SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR FOR 8 WEEKS AND SOFOSBUVIR/VELPATASVIR FOR 12 WEEKS ARE SAFE AND EFFECTIVE FOR PATIENTS WITH GENOTYPE 3 HCV INFECTION AND CIRRHOSIS: THE POLARIS-3 STUDY

Authors:
Strasser S1, Foster GR2, Thompson A3, Ruane PJ4, Borgia S5, Dore G6, Workowski K7, Hyland RH8, Wang J8, Svarovskaia ES8, Stamm LM8, Brainard DM8, Subramanian M8, McHutchison JG8, Berg T9, Agarwal K10, Conway B11, Feld J12, Willems B13, Roberts SK14

1Royal Prince Alfred Hospital, Sydney, Australia, 2Royal London Hospital, London, United Kingdom, 3St. Vincent’s Hospital, Melbourne, Australia, 4Ruane Medical and Liver Health Institute, Los Angeles, United States, 5Brampton Civic Hospital, Brampton, Canada, 6St Vincent's Public Hospital, Sydney, Australia, 7Emory University Hospital, Atlanta, United States, 8Gilead Sciences, Foster City, United States, 9Charité Universitätsmedizin, Berlin, Germany, 10Kings College Hospital, London, United Kingdom, 11Vancouver Infectious Disease Research and Care Centre, Vancouver, Canada, 12Toronto Western Hospital Liver Centre, Toronto, Canada, 13Centre Hospitalier de l'Université de Montréal, Montréal, Canada, 14Alfred Hospital, Melbourne, Australia.

Introduction: Patients with HCV genotype 3 (GT3) infection, particularly those with cirrhosis, have emerged as a more difficult to cure population. Voxilaprevir (VOX) is a pangenotypic inhibitor of the HCV protease. This Phase 3 study evaluated treatment with Sofosbuvir/Velpatasvir/VOX for 8 weeks and SOF/VEL for 12 weeks in DAA-naïve patients with GT3 HCV infection and compensated cirrhosis.

Methods: Patients in North America, Europe, Australia and New Zealand were randomized 1:1 to receive SOF/VEL (400/100 mg daily) for 12 weeks or SOF/VEL/VOX (400/100/100 mg daily) for 8 weeks. The primary endpoint compares the sustained virologic response 12 weeks after treatment (SVR12) to a pre-specified historic control rate of 83%. Secondary endpoints included safety, tolerability, and viral resistance.

Results: Of 219 patients treated, 72% were male, 90% were white, 42% had the IL28B CC genotype, and 31% had previously failed IFN-based treatment. Median platelet count was 139x103 cells/µL and mean Fibroscan was 23kPa in the SOF/VEL/VOX group and 22kPa in the SOF/VEL group. Treatment was well tolerated – two patients, both in the SOF/VEL group, discontinued therapy – 1) pelvic fracture and 2) viral breakthrough at week 8. No serious adverse events were attributed to medication were reported. Overall, SVR12 with SOF/VEL/VOX was 96% (106/110) and in the SOF/VEL was 96% (105/109). Both treatment arms were superior to the predefined performance goal of 83% (p<0.001).

Conclusion: The single tablet regimens of SOF/VEL/VOX for 8 weeks and SOF/VEL for 12 weeks are safe, well tolerated and effective treatment options for difficult-to-cure patients with GT3 infection with compensated cirrhosis.

Disclosure of Interest Statement: This study was funded by Gilead Sciences.
CHRONIC HEPATITIS C TREATMENT UPTAKE IN AUSTRALIA FOLLOWING AVAILABILITY OF INTERFERON-FREE THERAPY

Authors:
Hajarizadeh B1, Grebely J1, Matthews GV1, Martinello M1, Dore GJ1

1The Kirby Institute, UNSW Sydney, Sydney, New South Wales, Australia

Introduction: Government-subsidised direct acting antiviral (DAA) treatment for hepatitis C virus (HCV) infection has been available in Australia since March 2016. This study assessed DAA treatment uptake between March-September 2016.

Methods: A 10% random sample of Pharmaceutical Benefits Scheme (PBS) DAA prescriptions processed for reimbursement between March-September 2016 were analysed.

Results: An estimated 25890 individuals initiated DAA treatment between March-September 2016, accounting for an estimated 11% of all individuals with chronic HCV in Australia. DAA regimens included sofosbuvir/ledipasvir (57%) sofosbuvir+daclatasvir (38%), sofosbuvir+other agents (4%), and paritaprevir/ritonavir/ombitasvir+dasabuvir (1%). Of those initiating DAA therapy, 66% were men and 40% were ≤50 years old. Gastroenterologists were the predominant prescriber group (52%), followed by general practitioners (GP; 13%), infectious diseases physicians (8%), other specialists (4%), and other physicians (22%). The proportion of individuals prescribed by GPs increased from 4% in March to 19% in September (Figure 1A). The proportion of individuals ≤50 years increased from 28% in March to 54% in September (Figure 1B). Among patients with HCV-related cirrhosis, an estimated 64% received DAA therapy between 2014 and September 2016 through PBS, clinical trials, early access programs or generic supply.

Conclusion: Rapid treatment scale-up was observed in the first seven months of government-subsidised DAA therapy in Australia. The proportion of prescriptions by GPs increased over time, crucial for broadened access. Further HCV elimination evaluation will include monitoring of treatment outcomes, treatment uptake among people who inject drugs and HIV-infected men who have sex with men, and HCV prevalence and incidence (both primary infection and reinfection).

Disclosure of Interest Statement: The Kirby Institute is funded by the Australian Government Department of Health and is affiliated with the Faculty of Medicine, UNSW Sydney. The views expressed in this publication do not necessarily represent the position of the Australian Government. No pharmaceutical grants were received in the development of this study.
Figure 1: Distribution of monthly DAA treatment initiation by prescriber type (A) and patient’s age (B) during March-September 2016 in Australia.
SUB-OPTIMAL PROTECTION AGAINST PAST HEPATITIS B VIRUS INFECTION WHERE SEROTYPE MISMATCH EXISTS BETWEEN VACCINE AND CIRCULATING VIRAL GENOTYPE IN NORTHERN AUSTRALIA

Authors:
Cheah BC¹, Davies J¹,², Singh G², Wood N³, Jackson K⁴, Davison B², McIntyre P³, Locarnini S⁴, Davis JS², Tong SYC²,⁵.

1. Royal Darwin Hospital, Darwin NT, Australia
2. Menzies School of Health Research, Darwin NT, Australia
3. National Centre for Immunisation Research and Surveillance for Vaccine Preventable Diseases, The Children's Hospital at Westmead, Westmead NSW, Australia
4. Victorian Infectious Diseases Reference Laboratory, Doherty Institute for Infection and Immunity, Melbourne VIC, Australia
5. Victorian Infectious Disease Service, The Royal Melbourne Hospital, and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Victoria, Australia

Introduction: In the Northern Territory, there is a serotype mismatch between the hepatitis B virus vaccine (adw2) and the circulating viral genotype (ayw3) in the Indigenous population.

Methods: We assessed serological markers of HBV infection in the Aboriginal Birth Cohort (ABC). Participants were recruited at birth at the Royal Darwin Hospital (1987–1990), with follow-up serology obtained at waves 3 (W3; 2006–2008) and 4 (W4; 2013–2015). A subset of non-immune participants at W3 received a booster. We determined the vaccine effectiveness (VE) against any (anti-HBc Ab+) and chronic infection (HBs Ag+).

Results: Of 686 participants, HBV serology was obtained from 386 at W4, of whom 269 had received ≥1 vaccine dose, 113 were vaccinated in accordance with United States Centers for Disease Control recommendations and 117 had never been vaccinated. Seven participants were chronically infected and 94 had evidence of any infection. The VE against any infection was 66% (P = 0.06), and against chronic infection 100% (P = 0.20). For every dose of vaccine received, the odds of being anti-HBc Ab+ decreased by 41% (P < 0.001). The odds of being anti-HBc Ab+ was 87% lower in participants raised in urban compared to remote areas (P = 0.002). The W3 booster had no sustained effect.

Conclusion: The vaccine was effective in preventing chronic infection but sub-optimal against any infection. That anti-HBs titres and the presence of anti-HBc Ab were associated with remote dwelling rather than prior vaccination or boosting suggests ongoing exposure to circulating virus.

Disclosure of Interest Statement: This study was funded through NHMRC project and fellowship grants.
PREVALENCE OF ANTIVIRAL RESISTANCE IN AN AUSTRALIAN HEPATITIS C POPULATION

Ong ATL¹,²,³, Tay E¹, George J¹,³, Douglas MW¹,²,³

¹Storr Liver Centre, Westmead Millennium Institute, University of Sydney at Westmead Hospital, Sydney, Australia, ²Centre for Infectious Diseases and Microbiology, Westmead Hospital, Sydney, Australia, ³Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Sydney, Australia

Objective: To determine the prevalence of baseline resistance associated substitutions (RASs) in Australian patients with hepatitis C virus (HCV) genotype 1 infection.

Design: Single centre cross-sectional study.

Setting: Single tertiary centre. Large urban Australian public hospital pathology laboratory.

Participants: 380 patients whose blood samples were sent to the Institute for Clinical Pathology and Medical Research (ICPMR) for genotype testing, and found to be HCV genotype 1 or 1a infection. All patients were naive to new direct acting antivirals (DAAs) against HCV, which were approved for PBS subsidy in March 2016.

Main outcome measures: HCV RASs of greatest clinical relevance are those present in the NS3 and NS5A regions of the HCV genome. DAAs targeting these regions are being widely prescribed in Australia. Viral genome sequences from these regions were generated and analysed with epidemiological data.

Results: 380 samples were tested. The median age of the patients was 41.7, interquartile range (IQR) 33.7 - 49.9 years. Patients were predominantly male (71%). A significant proportion of patients were from correctional centres (31%). The most prevalent NS3 RAS was Q80K at 5.6%, and for NS5A was M30V at 6.0%.

Conclusions: This is the first and largest examination of the prevalence of HCV resistant mutations in Australia. The most prevalent NS3 RAS, Q80K confers resistance to simeprevir, a previous generation DAA no longer in use. The most prevalent NS5A RAS, M30V potentially confers resistance to ombitasvir. It is important to monitor for the potential emergence of drug resistance.

Disclosure of Interest Statement: No conflicts to declare.
POSTCARDS FROM THE DIGITAL HEALTH FRONTIER; TELEHEALTH FOR HEPATITIS C CARE IN THE DAA ERA

Authors: Biggs BA1,2,3, Kanhutu K1,2,3,4, Sasadeusz J1,2, Schulz T1,2, Watkinson S1,2

1Royal Melbourne Hospital, 2Victorian Infectious Diseases Service, 3University of Melbourne Faculty of Medicine, Dentistry and Health Sciences, 4Health Informatics Society Australia

Introduction: The Victorian Infectious Diseases Service based at the Royal Melbourne Hospital currently provides telehealth care for rural and regional patients with hepatitis C. The progressive roll out of the national broadband network and increasing availability of web based videoconferencing platforms and mobile devices have provided unprecedented capacity to manage patients remotely. The primary outcome of this study is to demonstrate that telehealth delivered hepatitis C management achieves comparable virological outcomes to standard face to face care.

Methods: The study is part of a quality audit of the hepatitis service.

Key outcome and process measures include;

- Proportion of patients achieving a sustained virological response (SVR)
- Failure to attend rate (FTA)
- Frequency of technical difficulties
- Consult duration time

Results: Since March 1st 2016 over 50 patients have been managed via telehealth. Of those who have so far completed therapy an SVR rate of 94% of has been achieved. Expected SVR genotype 1 (>95%); genotype 3 (>85%). Technical difficulties occurred in less than 10% of consultations with FTA of 17%. Consult duration was on average 15 minutes or less.

Conclusion: Our completed patient cohort results suggest comparable outcomes for telehealth managed patients as compared to traditional modalities even when adjusted for age, gender, hepatic fibrosis status and co-existent co-morbidities. Following on from the 2017 publication of the Infectious Diseases Society of America position statement on Telehealth and Telemedicine, we discuss the challenges and benefits of an outpatient ID telehealth services as we enter the era of accelerating digitally enabled healthcare.

Disclosure of Interest Statement: No conflicts to disclose.
CHESS - CURING HEPATITIS C: EFFECT ON THE ENDOTHELIUM AND CARDIOVASCULAR RISK

Authors: Joshua S Davis¹,²,³, Melissa Young¹, Sandra Lennox¹, Tracey Jones¹, Kim Piera³, Robert Pickles¹,², Steven Oakley¹,²

1. Division of Medicine, John Hunter Hospital, Newcastle, NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW, Australia
3. Menzies School of Health Research, Darwin, NT, Australia

Introduction: Epidemiological data suggest that chronic hepatitis C virus infection (CHC) is associated with increased cardiovascular risk, but the mechanisms are unclear. We aimed to assess the effect of antiviral treatment on endothelial function in adults with CHC.

Methods: Adults with CHC, genotype 1, and no evidence of advanced fibrosis or cirrhosis were eligible. All patients were treated with 12 weeks of paritaprevir/ritonavir, ombitasvir and dasabuvir (PrOD), with additional ribavirin for genotype 1a. Endothelial function was assessed at multiple time-points before, during and after antiviral treatment. The main assessment tools were reactive hyperaemia peripheral arterial tonometry (RHPAT, higher values reflect better endothelial function), and serum angiopoietin-2 (ang-2) and e-Selectin (for both, higher values reflect worse endothelial cell activation and damage).

Results: Sixteen patients were enrolled. Mean (sd) age was 52.0 (6.9) years and 11 participants (69%) were male. All 16 achieved a sustained virological response. The mean (sd) pooled baseline RHPAT index was 2.05 (0.48), and there was no significant change during treatment (mean within-patient change from baseline to end of treatment= -0.23 (0.45), p=NS). There was significant improvement in mean ang-2 (baseline 2.44 (0.79) ng/ml, within-patient change -0.60 (0.44), p<0.001) and plasma e-Selectin (baseline 48.7 (21.5) ng/ml, within-patient change -14.4 (13.0), p<0.001).

Conclusions: Removing HCV viraemia is associated with a significant improvement in endothelial function as measured by serum markers, but not in bedside microvascular reactivity. Chronic HCV viraemia may be associated with endothelial cell dysfunction and therefore long term cardiovascular risk.

Disclosure of Interest Statement: This study was funded by an unconditional investigator-initiated research grant from Abbvie sciences, who market PrOD.
IS GENTAMICIN SAFE AND EFFECTIVE FOR SEVERE COMMUNITY ACQUIRED PNEUMONIA? A RETROSPECTIVE COHORT STUDY.

Authors:
Brereton CJ\textsuperscript{1,2}, Lennon D\textsuperscript{1}, Browning S\textsuperscript{1}, Dunn E\textsuperscript{1}, Ferguson JK\textsuperscript{1,2}, Davis JS\textsuperscript{1,2,3}

1. Division of Medicine, John Hunter Hospital, Newcastle NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW Australia
3. Global and Tropical Health Division, Menzies School of Health Research, Darwin NT Australia

Introduction: Current Australian guidelines recommend a third generation cephalosporin (3GC) plus azithromycin as first line therapy for severe community acquired pneumonia (CAP). Benzyl-penicillin plus gentamicin plus azithromycin is an alternative, which provides excellent Gram negative cover, while avoiding the host and ecological effects on antimicrobial resistance of 3GCs. However Gentamicin is not commonly used in this setting due to concerns about potential toxicity and a lack of published evidence assessing efficacy.

Methods: We conducted a single-centre retrospective cohort study at a university teaching hospital where benzyl-penicillin, gentamicin and azithromycin is the empiric antibiotic regimen of choice for severe CAP. We included all patients with radiologically-confirmed CAP admitted to the intensive care unit between January 2008 and December 2015. The key exposure of interest was the receipt of gentamicin within the first 72 hours of admission. The key outcomes were acute kidney injury (AKI), hospital mortality, and relapse.

Results: We enrolled 147 patients of whom 117 received gentamicin. There was no difference in the incidence of new acute kidney injury in the gentamicin (59/117, 50%) and the non-gentamicin (15/30, 50%) groups, regardless of the number of doses received. Hospital mortality and relapse were no different in the gentamicin group (17%, 10% respectively) than the non-Gentamicin group (23%, 10%, p=NS for both comparisons), even after adjusting for receipt of other agents active against Gram negatives.

Conclusions: Gentamicin is a safe and effective alternative to broad spectrum antimicrobials as initial empiric Gram negative treatment of severe CAP.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
MYCOBACTERIUM ABSCESSUS COMPLEX IN A MAJOR TERTIARY ADULT CYSTIC FIBROSIS CENTRE

Authors:
Tippett E1, Ellis S2, Wilson J3,4, Kotsimbos T3,4†, Spelman D1,4†

1Infectious Diseases, Alfred Hospital, Victoria, 2Radiology Department, Alfred Hospital, Victoria, 3Respiratory Department, Alfred Hospital, Victoria, 4Monash University, Victoria
†Equal Senior Author.

Introduction: Mycobacterium abscessus complex (MAbsC), a rapidly growing atypical mycobacterium, is an opportunistic respiratory pathogen significant to people with underlying lung pathology, particularly cystic fibrosis (CF). Treatment is in the order of months with multiple agents, potential significant adverse events and poor treatment outcomes. This study reviewed the patient population in whom MAbsC was isolated at The Alfred Hospital, which specialises in adult CF, examining the natural history, risk factors for persistent colonisation and treatment outcomes.

Methods: We undertook a retrospective cohort analysis of all patients in whom MAbsC was isolated between 2005 to 2014, particularly focussing on patients with CF. Factors examined included BMI, FEV₁, CF comorbidities and medications including corticosteroids and prophylactic antibiotics to determine factors which may predict transient compared to persistent colonisation.

Results: MAbsC was isolated from 45 patients of whom 26 had CF. Of the patients with CF, patients who were transiently colonised with MAbsC had higher baseline respiratory function. In one third of our cohort, MAbsC was isolated for a mean of one year prior to spontaneous clearance. There was no correlation between recurrent MAbsC isolation and the use of systemic or inhaled steroids. Four CF patients were initiated on treatment with only one successful outcome.

Conclusion: This analysis demonstrates there are no clear predictors of those patients who will become persistently colonised with MAbsC and that a significant proportion will spontaneously clear colonisation. As treatment success rate is poor more work is urgently required in improve patient outcomes.

Disclosure of Interest Statement: E Tippett was supported by the Alfred Junior Medical Workforce. Nothing else to disclose.
CO-MRSA INFECTIONS IN AUSTRALIA COST $3.5B PER ANNUM

Authors:
Cameron JK1, Paterson DL2, Britton PN3, Tong SYC4, Hall L1, Nimmo GR5, Bennett CM6, Halton K1.

1 Institute for Health and Biomedical Innovation and School of Public Health and Social Work, Queensland University of Technology, 2 The University of Queensland Centre for Clinical Research, University of Queensland and Royal Brisbane and Women’s Hospital, 3 The Children’s Hospital at Westmead and Sydney Medical School, University of Sydney, 4 Victorian Infectious Disease Service, The Royal Melbourne Hospital and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity and Menzies School of Health Research, Darwin, 5 Griffith University School of Medicine and Pathology Queensland, 6 Centre for Population Health Research, Deakin University

Introduction: The health and economic burdens of community-onset methicillin resistant Staphylococcus aureus (CO-MRSA) infections are needed to inform policy, planning and evidence-based practice. We aimed to synthesise data from a range of public sources to generate the first estimate of the national incidence and cost of CO-MRSA infections.

Methods: Incidences of CO-MRSA skin and soft tissue (SSTI), lower respiratory tract (LRTI) and bloodstream (BSI) infections were calculated for regions of Australia using data from existing literature and correspondence with specialists.

Simulations estimated costs using treatment models developed for children and adults in primary or tertiary care settings and including bed-stay, diagnostics, procedures, mortalities and loss of productivity.

Results: Annually, in Australia there were found to be 3702 CO-MRSA SSTIs, 559 CO-MRSA BSIs and 425 CO-MRSA LRTIs, occupying 147,000 bed-days, including 1600 bed-days in intensive care. Incidence ranged from 4 /100,000 person-years in Tasmania to 243 /100,000 person-years in central Australia.

The estimated cost of CO-MRSA was $3.5b annually in Australia. The higher incidence of SSTIs resulted in costs greater than summing the costs of BSIs and LRTIs. The greatest cost was mortality. The cost to the health system was found to be $1.9b, with bed occupancies accounting for ≥94%.

Conclusion: This first evaluation of the health and economic burden of CO-MRSA in Australia found a need for increased and more consistent data collection for a significant and expensive disease.

Disclosure of Interest Statement: This research was funded by NHMRC grant GNT1027589.
OPTIMISING LABORATORY METHODS FOR PRE-TRUS BIOPSY QUINOLONE RESISTANCE SCREENING

Authors:
Liu E¹, Seed D¹, Andresen D¹,², McKew G¹, Gray T¹, Cheong E¹, Gottlieb T¹.

¹Concord Repatriation General Hospital, Concord, NSW, Australia
²St Vincents Hospital, Darlinghurst, NSW, Australia

Introduction: Ciprofloxacin-resistant Enterobacteriaceae infections following TRUS biopsy cause significant morbidity, however no consensus exists on an optimal laboratory screening method. We evaluated 7 methods regarding test performance, cost-effectiveness and usability.

Methods: Using simulated rectal swabs, 105 faecal samples were tested in parallel:
A: Direct plating to MacConkey agar (MAC)+CIP 10mcg/mL
B: Direct plating to MAC+5mcg CIP disc (MAC+5CD)
C-F: 5mL BHI broth+1, 2, 5 & 10mcg/mL CIP respectively; subculture to MAC+5CD
G: 5mL BHI broth+2x5mcg CIP discs (approximating 2mcg/mL), subculture to MAC+5CD

A positive screen on MAC+5CD was defined as coliform growth within a CIP zone <22mm, criteria derived from our prior validation study. The nearest coliform growth to the ciprofloxacin disc was identified by MALDI-TOF and CIP MIC determined by gradient strip.

Results: CIP-R Enterobacteriaceae was detected in 13/105 samples (MIC 2 to >32mcg/mL).

The most sensitive was broth enrichment at CIP10mcg/mL (100%, CI 75-100%) with 97% specificity (CI 91-100%). Subcultures from CIP<5mcg/mL broths were more difficult to read without superior sensitivity.

Both direct plating methods had equal sensitivity of 62% (CI 32-86%) and specificity >99% (CI 94-100%).

Arm B was most cost-effective at AUD $7.57/$0.64 (positive/negative), compared to Arm A ($7.93/$1.00) A and broth enrichment ($10.15/$3.22).

Conclusion: Direct disc screening is comparable to direct plating to MAC+CIP10mcg/mL agar, is more cost-effective and could be readily incorporated into existing laboratory work practices. Broth enrichment trended towards higher sensitivity, with larger studies needed to further assess if statistically significant.

Disclosure of Interest Statement: No conflict of interest to disclose.
HEALTH OUTCOMES FROM MULTI-DRUG RESISTANT SALMONELLA IN HIGH INCOME COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors:
Parisi A¹, Vilkins S¹, Furuya-Kanamori L¹, Crump JA², Howden BP³, Gray D¹, Glass K¹, Kirk M¹

¹ Australian National University, ² University of Otago, ³ University of Melbourne

Introduction: Salmonella is a leading cause of foodborne enterocolitis worldwide. Nontyphoidal Salmonella (NTS) infections that are Multi-Drug Resistant (MDR) (non-susceptible to ≥1 agent in ≥3 antimicrobial categories) may result in more severe outcomes, although these effects have not been systematically examined. We conducted a systematic review and meta-analysis to examine impacts of MDR NTS on health in high-income settings.

Methods: We systematically reviewed the literature from scientific databases, including PubMed, Scopus and grey literature sources, using PRISMA guidelines. We searched for data from case-control studies, cohorts, outbreaks and theses, imposing no language restriction. We included only publications from January 1990 to September 2016 from high income countries as classified by World Bank. We extracted data from papers on duration of illness, hospitalisation rates, morbidity and mortality for MDR and non-MDR NTS strains.

Results: After removing duplicates, the initial search revealed 4258 articles. After further screening, we identified 16 eligible studies for the systematic review, and 9 of these were included in the meta-analysis. NTS serotypes differed among the reported studies but serotypes Typhimurium, Enteritidis, Newport and Heidelberg were the most often reported MDR pathogens. Salmonella infections that were MDR were associated with excess bloodstream infections (OR 1.63; 95%CI 1.18-2.26), excess hospitalisations (OR 2.77; 95%CI 1.47-5.21) and higher mortality (OR 3.54; 95%CI 1.10-11.40).

Conclusion: MDR NTS infections are a serious public health concern. With the emergence of MDR Salmonella strains in the high-income countries, it is crucial to restrict the use of antimicrobials both in animals and humans, and intervene to prevent foodborne infections.

Disclosure of Interest Statement: We declare that we have no conflicts of interest in the authorship or publication of this contribution.
SIGNALLING INDUCED BY HUMAN CYTOMEGALOVIRUS IN AN AUTOCRINE MANNER ALTERS EXPRESSION OF WNT RECEPTOR ROR2 AND MIGRATION OF INFECTED TROPHOBLASTS

Authors: van Zuylen WJ1,2, Paull W2, Ford C4 and Rawlinson WD1,2,3

1Serology and Virology Division, SEALS Microbiology, Prince of Wales Hospital, Sydney, Australia, 2School of Medical Sciences, University of New South Wales, Sydney, Australia, 3School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, Australia, 4Metastasis Research Group, Prince of Wales Clinical School, University of New South Wales, Sydney, Australia

Introduction: Primary maternal CMV infection, reactivation, or infection with a different viral strain may cause adverse pregnancy outcomes including sensorineural hearing loss and mental disability. Placental infection may indirectly cause fetal injury via impairing placental development. New approaches to disease prevention are urgently needed. Better understanding of the molecular mechanisms of CMV infection of the placenta is essential for therapeutic innovations to decrease the prevalence and societal impact of congenital CMV.

Methods: Our previous findings indicate CMV controls the expression of the Wnt5a-binding tyrosine kinase receptor ROR2 to alter placental cell motility, which could lead to abnormal placental development in congenital CMV disease. We used migration assays in 2 compartment models, with added exogenous signalling proteins (wnt5a) and inhibitors (siRNA) to infected and uninfected cultures.

Results: We now show CMV specifically inhibits Wnt5a-mediated migration of infected trophoblasts, but not migration of surrounding uninfected cells. Utilising supernatant from CMV-infected trophoblasts, we also show that this inhibition and ROR2 alteration is not dependent on a soluble factor, rather it requires cell-cell contact. Furthermore, we show that both viable laboratory CMV strain AD169 and clinical CMV strain Merlin, but not UV-inactivated CMV inhibits Wnt5a-mediated trophoblast motility, indicating de novo viral gene expression is required.

Conclusions: Taken together, our novel findings suggest that autocrine signalling induced by human Cytomegalovirus alters ROR2 expression and this affects migration of infected trophoblasts. Inhibition of this autocrine signalling is a specific target for therapeutic intervention for CMV-induced placental damage and consequent fetal damage in congenital CMV infections.

Disclosure of Interest Statement: No conflicts to declare.
CONGENITAL CYTOMEGALOVIRUS (cCMV) IN INFANTS WITH HEARING LOSS IDENTIFIED VIA THE UNIVERSAL NEWBORN HEARING SCREENING PROGRAM, AND RISK FOR POSTNATAL INFECTION IN CHILDCARE

Authors:
Palasanthiran P², Wilkinson M², Hall B¹, Al Yazidi L², Fennell M¹, Zheng J¹, van Zuyl W¹, Cottier C², Rawlinson W¹.

¹Serology and Virology Division, Department of Microbiology, SEALS, Level 4 Campus Centre Prince of Wales Hospital, Randwick, NSW, 2031, Australia, ²Sydney Children's Hospital, High St Randwick, NSW, 2031, Australia and School of Women's and Child Health, University of New South Wales, Kensington, NSW, 2052, Australia, ³School of Medical Sciences, School of Biotechnology and Biomolecular Sciences, and Australian Centre for Perinatal Sciences, University of New South Wales, Kensington NSW 2052 Australia

Introduction: Pregnant women are at risk for infection with CMV, particularly through close contact with their children. This may result in congenital infection, with resultant hearing loss, neurodevelopmental deficits and most severely fetal death. We assessed risk for infection for infants attending childcare, and cCMV in infants referred for audiology after failed UNHS.

Methods: Sampled CMV excretion in 130 nasal samples from 20 childcare staff of 2 centres over 5 weeks, with PCR of nasal and skin swabs. CMV testing of urine +/- saliva in infants with CMV detected by PCR at ≤ 30 days of age in urine/saliva, were diagnosed cCMV then followed for counselling and treatment.

Results: Childcare 8/130 carers CMV DNA positive a CMV excretion rate of 35% in staff. Hearing clinics 1520 children failing UNHS referred for audiology. 30% (469) confirmed hearing loss & 308 offered CMV testing, 10 declined, 123 had audiology by ≤21 days, and 203 by ≤30 days, of whom 195 were tested for CMV. CCMV was diagnosed in 10 infants (9 urine, 6 saliva, urine + saliva in 7), including 1 positive NBSC).

