DUNEDIN, NEW ZEALAND, NOVEMBER 2016

Infectious Diseases, Microbiology and Global Health in the home of New Zealand’s first medical school

ASID New Zealand
Annual Meeting 2016
Dunedin, 3-5 November
Welcome to the 2016 Annual Scientific Meeting of the New Zealand branch of the Australasian Society for Infectious Diseases, and welcome to Dunedin, the home of New Zealand’s first medical school.

This year marks ASID’s 40th anniversary and we look forward to celebrating this milestone with you at the conference and at the dinner.

For the first time, the ASID New Zealand conference will be held back to back with the Otago Global Health Institute (OGHI) Annual Scientific Meeting. The OGHI McKinlay Oration by Prof Sarah Cleaveland, on Thursday 3 November, will bridge the two events.

As with previous Meetings, we have a full and varied scientific programme. We welcome Prof Paul Newton as our international keynote speaker, who will deliver two presentations, A/Prof Scott Beatson as the other plenary speaker, and all the presenters who will be sharing their updates with us this year.

We are grateful to all conference supporters, in particular to the Otago Global Health Institute and the convenors of the OGHI meeting, Prof John Crump and Prof Philip Hill, for their active participation in the organising of both events. Our thanks also go to our sponsors, which include Merck Sharp & Dohme (MSD) NZ Ltd, now in their eleventh year of sponsorship of the meeting; Gilead, now in their fourth year as sponsors; the Webster Centre for Infectious Diseases; and Tourism New Zealand.

We trust you will enjoy the surroundings, the company and the conference dinner. We hope some of you will have the opportunity to stay around to enjoy the leisure activities that the Otago region has to offer.

Dr James Ussher, Dr Antje van der Linden (Convenors)

Dr Kerry Read (ASID New Zealand Branch Chair)
Conference
Dunedin Public Art Gallery, 30 The Octagon, Dunedin
Click here to view Google Maps

Dinner venue
The Dunedin Club, 33 Melville Street, Dunedin
Click here to view Google Maps
International Speakers

**Professor Sarah Cleaveland, UK**
Professor of Comparative Epidemiology (Institute of Biodiversity Animal Health and Comparative Medicine); Associate Academic (School of Veterinary Medicine) University of Glasgow, UK

Professor Cleaveland was the first woman to be awarded the British Veterinary Association Trevor Blackburn Award in 2008 in recognition of her work on animal and human infectious diseases in Africa. She is a founding director of the Alliance for Rabies Control whose mission is to prevent human deaths caused by infection with the rabies virus and reduce the burden of this disease in animals. Research interests: Understanding the ecology of diseases affecting human, domestic animal and wildlife health in natural ecosystems and mitigating their impacts. Zoonoses, neglected tropical diseases, intervention science, ecosystem health research, One Health.

**Professor Paul Newton, Laos**
Director, Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit, Laos
Research Area: Clinical Epidemiology; Scientific Themes: Tropical Medicine & Global Health

After junior doctor training in infectious disease and internal medicine in the UK, Professor Newton worked in the Mahidol Oxford Research Unit in Bangkok on malaria and melioidosis for four years before moving to Laos, where his small clinical tropical medicine research group conduct clinical research to help improve global, regional and Lao public health and to build capacity for this in Laos. Paul has more than 200 publications on infectious diseases in low-resource settings.

**Associate Professor Scott Beatson, Australia**
School of Chemistry and Molecular Biosciences, University of Queensland

Scott Beatson obtained a MSc from the University of Otago and a PhD from the University of Queensland. He undertook post-doctoral fellowships at the University of Oxford and the University of Birmingham. He returned to the University of Queensland in 2006 where he leads a research group. The Beatson group aims to better understand the molecular mechanisms of infectious disease and identify potential therapeutic and diagnostic targets by exploiting “Next-gen” genomic data. A major focus of the group is the comparative analysis of genomes obtained from local clinical isolates of important human pathogens.
## ASID New Zealand Meeting, 3-5 November 2016
### Program

*Program current at 25 October and subject to change*

### Thursday, 3 November

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<td>Introduction of joint Public Lecture with Otago Global Health Institute</td>
<td>John Crump</td>
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<td><strong>OGHI McKinlay Oration:</strong> Towards Global Elimination of Rabies</td>
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<td>Implementation of an Infectious Disease Consultation Service at Waikato Hospital - a prospective audit</td>
<td>Paul Huggan</td>
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<td>Emergency department sepsis pathway using electronic prompts and predictive value of the SOFA score on 30 day infection mortality</td>
<td>Nigel Raymond</td>
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<td>SCRIPT: a mobile app that makes the ACH antibiotic prescribing guidelines readily available</td>
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<td>Previous antibiotic-related adverse drug reactions do not reduce expectations for antibiotic treatment of upper respiratory tract infections</td>
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<td>Antibiotic consumption by New Zealand children: exposure near-universal by the age of five years</td>
<td>Mark Hobbs</td>
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<td>The longevity and acceptability of treatment to eradicate nasal Staphylococcus aureus carriage amongst haemodialysis patients</td>
<td>Stephen Ritchie</td>
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<td>Taking flucloxacin with food does not compromise effective plasma concentrations in healthy volunteers</td>
<td>Stephen Chambers</td>
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<td>An update on HQSC IPC programmes</td>
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<td>Routine ertapenem prophylaxis for transrectal ultrasound-guided prostate biopsy does not select for carbapenem-resistant organisms: a prospective ...</td>
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<td>Prosthetic Hip and Knee Joint Infection with NDM-1 positive Klebsiella Pneumoniae at Middlemore Hospital: a case study</td>
<td>Michael Borrie</td>
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<td>A rare case of Mycobacterium xenopi in an HIV positive</td>
<td>Ritesh Chandra</td>
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<td>16s rRNA PCR at Middlemore Hospital: A review of its use and clinical utility</td>
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<td>Anti-cytokine autoantibodies in infectious disease - case report and recent experience</td>
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<td>Trends in invasive bacterial disease in New Zealand children: a population based observational study</td>
<td>Tony Walls</td>
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4.15-4.30  Appropriateness of antibiotic prescribing following major surgery at Auckland City Hospital
Mary DeAlmeida

4.30-4.45  Analysis of patients admitted for community acquired pneumonia (CAP) - focus on clinical and laboratory diagnostics and antimicrobial stewardship
Hasan Bhally

4.45-5.00  AD-SCAP: Adaptive Design trial for Severe Community-Acquired Pneumonia
Susan Morpeth

5.00-5.30  LeginZ
David Murdoch

7.30pm  Conference Dinner, arrivals from 7pm
Dinner presentation  Stephen Chambers

Saturday, 5 November
9am - 10am  Session 7, Plenary 3
Fevers around the Mekong  Paul Newton

10.00-10.30am  Session 8, Plenary 4
WGS and outbreak investigation  Scott Beatson

10.30am - 10.45am  Morning Tea

10.45am - 12.25pm  Session 6, Proffered papers continued
Investigation of a prolonged outbreak of Staphylococcus capitis in the Dunedin Hospital Neonatal Intensive Care Unit  James Ussher
Mycobacterium chimera and cardiac bypass heater cooler units - an update  Sally Roberts
The effect of food on the posaconazole pharmacokinetics investigated during the development of a new tablet formulation  Andree Hubber
Pilot study of flucloxacillin and probenecid twice daily versus flucloxacillin four times daily for acute bacterial skin infections  Richard Everts
Case series of adult patients treated with high-dose probenecid-boosted flucloxacillin  Richard Everts
Leptospira borgpetersenii infection presenting as acalculous cholecystitis: a case report and review of the literature  Peter Davies
Fusobacterial Pyogenic Liver Abscess: a case report and review of the literature  Paul Huggan
Trainee Award Presentation & Conference Close

12.35pm  Lunch
Adult Septic Arthritis in South Auckland 2009-2014


Background / Aims: Native joint septic arthritis (NJSA) in adults is poorly understood but seen frequently at Middlemore. We describe its epidemiology, clinical features and outcomes.

