required further surgery in 2011, complicated by a leak of cerebrospinal fluid (CSF) managed with a dural patch. She also had a minor superficial wound breakdown, wound swabs from which grew P. aeruginosa. She then developed recurrent fevers, requiring empirical antibiotics for suspected urinary tract infections.

Following several admissions for fever, culture of CSF from the operative region while off antibiotics grew P. aeruginosa. On the advice of microbiology, the dural patch was removed and the patient was treated with two weeks of intravenous piperacillin/tazobactam. Shortly after completion of antibiotics, the patient relapsed with high fevers and back pain. P. aeruginosa was cultured from a repeat CSF. On second exposure to the piperacillin/tazobactam the patient developed a rash, so was commenced on intravenous ceftazidime and gentamicin. Despite this, four days into treatment, P. aeruginosa was isolated from a further CSF. Management was then complicated by a ceftazidime-induced drug rash necessitating a change to meropenem. However, fever and meningism continued. High dose oral ciprofloxacin was added and the patient also received two doses of intra-thecal gentamicin. She then clinically improved and repeat CSF cultures became sterile. Questions were raised as to why the patient had failed to settle despite removal of prosthetic material as well as appropriate antibiotic therapy.

Treatment Complexities:
Prosthetic material: Further enquiry into the patient's past surgical history revealed the presence of an old dural graft inserted at the time of her previous surgery. Neurosurgical opinion was that any attempt at surgical clearance of the

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infection would require deloculation of the extensive arachnoid scar tissue and residual tumour with certain loss of lower limb function. Realistically this would be best achieved by total removal of all affected tissues with sacrifice of lower limb function in an attempt to save life.

Drug allergies: Drug rashes to both piperacillin/tazobactam and ceftazidime precluded the use of penicillins and cephalosporins in this patient's treatment. Although the organism tested sensitive to meropenem, this is not the optimal treatment for a deep-seated infection with P. aeruginosa.

Antibiotic resistance: The team elected to treat the patient with long-term oral ciprofloxacin suppressive therapy. There is an ongoing risk that the organism will develop resistance to this antibiotic.

Discussion: Our case highlights the difficulty of treating a proven P. aeruginosa infection of the central nervous system, particularly if prosthetic material is present and emphasises the importance of establishing previous surgical and implant history.

Evaluation of the Colonisation and Transmission Risk of Needle-Free Valves at Venous Access Ports
Richardson, J A T; Hodges, E; Rogerson, G; Young, P.
King's Lynn Institute for Patient Safety (KLIPS), Critical Care Centre, The Queen Elizabeth Hospital, King's Lynn

Needle-Free valves with a wipe-able stop–valve mechanism are increasingly used in an effort to prevent sharps injury in the NHS, however a simple plastic cap offers a needle-free solution at a 1/100th of the cost. The external surface of the Needle-Free valve can be wiped with antiseptic, however we hypothesized that a Needle-Free valve may present an increased infective risk to patients by acting as a trap for bacteria caught within the valve chamber. The manufacturer has performed studies with Staphylococcus aureus and with low colony forming unit inoculation of the outer surface (http://www.carefusion.co.uk/pdf/Infusion). We chose to perform a more extensive inoculation with mixed critical care pathogens.

Methods: We designed a blinded controlled trial to evaluate the transmission of pathogenic bacteria on a standard open port three-way tap (BD Connecta, Becton Dickinson, Helsingborg, Sweden) compared with the Needle-Free valve (Smartsite, Carefusion, UK). We introduced a heavily contaminated syringe tip (pre-dipped in a microbial broth of critical care pathogens) into each group port to simulate a serious breakdown in infection control. The Needle-Free valve surface was wiped in the recommended way and the open port wiped externally. A chlorhexidine 2%/ isopropyl alcohol wipe (Sani-Cloth, PDI, Flint, UK) was used for both. Ten minutes later, a 5mL sterile sample of saline was injected through port and collected at the "patient" end of the apparatus into sterile growth media, representing the passage of colonising bacteria to the patient on subsequent injection. This was then incubated for 48hr and plated onto blood agar. Fisher's Exact Test was used for comparisons.