Conclusion: We identified ~6% of congenital CMV in children failing UNHS and had permanent SNHL confirmed. It did not require significant additional assets to those already existing in the tertiary referral paediatric centre, and provided useful and timely information for clinical and audiological follow up. Increased awareness of childcare CMV infection among parents & healthcare providers is necessary to minimise CMV acquisition during pregnancy and subsequently congenital CMV infection.

Disclosure of Interest Statement: No conflicts to declare.
NATIONWIDE SURVEILLANCE OF PAEDIATRIC EMPYEMA IN NEW ZEALAND - 2014 TO 2016

Authors:
Rix-Trott KJ¹, Byrnes C¹,², Twiss J¹, Matsas R³, Hamill J¹, Evans S¹, Mahon C², Williamson D⁴, Dickson N⁵, Walls T⁶, Voss L¹, Best E¹,².

¹ Starship Children’s Health, Auckland District Health Board, Auckland, New Zealand ² Department of Paediatrics, University of Auckland ³ KidzFirst Hospital, Counties Manukau District Health Board, Auckland, ⁴ Institute of Environmental Science and Research, Wellington, ⁵ Paediatric Department, University of Otago, Wellington, ⁶ Paediatric Department, University of Otago, Christchurch.

Introduction: The aim was to document the burden of empyema in children aged <15 years in New Zealand including infectious aetiology, demographics and management.

Methods: Empyema was added as a notifiable disease in children <15 years of age on the New Zealand Paediatric Surveillance Unit (NZPSU) monthly report request from May 2014 to June 2016. A questionnaire recording demographics, presentation, infectious aetiology, medical and surgical management, complications, and short term outcomes was then requested from the lead paediatrician.

Results: 117 notifications were made with 99 fitting the case definition and complete data for 87 cases (88%). The median age was 3.8 years (range 2 months to 14.9 years) with 61% occurring in children under 5 years. 22% had co-morbid conditions ranging from mild asthma to immune-compromising conditions. Ethnicities were 34% Maori, 23% Pacific, 22% European, 13% Asian, and 5% Indian and 3% other. S. pneumoniae and S. aureus (MRSA + MSSA) made up 38% and 35% of causative organisms respectively. 60% of children had received 3-4 doses of PCV. 83% of cases required some form of surgical intervention, 1/3 required ICU and the mean length of stay was 19 days (6-56 days).

Conclusion: The burden of empyema in New Zealand children is seen predominantly in younger children and those of Maori and Pacific ethnicity. Streptococcal and staphylococcal infection were identified in nearly equal numbers, and 18% of S. aureus cases were MRSA. Empyema cases reflect a significant morbidity burden due to requirement for surgical intervention, ICU care, and prolonged hospitalization.

Disclosure of Interest Statement: Nil.
THE EFFECT OF INTRAVENOUS ANTIBIOTICS ON THE NASAL MICROBIOME IN CHILDREN – NOVEL ASSOCIATION WITH STAPHYLOCOCCUS AUREUS ACQUISITION

Authors: Bryant PA1,2,3, Curtis N1,2,3, Gordon L4, Parker K1, Hopper SM1,5, Holt K6, Babl FE1,2,5, Ibrahim LF1,2

1Murdoch Children’s Research Institute, Melbourne, 2Department of Paediatrics, The University of Melbourne, 3Infectious Diseases Unit, Department of General Medicine, Royal Children’s Hospital Melbourne, 4The Australian Genome Research Facility, Melbourne, 5Emergency Department, Royal Children’s Hospital Melbourne, 6Department of Biochemistry and Molecular Biology, The University of Melbourne

Introduction: Antibiotic use is almost universal in Australasian children. The risks of this include acquisition of pathogenic and resistant bacteria, including nasal carriage of Staphylococcus aureus. We investigated the effect of antibiotics on the nasal microbiome in previously healthy children.

Methods: Children aged 6 months-18 years with cellulitis receiving short-course intravenous followed by oral antibiotics were included. Nasal swabs were collected at 3 timepoints: baseline, 1 week (maximal antibiotic pressure) and 3 months (post antibiotic washout) after starting intravenous antibiotics. After DNA extraction, microbiome abundance and diversity were assessed by amplicon sequencing analysis of the 16S rRNA V3-V4 region.

Results: 33 nasal swabs were collected from 11 children. There was no difference in overall bacterial abundance or diversity between baseline or the 1 week or 3 month timepoints. However, phylogenetic analysis showed a dramatic shift in the Gram-positive phyla with Firmicutes increasing from 27% abundance at baseline to 46% at 1 week (p=0.005) at the expense of Actinobacteria (33% to 16%, p=0.006), while Gram-negative phyla Proteobacteria and Bacteroidetes remained the same. Four patients acquired S. aureus on nasal culture after antibiotics, and there was a significant difference in diversity compared to baseline and to those who did not acquire S. aureus (p<0.05)(figure).

Conclusion: Short-course antibiotics are associated with changes in nasal microbiome composition, with the novel finding of reduced diversity associated with S. aureus acquisition. This has potential implications on selection of resistant bacteria. Whether changes can be predicted and therefore reversed will be part of a larger study.

Disclosure of Interest Statement: This study was funded in part through grants from The Royal Children’s Hospital Foundation, and the Infection and Immunity Theme at the Murdoch Children’s Research Institute. Dr. Ibrahim was funded by an Avant Scholarship. No pharmaceutical grants were received in the development of this study.

Figure:
INFLUENCE OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION IN NEONATAL INTENSIVE CARE

Authors:
Villanueva P\textsuperscript{1}, Freyne B\textsuperscript{1,2}, Carr J\textsuperscript{1,2}, Hickey L\textsuperscript{3}, Bryant PA \textsuperscript{1,2}

\textsuperscript{1}Department of General Medicine, The Royal Children’s Hospital Melbourne.
\textsuperscript{2}Infectious Diseases Unit, The Royal Children’s Hospital Melbourne.
\textsuperscript{3}Department of Neonatal Medicine, The Royal Children’s Hospital Melbourne.

Introduction: Antimicrobial stewardship (AMS) is vital in the critical care environment of the neonatal intensive care unit (NICU) but evidence for specific interventions is lacking. Our objectives were:
\textbf{1)} To describe patterns and appropriateness of antimicrobial prescribing in NICU;
\textbf{2)} To assess the influence of AMS ward rounds on inappropriate prescribing

Methods: A weekly AMS round involving senior NICU medical staff and a paediatric infectious diseases fellow was introduced and assessed over 6 months. Audit-feedback recommendations were made regarding appropriateness of decision to prescribe antimicrobials, drug choice and application (dose, interval, route, duration), and were reviewed the following day to assess acceptance of recommendations.

Results: During the study period, 249 infants were assessed for 627 review episodes. The proportion on antimicrobials at each AMS round was 19-59\% (mean 37\%). Of the 627 episodes, 233 (37\%) reviews comprised patients receiving antimicrobials: 79 (34\%) received targeted antimicrobial treatment, 111 (48\%) empirical antimicrobial treatment and 43 (18\%) prophylaxis. Of the 233 episodes on antimicrobials, 58 (25\%) were deemed as having inappropriate prescriptions: 19\% inappropriate decision to prescribe antimicrobials, 71\% inappropriate antimicrobial choice, 10\% inappropriate application. The commonest recommendations were to narrow (53\%) or stop (19\%) antimicrobials. The majority (73\%) of recommendations were accepted.

Conclusion: A high proportion of infants in the NICU were on antimicrobials, and a quarter had recommendations to change/stop. Three-quarters of recommendations were actioned, showing that AMS rounds are effective in influencing prescribing. Education or more frequent rounds may increase this further.

Disclosure of Interest Statement: We have no conflict of interest to declare.
β-LACTAM ANTIBIOTICS: TOO MUCH OF A GOOD THING

Authors: Imani S 1,4, Marriott D 1,2, Buscher H 1,2, Gentili S 3, Sandaradura I 1,2

1 St Vincent’s Hospital, Sydney
2 University of New South Wales
3 University of South Australia
4 University of Notre Dame, Australia

Introduction: The potential for high-dose β-lactam antibiotics (BLA) to precipitate toxicity is becoming increasingly apparent in clinical practice. Adverse events, such as neurotoxicity, which were previously considered idiosyncratic, are now recognised as concentration-dependent. There is limited data, however, on the utility of BLA concentration in predicting toxicity.

Methods: Retrospective review of consecutive patients (n=378) treated with piperacillin (PIP, n=223), meropenem (MER, n=94) or flucloxacillin (FLU, n=61) who underwent therapeutic drug monitoring (TDM) at St Vincent’s Hospital Sydney between Jan 2013- Dec 2015. Adverse events investigated included neurotoxicity, nephrotoxicity, hepatotoxicity and opportunistic Clostridium difficile infection (CDI). Toxicity was measured using observational grading criteria, clinical judgment and relevant serum biomarkers. These findings were correlated with trough TDM measurements at the time of toxicity determination.

Results: Adverse event rates per antibiotic are summarised in Table 1.

Table 1: Toxicity event rates in study

<table>
<thead>
<tr>
<th></th>
<th>PIP</th>
<th>MER</th>
<th>FLU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>11.4%</td>
<td>15.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>8.5%</td>
<td>6.9%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>6.7%</td>
<td>8.3%</td>
<td>8.7%</td>
</tr>
<tr>
<td>CDI</td>
<td>7.9%</td>
<td>2.6%</td>
<td>0%</td>
</tr>
</tbody>
</table>

We found a significant increase in mean BLA trough concentration (C_{min}) in all patients diagnosed with neurotoxicity (p<0.05) and those with nephrotoxicity treated with PIP (p<0.01) or MER (p<0.01). Incidence of hepatotoxicity and CDI was not related to antibiotic concentration levels. Threshold C_{min} for which there was >50% risk of developing neurotoxicity (C_{PIP}>361.4mg/L, C_{MER}>64.2mg/L, C_{FLU}>125.1mg/L) and nephrotoxicity (C_{PIP}>452.65mg/L, C_{MER}>44.45mg/L) were identified.

Conclusion: Incidence of BLA toxicity is likely underestimated clinically. By utilising TDM early in the course of BLA treatment clinicians should aim to achieve the highest serum concentrations that can be safely attained, whilst ensuring that these toxicity thresholds are not surpassed. Additionally, TDM may be useful to diagnose BLA toxicity, avoiding other unnecessary investigations.

Disclosure of Interest Statement: The study was funded by a grant from the University of Notre Dame Australia.
INTRODUCTION: National antimicrobial shortages have become increasingly common over the past few years. Ampicillin and azithromycin shortages occurred in 2015. Concurrent shortages of a broad range of critical agents (including: vancomycin, daptomycin, aztreonam, tigecycline, metronidazole and aciclovir) occurred in late 2016 - threatening patient safety and stretching antimicrobial stewardship (AMS) team capability.

METHODS: We describe interventions, antimicrobial usage, and adverse events during this shortage period in a principal tertiary referral centre. Additional intensive, targeted antimicrobial stewardship processes were instituted ensuring the remaining stocks were used appropriately.

RESULTS: Targeted AMS towards these agents was achieved through education memos, one-on-one phone calls, electronic AMS approval system and physical removal of affected antimicrobials from general ward imprest settings. During the shortage period, a 70% decrease was seen in IV azithromycin usage / 100 OBDs and a 30% reduction in average monthly usage of vancomycin was noted. No adverse events have been attributable to the shortage on review of bacteraemia outcomes and IIMS notifications.

CONCLUSION: The wave of recent shortages led to enhanced antimicrobial stewardship team physical control of specific antimicrobials, however required significant additional vigilance and human resources. A marked reduction of use was noted in the antimicrobials affected without an increase in alternate antimicrobials. The externally caused shortage appeared to create a strong motivation of responsible prescribing in our hospital. Mitigating measures coordinated at the state and/or national level are required to ensure such shortages can be avoided in the future and that patient safety is not compromised.

Disclosure of Interest Statement: We declare no conflict of interest and there was no funding received for this study.
EFFECTS OF AGEING ON PARASITE BIOMASS, INFLAMMATION, ENDOTHELIAL ACTIVATION AND MICROVASCULAR DYSFUNCTION IN PLASMODIUM KNOWLESI AND P. FALCIPARUM MALARIA

Authors:
Barber BE1,2, Grigg MJ1,2, William T2,3, Piera KA1, Boyle M1,4, Yeo TW1,5,6, Anstey NM1,7

1. Menzies School of Health Research and Charles Darwin University, Darwin, Northern Territory, Australia
2. Infectious Diseases Society Sabah-Menzies School of Health Research Clinical Research Unit, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia
3. Jesselton Medical Centre, Kota Kinabalu, Sabah, Malaysia
4. Centre for Biomedical Research, Burnet Institute, Melbourne, Australia
5. Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
6. Institute of Infectious Disease and Epidemiology, Tan Tock Seng Hospital, Singapore
7. Department of Infectious Diseases, Royal Darwin Hospital, Darwin, Northern Territory, Australia

Introduction: In populations with low immunity to malaria, the risk of severe malaria increases with age. This is particularly apparent in Plasmodium knowlesi malaria. However; the pathophysiological mechanisms underlying knowlesi malaria, and of the age-related increase in risk in severe malaria in general, are poorly understood. We evaluated the effects of ageing on factors contributing to pathogenesis of severe knowlesi and falciparum malaria.

Methods: Malaysian patients aged ≥12 years with severe (n=47) and non-severe (n=99) knowlesi malaria, severe (n=21) and non-severe (n=109) falciparum malaria, and healthy controls (n=50) were enrolled. We measured parasite biomass, and markers of systemic inflammation (interleukin-6; IL-6), endothelial activation (angiopoietin-2), and microvascular function, and evaluated effects of age.

Results: Patients with severe knowlesi malaria were older than those with non-severe knowlesi malaria (median 55 vs. 42 years, p<0.0001). P. knowlesi parasitemia correlated with age (r=0.36, p<0.0001). In patients with knowlesi malaria, IL-6, angiopoietin-2 and microvascular dysfunction were increased in severe compared to non-severe disease, and all correlated with age, independent of parasitemia. In falciparum malaria, angiopoietin-2 increased with age, after controlling for parasite biomass (histidine-rich protein-2). Independent risk factors for severe malaria included parasitemia and angiopoietin-2 in knowlesi malaria, and HRP2, angiopoietin-2 and microvascular dysfunction in falciparum malaria.

Conclusion: Parasite biomass, endothelial activation and microvascular dysfunction are associated with severe disease in knowlesi malaria and likely contribute to pathogenesis. The independent association of each of these processes with ageing may account for the greater severity of malaria observed in older adults in regions of low endemicity.

Disclosure of Interest Statement: All authors state no conflict of interest.
PREVALENCE OF SCABIES AND IMPETIGO IN SCHOOL CHILDREN IN TIMOR-LESTE

Authors:
Korte L1,2, Draper A3,4, Davis K1, Appelbe A5, Dingle B6, Bowen A7, Francis J1,8

1 Royal Darwin Hospital, 2 Hospital Nacional Guido Valadares, 3 NT Centre for Disease Control, 4 National Centre for epidemiology and population health, Australian National University, 5 Kensington Hill Medical Centre, 6 St John of God, 7 Princess Margaret Hospital for Children, 8 Telethon Kids Institute, 9 Menzies School of Health Research

Introduction: Scabies and impetigo are common and important skin conditions which are often neglected in developing countries. The prevalence of these conditions in Timor-Leste is unknown. Sequelae including cellulitis, bacteraemia, nephritis, acute rheumatic fever and rheumatic heart disease contribute significantly to the burden of disease.

Methods: We conducted an epidemiological survey in October 2016. School students were recruited from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste. We used a standard questionnaire to record demographics, anthropometry and skin examination results. Prevalence of scabies and impetigo were calculated and binary risk factors described using relative risks and 95% confidence intervals. Continuous variables for were analysed for associations using the Mann-Whitney Rank Sum test. Results were considered significant if p<0.05.

Results: 1407 students were enrolled; with median student age of 12 years (range 4-24). The prevalence of scabies was 22% and active impetigo 10%; 68% of students had evidence of either active or healed impetigo. Students in Ermera were more likely than those in Dili to have scabies (RR 6.3; 95%CI 4.3 - 9.2, p<0.01) and scabies and active impetigo co-infection (RR 8.9; 95%CI 3.3 - 24, p<0.01). There was no difference in the prevalence of active impetigo between urban and rural sites.

Conclusion: Scabies and impetigo are prevalent in Timor-Leste, with particularly high prevalence of scabies in the rural district of Ermera. Improvements in prevention and treatment are needed, and consideration should be given for implementing strategies at a community level, focusing on rural areas.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer.
TREATMENT OF LATENT TB INFECTION IN THE DARWIN REGION OF AUSTRALIA

Boyd R 1, Johnston V 1,2, Farmer B 1, Krause V 1

1 Centre for Disease Control, Northern Territory
2 Honorary Fellow, Menzies School of Health Research, Northern Territory

Introduction: Preventing active tuberculosis (TB) disease through treatment of latent tuberculosis infection (LTBI) is an essential component of the World Health Organization’s End TB Strategy. To evaluate and inform practice we identified LTBI treatment uptake and compliance amongst Northern Territory populations.

Methods: We undertook a cohort study, including people diagnosed with LTBI June 2013-July 2014, Darwin; Population 140,000 including 25% Indigenous and 25% overseas-born. Demographic, treatment acceptance and compliance data were collected from the Darwin TB service.

Results: Of 573 people diagnosed with LTBI, 374 (65%) were offered; 265/374 (71%) accepted and 147/241 (55%) completed treatment. 74% were overseas-born, 14% non-Indigenous and 12% Indigenous. Indigenous people were more likely to accept treatment than overseas-born (OR 4.46; 95%CI 1.55-12.83) and non-Indigenous (OR 7.69; 95%CI 2.33-25.39). Overseas-born were least likely to complete treatment (Indigenous OR 1.34; 95%CI 0.66-2.72; non-Indigenous OR 1.38 95%CI 0.56-3.41).

All children under 6 years accepted treatment; 12/28(43%) completed treatment.

The cohort primarily comprised health care workers (HCW) 106(19%); contacts of active TB 97(17%) and asylum-seekers 94(16%). Of 106 HCW’s, 77(73%) were overseas-born. Supported by school nurses, students were most likely to complete treatment, with odds of completing 3.86 times higher than HCW’s (95%CI 1.02–14.58).

Conclusions: While comparable to previous studies, 45% did not complete treatment, representing missed opportunities to prevent disease. Encouragingly, we found high uptake of treatment amongst Indigenous people. Interventions should target optimising treatment completion in high risk populations of overseas-born and children under 6. Successful treatment in students supports ongoing engagement of school-based nurses.

Disclosure of Interest Statement: The Centre for Disease Control is funded by the Northern Territory Government. No additional funding was received for this study.
SHORTER MDR-TB TREATMENT COMPARED WITH CONVENTIONAL TREATMENT IN UZBEKISTAN: SPUTUM CULTURE CONVERSION AFTER 2 MONTHS

Authors:
A Ronnachit, A Khamraev, P du Cros, J Greig, T Pylypenko, Z Tigay, N Parpieva, J Achar

1 Médecins Sans Frontières, Nukus, Uzbekistan, 2 Ministry of Health, Nukus, Uzbekistan, 3 Médecins Sans Frontières UK, Manson Unit, London, United Kingdom, 4 National Institute of TB and Pulmonology, Tashkent, Uzbekistan

Introduction: The shorter multi-drug resistant tuberculosis (MDR-TB) regimen has been recommended by the World Health Organisation (WHO) for eligible patients. However, little comparative data about its efficacy has been published. We compared 2-month culture-conversion status from a single-arm, prospective observational study of the shorter MDR-TB regimen (SR) with patients treated with WHO-approved conventional care (CC) under programmatic conditions in Uzbekistan, a country listed by the WHO as a high-burden MDR-TB country with high rates of second-line drug resistance.

Methods: SR data was compared with CC data from culture confirmed MDR-TB patients treated within the same TB program. Exclusion criteria included documented exposure to second-line drugs and second-line drug resistance. Multivariate-logistic regression was used to estimate associations between regimen and culture-conversion status after 2-months. Ethics approval was obtained.

Results: 241 CC and 88 SR patients were included. Patients treated with SR had an aOR of 1.91 (95%CI 1.08-3.38, p=0.026) of culture-conversion by 2-months compared with CC. Higher baseline sputum smear-positivity was negatively associated with culture-conversion, aOR 0.37 (95%CI 0.21-0.65, p<0.001) for scanty/1+, and 0.11 (95%CI 0.05-0.24, p <0.001) for 2+/3+. Poor adherence was negatively associated: aOR 0.42 (95%CI 0.21-0.83, p=0.013) with culture-conversion. A negative association with age was found, for every increasing year aOR 0.98 (95%CI 0.96-0.99, p=0.006).

Conclusion: There was an almost two-fold greater odds of culture-conversion by 2-months following treatment with the SR. Earlier culture-conversion has important infection-control and treatment implications, and use of SR may reduce transmission.

Disclosure of Interest Statement: The authors declare that there is no conflict of interest.
INITIAL PROGRAMMATIC EXPERIENCE OF BEDAQUILINE CONTAINING TREATMENT REGIMENS FOR DRUG-RESISTANT TUBERCULOSIS IN SOUTH FLY DISTRICT, WESTERN PROVINCE, PAPUA NEW GUINEA

Authors:
Taune M1,2, Hiasihri S3, Huang K4, Ronnachit A4, Wallis P, Morris L3, Tugo O1, Dakulala P2, Bieb S2, John L2, Aia P2, Lavu E5, Coulter C6, Madjus S7, Innes A8, Islam T9, Chan G4, O’Brien D4, Graham S4, Majumdar S4

1Daru General Hospital, Western Province, PNG, 2National Department of Health PNG, 3Provincial Health Office, Western Province, PNG, 4Burnet Institute, Australia, 5Central Public Health Laboratory, PNG, 6Queensland Mycobacterial Reference Laboratory, Australia 7World Vision PNG, 8FHI 360 Asia Pacific Region, 9World Health Organisation, PNG.

Introduction: Treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) globally remain poor. The World Health Organization (WHO) for programmatic use has recently recommended Bedaquiline (BDQ), a novel drug for the treatment of MDR-TB. Daru Island, South Fly District (SFD), Western Province is the epicenter an outbreak of MDR-TB, including community transmission of extensively drug-resistant (XDR-TB) strains. Bedaquiline was introduced in the program in October 2015 and we describe the first programmatic use in PNG.

Methods: We conducted a cohort analysis using routine programmatic data for patients on BDQ-containing regimens enrolled from July 2015 to December 2016. Interim cohort outcomes (culture negative rate by month 6 of treatment) were assessed in patients with culture confirmed TB from 1 July 2015 to 30 June 2016. A core package of Active TB drug-safety monitoring and management (aDSM) was implemented.

Results: 21 patients received BDQ containing regimens. The median age was 36 years. 6 of 21 patients had microbiologically confirmed XDR TB. All patients are retained in care with no evidence of clinical or microbiological failure. In the interim cohort analysis (n=8), 7 (87.5%) patients on BDQ had a negative culture by month 6 of treatment, compared with 37 (44%) on non-BDQ containing regimens (n=85). A single serious adverse drug event was observed, unlikely related to Bdq.

Conclusion: Early experience with BDQ containing regimens in PNG demonstrates excellent interim treatment outcomes and a good safety profile and supports further scale up. New TB drugs with greater efficacy and better tolerability have the potential for great impact in the setting of a DR-TB outbreak and in routine use in resource-limited settings.

Disclosure of Interest Statement: No conflicts of interest to declare.
PREDICTORS FOR PNEUMOCOCCAL CONJUGATE VACCINATION (PCV) IN A LOW PCV COVERAGE SETTING IN THE EASTERN HIGHLANDS OF PAPUA NEW GUINEA

Authors:
Chan J1, Russell F1,2, Pomat W3, Sapura J3, Masiria G3, Kave J3, Ford R3, Kirarock W3, Kumani T3, Lehmann D4, Blyth CC4,5 on behalf of the PNG Aetiology Study Team

1 Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia
2 Centre for International Child Health- Dept. of Paediatrics, University of Melbourne, Melbourne, Australia
3 Infection and Immunity Unit, Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea
4 Telethon Kids Institute, University of Western Australia, Perth, Australia
5 School of Medicine, University of Western Australia, Perth, Australia.

Introduction: Pneumonia is the most important cause of childhood mortality and morbidity in Papua New Guinea (PNG). The 13-valent pneumococcal conjugate vaccine (PCV) was introduced to PNG in 2014 and in this study we describe PCV coverage over time and predictors for vaccination.

Methods: We completed a post-hoc analysis of vaccination coverage among children 2-59 months old, enrolled in a case-control study of pneumonia and meningitis. Cases were recruited at the Eastern Highlands Provincial Hospital and urban health clinics. Controls were recruited from the same villages as cases within an hour’s drive. Children were considered vaccinated if they had received two doses of PCV <12 months of age or one dose over 12 months of age. We calculated three-monthly rolling PCV coverage rates and determined predictors for vaccination using univariate and multivariate regression.

Results: Among the 1391 cases and controls enrolled from 2014-2015, PCV vaccination coverage started to increase from January 2015, reaching 30% coverage in December 2015 (figure 1). After adjustment, receipt of diphtheria-tetanus-pertussis vaccines was associated with an increased likelihood of PCV vaccination (aOR 9.3; 95% CI 5.8-14.8; p=0.000). In cases, distance from EHP hospital was also predictive of being vaccinated (aOR 3.0; 95% CI 1.2-7.4; p=0.02).

Figure 1: Three-month rolling vaccination coverage rate among cases and controls, Eastern Highlands Province, Papua New Guinea
**Conclusion:** PCV coverage remains low, however there is a trend towards increasing PCV coverage from 2015 onwards. Strategies to improve PCV coverage are required and should include programs targeting children from rural villages.

**Disclosure of Interest Statement:** This was an investigator-led study, funded by Pfizer Global and the PNG Institute of Medical Research.
CONJUGATE PNEUMOCOCCAL VACCINATION AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION REDUCES INVASIVE PNEUMOCOCCAL DISEASE

Authors:
Roberts MB¹, Lewis I², Bak N¹

¹Infectious Diseases Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA
²Haematology Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA

Introduction: Immunosuppressed patients, especially haematopoietic stem cell transplant (HSCT) recipients, are particularly vulnerable to invasive pneumococcal disease (IPD) with reported rates between 3.81 and 22.5/1000 transplants. However, uptake of pneumococcal vaccination tends to be lower in the immunosuppressed, partly due to concerns of vaccine effectiveness. The Royal Adelaide Hospital (RAH) introduced protocolised conjugate pneumococcal vaccination (13vPCV) to all HSCT patients in 2010.

Methods: We conducted a retrospective study of all RAH HSCT patients from 2004 to 2015 to assess the impact of introduced 13vPCV on IPD incidence. Microbiological results from sterile sites for all HSCT patients in this period were reviewed for IPD. Individuals with IPD had clinical records evaluated for further data.

Results: Fourteen episodes of IPD occurred in twelve patients between 2004 and 2015. Twelve episodes occurred in the pre-2010 group who did not receive 13vPCV, 40% of serotyped isolates would have been covered by 13vPCV. Two episodes occurred in the post-2010 group who did receive 13vPCV, neither isolate serotype was covered by 13vPCV. In the equivalent period there were 936 HSCT, of which there was >90% enrolment and >90% vaccination protocol completion rates for surviving patients. There was a significant reduction in overall IPD rate from 28.4/1000 transplants pre-2010, to 3.6/1000 transplants in the post-2010 group. Similar reductions occurred in the autologous group from 25.5 to 2.8/1000 transplants and allogeneic group from 44.2 to 5.3/1000 transplants.

Conclusion: This is the first study to demonstrate the clinical effectiveness of 13vPCV in this cohort, highlighting its importance in preventing infectious complications of HSCT.

Disclosure of Interest Statement: No conflicts to disclose.
ROUTINE ERTAPENEM PROPHYLAXIS FOR TRANSRECTAL ULTRASOUND-GUIDED PROSTATE BIOPSY DOES NOT SELECT FOR CARBAPENEM-RESISTANT ORGANISMS: A PROSPECTIVE COHORT STUDY

Authors: Bloomfield M\textsuperscript{1,2}, Page M\textsuperscript{3}, McLachlan A\textsuperscript{3}, Studd R\textsuperscript{3}, Blackmore T\textsuperscript{1,2}

1 Department of Infection Services, Wellington Regional Hospital, Wellington, New Zealand, 2 Department of Microbiology, Wellington Southern Community Laboratories, Wellington, New Zealand, 3 Department of Urology, Wellington Regional Hospital, Wellington, New Zealand

Introduction: Post-transrectal ultrasound-guided prostate biopsy sepsis (PBS) is an increasing problem in this era of rising antibiotic resistance. Ertapenem prophylaxis has proven very effective at our institution for reducing this, however has raised local and regional antimicrobial stewardship concerns. This study investigated the possible selective effect of single dose ertapenem prophylaxis on faecal colonisation with carbapenem-resistant Enterobacteriaceae.

Methods: Patients had a rectal swab taken prior to receiving pre-biopsy ertapenem prophylaxis. A second swab was taken at follow-up 4-6 weeks later. Swabs were screened for carbapenem-resistant Enterobacteriaceae (CRE) using an enhanced Centers for Disease Control method. Pre-biopsy swabs were also screened for extended-spectrum and 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. Three cases (0.9%, 95%-CI 0.2-2.8%) of probable PBS were identified during the study period. None were bacteraemic or required ICU admission.