Methods: Retrospective audit of NJSA in patients ≥16 years of age, identified using coding data, between 2009 to 2014. Electronic records were reviewed for demographic, clinical, laboratory, treatment and outcome data. Prosthetic joint infections were excluded.

Results: 543 episodes in 521 patients were included. Median age was 49 years and gender 70% male. Ethnicity was Pacific in 36%. NJSA incidence was higher than any previous report, 21/100,000 person years. Incidence was higher in Maori and Pacific people (30 and 43/100,00 person years respectively) and correlated strongly with age ($R^2=0.79$) and socioeconomic deprivation ($R^2=0.76$).

Commonly involved joints were knee (21%), hand interphalangeal (20%), metacarpophalangeal (18%) and glenohumeral (12%). Arthritis was monoarticular in 93%.

Underlying conditions included current smoking (35%), osteoarthritis (29%), diabetes (24%), gout (15%). Prior skin/soft tissue infection occurred in 38%. Sources of infection included haematogenous (42%), traumatic (36%), and iatrogenic (17%).

Causative organism(s) were isolated in 80%, most commonly *Staphylococcus aureus* (53%, 13% MRSA). 28% of culture-positive episodes were polymicrobial.

Treatment was with medians of 4 weeks of antibiotics and 1 surgical procedure.

90-day mortality was low at 5% (9% in large joint infection and 0% in solely small joint infection). Treatment failure occurred in 17% and on multivariate logistic regression was independently associated with large joint infection (OR 1.71), intra-articular prosthesis (OR3.38), age (OR 1.14 per 5 year increase) and number of surgical procedures (OR 1.42 per procedure).

Conclusions: This is the largest comprehensive series of adult NJSA to date. The high incidence, particularly among Maori and Pacific people is concerning. Large joint infection and the presence of prosthetic material are associated with poor outcome. NJSA mortality is lower than previously reported.
Implementation of an Infectious Disease Consultation Service at Waikato Hospital - a prospective audit


Background: A consultation-liaison service for infectious disease (ID) was introduced at Waikato Hospital in 2015. Prospective audit of service workload was undertaken for 19 weeks between December 2015 and June 2016.

Methods: Included were newly referred patients seen and examined by a member of the ID medical team (senior medical officer or registrar).

Excluded were all consultations conducted solely by telephone, patients under 16, urgent reviews of patients from the community and second or subsequent consultations within the study period.

Demographic, clinical and microbiologic details were collected for all patients.

Results: 220 consultations were undertaken. The mean age of patients was 60 (range 16-96). 25% were of Maori or Pacific Island ethnicity. 15% of patients were diagnosed with Type II diabetes, 6% were on long-term steroids and 5% had end-stage renal failure. The majority of referrals were from surgical departments (n=156; 71%), primarily orthopaedics (n=73; 33%), and general surgery (n=29; 13%). 50% of infections were of musculo-skeletal (n=72; 33%) or soft tissue origin (n=38; 17%). Prosthetic material or medical devices were involved in 31% (n=68) of cases. Over a quarter of patients (27%, 51/191) with proven or suspected bacterial infection were discharged to receive out-patient intravenous antibiotics (OPIVA).

Non-infectious disease (n=14; 6.5%), viral infection (n=10; 4.6%), fungal or mycobacterial infections (n=5, 2.3%) and overseas travel (n=4, 1.8%) together accounted for 15% of consults. Staphylococcus aureus was the most common pathogen, implicated in 35% (67/151) of proven bacterial infections. 8% (15/158) of proven bacterial infections involved resistant organisms (MRSA (n=10; 5.2%), non-ampC ESBL producing Enterobacteriaceae (n=4; 2.1%) or ampC producers (n=1; 0.5%)).

Consultation was judged to have resulted in a significant change in management (additional investigation, change in antibiotic choice or duration or acceptance onto OPIVA) in 91% cases (n=201).

Conclusions: In keeping with other services in Australasia the bulk of inpatient ID consultation concerns bacterial infection in patients with complex co-morbidity, often involving prosthetic or medical devices.
Emergency department sepsis pathway using electronic prompts and predictive value of the SOFA score on 30 day infection mortality.

Raymond N, Allmark S, Nguyen M.

Background: A sepsis pathway was introduced to Wellington Hospital Emergency Department (ED) in 2013 and updated since. In 2015, an electronic prompt was introduced at nursing triage and the medical assessment, asking whether ‘severe sepsis’ could be present, and if so to record electronically and to consider use of the sepsis pathway. During 2015, international definitions of sepsis recommended the Sequential Organ Failure Assessment (SOFA) score could be useful in assessing sepsis. We examined the application of the SOFA score in the ED setting.

Methods: Two sources of information were reviewed for the 1 year period July 2015 to June 2016. These were provided by the hospital’s Decision Support Unit.

(i) The outcome and features of those electronically identified with sepsis by ED staff. The qSOFA at ED triage was used as a guide to severity of infection.
(ii) All those people who died within 30 days of an ED visit with acute hospital admission for infection. The first 3 discharge diagnostic related groups (DRGs) were used to screen for possible infection.

Electronic clinical records were used to review a subset of both groups. Sepsis was assessed using the SOFA score criteria.

Results:

(i) Over the 1 year period there were 479 people electronically recorded in ED as suspected severe sepsis. On retrospective review of these and estimated 90% had infection as a major factor in their ED presentation. The 30 day mortality of those recorded in ED as severe sepsis was 53/497 (10.7%).
(ii) There were 208 people identified with likely infection, 9.2% of 2271 who had died within 30 days of having been acutely admitted to hospital during the one year period.

Results of the SOFA score assessments of a sample of both groups above will be presented. It was noted that sepsis often occurs in settings of people with multiple or advanced comorbidities, dementia, marked frailty, palliative intent, and advanced age.

Conclusions: Electronic prompts and surveillance of suspected ED sepsis in conjunction with a sepsis pathway may contribute to improving outcomes in people with acute infection. The SOFA score may be a useful tool in the ED setting.
SCRIPT: a mobile app that makes the ACH antibiotic prescribing guidelines readily available

Duffy E¹, Yoon C H¹, Thomas M¹,², Ritchie S¹,², Read K³, Holland D⁴ and Humphrey G²

¹ Auckland District Health Board  
² University of Auckland  
³ Waitemata District Health Board  
⁴ Counties Manukau District Health Board

Adherence by clinicians to evidence-based empirical antibiotic treatment guidelines has been associated with a relative risk reduction for mortality of 35%. Poor adherence to guidelines may often result in over prescribing of antibiotics, particularly of very broad spectrum antibiotics. Active antimicrobial stewardship programmes, electronic medicine prescribing tools, and web-based guidelines have contributed to improvements in prescribing; however, there remains great potential for improvement. A smartphone application (‘app’) provides the ability to have information readily accessible, understandable, and directly actionable at the time medicines are being prescribed, and opens a new era of possibilities for improving patient care and health care efficiency without compromising quality. However, research into the impact of antibiotic guidelines provided via a smartphone app is sparse and impact on patient care has not been studied.