Results: In the needle-free group 19/20 samples were heavily contaminated and one was negative. In the standard open port three-way tap group 6/20 were heavily contaminated and fourteen were negative ($p<0.001$).
Conclusions: Both the Needle-Free valve and the open port were easily contaminated. External cleaning with a chlorhexidine/alcohol swap was more likely to eliminate bacteria when the barrier of the stop valve on the Needle-Free valve was not present with the standard open port three-way tap. This may be due to the ability of antiseptic to ingress into the open port. We believe this has serious safety implications for Needle-Free valves because once contaminated they may serve as a bacterial trap.

BSAC Resistance Surveillance Project – Encore presentations
The BSAC Resistance Surveillance Project has carried out surveillance of antibiotic resistance continuously since 1999 in lower respiratory tract infections and 2001 in bacteraemia and collects up to 3,500 isolates for each surveillance programme each year. Forty sentinel laboratories based in the United Kingdom and the Republic of Ireland contribute to both surveillance programmes. The project is run by a working party of independent experts and industry representatives and has been funded by a total of 17 pharmaceutical companies at different times. The current collection of over 30,000 bacteraemia and 25,000 respiratory isolates is available for further research and several large-scale gene-sequencing projects using our surveillance isolates are in progress.

There have been over 50 publications from the study group, with abstracts published every year at ICAAC since 2001 and ECCMID since 2003. The four following posters were presented at national and international conferences during 2012 and will be shown at the 2013 BSAC Spring Meeting:

Vancomycin MICs compared between MRSA and MSSA in 9 countries. Reynolds, R., Jones, R.N., Stilwell, M.G., Zhanel, G., Hope, R., and on behalf of the BSAC Working Party on Resistance Surveillance. 22nd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). 2012 London, UK. Clinical Microbiology and Infection vol 18 suppl 3 p. S304-5, Abstract. P1215

Enterobacteriaceae in the UK and Ireland 2011: Susceptibility to Old and New Agents. Reynolds, R., Mushtaq, S., Kidney, A., and on behalf of the BSAC Working Party on Resistance Surveillance. 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). 2012. San Francisco, USA, Abstract. C2-152

BSAC Bacteraemia Resistance Surveillance Update 2011. Martin, V., Mushtaq, S., Livermore, D.M., Reynolds, R., and BSAC Working Party on Resistance Surveillance. Federation of Infection Societies (FIS) Scientific Meeting. 2012. Liverpool, UK, Abstract. AM14

BSAC Respiratory Resistance Surveillance Update 2010/11. Martin, V., Kidney, A., Janes, R., Reynolds, R., and BSAC Working Party on Resistance Surveillance. Federation of Infection Societies (FIS) Scientific Meeting. 2012. Liverpool, UK, Abstract. AM19

Notes

Expanded broad-spectrum coverage is on your side

TYGACIL has *in vitro* activity against a wide range of pathogens[1,2]

For the treatment of complicated intra-abdominal infections (cIAI) and complicated skin and soft tissue infections (cSSTI) excluding diabetic foot infections[2]

Tygacil should be used only in situations where it is known or suspected that other alternatives are not suitable[2]

References:
1. Wilcox MH. Surg Infect 2006; 7(1): 69–80.
2. TYGACIL® Summary of Product Characteristics. Accessed from www.medicines.org.uk.

Prescribing information can be found overleaf

Tygacil® tigecycline

Abbreviated Prescribing Information

TYGACIL® ▼ (tigecycline). See Summary of Product Characteristics (SmPC) before Prescribing.