Conclusion: Single dose ertapenem prophylaxis 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. It is highly effective prophylaxis for transrectal ultrasound-guided prostate biopsy. Ertapenem may, in the right setting, represent a useful prophylactic option for prevention of post-transrectal ultrasound-guided prostate biopsy sepsis.

Disclosure of Interest Statement: The study was funded by internal departmental funds allocated to research. No pharmaceutical or other industry grants were received in the development of this study.
IMPACT OF A DEDICATED POST-TRANSPLANT VACCINATION SERVICE ON COMPLIANCE RATES AT A LARGE AUSTRALIAN CANCER CENTRE

Authors:
Teh B¹,², Joyce T¹,³, Slavin M¹,²,⁴, Thursky K¹,²,⁴, Worth L¹,²,⁴

¹Department of Infectious Diseases, Peter MacCallum Cancer Centre, ²NHMRC Centre of Research Excellence, Infections in Cancer, ³Department of Haematology, Peter MacCallum Cancer Centre, ⁴Department of Medicine, University of Melbourne.

Introduction: Autologous haematopoietic stem cell transplantation (ASCT) results in impaired immunity to vaccine-preventable infections. Frequently, compliance with vaccination consensus guidelines is poor. We evaluated the impact of a dedicated vaccination service on post-transplant vaccination compliance with prevailing national immunisation guidelines.

Methods: A vaccination service for ASCT recipients was established at the Peter MacCallum Cancer Centre in March 2014, consisting of regular scheduled reviews, face-to-face education with nursing and medical staff and a vaccination schedule aligned with national guidelines. ASCT patients were retrospectively classified as ‘pre-clinic’ (Sept 2012-Sept 2013) or ‘post-clinic’ cohorts (Oct 2013-2014), according when the service became available. Uniform data were collated from clinical and pharmacy databases, including: type and timing of vaccine/s, number of cycles completed, and reasons for non-compliance with guidelines. Vaccination uptake and compliance in each cohort were compared.

Results: Post-clinic and pre-clinic cohorts consisted of 87 and 81 patients, respectively, with similar patient characteristics. The proportion commencing vaccination was not significantly different between groups (83.9% vs. 71.4%, \( p=0.12 \)). Of 74 patients eligible for vaccination in post-clinic cohort only 1 patient lost to follow up (1.4%) whilst the loss to follow up rate was 6.3% in pre-clinic cohort. Of patients vaccinated, the proportion administered according to national guidelines was significantly higher in the clinic cohort (70.8% vs. 19.0%, \( p<0.01 \)). More patients in this cohort completed all recommended vaccines (47.2% vs 32.8%, \( p=0.11 \)).

Conclusion: Implementing a dedicated post-ASCT vaccination service increased compliance with national immunisation guidelines (vaccination uptake, timing of administration) with near complete vaccination coverage.

Disclosure of Interest Statement: No conflicts of interest for all authors.
HIGH BURDEN OF FIRST PRESENTATION AND RECURRENCE OF SEVERE LOWER LIMB BACTERIAL CELLULITIS: A LONGITUDINAL STUDY

Authors:
Rajakaruna G1, Cannon J2, Dyer J1, Carapetis J2,3,4, Manning L1,4

1Fiona Stanley Hospital, 2Telethon Kids Institute WA, 3Perth Children's Hospital, 4University of Western Australia

Introduction: Lower limb bacterial cellulitis (LLBC) is a common and serious infection of skin and subcutaneous tissue. High rates of incidence, recurrence, morbidity and economic costs have been reported worldwide. Given the lack of good quality, contemporary data, we aimed to describe the epidemiology of first presentation, recurrence and excess mortality in Australian patients with LLBC.

Methods: The state-wide data-linkage system was used to extract records of adults presenting to Western Australian (WA) hospitals with first episode LLBC from January 2002 to December 2013. Incidence and recurrence rates were calculated and matched controls were used to describe excess mortality.

Results: Over 12 years, 43,410 LLBC episodes were reported in 36,276 patients. There was an annual increase in incidence (4.7% p.a.), with an overall incidence of 204.8 (95% CI 198.6-211.1) per 100,000 population in 2013. There were higher incidence rate ratios (IRR) in older patients aged 65-84 years (IRR 2.59 [2.50-2.69], P<0.001) and >85 years (IRR 7.04 [6.73-7.37], P<0.001) compared with 16-24 years. Males and Indigenous Australians also had higher IRR. There was significant seasonal variability with increased rates during summer. LLBC recurrence occurred in 4,598 (12.7%) patients, with increased risk in older patients, females and Indigenous Australians. When compared with matched controls, patients with LLBC had a higher mortality (P<0.0001).

Conclusion: There is a large and increasing burden of LLBC, especially amongst older Australians. Given the frequent recurrence, long term morbidity and association with increased mortality, efforts to reduce primary episodes and minimise the risk of recurrence should be a priority.

Disclosure of Interest Statement: This study was funded from internal funds held by the Department of Infectious Diseases at Fiona Stanley Hospital. No pharmaceutical grants were received in the development of this study.
A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL OF IBUPROFEN COMPARED WITH PLACEBO FOR UNCOMPLICATED CELLULITIS OF THE UPPER OR LOWER LIMB

Joshua S Davis¹,², Carol Mackrow³, Paula Binks¹, Wendy Fletcher³, Pascale Dettwiller⁴, Catherine Marshall³, Jane Day⁵, William Pratt⁵, Steven YC Tong¹,⁶

1. Global and Tropical Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, NT, Australia
2. Department of Infectious Diseases, John Hunter Hospital, Newcastle, NSW, Australia and the University of Newcastle
3. Hospital in the Home Program, Royal Darwin Hospital, Darwin, NT, Australia
4. Katherine Rural Clinical School, Flinders University, Katherine, NT
5. Hospital in the Home Program, Shoalhaven Hospital, Nowra, NSW, Australia
6. Victorian Infectious Diseases Service, the Royal Melbourne Hospital, and the University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia

Introduction: Cellulitis is a common skin and soft tissue infection resulting in substantial inflammation that may take weeks to resolve despite appropriate antibiotics. It is unclear whether the adjunctive use of non-steroidal anti-inflammatory drugs hastens the resolution of inflammation in patients with cellulitis.

Methods: We conducted a double-blind randomised controlled trial comparing ibuprofen 400mg three times daily orally for five days with identical placebo in adults with uncomplicated cellulitis of the upper or lower limb, treated with intravenous cefazolin via an outpatient parenteral antibiotic treatment service at one of two Australian hospitals. Participants were assessed twice daily by a study nurse. The primary outcome measure was the proportion of patients with regression of inflammation 48 hours following the first effective dose of parenteral antibiotics. This trial was registered (ANZCTR 12611000515998).

Results: Fifty-one patients were enrolled; 48 had sufficient data available to be included in the modified intention to treat analysis. Inflammation had begun to regress at 48 hours in 20 participants (80%) in the ibuprofen group compared with 15 (65%) in the placebo group (Absolute risk difference + 15% [95% CI -10% to +40%]), p>0.05). There was no significant difference in any of the secondary outcomes. Ibuprofen treatment appeared safe, with no patients developing renal impairment or necrotising fasciitis.

Conclusions: This trial demonstrated no significant benefit of adjunctive ibuprofen in adults with uncomplicated cellulitis. The trial was powered to detect a large effect, and hence it is unclear if the 15% absolute increase in the primary endpoint in the ibuprofen group was attributable to chance or not.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
ERTAPENEM FOR OSTEOARTICULAR INFECTIONS IN OBESE PATIENTS: A PHARMACOKINETIC STUDY OF PLASMA AND BONE CONCENTRATIONS

Authors:
Chambers J T¹, Page-Sharp M², Salman S³, Dyer J¹, Davis T³, Batty K T², Manning L³,⁴

¹ Department of Infectious Diseases, Fiona Stanley Hospital, Murdoch, Western Australia
² School of Pharmacy, Curtin University, Bentley, Western Australia
³ School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia
⁴ Harry Perkins Research Institute, Fiona Stanley Hospital, Murdoch, Western Australia

Introduction: Ertapenem is used off-label to treat osteoarticular infections, but there are few pharmacokinetic (PK) data to guide optimal dosing strategies or the probability of PK-pharmacodynamic target attainment (PTA) in this patient group who may be obese and/or frail with multiple co-morbidities.

Methods: Participants undergoing elective joint arthroplasty or lower limb and/or partial foot amputation received a dose of intravenous ertapenem prior to surgery, in addition to routine perioperative antibiotic prophylaxis. Plasma samples were collected at 8 time-points over 24 h and at least one bone sample per patient was collected at varying time-points post-infusion. Ertapenem concentrations in plasma and bone were measured using liquid-chromatography/mass-spectroscopy and analysed using non-linear mixed effects PK modelling.

Results: Plasma and bone concentrations were obtained from 10 participants. The final population PK model showed that a fat free body mass was the most appropriate body size adjustment. The model also demonstrated a strong effect of frailty on clearance with a doubling of plasma half-life in patients with moderate/severe frailty. Ertapenem equilibrated rapidly into bone, but concentrations were 40-fold higher in plasma and highly variable between individuals. Simulations demonstrated that the PTA for free plasma concentrations was ≤50% when the minimum inhibitory concentration (MIC) was ≥0.5mg/L. In bone, the PTA was ≤55% when the MIC was ≥0.25mg/L.

Conclusion: Local bone and free plasma concentrations appear adequate for osteoarticular infections where Enterobacteriaceae are the main causative pathogens, but for Staphylococcus spp., Bacteroides fragilis and Acinetobacter spp., standard dosing is unlikely to result in adequate PTA. Frailty may alter ertapenem PK.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study.
Introduction: Studies have demonstrated high rates of bacterial colonisation of hand-held mobile devices in hospital settings, but have not established a molecular epidemiological link between organisms colonising mobile devices and those causing disease in patients.

Methods: Over a 12-week period, all routine clinical isolates defined as multi-drug resistant (MDR) (MRSA, VRE and ESBL producing Enterobacteriaceae) were prospectively collected and stored. During the same time period, the mobile devices of all medical staff were swabbed. Swabs were cultured for resistant organisms, with identification by matrix – assisted laser desorption ionisation. Illumina whole genome sequencing was used to assess the genetic relatedness of MDR organisms found on phones and in clinical isolates.

Results: 90 MDR clinical isolates were collected from patients. A total of 45 mobile devices used by medical staff were swabbed. Of these, two phones cultured MRSA and one phone cultured A. baumannii. WGS was performed on the 17 MRSA and Acinetobacter isolates from phones and patient isolates. The two MRSA isolates from the phones were genetically similar, but were genetically different to all the clinical isolates. These two phones were spatio-temporally linked and came from the same 14-bed area of the ICU. All four MDR Acinetobacter isolates were genetically different.

Conclusion: To the authors' knowledge, this is the first study to assess the molecular epidemiological link between MDR organisms found on mobile devices and those from patients. Despite MDR organisms being able to colonise physician mobile devices, these organisms were genetically different to those seen in patient isolates during the same time period.

Figure 1. MRSA dendrogram
Disclosure of Interest Statement:
There are no disclosures of interest to declare from any contributor to this research project.
POSTEXPOSURE IMMUNOPROPHYLAXIS USING THE HUMAN MONOCLONAL ANTIBODY m102.4 FOLLOWING HUMAN EXPOSURE TO EQUINE HENDRA VIRUS INFECTION

Authors:
Playford EG\textsuperscript{1,2}, Broder CC\textsuperscript{3}, Bossart KN\textsuperscript{4,5}, Zhu Z\textsuperscript{6,7}, Dimitrov AS\textsuperscript{8}, Yan L\textsuperscript{3}, Feng Y\textsuperscript{3}, Barr J\textsuperscript{9}, Hendry S\textsuperscript{1}, Cramri G\textsuperscript{9}, Broom JK\textsuperscript{2,10}, Hickey AC\textsuperscript{4,5}, Langley A\textsuperscript{11}, Neucom D\textsuperscript{11}, Dimitrov DS\textsuperscript{6}, Wang L\textsuperscript{9,12}

\textsuperscript{1}Infection Management Services, Princess Alexandra Hospital, Brisbane, Australia, \textsuperscript{2}School of Medicine, The University of Queensland, Brisbane, Australia, \textsuperscript{3}Department of Microbiology and Immunology, Uniformed Services University, Bethesda, MD 20814, \textsuperscript{4}National Emerging Infectious Diseases Laboratories Institute and \textsuperscript{5}Department of Microbiology, Boston University School of Medicine, Boston, MA 02118, \textsuperscript{6}Protein Interactions Group, CCRNP, CCR, NCI-Frederick, National Institutes of Health, Frederick, MD, \textsuperscript{7}BRP, SAIC-Frederick, Inc., Frederick, MD 21702, \textsuperscript{8}Profectus BioSciences Inc., Baltimore, MD 21224, \textsuperscript{9}CSIRO Livestock Industries, Australian Animal Health Laboratory, Geelong, Victoria; \textsuperscript{10}Department of Infectious Diseases, Nambour Hospital, Nambour, Australia, \textsuperscript{11}Sunshine Coast Public Health Unit, Maroochydore, Australia, \textsuperscript{12}Emerging Infectious Diseases Program, Duke-NUS Graduate Medical School, Singapore 169857, Republic of Singapore

Introduction: Hendra virus is associated with a significant mortality rate in both equine and human hosts. Human exposure to infected horse respiratory secretions or blood products carries a high risk of infection. There is no establish medical therapy to treat or prevent this disease in humans. The human monoclonal antibody m102·4 has been shown to be an effective postexposure prophylactic agent in animal models, for both Hendra and Nipah virus.

Methods: Retrospective data was collected from ten patients with high level exposure to Hendra virus who received m102.4. The data collected included patient demographics, drug pharmacokinetic data, adverse reactions and serology/biochemical data from a time period between 2014 to 2016.

Results: We describe ten cases where humans with high level exposure to Hendra virus have received m102·4. All of these patients remained disease free without clinical or serological evidence of Hendra virus infection. There were minimal associated adverse reactions.

Conclusion: The human monoclonal antibody m102·4 may play a role in preventing Hendra virus infection in humans. This is concordant with the data demonstrated in animal models and highlights the potential role for preventing and treating both Hendra and Nipah virus infection in humans.

Disclosure of Interest Statement: No conflicts of interest to declare.
AN INTEGRATED FIRST-IN-HUMAN STUDY OF THE NOVEL LONG-ACTING ANTIMALARIAL DSM265 DEMONSTRATES A FAVOURABLE SAFETY AND TOLERABILITY PROFILE, AND PREDICTS A CLINICALLY EFFICACIOUS DOSE FOR TREATMENT OF FALCIPARUM MALARIA

Authors:
McCarthy JS1,4, Lotharius J2, Rückle T2, Chalon S2, Phillips MA3, Elliott S4, Sekuloski S1, Griffin P1,4, Ng CL5, Fidock DA5, Marquart L1, Williams NS3, Gobeau N2, Bebrevska L2, Rosario M6, Marsh K7, Möhrle JJ2

1 QIMR Berghofer MRI; 2 Medicines for Malaria Venture; 3 University of Texas Southwestern Medical Center, Dallas, TX, USA; 4 Q-Pharm Pty Ltd, Herston, Australia; 5 Columbia University, NY, NY, USA; 6 Takeda Pharmaceuticals; 7 AbbVie, Chicago, IL, USA.

Introduction: DSM265 is a novel antimalarial that selectively inhibits Plasmodium dihydroorotate dehydrogenase (DHODH), an enzyme essential for pyrimidine biosynthesis. In this first-in-human study, we investigated its safety, tolerability and pharmacokinetics, and tested its in vivo activity against P. falciparum.

Methods: Part 1 was a single ascending dose (25–1200 mg), double-blind, randomised, placebo-controlled study; part 2 was an induced blood-stage malaria (IBSM), open-label, randomised, active-comparator controlled study, where participants were inoculated with P. falciparum and treated with a single dose of DSM265 (150 mg) or mefloquine (10 mg/kg).

Results: In part 1, 73 participants were enrolled (DSM265, n=55; placebo, n=18). In part 2, nine participants were enrolled (DSM265, n=7; mefloquine, n=2). DSM265 showed a good safety profile, with no drug-related serious or severe adverse events. The most common drug-related adverse event was headache. The mean plasma Cmax ranged between 1.3 and 34.8 µg/mL across doses tested; median Tmax was between 1.5 and 4 h; mean elimination half-life was 86 - 118 h. The DSM265 (150 mg) parasite reduction ratio was 1.55 (95% CI 1.42-1.67), with a corresponding parasite clearance half-life of 9.4 h (95% CI 8.7-10.2). The median MIC in blood was 1.04 µg/mL (range 0.55-1.50), resulting in a predicted single efficacious dose of 340 mg.

Conclusion: This is the first report of an integrated Phase 1 and IBSM study in antimalarial drug development. Its good safety profile, long elimination half-life and antimalarial effect support its development as partner drug in a single-dose antimalarial combination treatment.

Disclosure of Interest Statement: This study was funded by the Global Health Innovation and Technology Fund, Bill & Melinda Gates Foundation, Wellcome Trust, UK Department of International Development.
A NOVEL ASSAY TO ASSESS IMMUNE COMPROMISE AND RISK OF INFECTION POST HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Authors:
Douglas AP\textsuperscript{1,5},  Yu J\textsuperscript{2,4}, Szer J\textsuperscript{3,4}, Ritchie D\textsuperscript{3,4}, Slavin MA\textsuperscript{1,4,5}, Sasadeusz J\textsuperscript{1,4}, Visvanathan K\textsuperscript{2,4}

1. Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia
2. Immunology Research Centre, St Vincent’s Hospital, Melbourne, Australia
3. Department of Clinical Haematology and Bone Marrow Transplant Service, Royal Melbourne Hospital, Melbourne, Australia
4. University of Melbourne, Melbourne, Australia
5. Peter MacCallum Cancer Centre, Melbourne, Australia

Introduction: Managing immunosuppression in patients post allogeneic haematopoietic stem cell transplantation (alloHSCT) is challenging. Excessive immunosuppression can be complicated by infection, while inadequate immunosuppression can result in graft versus host disease (GVHD). An accurate method to assess immune status in the setting of HSCT is lacking. Unlike other commercially available assays which assess the adaptive immune response alone, QuantiFERON Monitor\textsuperscript{®} (QFM) measures interferon-gamma (IFN-\gamma) release from whole blood following incubation with both innate (R848) and adaptive (CD3 antibody) immune stimulants.

Methods: Whole blood samples were prospectively collected from alloHSCTs at conditioning and days 10, 30, 60, 90, 120 and 180 and assayed by the QFM test. IFN-\gamma levels were plotted against time post alloHSCT and correlated to episodes of infection and GVHD.

Results: 40 patients were enrolled in the study (68\% male; median age 47 years; 33\% myeloablative, 67\% reduced intensity conditioning). IFN-\gamma levels rose steadily over the first 180 days post transplantation and there was a trend between those with and without acute or chronic GVHD although this did not reach statistical significance. IFN-\gamma levels were statistically significantly lower in those with active infection compared to those without (p=0.028 using logistic regression with IFN-\gamma as a continuous variable).

Conclusion: Immune function, as measured by the QFM assay, appears to steadily increase over the first 180 days post alloHSCT. Lower IFN-\gamma levels correlated with risk of infection. This assay is promising as a means to monitor immune recovery and predict risk of infection and hence tailor immunosuppression and prophylaxis accordingly.

Disclosure of Interest Statement: No conflicts to disclose.
DEVELOPMENT OF A MOBILE LABORATORY FOR SUDDEN ONSET DISASTERS

Authors:
Marr I¹, Baird RW², Quilty S³, Coatsworth N⁴

¹National Critical Care and Trauma Response Centre, Level 8 Royal Darwin Hospital, NT, Australia, ²Territory Pathology, Royal Darwin Hospital, Darwin, Australia, ³Department of Medicine, Katherine District Hospital, Katherine, Australia, ⁴Infectious Disease Unit, The Canberra Hospital, Canberra, Australia.

Introduction: Sudden onset disasters (SOD) require a rapid medical response to limit ongoing death and injury. As part of Australia’s preparedness, the National Critical care and Trauma Response centre is equipped to deploy a surgical field hospital to both national and international disasters. We developed a mobile field laboratory to enhance the clinical services offered in SOD.

Objectives: Design and trial a mobile laboratory unit for use in Sudden Onset Disasters (SOD) that meets a WHO Emergency Medical Team (EMT) 2 standard.

Methods: Using RT-PCR FilmArray®, iSTAT®, HemoCue301®, HemoCueWBC® and portable microscopy a mobile laboratory was developed with field appropriate standard operating procedures meeting ISO guidelines. A 12 day deployment to a remote Northern Territory Hospital (Katherine) with limited laboratory capacity tested functionality and reproducibility of results with validation against current NATA accredited results.

Results: Over the study period 11 RT-PCR FilmArray multiplex tests provided 9 positive and 3 negatives, including blood culture (n=4), gastrointestinal (n=4), respiratory multiplex screens (n=3). All results were confirmed with NATA standardised testing. There were 20 WBC HemoCue and HemoCue301 tests performed, with non-significant differences (p>0.05) on each parameter when compared to Sysmex XN 550. iSTAT tests were run in parallel against Vitros 250 showing non-significant differences for CHEM4 (n=10), CG8 (n=10) and TnI (n=5) cards, p>0.05.

Conclusions: This small pilot trial shows a EMT2 mobile field laboratory can provide reproducible results when compared to NATA accredited testing in an isolated Northern Territory location.

Disclosure of Interest Statement: Nothing to disclose.
A SMARTPHONE-BASED SYSTEM FOR MEASURING AND SUPPORTING ADHERENCE TO MEDICATION

Authors:
Molton JS¹,², Pang Y¹, Wang ZC², Qiu BQ², Wu P², Rahman-Shepherd A¹, Ooi WT², Paton NI¹,²

¹ National University Health System, Singapore, ² National University of Singapore

Introduction: Suboptimal adherence for infectious diseases such as tuberculosis (TB) results in poor clinical outcomes and ongoing infectivity. Directly Observed Therapy (DOT) has a number of limitations. We aimed to develop and evaluate a smartphone-based system to facilitate remotely observed therapy rather than in-person observation.

Methods: We developed an integrated smartphone and web-based system to provide medication reminders and facilitate video recording of pill ingestion, for upload and later review.

We evaluated the system in a single arm, prospective study. Healthy volunteers age ≥21 were instructed to take a supplement pill once, twice or three-times a day, for 2 months, and to video each pill taking episode using the system. Adherence was measured by the smartphone system and by pill count.

Additionally we developed face and image recognition modules to automate the verification process, and a conditional cash transfer module to encourage adherence by rewarding successful video uptake with small cash incentives.

Results: 42 eligible participants were recruited (median age 24). Overall median estimated participant adherence by MIST was 90.0%, similar to that obtained by pill count (93.8%). There was a good relationship between adherence as measured by the system and by pill count (Spearmans r= 0.66, p<0.001).

Conclusions: We have demonstrated the feasibility, acceptability and accuracy of a smartphone-based adherence support and monitoring system that has applicability for infectious diseases such as TB and HIV.

Disclosure of Interest Statement: This study was funded by National University of Singapore. No pharmaceutical grants were received in the development of this study. All authors declare no conflicts of interest.
IMPLEMENTING MOBILE HEALTH FOR TUBERCULOSIS CARE IN SYDNEY: EXPERIENCE WITH VIDEO DIRECTLY OBSERVED THERAPY

Authors: Chapman, S1 Holzman, S2,3, Rios KC2,4, Shah, M2

1 Western Sydney University, New South Wales, Sydney, Australia
2 Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
3 Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
4 Emocha Mobile Health, Inc., Baltimore, Maryland, USA

Introduction: Tuberculosis (TB) remains a disease of public health interest in Australia, with over 1,300 cases annually. Directly observed therapy (DOT) remains the standard of care in New South Wales, but is logistically challenging and resource intensive for patients and providers. Video-based DOT represents a promising potential alternative methodology to ensure high rates of treatment adherence and completion. We evaluated an asynchronous video-DOT application, miDOT, that allows patients to securely record and transmit videos of themselves taking medication to a secure website, where providers can view and verify adherence at their convenience.

Methods: We conducted a prospective implementation study of video-DOT at the Parramatta Chest Clinic in Western Sydney. All TB patients were eligible, and were enrolled at the discretion of the TB clinic providers. Upon enrollment, participants utilized the video-DOT system to document adherence to treatment. The primary outcome was percentage of total doses that were verified by observation (i.e. DOT), comparing the time period before (i.e. in-person DOT) and after enrollment (i.e. miDOT).

Results: 19 participants uploaded 1389 videos documenting treatment (mean 73 videos/person, most frequently with daily dosing schedule). The proportion of observed (i.e. verified in-person, or uploaded video) treatment doses increased from a median of 66% (IQR 56%-73%) prior to enrollment (pre-miDOT period) to a median of 95% using miDOT (IQR 90%-98%, p=0.0003).

Conclusion: Asynchronous video-DOT is an effective tool for expanding capacity to perform DOT in TB clinics, with high adherence. Additional research is needed to evaluate generalizability of findings in Australia.

Disclosure of Interest Statement: Maunank Shah is the inventor of the miDOT system, which is licensed to Emocha Mobile Health Inc. Katrina Rios is an employee of Emocha Mobile Health Inc. Emocha Mobile Health provided the miDOT system without charge to the Parramatta Chest Clinic for the duration of the study and had no role in the study design, data collection or analysis. Scott Chapman (PI) has no conflicts and provided oversight of the study and data abstraction. Samuel Holzman has no conflicts to disclose and led data analysis.
AN EVIDENCE-BASED APPROACH TO UNDERSTANDING THE TRANSMISSION CYCLE AND RISKS OF COXIELLA BURNETTI INFECTION IN COMPANION ANIMALS

Authors:
Bosward KL¹, Norris JM¹

¹ Sydney School of Veterinary Science (SSVS), Faculty of Science, University of Sydney

Introduction: Confirmed cases of Q fever in veterinary personnel in small animal practice and companion animal handlers such as cat breeders have illustrated that cats and dogs, especially periparturient ones, can be a source of transmission. Determining the extent of this risk to humans and the source of transmission to companion animals is vital and requires a multifaceted approach.

Methods: Studies at SSVS have included cross-sectional surveys of knowledge attitudes and practices of cat breeders, veterinarians, veterinary nurses; seroprevalence studies in cats and dogs from a range of subpopulations (pet, breeding, feral/stray, camp dogs in remote Indigenous communities); and molecular studies of raw milk and pet meat to determine the presence of C. burnetti DNA.

Results: Cat breeders and veterinary nurses in Australia reported low levels of knowledge and awareness of Q fever disease and vaccination, resulting in a poor vaccination rates. Seroprevalence studies showed increased evidence of prior/current infection in breeding cats and camp dogs in indigenous communities. Pilot studies investigating the potential sources of C. burnetii in raw pet meat and unpasteurized ‘cosmetic bath’ milk has found modest concentrations of C. burnetii DNA in bulk-tank samples of unpasteurised ‘cosmetic bath’ milk collected from health food stores and raw meat containing kangaroo from pet food distributors.

Conclusion: Further carefully constructed cross-sectional and multi-disciplined studies with an open mind and attention to detail are required to follow our research leads to date in this complex area, if we are to truly understand the cycle of transmission of C. burnetii in animals and humans.

Disclosure of Interest Statement: The authors have been funded by Australian Companion Animal Health Foundation, NH&MRC and the Canine Research Fund. No pharmaceutical grants were received in the development of these studies.
Introduction: Rheumatic heart disease (RHD) causes significant morbidity and mortality in school-aged children in Timor-Leste, but its prevalence has not been evaluated or described. We conducted the first echocardiography-based screening study to determine the prevalence of RHD in school-aged Timorese children.

Methods: School students were enrolled from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste, using opt-out consent. Demographic and anthropometric data were collected and all students had a limited echocardiogram looking for evidence of RHD. RHD was classified as borderline or definite, according to World Heart Federation criteria. Patients with RHD were entered into a register for ongoing secondary prophylaxis, with the first dose of benzathine penicillin G administered on the day of the study.

Results: 1413 children were screened; 739 (52%) were girls and the median age was 12 years (range 4-24). The prevalence of definite RHD was 1.8% and borderline 1.6% (total 3.4%). Borderline or definite RHD was more common in Ermera than Dili though the difference was not statistically significant (4.1% vs 2.2%; p=0.07). Definite RHD was more prevalent in girls than boys (2.8% vs 0.7%; p<0.01). Congenital heart disease was identified in 20 children (1.4%). Of the 26 definite RHD cases, 23 (88%) received education and a first dose of BPG during the study.

Conclusion: RHD is prevalent in Timor-Leste, with some of the highest rates observed in the world. Girls are affected more commonly than boys. Community engagement is essential to ongoing follow-up and effective delivery of secondary prophylaxis.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer. Pfizer has no role in the design, implementation or analysis of the study.
RESPONDING TO THE OUTBREAK OF DRUG-RESISTANT TUBERCULOSIS IN DARU, SOUTH FLY DISTRICT, WESTERN PROVINCE, PNG

Authors: Majumdar S1, Chan G1, Adepojib T1, Lawson J1, Wallis P1, Huang K1, Ronnachit A1, Wallis A1, O’Brien D1, Graham S1,

1Burnet Institute, Melbourne, Australia.