A co-design approach was undertaken to develop SCRIPT, a smartphone application that contains the existing ACH internet based guidelines. With help from DHW designers, the look and feel was shaped to make app use easy and intuitive.

The impact of the app on antibiotic prescribing is being measured through retrospective case audits of the initial treatment of 200 cases of community acquired pneumonia and urinary tract infections, pre- and post- intervention. The initial antibiotic treatment of control cohorts is also being audited in patients admitted to CMDHB and WDHB.

Engagement with clinicians has been positive with good uptake and use to date.

Previous antibiotic-related adverse drug reactions do not reduce expectations for antibiotic treatment of upper respiratory tract infections.

Stephen R Ritchie\textsuperscript{1,2}, Kalpa J Jayanatha\textsuperscript{1}, Eamon J Duffy\textsuperscript{1}, James Chancellor\textsuperscript{2}, Zarah Allport\textsuperscript{1}, Mark G Thomas\textsuperscript{1,2}.

\textsuperscript{1}Auckland District Health Board  
\textsuperscript{2}Faculty of Medical and Health Sciences, University of Auckland

Patients’ expectations may influence prescribers’ decisions about antibiotic prescribing for upper respiratory tract infection (URTI). We examined whether patients’ personal experiences of antibiotic related adverse drug reactions (aADR) was associated with perceptions about antibiotic safety or with expectations to be prescribed antibiotics for an URTI.

We developed a questionnaire and surveyed 103 hospital inpatients, 38 of whom (37\%) reported past experience of aADR. Participants who had received antibiotics in the past five years perceived the treatment to be effective (median score of 8, IQR 5–9, on a scale of 1 to 10) and safe (median score of 8/10, IQR 5–10). Overall, 41/103 (40\%) participants expected their doctors to prescribe antibiotics to treat an URTI; participants with a tertiary level of education were less likely to expect antibiotics. Participants’ perceptions of antibiotic safety or expectation of antibiotic treatment for an URTI did not differ between those who had personal experience of an aADR compared with those with no history of aADR.

The almost universal belief that antibiotics are not harmful, despite the high prevalence of prior personal experience of an aADR helps to explain the strong patient expectations for antibiotic treatment in a range of conditions. Educational campaigns about the prescription of antibiotics for URTI should include information about the high risk of aADR as well as the negligible chance of benefit.
Study for Monitoring Antimicrobial Resistance Trends (SMART) in Australia and New Zealand, 2002-2015

Robert Badal¹, Geoffrey Coombs², Dragana Drinkovic³, Narelle George⁴, Andree Hubber⁵, Tony Korman⁶, Sally Roberts⁷, Mandeep Semb⁻⁵, Susan Taylor⁸

The longitudinal Study for Monitoring Antimicrobial Resistance Trends (SMART) has collected aerobic and facultative Gram-negative bacilli causing intra-abdominal infections (IAI), urinary tract infections (UTI) and respiratory tract infections (RTI) from most global regions. Isolate analysis includes antibiotic susceptibility and phenotypic extended-spectrum β-lactamase (ESBLp) testing, which is performed independently by IHMA, Inc (USA). Currently, eight sites from Australia and New Zealand (ANZ) participate in SMART. A total of 9117 organisms, comprised of 64% IAI, 28% UTI and 8% RTI isolates, were identified from ANZ between 2002 and 2015. The Enterobacteriaceae family predominated (85.4%, n=7787); the most common genera were Escherichia spp. (55.1%), Klebsiella spp. (19.5%), and Enterobacter spp. (9.2%). Amongst Enterobacteriaceae, rank order % susceptibility of common agents were piperacillin/tazobactam (PTZ, 90.1%), ceftriaxone (CRO, 85%), and cefotaxime (CTX, 84.8%). Susceptibility to these agents decreased over time amongst IAI-Enterobacteriaceae isolates (PTZ, 2002-2008, 92.3%; 2009-2011, 90.5%; 2012-2013, 90%; 2014-2015, 88.3%; CRO, 2002-2008, 86.4%; 2009-2011, 86.5%; 2012-2013, 82.8%; 2014-2015, 83.8%; CTX, 2002-2008, 86.6%; 2009-2011, 86.3%; 2012-2013, 82.6%; 2014-2015, 83.9%). ESBLp-detection amongst E. coli, K. pneumoniae, K. oxytoca and Proteus mirabilis was higher in isolates collected from patients with ≥48 hours hospitalization (10.6% ESBL; ESBL-E. coli 9.4%, -K. pneumoniae 16.7%, -K. oxytoca 8.9% and -P. mirabilis 4.2%) compared to <48 hours hospitalization (6.8% ESBL; ESBL-E. coli 6.4%, K. pneumoniae 4.2%, K. oxytoca 10.9% and -P. mirabilis 2.0%). The % ESBLp in these species shows an upwards trend (2002-2008, 6.2%; 2009-2011, 6.6%; 2012-2013, 11.2%; 2014-2015, 10.5%). This study contributes to the growing body of regional data.

† Susceptibility based on EUCAST breakpoints
Antibiotic consumption by New Zealand children: exposure near-universal by the age of five years

MR Hobbs, CC Grant, SR Ritchie, C Chelimo, SMB Morton, S Berry, MG Thomas

**Background:** Increasing concerns about antibiotic resistance and microbiome disruption have stimulated interest in describing antibiotic consumption in young children. Young children are an age group for whom antibiotics are frequently prescribed.

**Objectives:** To describe community antibiotic dispensing during the first five years of life in a large, socioeconomically and ethnically diverse cohort of children, and to determine how antibiotic dispensing varied between population subgroups.

**Methods:** This study was performed within the Growing Up in New Zealand longitudinal cohort study (www.growingup.co.nz) with linkage to national administrative antibiotic dispensing data. Descriptive statistics, univariate and multivariable associations were determined.

**Results:** The 5822 cohort children received 53,068 antibiotic courses, of which 54% were for amoxicillin. By age 5, 97% of children had received one or more antibiotic courses, and each child had received a median of 8 antibiotic courses (interquartile range 4 – 13). The mean incidence of antibiotic dispensing was 1.9 courses per child per year. Multivariable negative binomial regression showed that Māori and Pacific children received more antibiotic courses than European children, as did children in the most compared to the least deprived areas. A distinct seasonal pattern was noted.

**Conclusions:** This study provided a detailed description of antibiotic dispensing within a large and diverse child cohort. Antibiotic exposure was near universal by age 5. The predominance of amoxicillin use and the seasonal pattern suggest much antibiotic use may have been for self-limiting respiratory infections. There is a need for safe and effective interventions to improve antibiotic prescribing practices for New Zealand children.
The longevity and acceptability of treatment to eradicate nasal *Staphylococcus aureus* carriage amongst haemodialysis patients.

SR Ritchie¹,², E Burrett¹, P Priest³, PB Rainey⁴, S Taylor⁵, J Drown¹, MG Thomas¹,², J Collins².

¹School of Medical Sciences, University of Auckland
²Auckland District Health Board
³Dunedin School of Medicine, University of Otago
⁴NZ Institute for Advanced Study, Massey University
⁵Counties Manukau District Health Board

**Background:** *S. aureus* colonisation is the main risk factor for the development of disease. Although commonly used, nasal decolonisation of *S. aureus* to prevent infections in patients with chronic medical conditions is not an evidence-based strategy. Advocates of decolonisation strategies (e.g. in haemodialysis units) justify this approach using results from studies showing short term success in surgical patients.