Presentation: Tygacil 50mg Powder for Solution for Infusion (powder for infusion). Each 5ml Tygacil vial contains 50mg of tigecycline. After reconstitution, 1 ml contains 10mg of tigecycline. **Indications:** Tygacil is indicated in adults for the treatment of complicated skin and soft tissue infections (cSSTI), excluding diabetic foot infections and complicated intra-abdominal infections (cIAI). Tygacil should be used only in situations where it is known or suspected that other alternatives are not suitable. Consideration should be given to official guidance on the appropriate use of antibacterial agents. **Dosage:** (Intravenous infusion only over 30 to 60 minutes): The recommended dose for adults is an initial dose of 100mg followed by 50mg every 12 hours for 5 to 14 days. The duration of therapy should be guided by the severity, site of infection, and the patient's clinical response. Hepatic Insufficiency: In patients with severe hepatic impairment (Child Pugh C), the dose of Tygacil should be reduced to 25mg every 12 hours following the 100mg initial dose. Patients with severe hepatic impairment (Child Pugh C) should be treated with caution and monitored for treatment response. Renal Insufficiency: No dosage adjustment is necessary in patients with renal impairment or patient undergoing haemodialysis. Elderly patients: No dosage adjustment is necessary in elderly patients. Paediatric population: The safety and efficacy of Tygacil in children below 18 years have not yet been established. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Patients hypersensitive to tetracycline class antibiotics may be hypersensitive to tigecycline. **Special Warnings and Precautions:** In clinical studies in cSSTI, cIAI, diabetic foot infections, nosocomial pneumonia and studies in resistant pathogens, a numerically higher mortality rate among Tygacil treated patients has been observed as compared to the comparator treatment. The causes of these findings remain unknown, but poorer efficacy and safety than the study comparators cannot be ruled out. In clinical trials in cIAI patients, impaired healing of the surgical wound has been associated with superinfection. A patient developing impaired healing should be monitored for the detection of superinfection. Patients who develop super-infections, in particular nosocomial pneumonia, appear to be associated with poorer outcomes. Patients should be closely monitored for the development of super-infection. The use of Tygacil in non-approved indications is not recommended. Anaphylaxis/anaphylactoid reactions, potentially life-threatening, have been reported with tigecycline. Cases of liver injury with a predominantly cholestatic pattern have been reported in patients receiving tigecycline treatment, including some cases of hepatic failure with a fatal outcome. Glycylcycline class antibiotics are structurally similar to tetracycline class antibiotics and may have similar adverse event profiles. Acute pancreatitis, which can be serious, has occurred in association with tigecycline treatment. Combination antibacterial therapy should be considered in patients with clinically apparent intestinal perforation or patients with incipient sepsis or septic shock. In case of severe, persistent diarrhoea, the possibility of antibiotic-induced, life threatening pseudomembranous colitis must be taken into consideration. Experience in the use of tigecycline for treatment of infections in patients with severe underlying diseases is limited. **Drug Interactions: See SmPC. Pregnancy and Lactation:** Tigecycline should not be used during pregnancy or lactation unless clearly necessary. **Side Effects:** *Very common:* Nausea, vomiting, diarrhoea. Common: Pneumonia, abscess, infections, prolonged activated partial thromboplastin time (aPTT), prolonged prothrombin time (PT), hypoglycaemia, dizziness, phlebitis, abdominal pain, dyspepsia, anorexia, elevated aspartate aminotransferase (AST), elevated alanine aminotransferase (ALT), hyperbilirubinaemia, pruritus, rash, headache, impaired healing, elevated amylase, increased blood urea nitrogen (BUN). **Overdose:** Intravenous administration of tigecycline at a single dose of 300mg over 60 minutes resulted in an increased incidence of nausea and vomiting. **Presentation:** 5ml clear glass vials with snap-off aluminium crimp seal. Tygacil is distributed in a ten vial tray pack. **Legal Category:** POM **Basic NHS Price:** 10 Vials £323.10 **MA Number:** EU/1/06/336/001 **Marketing Authorisation Holder:** Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom.

Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard Adverse events should also be reported to Pfizer Medical Information on 01304 616161

TYG063

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Tygacil® tigecycline

The British Society for
Antimicrobial Chemotherapy

Griffin House
53 Regent Place
Birmingham
B1 3NJ
T: +44 (0)121 236 1988
F: +44 (0)121 212 9822
www.bsac.org.uk