Introduction: There is a major outbreak of drug-resistant tuberculosis (DR-TB) that is having a devastating effect on the population of the South Fly District (SFD) of the Western Province of Papua New Guinea (PNG) with the majority of cases resident on Daru Island. The local epidemic is characterised by high rates of primary transmission of DR-TB, with a population incidence of among the highest ever recorded (503 per 100 000 in 2016). Operational research (OR) to test interventions and innovations that will increase the efficiency of the response is needed.

In 2014, the Government of PNG convened an emergency response taskforce for DR-TB hotspots, with significant support from the Australian government. The Burnet Institute’s Reducing the Impact of Drug-Resistant TB (RID-TB) in Western Province supports the design and implementation of an effective SFD TB program, working in partnership with the Provincial Health Office (PHO), Daru General Hospital (DGH), the National Department of Health (NDoH), World Vision PNG and the World Health Organisation.

Significant progress has been made by the SFD TB program and partners since 2014 through health and community systems strengthening that has resulted in an improvement in case detection and treatment outcomes for all forms of TB. Through the Tropical Disease Research Regional Collaboration Initiative (TDRRCI), Burnet will partner with PNG institutions to develop an OR framework using the Structured Operational Research Training (SORT-IT) model. This session will provide an outline of the response, progress, and challenges and describe the SORT-IT model.

Disclosure of Interest Statement: The RID-TB Project is funded by the Australian Government’s Department of Foreign Affairs and Trade. No other relevant disclosures.
USING NASOPHARYNGEAL CARRIAGE SURVEILLANCE IN CHILDREN HOSPITALISED WITH ACUTE RESPIRATORY INFECTION TO DETERMINE THE PNEUMOCOCCAL CONJUGATE VACCINE COVERAGE REQUIRED FOR INDIRECT IMMUNITY

Authors:
Chan J¹, Nguyen CD¹,², Xeuatvongsa A³, Lai JYR¹, Mungun T⁴, Blyth C⁵, Pomat W⁶, Dunne EM⁷, Lim R¹, Phetsouvahn R⁷,⁸, Datta S⁹, Hinds J¹⁰,¹¹, Fox K¹², Newton PN⁷,⁸, Lehmann D¹³, Ford R⁶, La Vincente S¹,¹⁴,¹⁵, Dance DAB⁷,⁸,¹⁶, Satzke C¹,²,¹⁷, Mulholland EK¹,¹⁵,¹⁸, Russell FM¹,¹⁴

¹ Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia.
² Department of Paediatrics, University of Melbourne, Melbourne, Australia.
³ National Immunization Programme, Ministry of Health, Vientiane, Lao PDR.
⁴ Ministry of Health, Ulaanbaatar, Mongolia.
⁵ School of Medicine, University of Western Australia, Perth, Australia.
⁶ Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea.
⁷ Wellcome Trust Research Unit, Lao-Oxford-Mahosot Hospital, Vientiane, Lao PDR.
⁸ Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, United Kingdom.
⁹ World Health Organization, Vientiane, Lao PDR.
¹⁰ Institute for Infection and Immunity, St George's-University of London, London, United Kingdom.
¹¹ BUGS Bioscience, London Bioscience Innovation Centre, London, United Kingdom.
¹² Regional Office for the Western Pacific, World Health Organization, Manila, Philippines.
¹³ Telethon Kids Institute, University of Western Australia, Perth, Australia.
¹⁴ Centre for International Child Health-Dept. of Paediatrics, The University of Melbourne, Melbourne, Australia.
¹⁵ International Child Health, Menzies School of Health Research, Darwin, Australia.
¹⁶ Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom.
¹⁷ Department of Microbiology and Immunology, University of Melbourne, Melbourne, Australia.
¹⁸ Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom.

Introduction: Pneumococcal conjugate vaccines (PCVs) prevent disease through direct protection of vaccinated individuals, and indirect protection by reducing nasopharyngeal (NP) carriage and transmission of vaccine-type pneumococci. While the indirect effects of PCV vaccination are well described, the PCV coverage required to achieve the indirect effects is unknown. We will determine this using hospital-based NP pneumococcal carriage surveillance.

Methods: Surveillance includes children aged 2-59 months admitted to participating hospitals at three sites with acute respiratory tract infection. Thirteen-valent PCV (PCV13) status is obtained from written records. An NP swab is collected according to standard methods and examined by lytA qPCR, with positives serotyped by microarray. PCV13 coverage is determined using administrative data or community survey.

Results: In Lao PDR, Papua New Guinea, and Mongolia, we have recruited 973, 204, and 240 children, respectively. For each site, we will present monthly PCV13 carriage rates. In Laos PDR, where PCV13 coverage is <50%, PCV13 carriage rates are declining among vaccinated children (direct effects) but not unvaccinated children (indirect effects, figure 1).
Data will also be pooled across sites to examine relationships between PCV13 coverage and carriage.

**Conclusion:** As PCV13 coverage increases, we hypothesise that PCV13 carriage to decline in vaccinated and unvaccinated individuals. These results will inform vaccine policy makers about the PCV coverage required to maximise the effects of PCV.

**Disclosure of Interest Statement:** This study received funding from the Bill and Melinda Gates Foundation. No pharmaceutical grants were received in the development of this study.
Introduction: Patients with HCV genotype 3 (GT3) infection, particularly those with cirrhosis, have emerged as a more difficult to cure population. Voxilaprevir (VOX) is a pangenotypic inhibitor of the HCV protease. This Phase 3 study evaluated treatment with Sofosbuvir/Velpatasvir/VOX for 8 weeks and SOF/VEL for 12 weeks in DAA-naïve patients with GT3 HCV infection and compensated cirrhosis.

Methods: Patients in North America, Europe, Australia and New Zealand were randomized 1:1 to receive SOF/VEL (400/100 mg daily) for 12 weeks or SOF/VEL/VOX (400/100/100 mg daily) for 8 weeks. The primary endpoint compares the sustained virologic response 12 weeks after treatment (SVR12) to a pre-specified historic control rate of 83%. Secondary endpoints included safety, tolerability, and viral resistance.

Results: Of 219 patients treated, 72% were male, 90% were white, 42% had the IL28B CC genotype, and 31% had previously failed IFN-based treatment. Median platelet count was 139x103 cells/µL and mean Fibroscan was 23kPa in the SOF/VEL/VOX group and 22kPa in the SOF/VEL group. Treatment was well tolerated – two patients, both in the SOF/VEL group, discontinued therapy – 1) pelvic fracture and 2) viral breakthrough at week 8. No serious adverse events were attributed to medication were reported. Overall, SVR12 with SOF/VEL/VOX was 96% (106/110) and in the SOF/VEL was 96% (105/109). Both treatment arms were superior to the predefined performance goal of 83% (p<0.001).

Conclusion: The single tablet regimens of SOF/VEL/VOX for 8 weeks and SOF/VEL for 12 weeks are safe, well tolerated and effective treatment options for difficult-to-cure patients with GT3 infection with compensated cirrhosis.

Disclosure of Interest Statement: This study was funded by Gilead Sciences.
CHRONIC HEPATITIS C TREATMENT UPTAKE IN AUSTRALIA FOLLOWING AVAILABILITY OF INTERFERON-FREE THERAPY

Authors:
Hajarizadeh B1, Grebely J1, Matthews GV1, Martinello M1, Dore GJ1

1The Kirby Institute, UNSW Sydney, Sydney, New South Wales, Australia

Introduction: Government-subsidised direct acting antiviral (DAA) treatment for hepatitis C virus (HCV) infection has been available in Australia since March 2016. This study assessed DAA treatment uptake between March-September 2016.

Methods: A 10% random sample of Pharmaceutical Benefits Scheme (PBS) DAA prescriptions processed for reimbursement between March-September 2016 were analysed.

Results: An estimated 25890 individuals initiated DAA treatment between March-September 2016, accounting for an estimated 11% of all individuals with chronic HCV in Australia. DAA regimens included sofosbuvir/ledipasvir (57%) sofosbuvir+daclatasvir (38%), sofosbuvir+other agents (4%), and paritaprevir/ritonavir/ombitasvir+dasabuvir (1%). Of those initiating DAA therapy, 66% were men and 40% were ≤50 years old. Gastroenterologists were the predominant prescriber group (52%), followed by general practitioners (GP; 13%), infectious diseases physicians (8%), other specialists (4%), and other physicians (22%). The proportion of individuals prescribed by GPs increased from 4% in March to 19% in September (Figure 1A). The proportion of individuals ≤50 years increased from 28% in March to 54% in September (Figure 1B). Among patients with HCV-related cirrhosis, an estimated 64% received DAA therapy between 2014 and September 2016 through PBS, clinical trials, early access programs or generic supply.

Conclusion: Rapid treatment scale-up was observed in the first seven months of government-subsidised DAA therapy in Australia. The proportion of prescriptions by GPs increased over time, crucial for broadened access. Further HCV elimination evaluation will include monitoring of treatment outcomes, treatment uptake among people who inject drugs and HIV-infected men who have sex with men, and HCV prevalence and incidence (both primary infection and reinfection).

Disclosure of Interest Statement: The Kirby Institute is funded by the Australian Government Department of Health and is affiliated with the Faculty of Medicine, UNSW Sydney. The views expressed in this publication do not necessarily represent the position of the Australian Government. No pharmaceutical grants were received in the development of this study.
Figure 1: Distribution of monthly DAA treatment initiation by prescriber type (A) and patient’s age (B) during March-September 2016 in Australia.
SUB-OPTIMAL PROTECTION AGAINST PAST HEPATITIS B VIRUS INFECTION WHERE SEROTYPE MISMATCH EXISTS BETWEEN VACCINE AND CIRCULATING VIRAL GENOTYPE IN NORTHERN AUSTRALIA

Authors: Cheah BC1, Davies J1,2, Singh G2, Wood N3, Jackson K4, Davison B2, McIntyre P3, Locarnini S4, Davis JS2, Tong SYC2,5.

1. Royal Darwin Hospital, Darwin NT, Australia
2. Menzies School of Health Research, Darwin NT, Australia
3. National Centre for Immunisation Research and Surveillance for Vaccine Preventable Diseases, The Children's Hospital at Westmead, Westmead NSW, Australia
4. Victorian Infectious Diseases Reference Laboratory, Doherty Institute for Infection and Immunity, Melbourne VIC, Australia
5. Victorian Infectious Disease Service, The Royal Melbourne Hospital, and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Victoria, Australia

Introduction: In the Northern Territory, there is a serotype mismatch between the hepatitis B virus vaccine (adw2) and the circulating viral genotype (ayw3) in the Indigenous population.

Methods: We assessed serological markers of HBV infection in the Aboriginal Birth Cohort (ABC). Participants were recruited at birth at the Royal Darwin Hospital (1987–1990), with follow-up serology obtained at waves 3 (W3; 2006–2008) and 4 (W4; 2013–2015). A subset of non-immune participants at W3 received a booster. We determined the vaccine effectiveness (VE) against any (anti-HBc Ab+) and chronic infection (HBs Ag+).

Results: Of 686 participants, HBV serology was obtained from 386 at W4, of whom 269 had received ≥1 vaccine dose, 113 were vaccinated in accordance with United States Centers for Disease Control recommendations and 117 had never been vaccinated. Seven participants were chronically infected and 94 had evidence of any infection. The VE against any infection was 66% (P = 0.06), and against chronic infection 100% (P = 0.20). For every dose of vaccine received, the odds of being anti-HBc Ab+ decreased by 41% (P < 0.001). The odds of being anti-HBc Ab+ was 87% lower in participants raised in urban compared to remote areas (P = 0.002). The W3 booster had no sustained effect.

Conclusion: The vaccine was effective in preventing chronic infection but sub-optimal against any infection. That anti-HBs titres and the presence of anti-HBc Ab were associated with remote dwelling rather than prior vaccination or boosting suggests ongoing exposure to circulating virus.

Disclosure of Interest Statement: This study was funded through NHMRC project and fellowship grants.
PREVALENCE OF ANTIVIRAL RESISTANCE IN AN AUSTRALIAN HEPATITIS C POPULATION

Ong ATL,1,2,3 Tay E1, George J1,3, Douglas MW1,2,3

1Storr Liver Centre, Westmead Millennium Institute, University of Sydney at Westmead Hospital, Sydney, Australia, 2Centre for Infectious Diseases and Microbiology, Westmead Hospital, Sydney, Australia, 3Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Sydney, Australia

Objective: To determine the prevalence of baseline resistance associated substitutions (RASs) in Australian patients with hepatitis C virus (HCV) genotype 1 infection.

Design: Single centre cross-sectional study.

Setting: Single tertiary centre. Large urban Australian public hospital pathology laboratory.

Participants: 380 patients whose blood samples were sent to the Institute for Clinical Pathology and Medical Research (ICPMR) for genotype testing, and found to be HCV genotype 1 or 1a infection. All patients were naive to new direct acting antivirals (DAAs) against HCV, which were approved for PBS subsidy in March 2016.

Main outcome measures: HCV RASs of greatest clinical relevance are those present in the NS3 and NS5A regions of the HCV genome. DAAs targeting these regions are being widely prescribed in Australia. Viral genome sequences from these regions were generated and analysed with epidemiological data.

Results: 380 samples were tested. The median age of the patients was 41.7, interquartile range (IQR) 33.7 - 49.9 years. Patients were predominantly male (71%). A significant proportion of patients were from correctional centres (31%). The most prevalent NS3 RAS was Q80K at 5.6%, and for NS5A was M30V at 6.0%.

Conclusions: This is the first and largest examination of the prevalence of HCV resistant mutations in Australia. The most prevalent NS3 RAS, Q80K confers resistance to simeprevir, a previous generation DAA no longer in use. The most prevalent NS5A RAS, M30V potentially confers resistance to ombitasvir. It is important to monitor for the potential emergence of drug resistance.

Disclosure of Interest Statement: No conflicts to declare.
POSTCARDS FROM THE DIGITAL HEALTH FRONTIER; TELEHEALTH FOR HEPATITIS C CARE IN THE DAA ERA

Authors: 
Biggs BA¹,²,³, Kanhutu K¹,²,³,⁴, Sasadeusz J¹,², Schulz T¹,², Watkinson S¹,²

¹Royal Melbourne Hospital, ²Victorian Infectious Diseases Service, ³University of Melbourne Faculty of Medicine, Dentistry and Health Sciences, ⁴Health Informatics Society Australia

Introduction: The Victorian Infectious Diseases Service based at the Royal Melbourne Hospital currently provides telehealth care for rural and regional patients with hepatitis C. The progressive roll out of the national broadband network and increasing availability of web based videoconferencing platforms and mobile devices have provided unprecedented capacity to manage patients remotely. The primary outcome of this study is to demonstrate that telehealth delivered hepatitis C management achieves comparable virological outcomes to standard face to face care.

Methods: The study is part of a quality audit of the hepatitis service.

Key outcome and process measures include;

- Proportion of patients achieving a sustained virological response (SVR)
- Failure to attend rate (FTA)
- Frequency of technical difficulties
- Consult duration time

Results: Since March 1⁰ 2016 over 50 patients have been managed via telehealth. Of those who have so far completed therapy an SVR rate of 94% of has been achieved. Expected SVR genotype 1 (>95%); genotype 3 (>85%). Technical difficulties occurred in less than 10% of consultations with FTA of 17%. Consult duration was on average 15 minutes or less.

Conclusion: Our completed patient cohort results suggest comparable outcomes for telehealth managed patients as compared to traditional modalities even when adjusted for age, gender, hepatic fibrosis status and co - existent co-morbidities. Following on from the 2017 publication of the Infectious Diseases Society of America position statement on Telehealth and Telemedicine, we discuss the challenges and benefits of an outpatient ID telehealth services as we enter the era of accelerating digitally enabled healthcare.

Disclosure of Interest Statement: No conflicts to disclose.
CHESS - CURING HEPATITIS C: EFFECT ON THE ENDOTHELIUM AND CARDIOVASCULAR RISK

Authors:
Joshua S Davis\textsuperscript{1,2,3}, Melissa Young\textsuperscript{1}, Sandra Lennox\textsuperscript{1}, Tracey Jones\textsuperscript{1}, Kim Piera\textsuperscript{3}, Robert Pickles\textsuperscript{1,2}, Steven Oakley\textsuperscript{1,2}

1. Division of Medicine, John Hunter Hospital, Newcastle, NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW, Australia
3. Menzies School of Health Research, Darwin, NT, Australia

Introduction: Epidemiological data suggest that chronic hepatitis C virus infection (CHC) is associated with increased cardiovascular risk, but the mechanisms are unclear. We aimed to assess the effect of antiviral treatment on endothelial function in adults with CHC.

Methods: Adults with CHC, genotype 1, and no evidence of advanced fibrosis or cirrhosis were eligible. All patients were treated with 12 weeks of paritaprevir/ritonavir, ombitasvir and dasabuvir (PrOD), with additional ribavirin for genotype 1a. Endothelial function was assessed at multiple time-points before, during and after antiviral treatment. The main assessment tools were reactive hyperaemia peripheral arterial tonometry (RHPAT, higher values reflect better endothelial function), and serum angiopoietin-2 (ang-2) and e-Selectin (for both, higher values reflect worse endothelial cell activation and damage).

Results: Sixteen patients were enrolled. Mean (sd) age was 52.0 (6.9) years and 11 participants (69%) were male. All 16 achieved a sustained virological response. The mean (sd) pooled baseline RHPAT index was 2.05 (0.48), and there was no significant change during treatment (mean within-patient change from baseline to end of treatment= -0.23 (0.45), p=NS). There was significant improvement in mean ang-2 (baseline 2.44 (0.79) ng/ml, within-patient change -0.60 (0.44), p<0.001) and plasma e-Selectin (baseline 48.7 (21.5) ng/ml, within-patient change -14.4 (13.0), p<0.001).

Conclusions: Removing HCV viraemia is associated with a significant improvement in endothelial function as measured by serum markers, but not in bedside microvascular reactivity. Chronic HCV viraemia may be associated with endothelial cell dysfunction and therefore long term cardiovascular risk.

Disclosure of Interest Statement: This study was funded by an unconditional investigator-initiated research grant from Abbvie sciences, who market PrOD.
IS GENTAMICIN SAFE AND EFFECTIVE FOR SEVERE COMMUNITY ACQUIRED PNEUMONIA? A RETROSPECTIVE COHORT STUDY.

Authors:
Brereton CJ¹,², Lennon D¹, Browning S¹, Dunn E¹, Ferguson JK¹,², Davis JS¹,²,³

1. Division of Medicine, John Hunter Hospital, Newcastle NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW Australia
3. Global and Tropical Health Division, Menzies School of Health Research, Darwin NT Australia

Introduction: Current Australian guidelines recommend a third generation cephalosporin (3GC) plus azithromycin as first line therapy for severe community acquired pneumonia (CAP). Benzyl-penicillin plus gentamicin plus azithromycin is an alternative, which provides excellent Gram negative cover, while avoiding the host and ecological effects on antimicrobial resistance of 3GCs. However Gentamicin is not commonly used in this setting due to concerns about potential toxicity and a lack of published evidence assessing efficacy.

Methods: We conducted a single-centre retrospective cohort study at a university teaching hospital where benzyl-penicillin, gentamicin and azithromycin is the empiric antibiotic regimen of choice for severe CAP. We included all patients with radiologically-confirmed CAP admitted to the intensive care unit between January 2008 and December 2015. The key exposure of interest was the receipt of gentamicin within the first 72 hours of admission. The key outcomes were acute kidney injury (AKI), hospital mortality, and relapse.

Results: We enrolled 147 patients of whom 117 received gentamicin. There was no difference in the incidence of new acute kidney injury in the gentamicin (59/117, 50%) and the non-gentamicin (15/30, 50%) groups, regardless of the number of doses received. Hospital mortality and relapse were no different in the gentamicin group (17%, 10%) respectively than the non-Gentamicin group (23%, 10%, p=NS for both comparisons), even after adjusting for receipt of other agents active against Gram negatives.

Conclusions: Gentamicin is a safe and effective alternative to broad spectrum antimicrobials as initial empiric Gram negative treatment of severe CAP.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
MYCOBACTERIUM ABSCESSUS COMPLEX IN A MAJOR TERTIARY ADULT CYSTIC FIBROSIS CENTRE

Authors:
Tippett E¹, Ellis S², Wilson J³,⁴, Kotsimbos T³,⁴†, Spelman D¹,⁴†

¹Infectious Diseases, Alfred Hospital, Victoria, ²Radiology Department, Alfred Hospital, Victoria, ³Respiratory Department, Alfred Hospital, Victoria, ⁴Monash University, Victoria
†Equal Senior Author.

Introduction: Mycobacterium abscessus complex (MAbsC), a rapidly growing atypical mycobacterium, is an opportunistic respiratory pathogen significant to people with underlying lung pathology, particularly cystic fibrosis (CF). Treatment is in the order of months with multiple agents, potential significant adverse events and poor treatment outcomes. This study reviewed the patient population in whom MAbsC was isolated at The Alfred Hospital, which specialises in adult CF, examining the natural history, risk factors for persistent colonisation and treatment outcomes.

Methods: We undertook a retrospective cohort analysis of all patients in whom MAbsC was isolated between 2005 to 2014, particularly focussing on patients with CF. Factors examined included BMI, FEV₁, CF comorbidities and medications including corticosteroids and prophylactic antibiotics to determine factors which may predict transient compared to persistent colonisation.

Results: MAbsC was isolated from 45 patients of whom 26 had CF. Of the patients with CF, patients who were transiently colonised with MAbsC had higher baseline respiratory function. In one third of our cohort, MAbsC was isolated for a mean of one year prior to spontaneous clearance. There was no correlation between recurrent MAbsC isolation and the use of systemic or inhaled steroids. Four CF patients were initiated on treatment with only one successful outcome.

Conclusion: This analysis demonstrates there are no clear predictors of those patients who will become persistently colonised with MAbsC and that a significant proportion will spontaneously clear colonisation. As treatment success rate is poor more work is urgently required in improve patient outcomes.

Disclosure of Interest Statement: E Tippett was supported by the Alfred Junior Medical Workforce. Nothing else to disclose.
CO-MRSA INFECTIONS IN AUSTRALIA COST $3.5B PER ANNUM

Authors:
Cameron JK¹, Paterson DL², Britton PN³, Tong SYC⁴, Hall L¹, Nimmo GR⁵, Bennett CM⁶, Halton K¹.

¹ Institute for Health and Biomedical Innovation and School of Public Health and Social Work, Queensland University of Technology, ² The University of Queensland Centre for Clinical Research, University of Queensland and Royal Brisbane and Women’s Hospital, ³ The Children’s Hospital at Westmead and Sydney Medical School, University of Sydney, ⁴ Victorian Infectious Disease Service, The Royal Melbourne Hospital and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity and Menzies School of Health Research, Darwin, ⁵ Griffith University School of Medicine and Pathology Queensland, ⁶ Centre for Population Health Research, Deakin University

Introduction: The health and economic burdens of community-onset methicillin resistant Staphylococcus aureus (CO-MRSA) infections are needed to inform policy, planning and evidence-based practice. We aimed to synthesise data from a range of public sources to generate the first estimate of the national incidence and cost of CO-MRSA infections.

Methods: Incidences of CO-MRSA skin and soft tissue (SSTI), lower respiratory tract (LRTI) and bloodstream (BSI) infections were calculated for regions of Australia using data from existing literature and correspondence with specialists.

Simulations estimated costs using treatment models developed for children and adults in primary or tertiary care settings and including bed-stay, diagnostics, procedures, mortalities and loss of productivity.

Results: Annually, in Australia there were found to be 3702 CO-MRSA SSTIs, 559 CO-MRSA BSIs and 425 CO-MRSA LRTIs, occupying 147,000 bed-days, including 1600 bed-days in intensive care. Incidence ranged from 4/100,000 person-years in Tasmania to 243/100,000 person-years in central Australia.

The estimated cost of CO-MRSA was $3.5b annually in Australia. The higher incidence of SSTIs resulted in costs greater than summing the costs of BSIs and LRTIs. The greatest cost was mortality. The cost to the health system was found to be $1.9b, with bed occupancies accounting for ≥94%.

Conclusion: This first evaluation of the health and economic burden of CO-MRSA in Australia found a need for increased and more consistent data collection for a significant and expensive disease.

Disclosure of Interest Statement: This research was funded by NHMRC grant GNT1027589.
OPTIMISING LABORATORY METHODS FOR PRE-TRUS BIOPSY QUINOLONE RESISTANCE SCREENING

Authors:
Liu E, Seed D, Andresen D, McKew G, Gray T, Cheong E, Gottlieb T.

1Concord Repatriation General Hospital, Concord, NSW, Australia
2St Vincents Hospital, Darlington, NSW, Australia

Introduction: Ciprofloxacin-resistant Enterobacteriaceae infections following TRUS biopsy cause significant morbidity, however no consensus exists on an optimal laboratory screening method. We evaluated 7 methods regarding test performance, cost-effectiveness and usability.

Methods: Using simulated rectal swabs, 105 faecal samples were tested in parallel:
A: Direct plating to MacConkey agar (MAC)+CIP 10mcg/mL
B: Direct plating to MAC+5mcg CIP disc (MAC+5CD)
C-F: 5mL BHI broth+1, 2, 5 & 10mcg/mL CIP respectively; subculture to MAC+5CD
G: 5mL BHI broth+2x5mcg CIP discs (approximating 2mcg/mL), subculture to MAC+5CD

A positive screen on MAC+5CD was defined as coliform growth within a CIP zone <22mm, criteria derived from our prior validation study. The nearest coliform growth to the ciprofloxacin disc was identified by MALDI-TOF and CIP MIC determined by gradient strip.

Results: CIP-R Enterobacteriaceae was detected in 13/105 samples (MIC 2 to >32mcg/mL).

The most sensitive was broth enrichment at CIP10mcg/mL (100%, CI 75-100%) with 97% specificity (CI 91-100%). Subcultures from CIP<5mcg/mL broths were more difficult to read without superior sensitivity.

Both direct plating methods had equal sensitivity of 62% (CI 32-86%) and specificity >99% (CI 94-100%).

Arm B was most cost-effective at AUD $7.57/$0.64 (positive/negative), compared to Arm A ($7.93/$1.00) A and broth enrichment ($10.15/$3.22).

Conclusion: Direct disc screening is comparable to direct plating to MAC+CIP10mcg/mL agar, is more cost-effective and could be readily incorporated into existing laboratory work practices. Broth enrichment trended towards higher sensitivity, with larger studies needed to further assess if statistically significant.

Disclosure of Interest Statement: No conflict of interest to disclose.
HEALTH OUTCOMES FROM MULTI-DRUG RESISTANT SALMONELLA IN HIGH INCOME COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors:
Parisi A¹, Vilkins S¹, Furuya-Kanamori L¹, Crump JA², Howden BP³, Gray D¹, Glass K¹, Kirk M¹

¹ Australian National University, ² University of Otago, ³ University of Melbourne

Introduction: Salmonella is a leading cause of foodborne enterocolitis worldwide. Nontyphoidal Salmonella (NTS) infections that are Multi-Drug Resistant (MDR) (non-susceptible to ≥1 agent in ≥3 antimicrobial categories) may result in more severe outcomes, although these effects have not been systematically examined. We conducted a systematic review and meta-analysis to examine impacts of MDR NTS on health in high-income settings.

Methods: We systematically reviewed the literature from scientific databases, including PubMed, Scopus and grey literature sources, using PRISMA guidelines. We searched for data from case-control studies, cohorts, outbreaks and theses, imposing no language restriction. We included only publications from January 1990 to September 2016 from high income countries as classified by World Bank. We extracted data from papers on duration of illness, hospitalisation rates, morbidity and mortality for MDR and non-MDR NTS strains.

Results: After removing duplicates, the initial search revealed 4258 articles. After further screening, we identified 16 eligible studies for the systematic review, and 9 of these were included in the meta-analysis. NTS serotypes differed among the reported studies but serotypes Typhimurium, Enteritidis, Newport and Heidelberg were the most often reported MDR pathogens. Salmonella infections that were MDR were associated with excess bloodstream infections (OR 1.63; 95%CI 1.18-2.26), excess hospitalisations (OR 2.77; 95%CI 1.47-5.21) and higher mortality (OR 3.54; 95%CI 1.10-11.40).

Conclusion: MDR NTS infections are a serious public health concern. With the emergence of MDR Salmonella strains in the high-income countries, it is crucial to restrict the use of antimicrobials both in animals and humans, and intervene to prevent foodborne infections.