**Aims:** We performed a pilot study to measure the duration of decolonisation and the acceptability of two decolonisation treatment strategies.

**Methods:** As part of a larger study comparing *S. aureus* carriage patterns between healthy adults and patients requiring haemodialysis, we randomised 31 haemodialysis patients to receive either nasal mupirocin combined with chlorhexidine body wash or systemic antibiotic treatment. Both treatments were given for 7 days and serial nasal swabs were obtained over 10 weeks of follow up. At that time 23 patients crossed over to the alternate treatment followed by serial nasal swabbing. All *S. aureus* isolates were *spa* typed. At the end of each week’s treatment we interviewed the patients about their adherence and treatment acceptability.

**Results:** Approximately one third remained free of nasal *S. aureus* colonisation during follow-up; the median time to re-colonisation was just over one month. 30/54 (56%) treatments were acceptable to the patient – they would be happy to use that treatment again. 10/25 (40%) patients who received antibiotics developed an adverse drug reaction; 5/29 (17%) patients who received mupirocin/chlorhexidine developed an adverse drug reaction.

**Conclusion:** The short median duration of decolonisation is consistent with the time-frame of new *S. aureus* infection in the healthy population. Haemodialysis patients often found it difficult to use the treatments we provided. These findings highlight the need to develop new strategies to provide long-term cure of *S. aureus* colonisation.
Taking flucloxacillin with food does not compromise effective plasma concentrations in healthy volunteers.

Sharon J Gardiner1-3, Philip G Drennan1, Ronald Begg4, Mei Zhang4,5, Jared K Green1, Heather L Isenman1, Richard J Everts6, Stephen T Chambers1,7, and Evan J Begg4.

1 Department of Infectious Diseases, Christchurch Hospital, Christchurch, New Zealand; 2 Department of Clinical Pharmacology, Christchurch Hospital, Christchurch, New Zealand; 3 Pharmacy Services, Christchurch Hospital, Christchurch, New Zealand; 4 Department of Medicine, University of Otago-Christchurch, Christchurch, New Zealand; 5 Toxicology, Canterbury Health Laboratories, Christchurch, New Zealand; 6 Department of Medicine, Nelson Hospital, Nelson, New Zealand; 7 Department of Pathology, University of Otago-Christchurch, Christchurch, New Zealand;

Objectives: To compare the bioequivalence of oral flucloxacillin, given with and without food, based on total and free flucloxacillin concentrations.

Methods: Flucloxacillin 1000 mg orally was given to 12 healthy volunteers without food and following a high-fat high-calorie breakfast, on two days one week apart. Total and free plasma concentrations of flucloxacillin over 12 hours were measured by LC-MS/MS. Standard pharmacokinetic values, and pharmacodynamic endpoints related to target concentration achievement, were compared in the fed and fasting states.

Results: For free flucloxacillin, the fed/fasting AUC0∞ ratio was 0.8 (p<0.01, 90% CI 0.70-0.92), the Cmax ratio 0.5 (p<0.001, 0.42-0.62) and the Tmax ratio 2.2 (p<0.001, 1.87-2.55). These ratios for total flucloxacillin concentrations were similar. The mean (90% CI) fed/fasting ratios of free concentrations achieved or exceeded for 30%, 50% and 70% of the first 6 hours post-dose were 0.74 (0.63-0.87, fed inferior p<0.01), 0.95 (0.81-1.11, bioequivalent) and 1.15 (0.97-1.36, fed non inferior), respectively. Results for 8 hours post-dose and those predicted for steady state were similar. Comparison of probability of target attainments (PTAs) for fed versus fasting across a range of MICs supported these results.

Conclusions: Flucloxacillin taken orally in the fed state reduced the AUC and Cmax, and prolonged the Tmax of both free and total concentrations compared with the fasting state. However, achievement of free concentration targets associated with efficacy were in most circumstances equivalent. In the light of these results, the requirement for taking flucloxacillin only in the fasting state needs reconsideration.
Routine ertapenem prophylaxis for transrectal ultrasound-guided prostate biopsy does not select for carbapenem-resistant organisms: a prospective cohort study.


**Background:** TRUS-guided prostate biopsy (TGB) is a commonly used procedure for investigation of prostatic malignancy. Post-TGB sepsis (PBS) is an increasing problem in this era of rising antibiotic resistance. Ertapenem prophylaxis has proven very effective at our institution for reducing PBS, however has raised local and regional antimicrobial stewardship concerns. This study investigated the possible selective effect of single dose ertapenem prophylaxis for TGB on faecal colonisation with carbapenem-resistant Enterobacteriaceae (CRE).

**Methods:** Patients had a rectal swab taken prior to receiving antibiotic prophylaxis for TGB. A second swab was taken at follow up several weeks later. Swabs were screened for CRE using an enhanced Centers for Disease Control (CDC) method. Pre biopsy swabs were also screened for ESBL/AmpC beta-lactamase-producing (ESBL/AmpC-E), and ciprofloxacin-resistant Enterobacteriaceae. Patients were monitored for PBS.

**Results:** Three hundred and twenty six patients were enrolled. At baseline, 6.4% and 9.0% of patients had colonisation with ESBL/AmpC-E and ciprofloxacin-resistant Enterobacteriaceae, respectively. No patients had CRE detected at either baseline or follow up. Colonisation with non-fermentative organisms with intrinsic ertapenem resistance was detected in 29.4% of patients at both baseline and follow up (p=1.0). Three cases (0.9%, 95%-CI 0.2-2.8%) of PBS were identified during the study period. None of these were bacteraemic or required ICU admission.

**Conclusion:** Single dose ertapenem is effective prophylaxis for TGB. It did not appear to have a significant selective effect on faecal colonisation with CRE or other ertapenem-resistant Gram-negative organisms in this outpatient group. Ertapenem may, in the right setting, represent a useful prophylactic option for prevention of PBS.
Prosthetic Hip and Knee Joint Infection with NDM-1 Positive *Klebsiella Pneumoniae* at Middlemore Hospital: A difficult problem that required above knee amputation

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**Introduction:** New Delhi metallo-beta-lactamases (NDM) are increasingly reported worldwide. It is the most commonly identified carbapenemase among *Enterobacteriaceae* in New Zealand. Joint infections with carbapenem resistant *Enterobacteriaceae* are a concerning prospect; as effective antibiotics do not all have distribution in bone, joints and biofilms.

**Methods:** This is a single case report from 2015 and literature review.

**Results:** A 66 year old man underwent open reduction and internal fixation of right tibial plateau and acetabular fractures in India following a motor vehicle accident. Both sites became infected with NDM-1 positive *Klebsiella pneumonia*, and were treated. A year later elective total hip arthroplasty, then total knee arthroplasty were performed in New Zealand for ongoing pain. There was no clinical infection at the time of surgery. Six days later he was admitted to Middlemore hospital with signs of knee infection. Joint cultures isolated NDM-1 positive *K. pneumoniae* and ESBL positive *K. pneumoniae* from the knee and hip. He underwent right above knee amputation followed by 42 days of colistin, meropenem and cotrimoxazole followed by Cotrimoxazole suppression. At discharge he was found to be colonized with an NDM-1 positive *Proteus mirabilis* (intrinsically colistin resistant). At last follow-up he was independently mobile with an external prosthesis and tolerating cotrimoxazole.