Disclosure of Interest Statement: We declare that we have no conflicts of interest in the authorship or publication of this contribution.
SIGNALLING INDUCED BY HUMAN CYTOMEGALOVIRUS IN AN AUTOCRINE MANNER ALTERS EXPRESSION OF WNT RECEPTOR ROR2 AND MIGRATION OF INFECTED TROPHOBLASTS

Authors:
vanzuylen WJ$^{1,2}$, Paul W$^2$, Ford C$^4$ and Rawlinson WD$^{1,2,3}$

$^1$Serology and Virology Division, SEALS Microbiology, Prince of Wales Hospital, Sydney, Australia, $^2$School of Medical Sciences, University of New South Wales, Sydney, Australia, $^3$School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, Australia, $^4$Metastasis Research Group, Prince of Wales Clinical School, University of New South Wales, Sydney, Australia

Introduction: Primary maternal CMV infection, reactivation, or infection with a different viral strain may cause adverse pregnancy outcomes including sensorineural hearing loss and mental disability. Placental infection may indirectly cause fetal injury via impairing placental development. New approaches to disease prevention are urgently needed. Better understanding of the molecular mechanisms of CMV infection of the placenta is essential for therapeutic innovations to decrease the prevalence and societal impact of congenital CMV.

Methods: Our previous findings indicate CMV controls the expression of the Wnt5a-binding tyrosine kinase receptor ROR2 to alter placental cell motility, which could lead to abnormal placental development in congenital CMV disease. We used migration assays in 2 compartment models, with added exogenous signalling proteins (wnt5a) and inhibitors (siRNA) to infected and uninfected cultures.

Results: We now show CMV specifically inhibits Wnt5a-mediated migration of infected trophoblasts, but not migration of surrounding uninfected cells. Utilising supernatant from CMV-infected trophoblasts, we also show that this inhibition and ROR2 alteration is not dependent on a soluble factor, rather it requires cell-cell contact. Furthermore, we show that both viable laboratory CMV strain AD169 and clinical CMV strain Merlin, but not UV-inactivated CMV inhibits Wnt5a-mediated trophoblast motility, indicating de novo viral gene expression is required.

Conclusions: Taken together, our novel findings suggest that autocrine signalling induced by human Cytomegalovirus alters ROR2 expression and this affects migration of infected trophoblasts. Inhibition of this autocrine signalling is a specific target for therapeutic intervention for CMV-induced placental damage and consequent fetal damage in congenital CMV infections.

Disclosure of Interest Statement: No conflicts to declare.
CONGENITAL CYTOMEGALOVIRUS (cCMV) IN INFANTS WITH HEARING LOSS IDENTIFIED VIA THE UNIVERSAL NEWBORN HEARING SCREENING PROGRAM, AND RISK FOR POSTNATAL INFECTION IN CHILDCARE

Authors: Palasanthiran P\textsuperscript{2}, Wilkinson M\textsuperscript{2}, Hall B\textsuperscript{1}, Al Yazidi L\textsuperscript{2}, Fennell M\textsuperscript{1}, Zheng J\textsuperscript{1}, van Zuylen W\textsuperscript{1}, Cottier C\textsuperscript{2}, Rawlinson W \textsuperscript{1}.

\textsuperscript{1}Serology and Virology Division, Department of Microbiology, SEALS, Level 4 Campus Centre Prince of Wales Hospital, Randwick, NSW, 2031, Australia, \textsuperscript{2}Sydney Children’s Hospital, High St Randwick, NSW, 2031, Australia and School of Women's and Child Health, University of New South Wales, Kensington, NSW, 2052, Australia, \textsuperscript{3}School of Medical Sciences, School of Biotechnology and Biomolecular Sciences, and Australian Centre for Perinatal Sciences, University of New South Wales, Kensington NSW 2052 Australia

Introduction: Pregnant women are at risk for infection with CMV, particularly through close contact with their children. This may result in congenital infection, with resultant hearing loss, neurodevelopmental deficits and most severely fetal death. We assessed risk for infection for infants attending childcare, and cCMV in infants referred for audiology after failed UNHS.

Methods: Sampled CMV excretion in 130 nasal samples from 20 childcare staff of 2 centres over 5 weeks, with PCR of nasal and skin swabs. CMV testing of urine +/- saliva in infants with CMV detected by PCR at ≤ 30 days of age in urine/saliva, were diagnosed cCMV then followed for counselling and treatment.

Results: Childcare 8/130 carers CMV DNA positive a CMV excretion rate of 35% in staff. Hearing clinics 1520 children failing UNHS referred for audiology. 30% (469) confirmed hearing loss & 308 offered CMV testing, 10 declined, 123 had audiology by ≤21 days, and 203 by ≤30 days, of whom 195 were tested for CMV. CCMV was diagnosed in 10 infants (9 urine, 6 saliva, urine + saliva in 7), including 1 positive NBSC).

Conclusion: We identified ~6% of congenital CMV in children failing UNHS and had permanent SNHL confirmed. It did not require significant additional assets to those already existing in the tertiary referral paediatric centre, and provided useful and timely information for clinical and audiological follow up. Increased awareness of childcare CMV infection among parents & healthcare providers is necessary to minimise CMV acquisition during pregnancy and subsequently congenital CMV infection.

Disclosure of Interest Statement: No conflicts to declare.
NATIONWIDE SURVEILLANCE OF PAEDIATRIC EMPYEMA IN NEW ZEALAND - 2014 TO 2016

Authors:
Rix-Trott KJ\textsuperscript{1}, Byrnes C\textsuperscript{1,2}, Twiss J\textsuperscript{1}, Matsas R\textsuperscript{3}, Hamill J\textsuperscript{1}, Evans S\textsuperscript{1}, Mahon C\textsuperscript{2}, Williamson D\textsuperscript{4}, Dickson N\textsuperscript{5}, Walls T\textsuperscript{6}, Voss L\textsuperscript{1}, Best E\textsuperscript{1,2}.

\textsuperscript{1} Starship Children’s Health, Auckland District Health Board, Auckland, New Zealand\textsuperscript{2} Department of Paediatrics, University of Auckland, \textsuperscript{3} KidzFirst Hospital, Counties Manukau District Health Board, Auckland, \textsuperscript{4} Institute of Environmental Science and Research, Wellington, \textsuperscript{5} Paediatric Department, University of Otago, Wellington, \textsuperscript{6} Paediatric Department, University of Otago, Christchurch.

Introduction: The aim was to document the burden of empyema in children aged <15 years in New Zealand including infectious aetiology, demographics and management.

Methods: Empyema was added as a notifiable disease in children <15 years of age on the New Zealand Paediatric Surveillance Unit (NZPSU) monthly report request from May 2014 to June 2016. A questionnaire recording demographics, presentation, infectious aetiology, medical and surgical management, complications, and short term outcomes was then requested from the lead paediatrician.

Results: 117 notifications were made with 99 fitting the case definition and complete data for 87 cases (88\%). The median age was 3.8 years (range 2 months to 14.9 years) with 61\% occurring in children under 5 years. 22\% had co-morbid conditions ranging from mild asthma to immune-compromising conditions. Ethnicities were 34\% Maori, 23\% Pacific, 22\% European, 13\% Asian, and 5\% Indian and 3\% other. \textit{S. pneumoniae} and \textit{S. aureus} (MRSA + MSSA) made up 38\% and 35\% of causative organisms respectively. 60\% of children had received 3-4 doses of PCV. 83\% of cases required some form of surgical intervention, 1/3 required ICU and the mean length of stay was 19 days (6-56 days).

Conclusion: The burden of empyema in New Zealand children is seen predominantly in younger children and those of Maori and Pacific ethnicity. Streptococcal and staphylococcal infection were identified in nearly equal numbers, and 18\% of \textit{S. aureus} cases were MRSA. Empyema cases reflect a significant morbidity burden due to requirement for surgical intervention, ICU care, and prolonged hospitalization.

Disclosure of Interest Statement: Nil.
THE EFFECT OF INTRAVENOUS ANTIBIOTICS ON THE NASAL MICROBIOME IN CHILDREN – NOVEL ASSOCIATION WITH STAPHYLOCOCCUS AUREUS ACQUISITION

Authors: Bryant PA1,2,3, Curtis N1,2,3, Gordon L4, Parker K1, Hopper SM1,5, Holt K6, Babl FE1,2,5, Ibrahim LF1,2

1Murdoch Children’s Research Institute, Melbourne, 2Department of Paediatrics, The University of Melbourne, 3Infectious Diseases Unit, Department of General Medicine, Royal Children’s Hospital Melbourne, 4The Australian Genome Research Facility, Melbourne, 5Emergency Department, Royal Children’s Hospital Melbourne, 6Department of Biochemistry and Molecular Biology, The University of Melbourne

Introduction: Antibiotic use is almost universal in Australasian children. The risks of this include acquisition of pathogenic and resistant bacteria, including nasal carriage of Staphylococcus aureus. We investigated the effect of antibiotics on the nasal microbiome in previously healthy children.

Methods: Children aged 6 months-18 years with cellulitis receiving short-course intravenous followed by oral antibiotics were included. Nasal swabs were collected at 3 timepoints: baseline, 1 week (maximal antibiotic pressure) and 3 months (post antibiotic washout) after starting intravenous antibiotics. After DNA extraction, microbiome abundance and diversity were assessed by amplicon sequencing analysis of the 16S rRNA V3-V4 region.

Results: 33 nasal swabs were collected from 11 children. There was no difference in overall bacterial abundance or diversity between baseline or the 1 week or 3 month timepoints. However, phylogenetic analysis showed a dramatic shift in the Gram-positive phyla with Firmicutes increasing from 27% abundance at baseline to 46% at 1 week (p=0.005) at the expense of Actinobacteria (33% to 16%, p=0.006), while Gram-negative phyla Proteobacteria and Bacteroidetes remained the same. Four patients acquired S. aureus on nasal culture after antibiotics, and there was a significant difference in diversity compared to baseline and to those who did not acquire S. aureus (p<0.05)(figure).

Conclusion: Short-course antibiotics are associated with changes in nasal microbiome composition, with the novel finding of reduced diversity associated with S. aureus acquisition. This has potential implications on selection of resistant bacteria. Whether changes can be predicted and therefore reversed will be part of a larger study.

Disclosure of Interest Statement: This study was funded in part through grants from The Royal Children’s Hospital Foundation, and the Infection and Immunity Theme at the Murdoch Children’s Research Institute. Dr. Ibrahim was funded by an Avant Scholarship. No pharmaceutical grants were received in the development of this study.

Figure:
Antibiotic timing:
*S. aureus* culture:
Pre Negative, n=11
Post Negative, n=11
Post Positive, n=11

Alpha Diversity Index

Decreasing diversity of bacterial populations

p < 0.05
INFLUENCE OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION IN NEONATAL INTENSIVE CARE

Authors: Villanueva P¹, Freyne B¹,², Carr J¹,², Hickey L³, Bryant PA¹,²

¹Department of General Medicine, The Royal Children’s Hospital Melbourne.
²Infectious Diseases Unit, The Royal Children’s Hospital Melbourne.
³Department of Neonatal Medicine, The Royal Children’s Hospital Melbourne.

Introduction: Antimicrobial stewardship (AMS) is vital in the critical care environment of the neonatal intensive care unit (NICU) but evidence for specific interventions is lacking. Our objectives were:
1) To describe patterns and appropriateness of antimicrobial prescribing in NICU;
2) To assess the influence of AMS ward rounds on inappropriate prescribing

Methods: A weekly AMS round involving senior NICU medical staff and a paediatric infectious diseases fellow was introduced and assessed over 6 months. Audit-feedback recommendations were made regarding appropriateness of decision to prescribe antimicrobials, drug choice and application (dose, interval, route, duration), and were reviewed the following day to assess acceptance of recommendations.

Results: During the study period, 249 infants were assessed for 627 review episodes. The proportion on antimicrobials at each AMS round was 19-59% (mean 37%). Of the 627 episodes, 233 (37%) reviews comprised patients receiving antimicrobials: 79 (34%) received targeted antimicrobial treatment, 111 (48%) empirical antimicrobial treatment and 43 (18%) prophylaxis. Of the 233 episodes on antimicrobials, 58 (25%) were deemed as having inappropriate prescriptions: 19% inappropriate decision to prescribe antimicrobials, 71% inappropriate antimicrobial choice, 10% inappropriate application. The commonest recommendations were to narrow (53%) or stop (19%) antimicrobials. The majority (73%) of recommendations were accepted.

Conclusion: A high proportion of infants in the NICU were on antimicrobials, and a quarter had recommendations to change/stop. Three-quarters of recommendations were actioned, showing that AMS rounds are effective in influencing prescribing. Education or more frequent rounds may increase this further.

Disclosure of Interest Statement: We have no conflict of interest to declare.
**β-LACTAM ANTIBIOTICS: TOO MUCH OF A GOOD THING**

**Authors:**
Imani S 1,4, Marriott D1,2, Buscher H1,2, Gentili S3, Sandaradura I1,2

1 St Vincent’s Hospital, Sydney
2 University of New South Wales
3 University of South Australia
4 University of Notre Dame, Australia

**Introduction:** The potential for high-dose β-lactam antibiotics (BLA) to precipitate toxicity is becoming increasingly apparent in clinical practice. Adverse events, such as neurotoxicity, which were previously considered idiosyncratic, are now recognised as concentration-dependent. There is limited data, however, on the utility of BLA concentration in predicting toxicity.

**Methods:** Retrospective review of consecutive patients (n=378) treated with piperacillin (PIP, n=223), meropenem (MER, n=94) or flucloxacillin (FLU, n=61) who underwent therapeutic drug monitoring (TDM) at St Vincent’s Hospital Sydney between Jan 2013- Dec 2015. Adverse events investigated included neurotoxicity, nephrotoxicity, hepatotoxicity and opportunistic *Clostridium difficile* infection (CDI). Toxicity was measured using observational grading criteria, clinical judgment and relevant serum biomarkers. These findings were correlated with trough TDM measurements at the time of toxicity determination.

**Results:** Adverse event rates per antibiotic are summarised in Table 1.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>PIP</th>
<th>MER</th>
<th>FLU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>11.4%</td>
<td>15.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>8.5%</td>
<td>6.9%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>6.7%</td>
<td>8.3%</td>
<td>8.7%</td>
</tr>
<tr>
<td>CDI</td>
<td>7.9%</td>
<td>2.6%</td>
<td>0%</td>
</tr>
</tbody>
</table>

We found a significant increase in mean BLA trough concentration ($C_{\text{min}}$) in all patients diagnosed with neurotoxicity ($p<0.05$) and those with nephrotoxicity treated with PIP ($p<0.01$) or MER ($p<0.01$). Incidence of hepatotoxicity and CDI was not related to antibiotic concentration levels. Threshold $C_{\text{min}}$ for which there was >50% risk of developing neurotoxicity ($C_{\text{PIP}}$>361.4mg/L, $C_{\text{MER}}$>64.2mg/L, $C_{\text{FLU}}$>125.1mg/L) and nephrotoxicity ($C_{\text{PIP}}$>452.65mg/L, $C_{\text{MER}}$>44.45mg/L) were identified.

**Conclusion:** Incidence of BLA toxicity is likely underestimated clinically. By utilising TDM early in the course of BLA treatment clinicians should aim to achieve the highest serum concentrations that can be safely attained, whilst ensuring that these toxicity thresholds are not surpassed. Additionally, TDM may be useful to diagnose BLA toxicity, avoiding other unnecessary investigations.

**Disclosure of Interest Statement:** The study was funded by a grant from the University of Notre Dame Australia.
ANTIMICROBIAL STEWARDSHIP ACTIVITY AND RESULTS DURING ANTIMICROBIAL SHORTAGES

Authors:
Casula L, Figtree M, Hoyle P, Russell P

Northern Sydney Local Health District

Introduction: National antimicrobial shortages have become increasingly common over the past few years. Ampicillin and azithromycin shortages occurred in 2015. Concurrent shortages of a broad range of critical agents (including: vancomycin, daptomycin, aztreonam, tigecycline, metronidazole and aciclovir) occurred in late 2016 - threatening patient safety and stretching antimicrobial stewardship (AMS) team capability.

Methods: We describe interventions, antimicrobial usage, and adverse events during this shortage period in a principal tertiary referral centre. Additional intensive, targeted antimicrobial stewardship processes were instituted ensuring the remaining stocks were used appropriately.

Results: Targeted AMS towards these agents was achieved through education memos, one-on-one phone calls, electronic AMS approval system and physical removal of affected antimicrobials from general ward imprest settings. During the shortage period, a 70% decrease was seen in IV azithromycin usage / 1000 OBDs and a 30% reduction in average monthly usage of vancomycin was noted. No adverse events have been attributable to the shortage on review of bacteraemia outcomes and IIMS notifications.

Conclusion: The wave of recent shortages led to enhanced antimicrobial stewardship team physical control of specific antimicrobials, however required significant additional vigilance and human resources. A marked reduction of use was noted in the antimicrobials affected without an increase in alternate antimicrobials. The externally caused shortage appeared to create a strong motivation of responsible prescribing in our hospital. Mitigating measures coordinated at the state and/or national level are required to ensure such shortages can be avoided in the future and that patient safety is not compromised.

Disclosure of Interest Statement: We declare no conflict of interest and there was no funding received for this study.
EFFECTS OF AGEING ON PARASITE BIOMASS, INFLAMMATION, ENDOThelial ACTIVATION AND MICROVASCULAR DYSFUNCTION IN PLASMODIUM KNOWLESI AND P. FALCIPARUM MALARIA

Authors:
Barber BE1,2, Grigg MJ1,2, William T2,3, Piera KA1, Boyle M1,4, Yeo TW1,5,6, Anstey NM1,7

1. Menzies School of Health Research and Charles Darwin University, Darwin, Northern Territory, Australia
2. Infectious Diseases Society Sabah-Menzies School of Health Research Clinical Research Unit, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia
3. Jesselton Medical Centre, Kota Kinabalu, Sabah, Malaysia
4. Centre for Biomedical Research, Burnet Institute, Melbourne, Australia
5. Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
6. Institute of Infectious Disease and Epidemiology, Tan Tock Seng Hospital, Singapore
7. Department of Infectious Diseases, Royal Darwin Hospital, Darwin, Northern Territory, Australia

Introduction: In populations with low immunity to malaria, the risk of severe malaria increases with age. This is particularly apparent in Plasmodium knowlesi malaria. However, the pathophysiological mechanisms underlying knowlesi malaria, and of the age-related increase in risk in severe malaria in general, are poorly understood. We evaluated the effects of ageing on factors contributing to pathogenesis of severe knowlesi and falciparum malaria.

Methods: Malaysian patients aged ≥12 years with severe (n=47) and non-severe (n=99) knowlesi malaria, severe (n=21) and non-severe (n=109) falciparum malaria, and healthy controls (n=50) were enrolled. We measured parasite biomass, and markers of systemic inflammation (interleukin-6; IL-6), endothelial activation (angiopoietin-2), and microvascular function, and evaluated effects of age.

Results: Patients with severe knowlesi malaria were older than those with non-severe knowlesi malaria (median 55 vs. 42 years, p<0.0001). P. knowlesi parasitemia correlated with age (r=0.36, p<0.0001). In patients with knowlesi malaria, IL-6, angiopoietin-2 and microvascular dysfunction were increased in severe compared to non-severe disease, and all correlated with age, independent of parasitemia. In falciparum malaria, angiopoietin-2 increased with age, after controlling for parasite biomass (histidine-rich protein-2). Independent risk factors for severe malaria included parasitemia and angiopoietin-2 in knowlesi malaria, and HRP2, angiopoietin-2 and microvascular dysfunction in falciparum malaria.

Conclusion: Parasite biomass, endothelial activation and microvascular dysfunction are associated with severe disease in knowlesi malaria and likely contribute to pathogenesis. The independent association of each of these processes with ageing may account for the greater severity of malaria observed in older adults in regions of low endemicity.

Disclosure of Interest Statement: All authors state no conflict of interest.
PREVALENCE OF SCABIES AND IMPETIGO IN SCHOOL CHILDREN IN TIMOR-LESTE

Authors: Korte L1, Draper A3,4, Davis K1, Appelbe A5, Dingle B6, Bowen A7, Francis J1,8

1 Royal Darwin Hospital, 2 Hospital Nacional Guido Valadares, 3 NT Centre for Disease Control, 4 National Centre for epidemiology and population health, Australian National University, 5 Kensington Hill Medical Centre, 6 St John of God, 7 Princess Margaret Hospital for Children, 8 Telethon Kids Institute, 9 Menzies School of Health Research

Introduction: Scabies and impetigo are common and important skin conditions which are often neglected in developing countries. The prevalence of these conditions in Timor-Leste is unknown. Sequelae including cellulitis, bacteraemia, nephritis, acute rheumatic fever and rheumatic heart disease contribute significantly to the burden of disease.

Methods: We conducted an epidemiological survey in October 2016. School students were recruited from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste. We used a standard questionnaire to record demographics, anthropometry and skin examination results. Prevalence of scabies and impetigo were calculated and binary risk factors described using relative risks and 95% confidence intervals. Continuous variables for were analysed for associations using the Mann-Whitney Rank Sum test. Results were considered significant if p<0.05.

Results: 1407 students were enrolled; with median student age of 12 years (range 4-24). The prevalence of scabies was 22% and active impetigo 10%; 68% of students had evidence of either active or healed impetigo. Students in Ermera were more likely than those in Dili to have scabies (RR 6.3; 95%CI 4.3 - 9.2, p<0.01) and scabies and active impetigo co-infection (RR 8.9; 95%CI 3.3 - 24, p<0.01). There was no difference in the prevalence of active impetigo between urban and rural sites.

Conclusion: Scabies and impetigo are prevalent in Timor-Leste, with particularly high prevalence of scabies in the rural district of Ermera. Improvements in prevention and treatment are needed, and consideration should be given for implementing strategies at a community level, focusing on rural areas.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer.
TREATMENT OF LATENT TB INFECTION IN THE DARWIN REGION OF AUSTRALIA

Boyd R 1, Johnston V 1-2, Farmer B 1, Krause V 1

1 Centre for Disease Control, Northern Territory
2 Honorary Fellow, Menzies School of Health Research, Northern Territory

Introduction: Preventing active tuberculosis (TB) disease through treatment of latent tuberculosis infection (LTBI) is an essential component of the World Health Organization’s End TB Strategy. To evaluate and inform practice we identified LTBI treatment uptake and compliance amongst Northern Territory populations.

Methods: We undertook a cohort study, including people diagnosed with LTBI June 2013-July 2014, Darwin; Population 140,000 including 25% Indigenous and 25% overseas-born. Demographic, treatment acceptance and compliance data were collected from the Darwin TB service.

Results: Of 573 people diagnosed with LTBI, 374 (65%) were offered; 265/374 (71%) accepted and 147/241 (55%) completed treatment. 74% were overseas-born, 14% non-Indigenous and 12% Indigenous. Indigenous people were more likely to accept treatment than overseas-born (OR 4.46; 95%CI 1.55-12.83) and non-Indigenous (OR 7.69; 95%CI 2.33-25.39). Overseas-born were least likely to complete treatment (Indigenous OR 1.34; 95%CI 0.66-2.72; non-Indigenous OR 1.38 95%CI 0.56-3.41).

All children under 6 years accepted treatment; 12/28(43%) completed treatment.

The cohort primarily comprised health care workers (HCW) 106(19%); contacts of active TB 97(17%) and asylum-seekers 94(16%). Of 106 HCW’s, 77(73%) were overseas-born. Supported by school nurses, students were most likely to complete treatment, with odds of completing 3.86 times higher than HCW’s (95%CI 1.02–14.58).

Conclusions: While comparable to previous studies, 45% did not complete treatment, representing missed opportunities to prevent disease. Encouragingly, we found high uptake of treatment amongst Indigenous people. Interventions should target optimising treatment completion in high risk populations of overseas-born and children under 6. Successful treatment in students supports ongoing engagement of school-based nurses.

Disclosure of Interest Statement: The Centre for Disease Control is funded by the Northern Territory Government. No additional funding was received for this study.
SHORTER MDR-TB TREATMENT COMPARED WITH CONVENTIONAL TREATMENT IN UZBEKISTAN: SPUTUM CULTURE CONVERSION AFTER 2 MONTHS

Authors:
A Ronnachit¹, A Khamraev², P du Cros³, J Greig³, T Pylypenko¹, Z Tigay², N Parpieva⁴, J Achar³

¹Médecins Sans Frontières, Nukus, Uzbekistan, ²Ministry of Health, Nukus, Uzbekistan, ³Médecins Sans Frontières UK, Manson Unit, London, United Kingdom, ⁴National Institute of TB and Pulmonology, Tashkent, Uzbekistan

Introduction: The shorter multi-drug resistant tuberculosis (MDR-TB) regimen has been recommended by the World Health Organisation (WHO) for eligible patients. However, little comparative data about its efficacy has been published. We compared 2-month culture-conversion status from a single-arm, prospective observational study of the shorter MDR-TB regimen (SR) with patients treated with WHO-approved conventional care (CC) under programmatic conditions in Uzbekistan, a country listed by the WHO as a high-burden MDR-TB country with high rates of second-line drug resistance.

Methods: SR data was compared with CC data from culture confirmed MDR-TB patients treated within the same TB program. Exclusion criteria included documented exposure to second-line drugs and second-line drug resistance. Multivariate-logistic regression was used to estimate associations between regimen and culture-conversion status after 2-months. Ethics approval was obtained.

Results: 241 CC and 88 SR patients were included. Patients treated with SR had an aOR of 1.91 (95%CI 1.08-3.38, p=0.026) of culture-conversion by 2-months compared with CC. Higher baseline sputum smear-positivity was negatively associated with culture-conversion, aOR 0.37 (95%CI 0.21-0.65, p<0.001) for scanty/1+, and 0.11 (95%CI 0.05-0.24, p <0.001) for 2+/3+. Poor adherence was negatively associated: aOR 0.42 (95%CI 0.21-0.83, p=0.013) with culture-conversion. A negative association with age was found, for every increasing year aOR 0.98 (95%CI 0.96-0.99, p=0.006).

Conclusion: There was an almost two-fold greater odds of culture-conversion by 2-months following treatment with the SR. Earlier culture-conversion has important infection-control and treatment implications, and use of SR may reduce transmission.

Disclosure of Interest Statement: The authors declare that there is no conflict of interest.
INITIAL PROGRAMMATIC EXPERIENCE OF BEDAQUILINE CONTAINING TREATMENT REGIMENS FOR DRUG-RESISTANT TUBERCULOSIS IN SOUTH FLY DISTRICT, WESTERN PROVINCE, PAPUA NEW GUINEA

Authors: Taune M1,2, Hiasihri S3, Huang K4, Ronnachit A4, Wallis P, Morris L3, Tugo O1, Dakulala P2, Bieq S2, John L2, Aia P2, Lavu E5, Coulter C6, Madjus S7, Innes A8, Islam T9, Chan G4, O’Brien D4, Graham S4, Majumdar S4

1Daru General Hospital, Western Province, PNG, 2National Department of Health PNG, 3Provincial Health Office, Western Province, PNG, 4Burnet Institute, Australia, 5Central Public Health Laboratory, PNG, 6Queensland Mycobacterial Reference Laboratory, Australia 7World Vision PNG, 8FHI 360 Asia Pacific Region, 9World Health Organisation, PNG.

Introduction: Treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) globally remain poor. The World Health Organization (WHO) for programmatic use has recently recommended Bedaquiline (BDQ), a novel drug for the treatment of MDR-TB. Daru Island, South Fly District (SFD), Western Province is the epicenter an outbreak of MDR-TB, including community transmission of extensively drug-resistant (XDR-TB) strains. Bedaquiline was introduced in the program in October 2015 and we describe the first programmatic use in PNG.

Methods: We conducted a cohort analysis using routine programmatic data for patients on BDQ-containing regimens enrolled from July 2015 to December 2016. Interim cohort outcomes (culture negative rate by month 6 of treatment) were assessed in patients with culture confirmed TB from 1 July 2015 to 30 June 2016. A core package of Active TB drug-safety monitoring and management (aDSM) was implemented.

Results: 21 patients received BDQ containing regimens. The median age was 36 years. 6 of 21 patients had microbiologically confirmed XDR TB. All patients are retained in care with no evidence of clinical or microbiological failure. In the interim cohort analysis (n=8), 7 (87.5%) patients on BDQ had a negative culture by month 6 of treatment, compared with 37 (44%) on non-BDQ containing regimens (n=85). A single serious adverse drug event was observed, unlikely related to Bdq.

Conclusion: Early experience with BDQ containing regimens in PNG demonstrates excellent interim treatment outcomes and a good safety profile and supports further scale up. New TB drugs with greater efficacy and better tolerability have the potential for great impact in the setting of a DR-TB outbreak and in routine use in resource-limited settings.

Disclosure of Interest Statement: No conflicts of interest to declare.
PREDICTORS FOR PNEUMOCOCCAL CONJUGATE VACCINATION (PCV) IN A LOW PCV COVERAGE SETTING IN THE EASTERN HIGHLANDS OF PAPUA NEW GUINEA

Authors:
Chan J¹, Russell F¹,², Pomat W³, Sapura J³, Masiria G³, Kave J³, Ford R³, Kirarock W³, Kumani T³, Lehmann D⁴, Blyth CC⁴,⁵ on behalf of the PNG Aetiology Study Team

¹ Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia
² Centre for International Child Health- Dept. of Paediatrics, University of Melbourne, Melbourne, Australia
³ Infection and Immunity Unit, Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea
⁴ Telethon Kids Institute, University of Western Australia, Perth, Australia
⁵ School of Medicine, University of Western Australia, Perth, Australia.

Introduction: Pneumonia is the most important cause of childhood mortality and morbidity in Papua New Guinea (PNG). The 13-valent pneumococcal conjugate vaccine (PCV) was introduced to PNG in 2014 and in this study we describe PCV coverage over time and predictors for vaccination.

Methods: We completed a post-hoc analysis of vaccination coverage among children 2-59 months old, enrolled in a case-control study of pneumonia and meningitis. Cases were recruited at the Eastern Highlands Provincial Hospital and urban health clinics. Controls were recruited from the same villages as cases within an hour’s drive. Children were considered vaccinated if they had received two doses of PCV <12 months of age or one dose over 12 months of age. We calculated three-monthly rolling PCV coverage rates and determined predictors for vaccination using univariate and multivariate regression.

Results: Among the 1391 cases and controls enrolled from 2014-2015, PCV vaccination coverage started to increase from January 2015, reaching 30% coverage in December 2015 (figure 1). After adjustment, receipt of diphtheria-tetanus-pertussis vaccines was associated with an increased likelihood of PCV vaccination (aOR 9.3; 95% CI 5.8-14.8; p=0.000). In cases, distance from EHP hospital was also predictive of being vaccinated (aOR 3.0; 95% CI 1.2-7.4; p=0.02).

Figure 1: Three-month rolling vaccination coverage rate among cases and controls, Eastern Highlands Province, Papua New Guinea
**Conclusion:** PCV coverage remains low, however there is a trend towards increasing PCV coverage from 2015 onwards. Strategies to improve PCV coverage are required and should include programs targeting children from rural villages.

**Disclosure of Interest Statement:** This was an investigator-led study, funded by Pfizer Global and the PNG Institute of Medical Research.
CONJUGATE PNEUMOCOCCAL VACCINATION AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION REDUCES INVASIVE PNEUMOCOCCAL DISEASE

Authors: Roberts MB¹, Lewis I², Bak N¹

¹Infectious Diseases Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA
²Haematology Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA

Introduction: Immunosuppressed patients, especially haematopoietic stem cell transplant (HSCT) recipients, are particularly vulnerable to invasive pneumococcal disease (IPD) with reported rates between 3.81 and 22.5/1000 transplants. However, uptake of pneumococcal vaccination tends to be lower in the immunosuppressed, partly due to concerns of vaccine effectiveness. The Royal Adelaide Hospital (RAH) introduced protocolised conjugate pneumococcal vaccination (13vPCV) to all HSCT patients in 2010.

Methods: We conducted a retrospective study of all RAH HSCT patients from 2004 to 2015 to assess the impact of introduced 13vPCV on IPD incidence. Microbiological results from sterile sites for all HSCT patients in this period were reviewed for IPD. Individuals with IPD had clinical records evaluated for further data.

Results: Fourteen episodes of IPD occurred in twelve patients between 2004 and 2015. Twelve episodes occurred in the pre-2010 group who did not receive 13vPCV, 40% of serotyped isolates would have been covered by 13vPCV. Two episodes occurred in the post-2010 group who did receive 13vPCV, neither isolate serotype was covered by 13vPCV. In the equivalent period there were 936 HSCT, of which there was >90% enrolment and >90% vaccination protocol completion rates for surviving patients. There was a significant reduction in overall IPD rate from 28.4/1000 transplants pre-2010, to 3.6/1000 transplants in the post-2010 group. Similar reductions occurred in the autologous group from 25.5 to 2.8/1000 transplants and allogeneic group from 44.2 to 5.3/1000 transplants.

Conclusion: This is the first study to demonstrate the clinical effectiveness of 13vPCV in this cohort, highlighting its importance in preventing infectious complications of HSCT.

Disclosure of Interest Statement: No conflicts to disclose.
ROUTINE ERTAPENEM PROPHYLAXIS FOR TRANSRECTAL ULTRASOUND-GUIDED PROSTATE BIOPSY DOES NOT SELECT FOR CARBAPENEM-RESISTANT ORGANISMS: A PROSPECTIVE COHORT STUDY

Authors: Bloomfield M\textsuperscript{1,2}, Page M\textsuperscript{3}, McLachlan A\textsuperscript{3}, Studd R\textsuperscript{3}, Blackmore T\textsuperscript{1,2}

\textsuperscript{1} Department of Infection Services, Wellington Regional Hospital, Wellington, New Zealand, \textsuperscript{2} Department of Microbiology, Wellington Southern Community Laboratories, Wellington, New Zealand, \textsuperscript{3} Department of Urology, Wellington Regional Hospital, Wellington, New Zealand

Introduction: Post-transrectal ultrasound-guided prostate biopsy sepsis (PBS) is an increasing problem in this era of rising antibiotic resistance. Ertapenem prophylaxis has proven very effective at our institution for reducing this, however has raised local and regional antimicrobial stewardship concerns. This study investigated the possible selective effect of single dose ertapenem prophylaxis on faecal colonisation with carbapenem-resistant Enterobacteriaceae.

Methods: Patients had a rectal swab taken prior to receiving pre-biopsy ertapenem prophylaxis. A second swab was taken at follow-up 4-6 weeks later. Swabs were screened for carbapenem-resistant Enterobacteriaceae (CRE) using an enhanced Centers for Disease Control method. Pre-biopsy swabs were also screened for extended-spectrum and 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. Three cases (0.9%, 95%-CI 0.2-2.8%) of probable PBS were identified during the study period. None were bacteraemic or required ICU admission.

Conclusion: Single dose ertapenem prophylaxis 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. It is highly effective prophylaxis for transrectal ultrasound-guided prostate biopsy. Ertapenem may, in the right setting, represent a useful prophylactic option for prevention of post-transrectal ultrasound-guided prostate biopsy sepsis.

Disclosure of Interest Statement: The study was funded by internal departmental funds allocated to research. No pharmaceutical or other industry grants were received in the development of this study.
IMPACT OF A DEDICATED POST-TRANSPLANT VACCINATION SERVICE ON COMPLIANCE RATES AT A LARGE AUSTRALIAN CANCER CENTRE

Authors: Teh B¹,², Joyce T¹,³, Slavin M¹,²,⁴, Thursky K¹,²,⁴, Worth L¹,²,⁴

¹Department of Infectious Diseases, Peter MacCallum Cancer Centre, ²NHMRC Centre of Research Excellence, Infections in Cancer, ³Department of Haematology, Peter MacCallum Cancer Centre, ⁴Department of Medicine, University of Melbourne.

Introduction: Autologous haematopoietic stem cell transplantation (ASCT) results in impaired immunity to vaccine-preventable infections. Frequently, compliance with vaccination consensus guidelines is poor. We evaluated the impact of a dedicated vaccination service on post-transplant vaccination compliance with prevailing national immunisation guidelines.

Methods: A vaccination service for ASCT recipients was established at the Peter MacCallum Cancer Centre in March 2014, consisting of regular scheduled reviews, face-to-face education with nursing and medical staff and a vaccination schedule aligned with national guidelines. ASCT patients were retrospectively classified as ‘pre-clinic’ (Sept 2012-Sept 2013) or ‘post-clinic’ cohorts (Oct 2013-2014), according when the service became available. Uniform data were collated from clinical and pharmacy databases, including: type and timing of vaccine/s, number of cycles completed, and reasons for non-compliance with guidelines. Vaccination uptake and compliance in each cohort were compared.

Results: Post-clinic and pre-clinic cohorts consisted of 87 and 81 patients, respectively, with similar patient characteristics. The proportion commencing vaccination was not significantly different between groups (83.9% vs. 71.4%, p=0.12). Of 74 patients eligible for vaccination in post-clinic cohort only 1 patient lost to follow up (1.4%) whilst the loss to follow up rate was 6.3% in pre-clinic cohort. Of patients vaccinated, the proportion administered according to national guidelines was significantly higher in the clinic cohort (70.8% vs. 19.0%, p<0.01). More patients in this cohort completed all recommended vaccines (47.2% vs 32.8%, p=0.11).

Conclusion: Implementing a dedicated post-ASCT vaccination service increased compliance with national immunisation guidelines (vaccination uptake, timing of administration) with near complete vaccination coverage.

Disclosure of Interest Statement: No conflicts of interest for all authors.
HIGH BURDEN OF FIRST PRESENTATION AND RECURRENCE OF SEVERE LOWER LIMB BACTERIAL CELLULITIS: A LONGITUDINAL STUDY

Authors:
Rajakaruna G¹, Cannon J², Dyer J¹, Carapetis J²,³,⁴, Manning L¹,⁴

¹Fiona Stanley Hospital, ²Telethon Kids Institute WA, ³Perth Children's Hospital, ⁴University of Western Australia

Introduction: Lower limb bacterial cellulitis (LLBC) is a common and serious infection of skin and subcutaneous tissue. High rates of incidence, recurrence, morbidity and economic costs have been reported worldwide. Given the lack of good quality, contemporary data, we aimed to describe the epidemiology of first presentation, recurrence and excess mortality in Australian patients with LLBC.

Methods: The state-wide data-linkage system was used to extract records of adults presenting to Western Australian (WA) hospitals with first episode LLBC from January 2002 to December 2013. Incidence and recurrence rates were calculated and matched controls were used to describe excess mortality.

Results: Over 12 years, 43,410 LLBC episodes were reported in 36,276 patients. There was an annual increase in incidence (4.7% p.a.), with an overall incidence of 204.8 (95% CI 198.6-211.1) per 100,000 population in 2013. There were higher incidence rate ratios (IRR) in older patients aged 65-84 years (IRR 2.59 [2.50-2.69], P<0.001) and >85 years (IRR 7.04 [6.73-7.37], P<0.001) compared with 16-24 years. Males and Indigenous Australians also had higher IRR. There was significant seasonal variability with increased rates during summer. LLBC recurrence occurred in 4,598 (12.7%) patients, with increased risk in older patients, females and Indigenous Australians. When compared with matched controls, patients with LLBC had a higher mortality (P<0.0001).

Conclusion: There is a large and increasing burden of LLBC, especially amongst older Australians. Given the frequent recurrence, long term morbidity and association with increased mortality, efforts to reduce primary episodes and minimise the risk of recurrence should be a priority.

Disclosure of Interest Statement: This study was funded from internal funds held by the Department of Infectious Diseases at Fiona Stanley Hospital. No pharmaceutical grants were received in the development of this study.
A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL OF IBUPROFEN COMPARED WITH PLACEBO FOR UNCOMPLICATED CELLULITIS OF THE UPPER OR LOWER LIMB

Joshua S Davis¹,², Carol Mackrow³, Paula Binks¹, Wendy Fletcher³, Pascale Dettwiller⁴, Catherine Marshall³, Jane Day⁵, William Pratt⁵, Steven YC Tong¹,⁶

1. Global and Tropical Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, NT, Australia
2. Department of Infectious Diseases, John Hunter Hospital, Newcastle, NSW, Australia and the University of Newcastle
3. Hospital in the Home Program, Royal Darwin Hospital, Darwin, NT, Australia
4. Katherine Rural Clinical School, Flinders University, Katherine, NT
5. Hospital in the Home Program, Shoalhaven Hospital, Nowra, NSW, Australia
6. Victorian Infectious Diseases Service, the Royal Melbourne Hospital, and the University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia

Introduction: Cellulitis is a common skin and soft tissue infection resulting in substantial inflammation that may take weeks to resolve despite appropriate antibiotics. It is unclear whether the adjunctive use of non-steroidal anti-inflammatory drugs hastens the resolution of inflammation in patients with cellulitis.

Methods: We conducted a double-blind randomised controlled trial comparing ibuprofen 400mg three times daily orally for five days with identical placebo in adults with uncomplicated cellulitis of the upper or lower limb, treated with intravenous cefazolin via an outpatient parenteral antibiotic treatment service at one of two Australian hospitals. Participants were assessed twice daily by a study nurse. The primary outcome measure was the proportion of patients with regression of inflammation 48 hours following the first effective dose of parenteral antibiotics. This trial was registered (ANZCTR 12611000515998).

Results: Fifty-one patients were enrolled; 48 had sufficient data available to be included in the modified intention to treat analysis. Inflammation had begun to regress at 48 hours in 20 participants (80%) in the ibuprofen group compared with 15 (65%) in the placebo group (Absolute risk difference + 15% [95% CI -10% to +40%]), p>0.05). There was no significant difference in any of the secondary outcomes. Ibuprofen treatment appeared safe, with no patients developing renal impairment or necrotising fasciitis.

Conclusions: This trial demonstrated no significant benefit of adjunctive ibuprofen in adults with uncomplicated cellulitis. The trial was powered to detect a large effect, and hence it is unclear if the 15% absolute increase in the primary endpoint in the ibuprofen group was attributable to chance or not.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
ERTAPENEM FOR OSTEOARTICULAR INFECTIONS IN OBESE PATIENTS: A PHARMACOKINETIC STUDY OF PLASMA AND BONE CONCENTRATIONS

Authors: Chambers J T¹, Page-Sharp M², Salman S³, Dyer J¹, Davis T³, Batty K T², Manning L³,⁴

¹ Department of Infectious Diseases, Fiona Stanley Hospital, Murdoch, Western Australia
² School of Pharmacy, Curtin University, Bentley, Western Australia
³ School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia
⁴ Harry Perkins Research Institute, Fiona Stanley Hospital, Murdoch, Western Australia

Introduction: Ertapenem is used off-label to treat osteoarticular infections, but there are few pharmacokinetic (PK) data to guide optimal dosing strategies or the probability of PK-pharmacodynamic target attainment (PTA) in this patient group who may be obese and/or frail with multiple co-morbidities.

Methods: Participants undergoing elective joint arthroplasty or lower limb and/or partial foot amputation received a dose of intravenous ertapenem prior to surgery, in addition to routine perioperative antibiotic prophylaxis. Plasma samples were collected at 8 time-points over 24 h and at least one bone sample per patient was collected at varying time-points post-infusion. Ertapenem concentrations in plasma and bone were measured using liquid-chromatography/mass-spectroscopy and analysed using non-linear mixed effects PK modelling.

Results: Plasma and bone concentrations were obtained from 10 participants. The final population PK model showed that a fat free body mass was the most appropriate body size adjustment. The model also demonstrated a strong effect of frailty on clearance with a doubling of plasma half-life in patients with moderate/severe frailty. Ertapenem equilibrated rapidly into bone, but concentrations were 40-fold higher in plasma and highly variable between individuals. Simulations demonstrated that the PTA for free plasma concentrations was ≤50% when the minimum inhibitory concentration (MIC) was ≥0.5mg/L. In bone, the PTA was ≤55% when the MIC was ≥0.25mg/L.

Conclusion: Local bone and free plasma concentrations appear adequate for osteoarticular infections where Enterobacteriaceae are the main causative pathogens, but for Staphylococcus spp., Bacteroides fragilis and Acinetobacter spp., standard dosing is unlikely to result in adequate PTA. Frailty may alter ertapenem PK.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study.
Introduction: Studies have demonstrated high rates of bacterial colonisation of hand-held mobile devices in hospital settings, but have not established a molecular epidemiological link between organisms colonising mobile devices and those causing disease in patients.

Methods: Over a 12-week period, all routine clinical isolates defined as multi-drug resistant (MDR) (MRSA, VRE and ESBL producing Enterobacteriaceae) were prospectively collected and stored. During the same time period, the mobile devices of all medical staff were swabbed. Swabs were cultured for resistant organisms, with identification by matrix – assisted laser desorption ionisation. Illumina whole genome sequencing was used to assess the genetic relatedness of MDR organisms found on phones and in clinical isolates.

Results: 90 MDR clinical isolates were collected from patients. A total of 45 mobile devices used by medical staff were swabbed. Of these, two phones cultured MRSA and one phone cultured A. baumannii. WGS was performed on the 17 MRSA and Acinetobacter isolates from phones and patient isolates. The two MRSA isolates from the phones were genetically similar, but were genetically different to all the clinical isolates. These two phones were spatio-temporally linked and came from the same 14-bed area of the ICU. All four MDR Acinetobacter isolates were genetically different.

Conclusion: To the authors’ knowledge, this is the first study to assess the molecular epidemiological link between MDR organisms found on mobile devices and those from patients. Despite MDR organisms being able to colonise physician mobile devices, these organisms were genetically different to those seen in patient isolates during the same time period.

Figure 1. MRSA dendrogram
Disclosure of Interest Statement:
There are no disclosures of interest to declare from any contributor to this research project.
POSTEXPOSURE IMMUNOPROPHYLAXIS USING THE HUMAN MONOCLONAL ANTIBODY m102.4 FOLLOWING HUMAN EXPOSURE TO EQUINE HENDRA VIRUS INFECTION

Authors:
Playford EG1,2, Broder CC3, Bossart KN4,5, Zhu Z6,7, Dimitrov AS8, Yan L3, Feng Y3, Barr J9, Hendry S1, Cramri G9, Broom JK2,10, Hickey AC4,5, Langley A11, Neucom D11, Dimitrov DS6, Wang L9,12

1Infection Management Services, Princess Alexandra Hospital, Brisbane, Australia, 2School of Medicine, The University of Queensland, Brisbane, Australia, 3Department of Microbiology and Immunology, Uniformed Services University, Bethesda, MD 20814, 4National Emerging Infectious Diseases Laboratories Institute and 5Department of Microbiology, Boston University School of Medicine, Boston, MA 02118, 6Protein Interactions Group, CCRNP, CCR, NCI-Frederick, National Institutes of Health, Frederick, MD, 7BRP, SAIC-Frederick, Inc., Frederick, MD 21702, 8Profectus BioSciences Inc., Baltimore, MD 21224, 9CSIRO Livestock Industries, Australian Animal Health Laboratory, Geelong, Victoria; 3220, Australia 10Department of Infectious Diseases, Nambour Hospital, Nambour, Australia, 11Sunshine Coast Public Health Unit, Maroochydore, Australia, 12Emerging Infectious Diseases Program, Duke-NUS Graduate Medical School, Singapore 169857, Republic of Singapore

Introduction: Hendra virus is associated with a significant mortality rate in both equine and human hosts. Human exposure to infected horse respiratory secretions or blood products carries a high risk of infection. There is no established medical therapy to treat or prevent this disease in humans. The human monoclonal antibody m102·4 has been shown to be an effective postexposure prophylactic agent in animal models, for both Hendra and Nipah virus.

Methods: Retrospective data was collected from ten patients with high-level exposure to Hendra virus who received m102.4. The data collected included patient demographics, drug pharmacokinetic data, adverse reactions and serology/biochemical data from a time period between 2014 to 2016.

Results: We describe ten cases where humans with high-level exposure to Hendra virus have received m102·4. All of these patients remained disease free without clinical or serological evidence of Hendra virus infection. There were minimal associated adverse reactions.

Conclusion: The human monoclonal antibody m102·4 may play a role in preventing Hendra virus infection in humans. This is concordant with the data demonstrated in animal models and highlights the potential role for preventing and treating both Hendra and Nipah virus infection in humans.

Disclosure of Interest Statement: No conflicts of interest to declare.
AN INTEGRATED FIRST-IN-HUMAN STUDY OF THE NOVEL LONG-ACTING ANTIMALARIAL DSM265 DEMONSTRATES A FAVOURABLE SAFETY AND TOLERABILITY PROFILE, AND PREDICTS A CLINICALLY EFFICACIOUS DOSE FOR TREATMENT OF FALCIPARUM MALARIA

Authors:
McCarthy JS1,4, Lotharius J2, Rückle T2, Chalon S2, Phillips MA3, Elliott S4, Sekuloski S1, Griffin P1,4, Ng CL5, Fidock DA5, Marquart L1, Williams NS3, Gobeau N2, Bebrevska L2, Rosario M6, Marsh K7, Mührle JJ2

1 QIMR Berghofer MRI; 2 Medicines for Malaria Venture; 3 University of Texas Southwestern Medical Center, Dallas, TX, USA; 4 Q-Pharm Pty Ltd, Herston, Australia; 5 Columbia University, NY, NY, USA; 6 Takeda Pharmaceuticals; 7 AbbVie, Chicago, IL, USA.

Introduction: DSM265 is a novel antimalarial that selectively inhibits Plasmodium dihydroorotate dehydrogenase (DHODH), an enzyme essential for pyrimidine biosynthesis. In this first-in-human study, we investigated its safety, tolerability and pharmacokinetics, and tested its in vivo activity against P. falciparum.

Methods: Part 1 was a single ascending dose (25–1200 mg), double-blind, randomised, placebo-controlled study; part 2 was an induced blood-stage malaria (IBSM), open-label, randomised, active-comparator controlled study, where participants were inoculated with P. falciparum and treated with a single dose of DSM265 (150 mg) or mefloquine (10 mg/kg).

Results: In part 1, 73 participants were enrolled (DSM265, n=55; placebo, n=18). In part 2, nine participants were enrolled (DSM265, n=7; mefloquine, n=2). DSM265 showed a good safety profile, with no drug-related serious or severe adverse events. The most common drug-related adverse event was headache. The mean plasma Cmax ranged between 1.3 and 34.8 µg/mL across doses tested; median Tmax was between 1.5 and 4 h; mean elimination half-life was 86 - 118 h. The DSM265 (150 mg) parasite reduction ratio was 1.55 (95% CI 1.42-1.67), with a corresponding parasite clearance half-life of 9.4 h (95% CI 8.7-10.2). The median MIC in blood was 1.04 µg/mL (range 0.55-1.50), resulting in a predicted single efficacious dose of 340 mg.

Conclusion: This is the first report of an integrated Phase 1 and IBSM study in antimalarial drug development. Its good safety profile, long elimination half-life and antimalarial effect support its development as partner drug in a single-dose antimalarial combination treatment.

Disclosure of Interest Statement: This study was funded by the Global Health Innovation and Technology Fund, Bill & Melinda Gates Foundation, Wellcome Trust, UK Department of International Development.
A NOVEL ASSAY TO ASSESS IMMUNE COMPROMISE AND RISK OF INFECTION POST HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Authors:

1. Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia
2. Immunology Research Centre, St Vincent’s Hospital, Melbourne, Australia
3. Department of Clinical Haematology and Bone Marrow Transplant Service, Royal Melbourne Hospital, Melbourne, Australia
4. University of Melbourne, Melbourne, Australia
5. Peter MacCallum Cancer Centre, Melbourne, Australia

Introduction: Managing immunosuppression in patients post allogeneic haematopoietic stem cell transplantation (alloHSCT) is challenging. Excessive immunosuppression can be complicated by infection, while inadequate immunosuppression can result in graft versus host disease (GVHD). An accurate method to assess immune status in the setting of HSCT is lacking. Unlike other commercially available assays which assess the adaptive immune response alone, QuantiFERON Monitor® (QFM) measures interferon-gamma (IFN-γ) release from whole blood following incubation with both innate (R848) and adaptive (CD3 antibody) immune stimulants.

Methods: Whole blood samples were prospectively collected from alloHSCTs at conditioning and days 10, 30, 60, 90, 120 and 180 and assayed by the QFM test. IFN-γ levels were plotted against time post alloHSCT and correlated to episodes of infection and GVHD.

Results: 40 patients were enrolled in the study (68% male; median age 47 years; 33% myeloablative, 67% reduced intensity conditioning). IFN-γ levels rose steadily over the first 180 days post transplantation and there was a trend between those with and without acute or chronic GVHD although this did not reach statistical significance. IFN-γ levels were statistically significantly lower in those with active infection compared to those without (p=0.028 using logistic regression with IFN-γ as a continuous variable).

Conclusion: Immune function, as measured by the QFM assay, appears to steadily increase over the first 180 days post alloHSCT. Lower IFN-γ levels correlated with risk of infection. This assay is promising as a means to monitor immune recovery and predict risk of infection and hence tailor immunosuppression and prophylaxis accordingly.

Disclosure of Interest Statement: No conflicts to disclose.
DEVELOPMENT OF A MOBILE LABORATORY FOR SUDDEN ONSET DISASTERS

Authors:
Marr I¹, Baird RW², Quilty S³, Coatsworth N⁴

¹National Critical Care and Trauma Response Centre, Level 8 Royal Darwin Hospital, NT, Australia, ²Territory Pathology, Royal Darwin Hospital, Darwin, Australia, ³Department of Medicine, Katherine District Hospital, Katherine, Australia, ⁴Infectious Disease Unit, The Canberra Hospital, Canberra, Australia.

Introduction: Sudden onset disasters (SOD) require a rapid medical response to limit ongoing death and injury. As part of Australia’s preparedness, the National Critical Care and Trauma Response centre is equipped to deploy a surgical field hospital to both national and international disasters. We developed a mobile field laboratory to enhance the clinical services offered in SOD.

Objectives: Design and trial a mobile laboratory unit for use in Sudden Onset Disasters (SOD) that meets a WHO Emergency Medical Team (EMT) 2 standard.

Methods: Using RT-PCR FilmArray ®, iSTAT ®, HemoCue301 ®, HemoCueWBC ® and portable microscopy a mobile laboratory was developed with field appropriate standard operating procedures meeting ISO guidelines. A 12 day deployment to a remote Northern Territory Hospital (Katherine) with limited laboratory capacity tested functionality and reproducibility of results with validation against current NATA accredited results.

Results: Over the study period 11 RT-PCR FilmArray multiplex tests provided 9 positive and 3 negatives, including blood culture (n=4), gastrointestinal (n=4), respiratory multiplex screens (n=3). All results were confirmed with NATA standardised testing. There were 20 WBC HemoCue and HemoCue301 tests performed, with non-significant differences (p>0.05) on each parameter when compared to Sysmex XN 550. iSTAT tests were run in parallel against Vitros 250 showing non-significant differences for CHEM4 (n=10), CG8 (n=10) and TnI (n=5) cards, p>0.05.

Conclusions: This small pilot trial shows a EMT2 mobile field laboratory can provide reproducible results when compared to NATA accredited testing in an isolated Northern Territory location.

Disclosure of Interest Statement: Nothing to disclose.
A SMARTPHONE-BASED SYSTEM FOR MEASURING AND SUPPORTING ADHERENCE TO MEDICATION

Authors:
Molton JS1,2, Pang Y1, Wang ZC2, Qiu BQ2, Wu P2, Rahman-Shepherd A1, Ooi WT2, Paton NI1,2

1 National University Health System, Singapore, 2 National University of Singapore

Introduction: Suboptimal adherence for infectious diseases such as tuberculosis (TB) results in poor clinical outcomes and ongoing infectivity. Directly Observed Therapy (DOT) has a number of limitations. We aimed to develop and evaluate a smartphone-based system to facilitate remotely observed therapy rather than in-person observation.

Methods: We developed an integrated smartphone and web-based system to provide medication reminders and facilitate video recording of pill ingestion, for upload and later review.

We evaluated the system in a single arm, prospective study. Healthy volunteers age ≥21 were instructed to take a supplement pill once, twice or three-times a day, for 2 months, and to video each pill taking episode using the system. Adherence was measured by the smartphone system and by pill count.

Additionally we developed face and image recognition modules to automate the verification process, and a conditional cash transfer module to encourage adherence by rewarding successful video uptake with small cash incentives.

Results: 42 eligible participants were recruited (median age 24). Overall median estimated participant adherence by MIST was 90.0%, similar to that obtained by pill count (93.8%). There was a good relationship between adherence as measured by the system and by pill count (Spearmans $r_s$ 0.66, p<0.001).

Conclusions: We have demonstrated the feasibility, acceptability and accuracy of a smartphone-based adherence support and monitoring system that has applicability for infectious diseases such as TB and HIV.

Disclosure of Interest Statement: This study was funded by National University of Singapore. No pharmaceutical grants were received in the development of this study. All authors declare no conflicts of interest.
IMPLEMENTING MOBILE HEALTH FOR TUBERCULOSIS CARE IN SYDNEY: EXPERIENCE WITH VIDEO DIRECTLY OBSERVED THERAPY

Authors:
Chapman, S1 Holzman, S2,3, Rios KC2,4, Shah, M2

1 Western Sydney University, New South Wales, Sydney, Australia
2 Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
3 Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
4 Emocha Mobile Health, Inc., Baltimore, Maryland, USA

Introduction: Tuberculosis (TB) remains a disease of public health interest in Australia, with over 1,300 cases annually. Directly observed therapy (DOT) remains the standard of care in New South Wales, but is logistically challenging and resource intensive for patients and providers. Video-based DOT represents a promising potential alternative methodology to ensure high rates of treatment adherence and completion. We evaluated an asynchronous video-DOT application, miDOT, that allows patients to securely record and transmit videos of themselves taking medication to a secure website, where providers can view and verify adherence at their convenience.

Methods: We conducted a prospective implementation study of video-DOT at the Parramatta Chest Clinic in Western Sydney. All TB patients were eligible, and were enrolled at the discretion of the TB clinic providers. Upon enrollment, participants utilized the video-DOT system to document adherence to treatment. The primary outcome was percentage of total doses that were verified by observation (i.e. DOT), comparing the time period before (i.e. in-person DOT) and after enrollment (i.e. miDOT).

Results: 19 participants uploaded 1389 videos documenting treatment (mean 73 videos/person, most frequently with daily dosing schedule). The proportion of observed (i.e. verified in-person, or uploaded video) treatment doses increased from a median of 66% (IQR 56%-73%) prior to enrollment (pre-miDOT period) to a median of 95% using miDOT (IQR 90%-98%, p=0.0003).

Conclusion: Asynchronous video-DOT is an effective tool for expanding capacity to perform DOT in TB clinics, with high adherence. Additional research is needed to evaluate generalizability of findings in Australia.