**Conclusion:** This is the first case report of prosthetic joint infection caused by a NDM-1 positive *K. pneumoniae*. Robust analysis of clinical isolates and appropriate screening is needed throughout New Zealand hospitals. Clinicians need to be vigilant for possible chronic prosthetic joint infection despite clinical quiescence.

**Disclosure of Interest Statement:** None of the authors have any relevant disclosures. No grants were received for this study.
A rare case of *Mycobacterium xenopi* osteomyelitis in an HIV-infected patient

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We describe the case of a 58 year old female who presented with chronic back pain for 3 months prior to presenting to orthopaedic services. She was admitted and an MRI spine was consistent with thoracic vertebral osteomyelitis. A CT-guided biopsy was performed which was initially culture negative and she was empirically treated with intravenous flucloxacillin.

Her past medical history included Human Immunodeficiency Virus (HIV) infection with a CD4 nadir of 4. She had subsequently been on antiretroviral treatment with a fully suppressed virus and a CD4 count >450 for more than 5 years.

She was readmitted with no improvement on empiric 4-week therapy flucloxacillin and another CT-guided biopsy was performed. The next day, *Mycobacterium xenopi* was cultured from the original biopsy, after 40 days of incubation. Clinical deterioration led to a T9/10 corpectomy and stabilisation surgery. *M. xenopi* was subsequently cultured from the repeat CT-guided biopsy and surgical biopsies.

At last assessment she was continuing to improve on antimycobacterial treatment.

**Conclusion:** *M. xenopi* is a rare cause of spinal infection. We review the literature on *M. xenopi* spinal infections including cases occurring in HIV infected patients.
16s rRNA PCR at Middlemore Hospital: A review of its use and clinical utility

Playle V, Morpeth S, Taylor S

16s rRNA PCR is increasingly being used in the laboratory both for identification of bacterial isolates for which an identification cannot otherwise be determined and in clinical samples where infection is suspected but a causative organism has not been found through routine methods. Anecdotally the utility of this test in clinical samples has been mixed. Of particular interest is its use in culture-negative bone and joint infections particularly in those who have been pre-treated with antibiotics.

Middlemore Hospital has been using 16sPCR on clinical samples on a case by case basis through the infectious disease and microbiology service since 2006 with 114 clinical samples sent for 16sPCR (of which 82 were from joint aspirates/tissue).

We review the local experience looking at the frequency of positive results and factors that improve the likelihood of a positive result. This has allowed us to refine our algorithm for the use of 16sPCR.
How many patients with cellulitis are unnecessarily admitted to Auckland City Hospital?

T. Cutfield, S. Ritchie, A. Chuang, M. Thomas

Introduction: Cellulitis is a leading cause of avoidable hospitalisation at Auckland City Hospital (ACH), however there is no protocol for severity assessment to guide management of cellulitis. This pilot study aimed to apply the 2011 Dundee classification of cellulitis severity to find how many patients may have been unnecessarily hospitalised. The secondary aim was to gain a detailed understanding of the characteristics of patients with cellulitis seen at ACH.

Methods: 250 cases were randomly selected from a retrospective cohort of 1514 adult presentations with a primary coded diagnosis of cellulitis. Demographic data was obtained from coding resources. Electronic medical records were reviewed for all encounters to obtain clinical and laboratory data.

Results: 244 out of 250 were suitable for analysis. Demographics was well matched with the parent cohort of 1514. Maori were overrepresented compared with census data (12.4% vs 7.9%), but Pacific Island peoples were not (12.4% vs 11.2%). Asian people were under-represented (11.2% vs 29%). Rates of diabetes, obesity and chronic venous insufficiency were 19.7%, 19.3%, 20.0% respectively. Lower limbs were the most common site of cellulitis (70.2%). Median length of stay was 3.5 days. The most common microbiological isolates were Staphylococcus aureus and Streptococci. Dundee severity classification was class 1 in 54.9%, class 2 in 26.2%, class 3 in 16.8%, and class 4 in 2%. 30 day mortality was 1.6%, with a 30 day readmission rate for cellulitis of 9.0%. Rates of intravenous antibiotic prescription were 85.1% for class 1, 92.2% for class 2 and 100% for both class 3 and 4. The mean cost per encounter was $4698, with mean cost per Class I encounter $2990 and discharges from the emergency department $879.3.

Conclusion: Most cases of cellulitis had no systemic compromise, with almost all being admitted to hospital for intravenous antibiotics. A modest increase in the rate of discharge from the Emergency Department in these mild cases would result in significant reduction in avoidable admissions and cost.
Anti-cytokine autoantibodies in infectious disease – case report and recent experience

Huggan P

Autoantibodies to a range of cytokines have been associated with predisposition to infection. An immunocompetent male presented to our hospital with a *Nocardia* abscess at the site of a soft tissue injury and an acute paraparesis. Investigations revealed extensive neuraxial involvement with spinal cord and cerebral abscesses. Treatment was successful but the patient lives with significant disability. Anti- granulocyte macrophage colony stimulating factor (anti-GMCSF) antibodies were recently reported in association with disseminated nocardia infection in adults who would otherwise be considered immunocompetent. The literature on anti-cytokine autoantibodies as it relates to infection and the pathway to testing for this patient will be discussed.
Trends in invasive bacterial disease in New Zealand children: a population based observational study

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Background: The incidence of invasive bacterial infection is generally higher in infants and young children than at any other time in life. Historically *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* type B (Hib) have been the commonest organisms causing severe disease in this age group. Vaccines are now available to prevent each of these infections.

Aims: The aim of this study was to describe the long-term trends in hospital admissions and notifications for invasive infections caused by *S. pneumoniae*, *N. meningitidis* and Hib in New Zealand (NZ) children aged <15 years.

Methods: Two separate datasets were analysed to assess trends in hospital admissions and notifications for infections caused by *S. pneumoniae*, *N. meningitidis* and Hib from 1991 to 2014. The National Minimum Dataset (NMDS) provided data, using encrypted NHI numbers, as defined by hospital discharge coding for meningitis and septicaemia caused by each pathogen. Admission rates for epiglottitis were also analysed. EpiSurv provided data on notifications for each disease from 1997 onwards. Annual population estimates based on Census data (Statistics New Zealand) were used as the denominator to calculate rates of disease. The direct method of age standardisation using the European Standard Population was used to enable comparison with recent United Kingdom (UK) data.

Results: Following the introduction of the protein conjugate Hib vaccine in 1993 there were dramatic and sustained reductions in the rates of hospital admissions due to invasive Hib disease from 21.1/100,000 to 0.62/100,000 children annually. During the NZ meningococcal hyperepidemic of the 1990’s admission and notification rates fell substantially following the introduction of the MenZB vaccine (from 57.2/100,000 to 3.6/100,000) and remained low even when this vaccine was withdrawn. The greatest reduction in hospital admissions occurred in Maori children. The rates of hospital admission due to pneumococcal disease in children have also declined following the introduction of pneumococcal conjugate vaccines (from 13.9/100,000 to 2.6/100,000), with the greatest declines also occurring in Maori children.

Comparison with UK hospital admission rates demonstrated that rates of Hib disease are similar in the two countries. NZ had lower rates of meningococcal disease during 2007-11 despite there being no meningococcal vaccine on the national immunisation schedule. NZ rates of pneumococcal septicaemia have been consistently higher than in the UK throughout the study period.