Disclosure of Interest Statement: Maunank Shah is the inventor of the miDOT system, which is licensed to Emocha Mobile Health Inc. Katrina Rios is an employee of Emocha mobile health Inc. Emocha Mobile Health provided the miDOT system without charge to the Parramatta Chest Clinic for the duration of the study and had no role in the study design, data collection or analysis. Scott Chapman (PI) has no conflicts and provided oversight of the study and data abstraction. Samuel Holzman has no conflicts to disclose and led data analysis.
AN EVIDENCE-BASED APPROACH TO UNDERSTANDING THE TRANSMISSION CYCLE AND RISKS OF COXIELLA BURNETTI INFECTION IN COMPANION ANIMALS

Authors:
Bosward KL¹, Norris JM¹

¹ Sydney School of Veterinary Science (SSVS), Faculty of Science, University of Sydney

Introduction: Confirmed cases of Q fever in veterinary personnel in small animal practice and companion animal handlers such as cat breeders have illustrated that cats and dogs, especially periparturient ones, can be a source of transmission. Determining the extent of this risk to humans and the source of transmission to companion animals is vital and requires a multifaceted approach.

Methods: Studies at SSVS have included cross-sectional surveys of knowledge attitudes and practices of cat breeders, veterinarians, veterinary nurses; seroprevalence studies in cats and dogs from a range of subpopulations (pet, breeding, feral/stray, camp dogs in remote Indigenous communities); and molecular studies of raw milk and pet meat to determine the presence of C. burnetti DNA.

Results: Cat breeders and veterinary nurses in Australia reported low levels of knowledge and awareness of Q fever disease and vaccination, resulting in a poor vaccination rate. Seroprevalence studies showed increased evidence of prior/current infection in breeding cats and camp dogs in indigenous communities. Pilot studies investigating the potential sources of C. burnetii in raw pet meat and unpasteurized ‘cosmetic bath’ milk has found modest concentrations of C. burnetii DNA in bulk-tank samples of unpasteurised ‘cosmetic bath’ milk collected from health food stores and raw meat containing kangaroo from pet food distributors.

Conclusion: Further carefully constructed cross-sectional and multi-disciplined studies with an open mind and attention to detail are required to follow our research leads to date in this complex area, if we are to truly understand the cycle of transmission of C. burnetii in animals and humans.

Disclosure of Interest Statement: The authors have been funded by Australian Companion Animal Health Foundation, NH&MRC and the Canine Research Fund. No pharmaceutical grants were received in the development of these studies.
BROKEN HEARTS IN TIMOR-LESTE: AN ECHOCARDIOGRAPHY-BASED PREVALENCE STUDY OF RHEUMATIC HEART DISEASE IN SCHOOL CHILDREN

Authors:

1 East Timor Hearts Fund, 2 RhEACH, 3 Royal Darwin Hospital, 4 Menzies School of Health Research, 5 Centre for Disease Control, Darwin, 6 Cairns Base Hospital

Introduction: Rheumatic heart disease (RHD) causes significant morbidity and mortality in school aged children in Timor-Leste, but its prevalence has not been evaluated or described. We conducted the first echocardiography-based screening study to determine the prevalence of RHD in school-aged Timorese children.

Methods: School students were enrolled from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste, using opt-out consent. Demographic and anthropometric data were collected and all students had a limited echocardiogram looking for evidence of RHD. RHD was classified as borderline or definite, according to World Heart Federation criteria. Patients with RHD were entered into a register for ongoing secondary prophylaxis, with the first dose of benzathine penicillin G administered on the day of the study.

Results: 1413 children were screened; 739 (52%) were girls and the median age was 12 years (range 4-24). The prevalence of definite RHD was 1.8% and borderline 1.6% (total 3.4%). Borderline or definite RHD was more common in Ermera than Dili though the difference was not statistically significant (4.1% vs 2.2%; p=0.07). Definite RHD was more prevalent in girls than boys (2.8% vs 0.7%; p<0.01). Congenital heart disease was identified in 20 children (1.4%). Of the 26 definite RHD cases, 23 (88%) received education and a first dose of BPG during the study.

Conclusion: RHD is prevalent in Timor-Leste, with some of the highest rates observed in the world. Girls are affected more commonly than boys. Community engagement is essential to ongoing follow up and effective delivery of secondary prophylaxis.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer. Pfizer has no role in the design, implementation or analysis of the study.
RESPONDING TO THE OUTBREAK OF DRUG-RESISTANT TUBERCULOSIS IN DARU, SOUTH FLY DISTRICT, WESTERN PROVINCE, PNG

Authors:
Majumdar S1, Chan G1, Adepojibi T1, Lawson J1, Wallis P1, Huang K1, Ronnachit A1, Wallis A1, O’Brien D1, Graham S1,

1Burnet Institute, Melbourne, Australia.

Introduction: There is a major outbreak of drug-resistant tuberculosis (DR-TB) that is having a devastating effect on the population of the South Fly District (SFD) of the Western Province of Papua New Guinea (PNG) with the majority of cases resident on Daru Island. The local epidemic is characterised by high rates of primary transmission of DR-TB, with a population incidence of among the highest ever recorded (503 per 100,000 in 2016). Operational research (OR) to test interventions and innovations that will increase the efficiency of the response is needed.

In 2014, the Government of PNG convened an emergency response taskforce for DR-TB hotspots, with significant support from the Australian government. The Burnet Institute’s Reducing the Impact of Drug-Resistant TB (RID-TB) in Western Province supports the design and implementation of an effective SFD TB program, working in partnership with the Provincial Health Office (PHO), Daru General Hospital (DGH), the National Department of Health (NDoH), World Vision PNG and the World Health Organisation.

Significant progress has been made by the SFD TB program and partners since 2014 through health and community systems strengthening that has resulted in an improvement in case detection and treatment outcomes for all forms of TB. Through the Tropical Disease Research Regional Collaboration Initiative (TDRRCI), Burnet will partner with PNG institutions to develop an OR framework using the Structured Operational Research Training (SORT-IT) model. This session will provide an outline of the response, progress, and challenges and describe the SORT-IT model.

Disclosure of Interest Statement: The RID-TB Project is funded by the Australian Government’s Department of Foreign Affairs and Trade. No other relevant disclosures.
USING NASOPHARYNGEAL CARRIAGE SURVEILLANCE IN CHILDREN HOSPITALISED WITH ACUTE RESPIRATORY INFECTION TO DETERMINE THE PNEUMOCOCCAL CONJUGATE VACCINE COVERAGE REQUIRED FOR INDIRECT IMMUNITY

Authors:
Chan J¹, Nguyen CD¹,², Xeuatvongsa A³, Lai JYR¹, Mungun T⁴, Blyth C⁵, Pomat W⁶, Dunne EM⁷, Lim R¹, Phetsouvaph R⁷-⁸, Datta S⁹, Hinds J¹⁰,¹¹, Fox K¹², Newton PN⁷,⁸, Lehmann D¹³, Ford R⁶, La Vincente S¹,¹⁴,¹⁵, Dance DAB⁷,⁸,¹⁶, Satzke C¹,²,¹⁷, Mulholland EK¹,¹⁵,¹⁸, Russell FM¹,¹⁴

¹ Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia.
² Department of Paediatrics, University of Melbourne, Melbourne, Australia.
³ National Immunization Programme, Ministry of Health, Vientiane, Lao PDR.
⁴ Ministry of Health, Ulaanbaatar, Mongolia.
⁵ School of Medicine, University of Western Australia, Perth, Australia.
⁶ Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea.
⁷ Wellcome Trust Research Unit, Lao-Oxford-Mahosot Hospital, Vientiane, Lao PDR.
⁸ Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, United Kingdom.
⁹ World Health Organization, Vientiane, Lao PDR.
¹⁰ Institute for Infection and Immunity, St George's- University of London, London, United Kingdom.
¹¹ BUGS Bioscience, London Bioscience Innovation Centre, London, United Kingdom.
¹² Regional Office for the Western Pacific, World Health Organization, Manila, Philippines.
¹³ Telethon Kids Institute, University of Western Australia, Perth, Australia.
¹⁴ Centre for International Child Health- Dept. of Paediatrics, The University of Melbourne, Melbourne, Australia.
¹⁵ International Child Health, Menzies School of Health Research, Darwin, Australia.
¹⁶ Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom.
¹⁷ Department of Microbiology and Immunology, University of Melbourne, Melbourne, Australia.
¹⁸ Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom.

Introduction: Pneumococcal conjugate vaccines (PCVs) prevent disease through direct protection of vaccinated individuals, and indirect protection by reducing nasopharyngeal (NP) carriage and transmission of vaccine-type pneumococci. While the indirect effects of PCV vaccination are well described, the PCV coverage required to achieve the indirect effects is unknown. We will determine this using hospital-based NP pneumococcal carriage surveillance.

Methods: Surveillance includes children aged 2-59 months admitted to participating hospitals at three sites with acute respiratory tract infection. Thirteen-valent PCV (PCV13) status is obtained from written records. An NP swab is collected according to standard methods and examined by lytA qPCR, with positives serotyped by microarray. PCV13 coverage is determined using administrative data or community survey.

Results: In Lao PDR, Papua New Guinea, and Mongolia, we have recruited 973, 204, and 240 children, respectively. For each site, we will present monthly PCV13 carriage rates. In Laos PDR, where PCV13 coverage is <50%, PCV13 carriage rates are declining among vaccinated children (direct effects) but not unvaccinated children (indirect effects, figure 1).
Data will also be pooled across sites to examine relationships between PCV13 coverage and carriage.

**Conclusion:** As PCV13 coverage increases, we hypothesise that PCV13 carriage to decline in vaccinated and unvaccinated individuals. These results will inform vaccine policy makers about the PCV coverage required to maximise the effects of PCV.

**Disclosure of Interest Statement:** This study received funding from the Bill and Melinda Gates Foundation. No pharmaceutical grants were received in the development of this study.
SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR FOR 8 WEEKS AND
SOFOSBUVIR/VELPATASVIR FOR 12 WEEKS ARE SAFE AND EFFECTIVE FOR
PATIENTS WITH GENOTYPE 3 HCV INFECTION AND CIRRHOSIS: THE POLARIS-3
STUDY

Authors:
Strasser S1, Foster GR2, Thompson A3, Ruane PJ4, Borgia S5, Dore G6, Workowski K7,
Hyland RH8, Wang J8, Svarovskaia ES8, Stamm LM8, Brainard DM8, Subramanian M8,
McHutchison JG8, Berg T9, Agarwal K10, Conway B11, Feld J12, Willems B13, Roberts SK14

1Royal Prince Alfred Hospital, Sydney, Australia, 2Royal London Hospital, London, United
Kingdom, 3St. Vincent’s Hospital, Melbourne, Australia, 4Ruane Medical and Liver
Health Institute, Los Angeles, United States, 5Brampton Civic Hospital, Brampton, Canada, 6St
Vincent's Public Hospital, Sydney, Australia, 7Emory University Hospital, Atlanta, United
States, 8Gilead Sciences, Foster City, United States, 9Charité Universitätsmedizin, Berlin,
Germany, 10Kings College Hospital, London, United Kingdom, 11Vancouver Infectious
Disease Research and Care Centre, Vancouver, Canada, 12Toronto Western Hospital Liver
Centre, Toronto, Canada, 13Centre Hospitalier de l'Université de Montréal, Montréal,
Canada, 14Alfred Hospital, Melbourne, Australia.

Introduction: Patients with HCV genotype 3 (GT3) infection, particularly those with
cirrhosis, have emerged as a more difficult to cure population. Voxilaprevir (VOX) is a
pangenotypic inhibitor of the HCV protease. This Phase 3 study evaluated treatment with
Sofosbuvir/Velpatasvir/VOX for 8 weeks and SOF/VEL for 12 weeks in DAA-naïve patients
with GT3 HCV infection and compensated cirrhosis.

Methods: Patients in North America, Europe, Australia and New Zealand were randomized
1:1 to receive SOF/VEL (400/100 mg daily) for 12 weeks or SOF/VEL/VOX (400/100/100 mg
daily) for 8 weeks. The primary endpoint compares the sustained virologic response 12
weeks after treatment (SVR12) to a pre-specified historic control rate of 83%. Secondary
endpoints included safety, tolerability, and viral resistance.

Results: Of 219 patients treated, 72% were male, 90% were white, 42% had the IL28B CC
genotype, and 31% had previously failed IFN-based treatment. Median platelet count was
139x103 cells/µL and mean Fibroscan was 23kPa in the SOF/VEL/VOX group and 22kPa in
the SOF/VEL group. Treatment was well tolerated – two patients, both in the SOF/VEL
group, discontinued therapy – 1) pelvic fracture and 2) viral breakthrough at week 8. No
serious adverse events were attributed to medication were reported. Overall, SVR12 with
SOF/VEL/VOX was 96% (106/110) and in the SOF/VEL was 96% (105/109). Both treatment
arms were superior to the predefined performance goal of 83% (p<0.001).

Conclusion: The single tablet regimens of SOF/VEL/VOX for 8 weeks and SOF/VEL for 12
weeks are safe, well tolerated and effective treatment options for difficult-to-cure patients
with GT3 infection with compensated cirrhosis.

Disclosure of Interest Statement: This study was funded by Gilead Sciences.
CHRONIC HEPATITIS C TREATMENT UPTAKE IN AUSTRALIA FOLLOWING AVAILABILITY OF INTERFERON-FREE THERAPY

Authors:
Hajarizadeh B1, Grebely J1, Matthews GV1, Martinello M1, Dore GJ1

1The Kirby Institute, UNSW Sydney, Sydney, New South Wales, Australia

Introduction: Government-subsidised direct acting antiviral (DAA) treatment for hepatitis C virus (HCV) infection has been available in Australia since March 2016. This study assessed DAA treatment uptake between March-September 2016.

Methods: A 10% random sample of Pharmaceutical Benefits Scheme (PBS) DAA prescriptions processed for reimbursement between March-September 2016 were analysed.

Results: An estimated 25890 individuals initiated DAA treatment between March-September 2016, accounting for an estimated 11% of all individuals with chronic HCV in Australia. DAA regimens included sofosbuvir/ledipasvir (57%) sofosbuvir+daclatasvir (38%), sofosbuvir+other agents (4%), and paritaprevir/ritonavir/ombitasvir+dasabuvir (1%). Of those initiating DAA therapy, 66% were men and 40% were ≤50 years old. Gastroenterologists were the predominant prescriber group (52%), followed by general practitioners (GP; 13%), infectious diseases physicians (8%), other specialists (4%), and other physicians (22%). The proportion of individuals prescribed by GPs increased from 4% in March to 19% in September (Figure 1A). The proportion of individuals ≤50 years increased from 28% in March to 54% in September (Figure 1B). Among patients with HCV-related cirrhosis, an estimated 64% received DAA therapy between 2014 and September 2016 through PBS, clinical trials, early access programs or generic supply.

Conclusion: Rapid treatment scale-up was observed in the first seven months of government-subsidised DAA therapy in Australia. The proportion of prescriptions by GPs increased over time, crucial for broadened access. Further HCV elimination evaluation will include monitoring of treatment outcomes, treatment uptake among people who inject drugs and HIV-infected men who have sex with men, and HCV prevalence and incidence (both primary infection and reinfection).

Disclosure of Interest Statement: The Kirby Institute is funded by the Australian Government Department of Health and is affiliated with the Faculty of Medicine, UNSW Sydney. The views expressed in this publication do not necessarily represent the position of the Australian Government. No pharmaceutical grants were received in the development of this study.
Figure 1: Distribution of monthly DAA treatment initiation by prescriber type (A) and patient’s age (B) during March-September 2016 in Australia
SUB-OPTIMAL PROTECTION AGAINST PAST HEPATITIS B VIRUS INFECTION WHERE SEROTYPE MISMATCH EXISTS BETWEEN VACCINE AND CIRCULATING VIRAL GENOTYPE IN NORTHERN AUSTRALIA

Authors: Cheah BC1, Davies J1,2, Singh G2, Wood N3, Jackson K4, Davison B2, McIntyre P3, Locarnini S4, Davis JS2, Tong SYC2,5.

1. Royal Darwin Hospital, Darwin NT, Australia
2. Menzies School of Health Research, Darwin NT, Australia
3. National Centre for Immunisation Research and Surveillance for Vaccine Preventable Diseases, The Children's Hospital at Westmead, Westmead NSW, Australia
4. Victorian Infectious Diseases Reference Laboratory, Doherty Institute for Infection and Immunity, Melbourne VIC, Australia
5. Victorian Infectious Disease Service, The Royal Melbourne Hospital, and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Victoria, Australia

Introduction: In the Northern Territory, there is a serotype mismatch between the hepatitis B virus vaccine (adw2) and the circulating viral genotype (ayw3) in the Indigenous population.

Methods: We assessed serological markers of HBV infection in the Aboriginal Birth Cohort (ABC). Participants were recruited at birth at the Royal Darwin Hospital (1987–1990), with follow-up serology obtained at waves 3 (W3; 2006–2008) and 4 (W4; 2013–2015). A subset of non-immune participants at W3 received a booster. We determined the vaccine effectiveness (VE) against any (anti-HBc Ab+) and chronic infection (HBs Ag+).

Results: Of 686 participants, HBV serology was obtained from 386 at W4, of whom 269 had received ≥1 vaccine dose, 113 were vaccinated in accordance with United States Centers for Disease Control recommendations and 117 had never been vaccinated. Seven participants were chronically infected and 94 had evidence of any infection. The VE against any infection was 66% (P = 0.06), and against chronic infection 100% (P = 0.20). For every dose of vaccine received, the odds of being anti-HBc Ab decreased by 41% (P < 0.001). The odds of being anti-HBc Ab+ was 87% lower in participants raised in urban compared to remote areas (P = 0.002). The W3 booster had no sustained effect.

Conclusion: The vaccine was effective in preventing chronic infection but sub-optimal against any infection. That anti-HBs titres and the presence of anti-HBc Ab were associated with remote dwelling rather than prior vaccination or boosting suggests ongoing exposure to circulating virus.

Disclosure of Interest Statement: This study was funded through NHMRC project and fellowship grants.
PREVALENCE OF ANTIVIRAL RESISTANCE IN AN AUSTRALIAN HEPATITIS C POPULATION

Ong ATL$^{1,2,3}$, Tay E$^1$, George J$^{1,3}$, Douglas MW$^{1,2,3}$

$^1$Storr Liver Centre, Westmead Millennium Institute, University of Sydney at Westmead Hospital, Sydney, Australia, $^2$Centre for Infectious Diseases and Microbiology, Westmead Hospital, Sydney, Australia, $^3$Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Sydney, Australia

Objective: To determine the prevalence of baseline resistance associated substitutions (RASs) in Australian patients with hepatitis C virus (HCV) genotype 1 infection.

Design: Single centre cross-sectional study.

Setting: Single tertiary centre. Large urban Australian public hospital pathology laboratory.

Participants: 380 patients whose blood samples were sent to the Institute for Clinical Pathology and Medical Research (ICPMR) for genotype testing, and found to be HCV genotype 1 or 1a infection. All patients were naive to new direct acting antivirals (DAAs) against HCV, which were approved for PBS subsidy in March 2016.

Main outcome measures: HCV RASs of greatest clinical relevance are those present in the NS3 and NS5A regions of the HCV genome. DAAs targeting these regions are being widely prescribed in Australia. Viral genome sequences from these regions were generated and analysed with epidemiological data.

Results: 380 samples were tested. The median age of the patients was 41.7, interquartile range (IQR) 33.7 - 49.9 years. Patients were predominantly male (71%). A significant proportion of patients were from correctional centres (31%). The most prevalent NS3 RAS was Q80K at 5.6%, and for NS5A was M30V at 6.0%.

Conclusions: This is the first and largest examination of the prevalence of HCV resistant mutations in Australia. The most prevalent NS3 RAS, Q80K confers resistance to simeprevir, a previous generation DAA no longer in use. The most prevalent NS5A RAS, M30V potentially confers resistance to ombitasvir. It is important to monitor for the potential emergence of drug resistance.

Disclosure of Interest Statement: No conflicts to declare.
POSTCARDS FROM THE DIGITAL HEALTH FRONTIER; TELEHEALTH FOR HEPATITIS C CARE IN THE DAA ERA

Authors: Biggs BA\textsuperscript{1,2,3}, Kanhutu K\textsuperscript{1,2,3,4}, Sasadeusz J\textsuperscript{1,2}, Schulz T\textsuperscript{1,2}, Watkinson S\textsuperscript{1,2}

\textsuperscript{1}Royal Melbourne Hospital, \textsuperscript{2}Victorian Infectious Diseases Service, \textsuperscript{3}University of Melbourne
Faculty of Medicine, Dentistry and Health Sciences, \textsuperscript{4}Health Informatics Society Australia

Introduction: The Victorian Infectious Diseases Service based at the Royal Melbourne Hospital currently provides telehealth care for rural and regional patients with hepatitis C. The progressive roll out of the national broadband network and increasing availability of web based videoconferencing platforms and mobile devices have provided unprecedented capacity to manage patients remotely. The primary outcome of this study is to demonstrate that telehealth delivered hepatitis C management achieves comparable virological outcomes to standard face to face care.

Methods: The study is part of a quality audit of the hepatitis service. Key outcome and process measures include;

- Proportion of patients achieving a sustained virological response (SVR)
- Failure to attend rate FTA
- Frequency of technical difficulties
- Consult duration time

Results: Since March 1\textsuperscript{st} 2016 over 50 patients have been managed via telehealth. Of those who have so far completed therapy an SVR rate of 94\% of has been achieved. Expected SVR genotype 1 (>95\%); genotype 3 (>85\%). Technical difficulties occurred in less than 10\% of consultations with FTA of 17\%. Consult duration was on average 15 minutes or less.

Conclusion: Our completed patient cohort results suggest comparable outcomes for telehealth managed patients as compared to traditional modalities even when adjusted for age, gender, hepatic fibrosis status and co-existent co-morbidities. Following on from the 2017 publication of the Infectious Diseases Society of America position statement on Telehealth and Telemedicine, we discuss the challenges and benefits of an outpatient ID telehealth services as we enter the era of accelerating digitally enabled healthcare.

Disclosure of Interest Statement: No conflicts to disclose.
CHESS - CURING HEPATITIS C: EFFECT ON THE ENDOTHELIUM AND CARDIOVASCULAR RISK

Authors:
Joshua S Davis¹,²,³, Melissa Young¹, Sandra Lennox¹, Tracey Jones¹, Kim Piera³, Robert Pickles¹,², Steven Oakley¹,²

1. Division of Medicine, John Hunter Hospital, Newcastle, NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW, Australia
3. Menzies School of Health Research, Darwin, NT, Australia

Introduction: Epidemiological data suggest that chronic hepatitis C virus infection (CHC) is associated with increased cardiovascular risk, but the mechanisms are unclear. We aimed to assess the effect of antiviral treatment on endothelial function in adults with CHC.

Methods: Adults with CHC, genotype 1, and no evidence of advanced fibrosis or cirrhosis were eligible. All patients were treated with 12 weeks of paritaprevir/ritonavir, ombitasvir and dasabuvir (PrOD), with additional ribavirin for genotype 1a. Endothelial function was assessed at multiple time-points before, during and after antiviral treatment. The main assessment tools were reactive hyperaemia peripheral arterial tonometry (RHPAT, higher values reflect better endothelial function), and serum angiopoietin-2 (ang-2) and e-Selectin (for both, higher values reflect worse endothelial cell activation and damage).

Results: Sixteen patients were enrolled. Mean (sd) age was 52.0 (6.9) years and 11 participants (69%) were male. All 16 achieved a sustained virological response. The mean (sd) pooled baseline RHPAT index was 2.05 (0.48), and there was no significant change during treatment (mean within-patient change from baseline to end of treatment= -0.23 (0.45), p=NS). There was significant improvement in mean ang-2 (baseline 2.44 (0.79) ng/ml, within-patient change -0.60 (0.44), p<0.001) and plasma e-Selectin (baseline 48.7 (21.5) ng/ml, within-patient change -14.4 (13.0), p<0.001).

Conclusions: Removing HCV viraemia is associated with a significant improvement in endothelial function as measured by serum markers, but not in bedside microvascular reactivity. Chronic HCV viraemia may be associated with endothelial cell dysfunction and therefore long term cardiovascular risk.

Disclosure of Interest Statement: This study was funded by an unconditional investigator-initiated research grant from Abbvie sciences, who market PrOD.
IS GENTAMICIN SAFE AND EFFECTIVE FOR SEVERE COMMUNITY ACQUIRED PNEUMONIA? A RETROSPECTIVE COHORT STUDY.

Authors:
Brereton CJ\textsuperscript{1, 2}, Lennon D\textsuperscript{1}, Browning S\textsuperscript{1}, Dunn E\textsuperscript{1}, Ferguson JK\textsuperscript{1, 2}, Davis JS\textsuperscript{1, 2, 3}

1. Division of Medicine, John Hunter Hospital, Newcastle NSW Australia
2. School of Medicine and Public Health, University of Newcastle, NSW Australia
3. Global and Tropical Health Division, Menzies School of Health Research, Darwin NT Australia

Introduction: Current Australian guidelines recommend a third generation cephalosporin (3GC) plus azithromycin as first line therapy for severe community acquired pneumonia (CAP). Benzyl-penicillin plus gentamicin plus azithromycin is an alternative, which provides excellent Gram negative cover, while avoiding the host and ecological effects on antimicrobial resistance of 3GCs. However Gentamicin is not commonly used in this setting due to concerns about potential toxicity and a lack of published evidence assessing efficacy.

Methods: We conducted a single-centre retrospective cohort study at a university teaching hospital where benzyl-penicillin, gentamicin and azithromycin is the empiric antibiotic regimen of choice for severe CAP. We included all patients with radiologically-confirmed CAP admitted to the intensive care unit between January 2008 and December 2015. The key exposure of interest was the receipt of gentamicin within the first 72 hours of admission. The key outcomes were acute kidney injury (AKI), hospital mortality, and relapse.

Results: We enrolled 147 patients of whom 117 received gentamicin. There was no difference in the incidence of new acute kidney injury in the gentamicin (59/117, 50%) and the non-gentamicin (15/30, 50%) groups, regardless of the number of doses received. Hospital mortality and relapse were no different in the gentamicin group (17%, 10% respectively) than the non-Gentamicin group (23%, 10%, \(p=\text{NS}\) for both comparisons), even after adjusting for receipt of other agents active against Gram negatives.

Conclusions: Gentamicin is a safe and effective alternative to broad spectrum antimicrobials as initial empiric Gram negative treatment of severe CAP.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
MYCOBACTERIUM ABSCESSUS COMPLEX IN A MAJOR TERTIARY ADULT CYSTIC FIBROSIS CENTRE

Authors:
Tippett E, Ellis S, Wilson J, Kotsimbos T, Spelman D

1Infectious Diseases, Alfred Hospital, Victoria, 2Radiology Department, Alfred Hospital, Victoria, 3Respiratory Department, Alfred Hospital, Victoria, 4Monash University, Victoria

†Equal Senior Author.

Introduction: Mycobacterium abscessus complex (MAbsC), a rapidly growing atypical mycobacterium, is an opportunistic respiratory pathogen significant to people with underlying lung pathology, particularly cystic fibrosis (CF). Treatment is in the order of months with multiple agents, potential significant adverse events and poor treatment outcomes. This study reviewed the patient population in whom MAbsC was isolated at The Alfred Hospital, which specialises in adult CF, examining the natural history, risk factors for persistent colonisation and treatment outcomes.

Methods: We undertook a retrospective cohort analysis of all patients in whom MAbsC was isolated between 2005 to 2014, particularly focussing on patients with CF. Factors examined included BMI, FEV1, CF comorbidities and medications including corticosteroids and prophylactic antibiotics to determine factors which may predict transient compared to persistent colonisation.

Results: MAbsC was isolated from 45 patients of whom 26 had CF. Of the patients with CF, patients who were transiently colonised with MAbsC had higher baseline respiratory function. In one third of our cohort, MAbsC was isolated for a mean of one year prior to spontaneous clearance. There was no correlation between recurrent MAbsC isolation and the use of systemic or inhaled steroids. Four CF patients were initiated on treatment with only one successful outcome.

Conclusion: This analysis demonstrates there are no clear predictors of those patients who will become persistently colonised with MAbsC and that a significant proportion will spontaneously clear colonisation. As treatment success rate is poor more work is urgently required in improve patient outcomes.

Disclosure of Interest Statement: E Tippett was supported by the Alfred Junior Medical Workforce. Nothing else to disclose.
CO-MRSA INFECTIONS IN AUSTRALIA COST $3.5B PER ANNUM

Authors: Cameron JK¹, Paterson DL², Britton PN³, Tong SYC⁴, Hall L¹, Nimmo GR⁵, Bennett CM⁶, Halton K¹.

¹ Institute for Health and Biomedical Innovation and School of Public Health and Social Work, Queensland University of Technology, ² The University of Queensland Centre for Clinical Research, University of Queensland and Royal Brisbane and Women’s Hospital, ³ The Children’s Hospital at Westmead and Sydney Medical School, University of Sydney, ⁴ Victorian Infectious Disease Service, The Royal Melbourne Hospital and The University of Melbourne, at the Peter Doherty Institute for Infection and Immunity and Menzies School of Health Research, Darwin, ⁵ Griffith University School of Medicine and Pathology Queensland, ⁶ Centre for Population Health Research, Deakin University

Introduction: The health and economic burdens of community-onset methicillin resistant Staphylococcus aureus (CO-MRSA) infections are needed to inform policy, planning and evidence-based practice. We aimed to synthesise data from a range of public sources to generate the first estimate of the national incidence and cost of CO-MRSA infections.