Conclusions: Substantial reductions have occurred in hospital admissions for and notifications of vaccine-preventable bacterial infections in NZ children over the last 25 years. The impact of vaccination programmes appears to have been greatest for Maori children.
Appropriateness of antibiotic prescribing following major surgery at Auckland City Hospital (ACH)

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Background: In 2015, the Health Quality & Safety Commission introduced the ‘Infection and antibiotic use following major surgery’ domain of the Atlas of Healthcare Variation. A key finding was that on average, 34\% of patients discharged following major surgery at a public hospital were dispensed an antibiotic within 30 days of the procedure. This contrasts with the average 2.6\% of patients being recorded as having an infection after major surgery. At Auckland District Health Board, 32.4\% of patients discharged following a major surgery in 2013 were dispensed an antibiotic within 30 days of discharge. Of concern, was that 50\% of the prescribing occurred at discharge.

In light of the findings of the Atlas, we aimed to determine the indications and the appropriateness of antibiotic use in patients discharged following major surgery at ACH.

Method: A retrospective audit of antibiotic prescribing in patients discharged following major surgery was conducted for the period January to December 2013. The indication for antibiotic use was categorised into one of six categories: (i) infection present on admission; (ii) healthcare associated infection (HAI); (iii) prolonged surgical antimicrobial prophylaxis (SAP); (iv) empiric therapy; (v) no documented indication; (vi) other reason. The justification for antibiotic use was further classified as ‘appropriate’, ‘uncertain’ or ‘inappropriate’.

Results: The medical records of 414 patients were reviewed. 16 were excluded. For the 398 patients reviewed, an indication was not documented in 72 patients (18\%). Antibiotics were prescribed for an established infection in 171 patients (43\%), as prolonged SAP in 41 patients (10.3\%) and as empiric therapy in 100 patients (25.1\%). Overall, more than a third of patients received antibiotics inappropriately. Amoxicillin clavulanate was by far the most commonly prescribed antibiotic.

Conclusion: This study demonstrates that a significant proportion of antibiotics prescribed following surgery were inappropriate and this is an area where good antimicrobial stewardship may be effective.
Analysis of patients admitted for community acquired pneumonia (CAP)- focus on clinical and laboratory diagnostics and antimicrobial stewardship.

Ritesh Chandra, Nicola Williams, Minja Bojic, Kirsty Moffat, Hasan Bhally

**Background:** Lower respiratory tract infection (LRTI) is a common indication for use of antibiotics. In a recent study 50% of our inpatients with infection had LRTI as the admitting diagnosis, but only 40% were supported by either microbiological or radiological evidence. Variability exists in terms of utility of microbiological diagnostic testing, interpretation of results, and antibiotic management.

**Objective:** The main study objective is to assess the clinical, radiological and microbiological characteristics of inpatients managed as CAP, and to determine appropriateness of antibiotic therapy in these patients.

**Methods:** A 6 week observational study was conducted at WTK hospital in mid-2016. All adults (>15 yrs) admitted under General Medicine service with a clinical diagnosis of ‘chest infection’, ‘pneumonia’ or ‘COPD exacerbation’ were identified through daily admission lists and management was reviewed confidentially. Patients with 1 or more: fever>38, new or worsening cough, or pleurisy were included and divided into definite CAP (cases)- LRTI with new pulmonary infiltrate, and clinical CAP (controls)- LRTI without infiltrate but discharge diagnosis of pneumonia. Utilisation of diagnostic microbiology and antimicrobial therapy was assessed.

**Results:** A total of 145 patients- 77 cases and 68 controls were included, with no significant baseline differences in mean age, sex, ethnicity. Chronic lung disease was more common in controls (69% vs 45%), fever more common in cases (47% vs 32%), and new or worsening cough present in 80% in each group. Overall, yield of bacterial aetiology was only 2.3% (2/86) from bacterial cultures, 34% (25/72) from sputum cultures, and 8.3% (4/48) from urine antigen testing. None of the control group had a positive blood culture or urine antigen. *S.pneumoniae* (12% of cases and no controls) and *H.influenza* (7% cases and 8.5% controls) were commonest bacteria. Human metapneumovirus (n=6), Influenza (n=7), and RSV (n=8) were isolated in both cases and controls. All except 5 patients (1 case) received antibiotics. Average antibiotic duration was not significantly different in cases (mean 5.8 days in hospital and 4.6 days after discharge) and controls (mean 5.3 and 3.9 days). All 11 cases vs 6 of 11 controls with confirmed viral aetiology had prolonged antibiotic courses.

**Conclusion:** This study highlights the issues of over diagnosis of LRTI as pneumonia, poor diagnostic yield from routine microbiology tests, and excessive use of empiric antibiotics in treatment of LRTI.
AD-SCAP: Adaptive Design trial for Severe Community-Acquired Pneumonia


Background: Community-acquired pneumonia (CAP) causes ~1100 adult admissions to Intensive Care Units (ICUs) per year in New Zealand, with 20% mortality. AD-SCAP is a novel adaptive design platform trial that will take place in New Zealand, Australia and Europe.

Methods: The platform trial will consist of a registry of patients with CAP admitted to participating ICUs. Domains testing different interventions are layered onto the platform, using adaptive randomisation; meaning random allocation to interventions is in proportion to the likelihood that they are best treatment. Regular interim analyses will use Bayesian statistics; no fixed sample size means that conclusions will be drawn when there is sufficient data, with pre-specified thresholds to avoid types I & II error. Two of the first planned domains are the antibiotic and immune modulation domains. The antibiotic domain will study empiric antibiotic therapy and has up to five interventions; a) Ceftriaxone + Azithromycin, b) Moxifloxacin, c) Piperacillin-tazobactam + Azithromycin, d) Ceftaroline + Azithromycin, e) Amoxicillin-clavulanate + Azithromycin. The immune modulation domain will examine the effect of 14 vs 3 days of azithromycin among patients in whom infection with Legionella, Mycoplasma and Chlamydophila species has been excluded. The primary outcome will be 60-day mortality. Secondary outcomes include length-of-stay, functional capacity, lung abscess/empyema, and detection of multi-drug resistant bacteria or Clostridium difficile infection.

Discussion: The novel design means less effective interventions are dropped early and best treatment becomes standard of care immediately. Response adaptive randomisation results in lower trial mortality than fixed 1:1 randomisation, and a greater proportion of patients receive ‘best treatment’ in the trial compared to outside the trial.
LegiNZ: The New Zealand Legionnaires’ Disease Case Finding Study

David Murdoch, on behalf of the LegiNZ Investigators
University of Otago, Christchurch

**Background.** New Zealand has the highest reported incidence of Legionnaires’ disease globally. However, Legionnaires’ disease is almost certainly under-diagnosed because of the poor sensitivity and poor utilisation of diagnostic tests. This has resulted in an inaccurate national picture of disease burden and epidemiology, with a predominance of cases coming from Canterbury where the nation’s most rigorous testing strategy occurs. The Canterbury testing strategy involves the routine use of PCR to test sputum samples from hospitalised patients with suspected pneumonia. The LegiNZ study applied this testing strategy across New Zealand in order to better assess the burden and epidemiology of Legionnaires’ disease.

**Methods.** From May 2015 to May 2016, all sputum samples identified as from patients hospitalised with pneumonia in 20 hospitals from 17 District Health Boards were tested for *Legionella* spp. by PCR. Demographic and clinical data were collected from all patients, with additional clinical data collected from those with Legionnaires’ disease.

**Results.** Sputum samples from 5677 patients were tested, of which 211 (4%) tested positive for *Legionella* spp.. Two thirds of cases were due to *Legionella longbeachae*, while most of the remainder were due to *Legionella pneumophila*. Cases of Legionnaires’ disease were found throughout New Zealand, with the highest incidences coming from Bay of Plenty, Canterbury, the Auckland region and Hawkes Bay. Legionnaires’ disease notifications increased to approximately three times usual levels during the study period.

**Conclusions.** Legionnaires’ disease is not just a Canterbury phenomenon. This disease is under-diagnosed and a systematic testing strategy has revealed a previously unrecognised burden in several regions of New Zealand.
WGS and outbreak investigation

Scott Beatson - Abstract not available at the time of printing

Endemic Staphylococcus capitis subsp urealyticus in Neonatal Intensive Care: an international problem.

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Background/Objectives: Coagulase negative staphylococci (CoNS) are recognised as the most common cause of late serious bacterial sepsis (SBS) in very preterm infants in Neonatal Intensive Care Units (NICUs). Dunedin NICU has for more than a decade had a high proportion of S. capitis among its CoNS. The aim of this study was to characterise the local S. capitis, to compare it with S. capitis causing SBS in other NICUs, and to understand its biology to inform the development of preventive strategies.

Methods: S. capitis isolates from the following sources were investigated:

1) Blood culture isolates from:
   a. septic infants in Dunedin Hospital NICU
   b. blood cultures from adults in Dunedin
2) Skin surveillance isolates from non-septic infants in Dunedin Hospital NICU
3) Skin surveillance isolates from staff in Dunedin Hospital NICU
4) Cryopreserved S. capitis isolates from sterile sites from patients in Christchurch, Auckland, and Melbourne

The organisms were initially typed by pulsed-field gel electrophoresis (PFGE) and a subset (n=126) was analysed by whole genome sequencing (WGS) on an Illumina NextSeq platform. A complete local reference genome was generated using PacBio SMRT sequencing. Comparison was made with previously published reference S. capitis genomes, including sepsis-related NICU strains from Australia, Europe and USA. Phylogenetic and comparative genomic analyses were performed using in-house bioinformatic pipelines at MDU PHL.
**Results:** Isolates of *S. capitis* from infants in the Dunedin unit were shown to be clonally related by PFGE. Very preterm infants rapidly became colonised with the endemic strain of *S. capitis*, while staff were colonised with non-endemic strains. By WGS, *S. capitis* isolated from both septic and colonised infants in the Dunedin NICU were highly related, and were also closely related to the *S. capitis* clone reported from septic infants in NICUs in France, USA, and Australia. However, isolates from neonates in the Dunedin NICU were distantly related to *S. capitis* from septic adults and from staff in Dunedin NICU. NICU-related strains contained the ica (Intercellular Adhesion Locus) operon, which is associated with biofilm production, and the SCCmec element, which contains the methicillin resistance gene, *mecA*. There was also evidence that the Dunedin strain had acquired a plasmid encoding genes associated with fusidic acid resistance (*fusB*) and reduced susceptibility to chlorhexidine (*qacA*).

**Conclusions:** The endemic *S. capitis* in the Dunedin NICU is very closely related to published organisms causing similar endemic infections in NICUs in Melbourne, Lyon and other parts of France. It has multiple resistance features including resistance to methicillin. Of note, the Dunedin isolate has acquired a plasmid encoding genes associated with reduced susceptibility to chlorhexidine and fusidic acid. The NICU-related *S. capitis* strain has spread across the world, possibly carried by healthcare workers.
The effect of food on the posaconazole pharmacokinetics investigated during the development of a new tablet formulation

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Background: Posaconazole (POS) is a potent antifungal agent which is on the market as an oral suspension. However, it needs to be administered multiple times a day with food (preferably high fat meal) or nutritional supplements to increase exposure. Therefore, POS tablet was designed to enhance bioavailability and to reduce the requirement for food intake.

Methods: In 3 different studies, the effect of food on various formulations during the tablet development was investigated:

• In study 1, healthy subjects received single doses of prototype tablets A and B, a capsule and the oral suspension, all at 100 mg, in the presence or absence of a high fat meal.

• In study 2, patients received multiple doses of prototype tablet C and tablet D (the FMI) at a dose of 300 mg (3 x 100 mg) once daily, without regard to food.

• In study 3, healthy subjects received single doses of tablet D at 300 mg (3 x 100 mg) in the presence or absence of a high fat meal.

In all studies main PK parameters were Cmax and AUC_{0-last} and in study 2 Cavg was evaluated against predefined (safety and efficacy) target exposure ranges.

Results: • In study 1, no relevant food effects were noted for the capsule and prototype formulations: Cmax geometric mean ratios (GMRs) of Cmax_fed/Cmax_fasted and AUC_fed/AUC_fasted ranged from 0.85-0.96 and 1.02-1.11 respectively whereas for the oral suspension, 3.34 and 3.06 respectively.

• In study 2, in the majority of patients, POS exposures were within the target ranges when the tablets were taken without regard to food.
In Study 3, GMRs of Cmax,fed/Cmax,fasted and AUCfed/AUCfasted were 1.16 and 1.51, respectively.

**Conclusion:** Although a modest food effect is still present, the availability of a posaconazole tablet with a significant reduced food effect is an important advance in the treatment of patients that generally have a poor oral intake.

**Pilot study of flucloxacillin and probenecid twice daily versus flucloxacillin four times daily for acute bacterial skin infections**

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Pharmacokinetic studies in volunteers show that probenecid markedly increases flucloxacillin exposure and taking flucloxacillin plus probenecid with a small meal leads to equal or better flucloxacillin exposure than on an empty stomach. Modelling of these results suggests that flucloxacillin 1 g orally twice daily plus probenecid 500 mg orally twice daily will provide sufficient \( fT_{>MIC} \) to effectively treat almost all mild *Staphylococcus aureus* and beta-haemolytic streptococcal infections in immune-competent adults (bacteriostasis).

Thirty nine adult patients with mild to moderate skin infections were randomised to receive either flucloxacillin 1 g orally twice daily with probenecid 500 mg orally twice daily with food for 7 days (n=19) or flucloxacillin 500 mg four times daily alone on an empty stomach for 7 days (n=20). Baseline characteristics were similar between the two groups. Clinical outcomes were equally favourable and adverse effects were not worse for the probenecid group.

This small pilot study indicates that larger trials are feasible and warranted. Twice daily flucloxacillin with probenecid is more convenient, likely to be equally effective and no more likely to cause adverse effects than flucloxacillin four times daily alone for patients who have no contra-indications to taking probenecid.
Case series of adult patients treated with high-dose probenecid-boosted flucloxacillin

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Pharmacokinetic studies in volunteers show that probenecid markedly increases flucloxacillin exposure and taking flucloxacillin plus probenecid with a small meal leads to equal or better flucloxacillin exposure than on an empty stomach. Modelling of these volunteer results suggests that flucloxacillin 1 g orally four times daily plus probenecid 500 mg orally four times daily will provide sufficient flucloxacillin exposure to effectively treat almost all moderately severe Staphylococcus aureus and beta-haemolytic streptococcal infections, based on a PK/PD target of \( fT_{T>0.5} \) for at least 50% of the dose interval.

Since 2012 most adult patients in Nelson and Marlborough with severe infections known or suspected to be caused by flucloxacillin-susceptible pathogens have been treated as inpatients with IV antibiotics then discharged on flucloxacillin 1 g orally three or four times daily with probenecid 500 mg orally three or four times daily. Previously, such patients were usually treated with outpatient IV flucloxacillin infusions. Plasma flucloxacillin levels are measured 3 to 6 hours post-dose at least once and the dose is adjusted to achieve \( fT_{T>0.5} \) for at least 50% of the dosing interval. ID follow-up and blood monitoring is undertaken weekly.

Accurate total plasma flucloxacillin levels have been available through Canterbury Health Lab since August 2012. Free (unbound) plasma flucloxacillin levels are estimated from total levels based on an age-adjusted conversion formula. The results of 104 plasma free flucloxacillin tests in 68 patients receiving flucloxacillin 1 g plus probenecid 500 mg orally are presented; almost all were therapeutic.

The clinical outcome of oral flucloxacillin and probenecid treatment for 90 episodes of moderately severe infection (mostly orthopaedic infections caused by Staphylococcus aureus) in 84 adult patients between March 2011 and September 2016 is presented. Sixty six of 70 patients with known flucloxacillin-susceptible organisms responded clinically and biochemically to this regimen; under-dosing may have contributed to 2 of the 4 failures. Infection relapse occurred in 12 of 66 patients (18%). Possible toxicity requiring discontinuation of flucloxacillin or probenecid treatment occurred in 8 cases (9%): acute liver toxicity (4), nausea (2), rash (1) and acute kidney injury (1). Toxicity was not associated with high plasma flucloxacillin levels.

Although not a comparative trial, these data indicate that oral probenecid-boosted flucloxacillin is probably effective and well tolerated and is a potential replacement for outpatient IV infusion.
therapy in compliant patients with no contraindication to taking probenecid. Flucloxacillin concentration monitoring is important for avoiding potential under-dosing. Further PK analyses and comparative trials are warranted.

**Leptospira borgpetersenii infection presenting as acalculous cholecystitis: a case report and review of the literature**

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Authors: Davies. P, Aoyagi. Y.

Leptospirosis is the most common zoonosis worldwide and its incidence is increasing in New Zealand. To date in 2016 there have been 42 confirmed cases nationally with 10 in Northland alone, up from a yearly average of 4. Acalculus cholecystitis (AC) is an under-recognised complication/presentation of leptospirosis. We report a case of a 46 year old lady with farm/river water exposure presenting with fevers, myalgia, headache and lethargy. She was found to have right upper quadrant tenderness and deranged liver function, a clinical picture suggestive of acute cholecystitis. Given the prodrome she was started on doxycycline, treated empirically for leptospirosis. USS biliary tract demonstrated acute inflammation and gallbladder thickening without evidence of choledolithiasis or ductal obstruction consistent with AC. After a surgical review she was switched to cefuroxime and metronidazole for presumed biliary source and requested a MRCP which was negative. She subsequently recovered with doxycycline and serology confirmed infection with leptospira borgpetersenii.

We undertook a pubmed search identifying 15 cases in the literature, from 12 case reports, of AC associated with leptospirosis. Incidence is inferred from mass exposure following a triathlon, of 75 confirmed leptospirosis cases 2.6% presented with acute cholecystitis. Worldwide reported cases were varied in age 2-75 years (mean 38) and were mostly male (73%), likely representing occupational exposure in the developing world. Leptospirosis interrogans serovars icterohaemorrhagiae and autumnalis are the only reported species to have been associated with AC. This is the first reported case of AC associated with leptospirosis caused by the borgpetersenii species. Management compromises antibiotics and supportive therapy as in this case; however given under recognition of this association acute cholecystectomy was performed in a third of cases. Given the increasing incidence it is important that AC become well recognised as an atypical presentation of leptospirosis, especially with the typical preceding prodrome, this will serve to limit unnecessary investigations and operative interventions.
Fusobacterial Pyogenic Liver Abscess: a case report and review of the literature

Jayasimhan D, Huggan P.

Introduction: *Fusobacteria* are facultative anaerobic gram-negative bacilli. *Fusobacteria* cause a range of invasive infections, amongst which pyogenic liver abscess is a rare example. We describe a case of *Fusobacteria nucleatum* liver abscess and review the relevant literature.

Case: A 51 year old lady who had recently travelled to Samoa presented with a 4 day history of abdominal pain, diarrhoea, fever, rigors and lethargy. The liver was palpable and enlarged. A 9x9cm abscess of the left lobe of the liver was confirmed and then drained percutaneously with CT guidance. Anaerobic Gram negative bacilli identified as *Fusobacterium nucleatum* were grown from the aspirate and also blood cultures taken on the day of presentation. An emerging abscess was identified at follow-up ultrasound, an aspirate of which grew *Prevotella pleuritidis*. The patient made a full recovery with drainage and antibiotic therapy.

Literature Review

A MEDLINE search was undertaken using freetext and MeSH subject headings, keywords “Fusobacterium” and “Liver abscess”. Non-English language reports and cases without confirmed growth of *Fusobacterium spp* were excluded. Additional cases were identified by surveying the references of each report and by using the same keywords in Google.

Results: 52 cases were identified, 45 in men. The median age was 40, range 8 months to 78 years. 22 cases involved *F. nucleatum*, 25 *F. necrophorum* and 5 were not speciated. Among cases of *F. nucleatum* liver abscess nine were attributed to periodontal disease, four to lower gastrointestinal tract disease, one case to a presentation consistent with Lemierre’s Syndrome, and eight cases were cryptogenic. All patients treated made a full recovery.

Conclusion: *Fusobacterium nucleatum* is an uncommon cause of liver abscess associated with good clinical outcomes. The concurrent identification of a *Prevotella* spp points to a periodontal source of infection in our patient.
Thank you to our sponsors!

The Webster Centre for Infectious Diseases is a multidisciplinary research centre which aims to address important problems caused by infectious diseases in New Zealand today. We have over sixty experts from four universities, and key Crown Research Institutes working to translate discoveries into practical applications to help treat infectious diseases.

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Ruth Doone is responsible for both the HIV and Hepatitis portfolios, looking after both the Product Management and customer responsibilities for MSD. Ruth graduated as a Registered Comprehensive Nurse in 1993, she completed 2 years post grad at Waikato Hospital before spending 5 years based in the UK, working in both the private and public sector but finally finding a niche in Clinical Research based at the National Heart and Lung Institute, Charing Cross Hospital, London. Ruth returned to NZ and joined MSD in 2002 as a representative in the Waikato before relocating to Auckland and commencing her current role in December 2012.

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Delwyn is responsible for Gilead’s HIV, Hepatitis and Antifungal portfolio in NZ. She trained as a RGON at Auckland hospital followed by working in Neonatal Intensive Care, Haematology and Surgery. This was followed by 12 years as a Practice Nurse whilst raising 3 children, establishing a local kindergarten, organising and facilitating women’s conferences. The last 16 years Delwyn has had various medical device and Pharmaceutical roles, often project managing and facilitating new initiatives such as the IBD Paediatric Transition clinics in Auckland. Other interests include gardening, walking, and cycling, plus spending time with her grandchildren.

Tourism New Zealand is the organisation responsible for marketing New Zealand to the world as a tourist destination. Their major tool to do this is the 100% Pure New Zealand marketing campaign, which has evolved over the past 16 years to make New Zealand one of the world’s most well-respected tourism brands.