Methods: Incidences of CO-MRSA skin and soft tissue (SSTI), lower respiratory tract (LRTI) and bloodstream (BSI) infections were calculated for regions of Australia using data from existing literature and correspondence with specialists.

Simulations estimated costs using treatment models developed for children and adults in primary or tertiary care settings and including bed-stay, diagnostics, procedures, mortalities and loss of productivity.

Results: Annually, in Australia there were found to be 3702 CO-MRSA SSTIs, 559 CO-MRSA BSIs and 425 CO-MRSA LRTIs, occupying 147,000 bed-days, including 1600 bed-days in intensive care. Incidence ranged from 4 /100,000 person-years in Tasmania to 243 /100,000 person-years in central Australia.

The estimated cost of CO-MRSA was $3.5b annually in Australia. The higher incidence of SSTIs resulted in costs greater than summing the costs of BSIs and LRTIs. The greatest cost was mortality. The cost to the health system was found to be $1.9b, with bed occupancies accounting for ≥94%.

Conclusion: This first evaluation of the health and economic burden of CO-MRSA in Australia found a need for increased and more consistent data collection for a significant and expensive disease.

Disclosure of Interest Statement: This research was funded by NHMRC grant GNT1027589.
OPTIMISING LABORATORY METHODS FOR PRE-TRUS BIOPSY QUINOLONE RESISTANCE SCREENING

Authors: Liu E¹, Seed D¹, Andresen D¹,², McKew G¹, Gray T¹, Cheong E¹, Gottlieb T¹.

¹Concord Repatriation General Hospital, Concord, NSW, Australia
²St Vincents Hospital, Darlinghurst, NSW, Australia

Introduction: Ciprofloxacin-resistant Enterobacteriaceae infections following TRUS biopsy cause significant morbidity, however no consensus exists on an optimal laboratory screening method. We evaluated 7 methods regarding test performance, cost-effectiveness and usability.

Methods: Using simulated rectal swabs, 105 faecal samples were tested in parallel:
A: Direct plating to MacConkey agar (MAC)+CIP 10mcg/mL
B: Direct plating to MAC+5mcg CIP disc (MAC+5CD)
C-F: 5mL BHI broth+1, 2, 5 & 10mcg/mL CIP respectively; subculture to MAC+5CD
G: 5mL BHI broth+2x5mcg CIP discs (approximating 2mcg/mL), subculture to MAC+5CD

A positive screen on MAC+5CD was defined as coliform growth within a CIP zone <22mm, criteria derived from our prior validation study. The nearest coliform growth to the ciprofloxacin disc was identified by MALDI-TOF and CIP MIC determined by gradient strip.

Results: CIP-R Enterobacteriaceae was detected in 13/105 samples (MIC 2 to >32mcg/mL).

The most sensitive was broth enrichment at CIP10mcg/mL (100%, CI 75-100%) with 97% specificity (CI 91-100%). Subcultures from CIP<5mcg/mL broths were more difficult to read without superior sensitivity.

Both direct plating methods had equal sensitivity of 62% (CI 32-86%) and specificity >99% (CI 94-100%).

Arm B was most cost-effective at AUD $7.57/$0.64 (positive/negative), compared to Arm A ($7.93/$1.00) A and broth enrichment ($10.15/$3.22).

Conclusion: Direct disc screening is comparable to direct plating to MAC+CIP10mcg/mL agar, is more cost-effective and could be readily incorporated into existing laboratory work practices. Broth enrichment trended towards higher sensitivity, with larger studies needed to further assess if statistically significant.

Disclosure of Interest Statement: No conflict of interest to disclose.
HEALTH OUTCOMES FROM MULTI-DRUG RESISTANT SALMONELLA IN HIGH INCOME COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors:
Parisi A1, Vilkins S1, Furuya-Kanamori L1, Crump JA2, Howden BP3, Gray D1, Glass K1, Kirk M1

1 Australian National University, 2 University of Otago, 3 University of Melbourne

Introduction: Salmonella is a leading cause of foodborne enterocolitis worldwide. Nontyphoidal Salmonella (NTS) infections that are Multi-Drug Resistant (MDR) (non-susceptible to ≥1 agent in ≥3 antimicrobial categories) may result in more severe outcomes, although these effects have not been systematically examined. We conducted a systematic review and meta-analysis to examine impacts of MDR NTS on health in high-income settings.

Methods: We systematically reviewed the literature from scientific databases, including PubMed, Scopus and grey literature sources, using PRISMA guidelines. We searched for data from case-control studies, cohorts, outbreaks and theses, imposing no language restriction. We included only publications from January 1990 to September 2016 from high income countries as classified by World Bank. We extracted data from papers on duration of illness, hospitalisation rates, morbidity and mortality for MDR and non-MDR NTS strains.

Results: After removing duplicates, the initial search revealed 4258 articles. After further screening, we identified 16 eligible studies for the systematic review, and 9 of these were included in the meta-analysis. NTS serotypes differed among the reported studies but serotypes Typhimurium, Enteritidis, Newport and Heidelberg were the most often reported MDR pathogens. Salmonella infections that were MDR were associated with excess bloodstream infections (OR 1.63; 95%CI 1.18-2.26), excess hospitalisations (OR 2.77; 95%CI 1.47-5.21) and higher mortality (OR 3.54; 95%CI 1.10-11.40).

Conclusion: MDR NTS infections are a serious public health concern. With the emergence of MDR Salmonella strains in the high-income countries, it is crucial to restrict the use of antimicrobials both in animals and humans, and intervene to prevent foodborne infections.

Disclosure of Interest Statement: We declare that we have no conflicts of interest in the authorship or publication of this contribution.
SIGNALLING INDUCED BY HUMAN CYTOMEGALOVIRUS IN AN AUTOCRINE MANNER ALTERS EXPRESSION OF WNT RECEPTOR ROR2 AND MIGRATION OF INFECTED TROPHOBLASTS

Authors:
van Zuylen WJ1,2, Paull W2, Ford C4 and Rawlinson WD1,2,3

1Serology and Virology Division, SEALS Microbiology, Prince of Wales Hospital, Sydney, Australia, 2School of Medical Sciences, University of New South Wales, Sydney, Australia, 3School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, Australia, 4Metastasis Research Group, Prince of Wales Clinical School, University of New South Wales, Sydney, Australia

Introduction: Primary maternal CMV infection, reactivation, or infection with a different viral strain may cause adverse pregnancy outcomes including sensorineural hearing loss and mental disability. Placental infection may indirectly cause fetal injury via impairing placental development. New approaches to disease prevention are urgently needed. Better understanding of the molecular mechanisms of CMV infection of the placenta is essential for therapeutic innovations to decrease the prevalence and societal impact of congenital CMV.

Methods: Our previous findings indicate CMV controls the expression of the Wnt5a-binding tyrosine kinase receptor ROR2 to alter placental cell motility, which could lead to abnormal placental development in congenital CMV disease. We used migration assays in 2 compartment models, with added exogenous signalling proteins (wnt5a) and inhibitors (siRNA) to infected and uninfected cultures.

Results: We now show CMV specifically inhibits Wnt5a-mediated migration of infected trophoblasts, but not migration of surrounding uninfected cells. Utilising supernatant from CMV-infected trophoblasts, we also show that this inhibition and ROR2 alteration is not dependent on a soluble factor, rather it requires cell-cell contact. Furthermore, we show that both viable laboratory CMV strain AD169 and clinical CMV strain Merlin, but not UV-inactivated CMV inhibits Wnt5a-mediated trophoblast motility, indicating de novo viral gene expression is required.

Conclusions: Taken together, our novel findings suggest that autocrine signalling induced by human Cytomegalovirus alters ROR2 expression and this affects migration of infected trophoblasts. Inhibition of this autocrine signalling is a specific target for therapeutic intervention for CMV-induced placental damage and consequent fetal damage in congenital CMV infections.

Disclosure of Interest Statement: No conflicts to declare.
CONGENITAL CYTOMEGALOVIRUS (cCMV) IN INFANTS WITH HEARING LOSS IDENTIFIED VIA THE UNIVERSAL NEWBORN HEARING SCREENING PROGRAM, AND RISK FOR POSTNATAL INFECTION IN CHILDCARE

Authors: Palasanthiran P², Wilkinson M², Hall B¹, Al Yazidi L², Fennell M¹, Zheng J¹, van Zuylen W¹, Cottier C², Rawlinson W¹.

¹Serology and Virology Division, Department of Microbiology, SEALS, Level 4 Campus Centre Prince of Wales Hospital, Randwick, NSW, 2031, Australia, ²Sydney Children's Hospital, High St Randwick, NSW, 2031, Australia and School of Women's and Child Health, University of New South Wales, Kensington, NSW, 2052, Australia, ³School of Medical Sciences, School of Biotechnology and Biomolecular Sciences, and Australian Centre for Perinatal Sciences, University of New South Wales, Kensington NSW 2052 Australia

Introduction: Pregnant women are at risk for infection with CMV, particularly through close contact with their children. This may result in congenital infection, with resultant hearing loss, neurodevelopmental deficits and most severely fetal death. We assessed risk for infection for infants attending childcare, and cCMV in infants referred for audiology after failed UNHS.

Methods: Sampled CMV excretion in 130 nasal samples from 20 childcare staff of 2 centres over 5 weeks, with PCR of nasal and skin swabs. CMV testing of urine +/- saliva in infants with CMV detected by PCR at ≤30 days of age in urine/saliva, were diagnosed cCMV then followed for counselling and treatment.

Results: Childcare 8/130 carers CMV DNA positive a CMV excretion rate of 35% in staff. Hearing clinics 1520 children failing UNHS referred for audiology. 30% (469) confirmed hearing loss & 308 offered CMV testing, 10 declined, 123 had audiology by ≤21 days, and 203 by ≤30 days, of whom 195 were tested for CMV. CCMV was diagnosed in 10 infants (9 urine, 6 saliva, urine + saliva in 7), including 1 positive NBSC).

Conclusion: We identified ~6% of congenital CMV in children failing UNHS and had permanent SNHL confirmed. It did not require significant additional assets to those already existing in the tertiary referral paediatric centre, and provided useful and timely information for clinical and audiological follow up. Increased awareness of childcare CMV infection among parents & healthcare providers is necessary to minimise CMV acquisition during pregnancy and subsequently congenital CMV infection.

Disclosure of Interest Statement: No conflicts to declare.
NATIONWIDE SURVEILLANCE OF PAEDIATRIC EMPYEMA IN NEW ZEALAND - 2014 TO 2016

Authors:
Rix-Trott KJ¹, Byrnes C¹,², Twiss J¹, Matsas R³, Hamill J¹, Evans S¹, Mahon C², Williamson D⁴, Dickson N⁵, Walls T⁶, Voss L¹, Best E¹,².

¹ Starship Children’s Health, Auckland District Health Board, Auckland, New Zealand ² Department of Paediatrics, University of Auckland, ³ KidzFirst Hospital, Counties Manukau District Health Board, Auckland, ⁴ Institute of Environmental Science and Research, Wellington, ⁵ Paediatric Department, University of Otago, Wellington, ⁶ Paediatric Department, University of Otago, Christchurch.

Introduction: The aim was to document the burden of empyema in children aged <15 years in New Zealand including infectious aetiology, demographics and management.

Methods: Empyema was added as a notifiable disease in children <15 years of age on the New Zealand Paediatric Surveillance Unit (NZPSU) monthly report request from May 2014 to June 2016. A questionnaire recording demographics, presentation, infectious aetiology, medical and surgical management, complications, and short term outcomes was then requested from the lead paediatrician.

Results: 117 notifications were made with 99 fitting the case definition and complete data for 87 cases (88%). The median age was 3.8 years (range 2 months to 14.9 years) with 61% occurring in children under 5 years. 22% had co-morbid conditions ranging from mild asthma to immune-compromising conditions. Ethnicities were 34% Maori, 23% Pacific, 22% European, 13% Asian, and 5% Indian and 3% other. S. pneumoniae and S. aureus (MRSA + MSSA) made up 38% and 35% of causative organisms respectively. 60% of children had received 3-4 doses of PCV. 83% of cases required some form of surgical intervention, 1/3 required ICU and the mean length of stay was 19 days (6-56 days).

Conclusion: The burden of empyema in New Zealand children is seen predominantly in younger children and those of Maori and Pacific ethnicity. Streptococcal and staphylococcal infection were identified in nearly equal numbers, and 18% of S. aureus cases were MRSA. Empyema cases reflect a significant morbidity burden due to requirement for surgical intervention, ICU care, and prolonged hospitalization.

Disclosure of Interest Statement: Nil.
THE EFFECT OF INTRAVENOUS ANTIBIOTICS ON THE NASAL MICROBIOME IN CHILDREN – NOVEL ASSOCIATION WITH STAPHYLOCOCCUS AUREUS ACQUISITION

Authors: Bryant PA¹,²,³, Curtis N¹,²,³, Gordon L⁴, Parker K¹, Hopper SM¹,⁵, Holt K⁶, Babl FE¹,²,⁵, Ibrahim LF¹,²

¹Murdoch Children’s Research Institute, Melbourne, ²Department of Paediatrics, The University of Melbourne, ³Infectious Diseases Unit, Department of General Medicine, Royal Children’s Hospital Melbourne, ⁴The Australian Genome Research Facility, Melbourne, ⁵Emergency Department, Royal Children’s Hospital Melbourne, ⁶Department of Biochemistry and Molecular Biology, The University of Melbourne

Introduction: Antibiotic use is almost universal in Australasian children. The risks of this include acquisition of pathogenic and resistant bacteria, including nasal carriage of Staphylococcus aureus. We investigated the effect of antibiotics on the nasal microbiome in previously healthy children.

Methods: Children aged 6 months-18 years with cellulitis receiving short-course intravenous followed by oral antibiotics were included. Nasal swabs were collected at 3 timepoints: baseline, 1 week (maximal antibiotic pressure) and 3 months (post antibiotic washout) after starting intravenous antibiotics. After DNA extraction, microbiome abundance and diversity were assessed by amplicon sequencing analysis of the 16S rRNA V3-V4 region.

Results: 33 nasal swabs were collected from 11 children. There was no difference in overall bacterial abundance or diversity between baseline or the 1 week or 3 month timepoints. However, phylogenetic analysis showed a dramatic shift in the Gram-positive phyla with Firmicutes increasing from 27% abundance at baseline to 46% at 1 week (p=0.005) at the expense of Actinobacteria (33% to 16%, p=0.006), while Gram-negative phyla Proteobacteria and Bacteroidetes remained the same. Four patients acquired S. aureus on nasal culture after antibiotics, and there was a significant difference in diversity compared to baseline and to those who did not acquire S. aureus (p<0.05)(figure).

Conclusion: Short-course antibiotics are associated with changes in nasal microbiome composition, with the novel finding of reduced diversity associated with S. aureus acquisition. This has potential implications on selection of resistant bacteria. Whether changes can be predicted and therefore reversed will be part of a larger study.

Disclosure of Interest Statement: This study was funded in part through grants from The Royal Children’s Hospital Foundation, and the Infection and Immunity Theme at the Murdoch Children’s Research Institute. Dr. Ibrahim was funded by an Avant Scholarship. No pharmaceutical grants were received in the development of this study.

Figure:
Antibiotic timing:
*S. aureus* culture:

Pre Negative
n=11  

Post Negative
n=11  

Post Positive
n=11  

Decreasing diversity of bacterial populations

p < 0.05
INFLUENCE OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION IN NEONATAL INTENSIVE CARE

Authors:
Villanueva P¹, Freyne B¹,², Carr J¹,², Hickey L³, Bryant PA ¹,²

¹ Department of General Medicine, The Royal Children’s Hospital Melbourne.
² Infectious Diseases Unit, The Royal Children’s Hospital Melbourne.
³ Department of Neonatal Medicine, The Royal Children’s Hospital Melbourne.

Introduction: Antimicrobial stewardship (AMS) is vital in the critical care environment of the neonatal intensive care unit (NICU) but evidence for specific interventions is lacking. Our objectives were:
1) To describe patterns and appropriateness of antimicrobial prescribing in NICU;
2) To assess the influence of AMS ward rounds on inappropriate prescribing

Methods: A weekly AMS round involving senior NICU medical staff and a paediatric infectious diseases fellow was introduced and assessed over 6 months. Audit-feedback recommendations were made regarding appropriateness of decision to prescribe antimicrobials, drug choice and application (dose, interval, route, duration), and were reviewed the following day to assess acceptance of recommendations.

Results: During the study period, 249 infants were assessed for 627 review episodes. The proportion on antimicrobials at each AMS round was 19-59% (mean 37%). Of the 627 episodes, 233 (37%) reviews comprised patients receiving antimicrobials: 79 (34%) received targeted antimicrobial treatment, 111 (48%) empirical antimicrobial treatment and 43 (18%) prophylaxis. Of the 233 episodes on antimicrobials, 58 (25%) were deemed as having inappropriate prescriptions: 19% inappropriate decision to prescribe antimicrobials, 71% inappropriate antimicrobial choice, 10% inappropriate application. The commonest recommendations were to narrow (53%) or stop (19%) antimicrobials. The majority (73%) of recommendations were accepted.

Conclusion: A high proportion of infants in the NICU were on antimicrobials, and a quarter had recommendations to change/stop. Three-quarters of recommendations were actioned, showing that AMS rounds are effective in influencing prescribing. Education or more frequent rounds may increase this further.

Disclosure of Interest Statement: We have no conflict of interest to declare.
β-LACTAM ANTIBIOTICS: TOO MUCH OF A GOOD THING

Authors:  
Imani S 1,4, Marriott D1,2, Buscher H1,2, Gentili S3, Sandaradura I1,2  

1 St Vincent’s Hospital, Sydney  
2 University of New South Wales  
3 University of South Australia  
4 University of Notre Dame, Australia

Introduction: The potential for high-dose β-lactam antibiotics (BLA) to precipitate toxicity is becoming increasingly apparent in clinical practice. Adverse events, such as neurotoxicity, which were previously considered idiosyncratic, are now recognised as concentration-dependent. There is limited data, however, on the utility of BLA concentration in predicting toxicity.

Methods: Retrospective review of consecutive patients (n=378) treated with piperacillin (PIP, n=223), meropenem (MER, n=94) or flucloxacillin (FLU, n=61) who underwent therapeutic drug monitoring (TDM) at St Vincent’s Hospital Sydney between Jan 2013- Dec 2015. Adverse events investigated included neurotoxicity, nephrotoxicity, hepatotoxicity and opportunistic Clostridium difficile infection (CDI). Toxicity was measured using observational grading criteria, clinical judgment and relevant serum biomarkers. These findings were correlated with trough TDM measurements at the time of toxicity determination.

Results: Adverse event rates per antibiotic are summarised in Table 1.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>PIP</th>
<th>MER</th>
<th>FLU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>11.4%</td>
<td>15.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>8.5%</td>
<td>6.9%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>6.7%</td>
<td>8.3%</td>
<td>8.7%</td>
</tr>
<tr>
<td>CDI</td>
<td>7.9%</td>
<td>2.6%</td>
<td>0%</td>
</tr>
</tbody>
</table>

We found a significant increase in mean BLA trough concentration (C_{\text{min}}) in all patients diagnosed with neurotoxicity (p<0.05) and those with nephrotoxicity treated with PIP (p<0.01) or MER (p<0.01). Incidence of hepatotoxicity and CDI was not related to antibiotic concentration levels. Threshold C_{\text{min}} for which there was >50% risk of developing neurotoxicity (C_{\text{PIP}}>361.4mg/L, C_{\text{MER}}>64.2mg/L, C_{\text{FLU}}>125.1mg/L) and nephrotoxicity (C_{\text{PIP}}>452.65mg/L, C_{\text{MER}}>44.45mg/L) were identified.

Conclusion: Incidence of BLA toxicity is likely underestimated clinically. By utilising TDM early in the course of BLA treatment clinicians should aim to achieve the highest serum concentrations that can be safely attained, whilst ensuring that these toxicity thresholds are not surpassed. Additionally, TDM may be useful to diagnose BLA toxicity, avoiding other unnecessary investigations.

Disclosure of Interest Statement: The study was funded by a grant from the University of Notre Dame Australia.
ANTIMICROBIAL STEWARDSHIP ACTIVITY AND RESULTS DURING ANTIMICROBIAL SHORTAGES

Authors:
Casula L	extsuperscript{1}, Figtree M	extsuperscript{1}, Hoyle P	extsuperscript{1}, Russell P	extsuperscript{1}

	extsuperscript{1} Northern Sydney Local Health District

Introduction: National antimicrobial shortages have become increasingly common over the past few years. Ampicillin and azithromycin shortages occurred in 2015. Concurrent shortages of a broad range of critical agents (including: vancomycin, daptomycin, aztreonam, tigecycline, metronidazole and aciclovir) occurred in late 2016 - threatening patient safety and stretching antimicrobial stewardship (AMS) team capability.

Methods: We describe interventions, antimicrobial usage, and adverse events during this shortage period in a principal tertiary referral centre. Additional intensive, targeted antimicrobial stewardship processes were instituted ensuring the remaining stocks were used appropriately.

Results: Targeted AMS towards these agents was achieved through education memos, one-on-one phone calls, electronic AMS approval system and physical removal of affected antimicrobials from general ward imprest settings. During the shortage period, a 70% decrease was seen in IV azithromycin usage / 1000 OBDs and a 30% reduction in average monthly usage of vancomycin was noted. No adverse events have been attributable to the shortage on review of bacteraemia outcomes and IIMS notifications.

Conclusion: The wave of recent shortages led to enhanced antimicrobial stewardship team physical control of specific antimicrobials, however required significant additional vigilance and human resources. A marked reduction of use was noted in the antimicrobials affected without an increase in alternate antimicrobials. The externally caused shortage appeared to create a strong motivation of responsible prescribing in our hospital. Mitigating measures coordinated at the state and/or national level are required to ensure such shortages can be avoided in the future and that patient safety is not compromised.

Disclosure of Interest Statement: We declare no conflict of interest and there was no funding received for this study.
EFFECTS OF AGEING ON PARASITE BIOMASS, INFLAMMATION, ENDOTHELIAL ACTIVATION AND MICROVASCULAR DYSFUNCTION IN PLASMODIUM KNOWLESI AND P. FALCIPARUM MALARIA

Authors:
Barber BE1,2, Grigg MJ1,2, William T2,3, Piera KA1, Boyle M1,4, Yeo TW1,5,6, Anstey NM1,7

1. Menzies School of Health Research and Charles Darwin University, Darwin, Northern Territory, Australia
2. Infectious Diseases Society Sabah-Menzies School of Health Research Clinical Research Unit, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia
3. Jesselton Medical Centre, Kota Kinabalu, Sabah, Malaysia
4. Centre for Biomedical Research, Burnet Institute, Melbourne, Australia
5. Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
6. Institute of Infectious Disease and Epidemiology, Tan Tock Seng Hospital, Singapore
7. Department of Infectious Diseases, Royal Darwin Hospital, Darwin, Northern Territory, Australia

Introduction: In populations with low immunity to malaria, the risk of severe malaria increases with age. This is particularly apparent in Plasmodium knowlesi malaria. However, the pathophysiological mechanisms underlying knowlesi malaria, and of the age-related increase in risk in severe malaria in general, are poorly understood. We evaluated the effects of ageing on factors contributing to pathogenesis of severe knowlesi and falciparum malaria.

Methods: Malaysian patients aged ≥12 years with severe (n=47) and non-severe (n=99) knowlesi malaria, severe (n=21) and non-severe (n=109) falciparum malaria, and healthy controls (n=50) were enrolled. We measured parasite biomass, and markers of systemic inflammation (interleukin-6; IL-6), endothelial activation (angiopoietin-2), and microvascular function, and evaluated effects of age.

Results: Patients with severe knowlesi malaria were older than those with non-severe knowlesi malaria (median 55 vs. 42 years, p<0.0001). P. knowlesi parasitemia correlated with age (r=0.36, p<0.0001). In patients with knowlesi malaria, IL-6, angiopoietin-2 and microvascular dysfunction were increased in severe compared to non-severe disease, and all correlated with age, independent of parasitemia. In falciparum malaria, angiopoietin-2 increased with age, after controlling for parasite biomass (histidine-rich protein-2). Independent risk factors for severe malaria included parasitemia and angiopoietin-2 in knowlesi malaria, and HRP2, angiopoietin-2 and microvascular dysfunction in falciparum malaria.

Conclusion: Parasite biomass, endothelial activation and microvascular dysfunction are associated with severe disease in knowlesi malaria and likely contribute to pathogenesis. The independent association of each of these processes with ageing may account for the greater severity of malaria observed in older adults in regions of low endemicity.

Disclosure of Interest Statement: All authors state no conflict of interest.
PREVALENCE OF SCABIES AND IMPETIGO IN SCHOOL CHILDREN IN TIMOR-LESTE

Authors:
Korte L, Draper A, Davis K, Appelbe A, Dingle B, Bowen A, Francis J

1 Royal Darwin Hospital, 2 Hospital Nacional Guido Valadares, 3 NT Centre for Disease Control, 4 National Centre for epidemiology and population health, Australian National University, 5 Kensington Hill Medical Centre, 6 St John of God, 7 Princess Margaret Hospital for Children, 8 Telethon Kids Institute, 9 Menzies School of Health Research

Introduction: Scabies and impetigo are common and important skin conditions which are often neglected in developing countries. The prevalence of these conditions in Timor-Leste is unknown. Sequelae including cellulitis, bacteraemia, nephritis, acute rheumatic fever and rheumatic heart disease contribute significantly to the burden of disease.

Methods: We conducted an epidemiological survey in October 2016. School students were recruited from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste. We used a standard questionnaire to record demographics, anthropometry and skin examination results. Prevalence of scabies and impetigo were calculated and binary risk factors described using relative risks and 95% confidence intervals. Continuous variables for were analysed for associations using the Mann-Whitney Rank Sum test. Results were considered significant if \( p<0.05 \).

Results: 1407 students were enrolled; with median student age of 12 years (range 4-24). The prevalence of scabies was 22% and active impetigo 10%; 68% of students had evidence of either active or healed impetigo. Students in Ermera were more likely than those in Dili to have scabies (RR 6.3; 95%CI 4.3 - 9.2, \( p<0.01 \)) and scabies and active impetigo co-infection (RR 8.9; 95%CI 3.3 - 24, \( p<0.01 \)). There was no difference in the prevalence of active impetigo between urban and rural sites.

Conclusion: Scabies and impetigo are prevalent in Timor-Leste, with particularly high prevalence of scabies in the rural district of Ermera. Improvements in prevention and treatment are needed, and consideration should be given for implementing strategies at a community level, focusing on rural areas.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer.
TREATMENT OF LATENT TB INFECTION IN THE DARWIN REGION OF AUSTRALIA

Boyd R¹, Johnston V¹-², Farmer B¹, Krause V¹

¹ Centre for Disease Control, Northern Territory
² Honorary Fellow, Menzies School of Health Research, Northern Territory

Introduction: Preventing active tuberculosis (TB) disease through treatment of latent tuberculosis infection (LTBI) is an essential component of the World Health Organization’s End TB Strategy. To evaluate and inform practice we identified LTBI treatment uptake and compliance amongst Northern Territory populations.

Methods: We undertook a cohort study, including people diagnosed with LTBI June 2013-July 2014, Darwin; Population 140,000 including 25% Indigenous and 25% overseas-born. Demographic, treatment acceptance and compliance data were collected from the Darwin TB service.

Results: Of 573 people diagnosed with LTBI, 374 (65%) were offered; 265/374 (71%) accepted and 147/241 (55%) completed treatment. 74% were overseas-born, 14% non-Indigenous and 12% Indigenous. Indigenous people were more likely to accept treatment than overseas-born (OR 4.46; 95%CI 1.55-12.83) and non-Indigenous (OR 7.69; 95%CI 2.33-25.39). Overseas-born were least likely to complete treatment (Indigenous OR 1.34; 95%CI 0.66-2.72; non-Indigenous OR 1.38 95%CI 0.56-3.41).

All children under 6 years accepted treatment; 12/28(43%) completed treatment.

The cohort primarily comprised health care workers (HCW) 106(19%); contacts of active TB 97(17%) and asylum-seekers 94(16%). Of 106 HCW’s, 77(73%) were overseas-born. Supported by school nurses, students were most likely to complete treatment, with odds of completing 3.86 times higher than HCW’s (95%CI 1.02–14.58).

Conclusions: While comparable to previous studies, 45% did not complete treatment, representing missed opportunities to prevent disease. Encouragingly, we found high uptake of treatment amongst Indigenous people. Interventions should target optimising treatment completion in high risk populations of overseas-born and children under 6. Successful treatment in students supports ongoing engagement of school-based nurses.

Disclosure of Interest Statement: The Centre for Disease Control is funded by the Northern Territory Government. No additional funding was received for this study.
SHORTER MDR-TB TREATMENT COMPARED WITH CONVENTIONAL TREATMENT IN UZBEKISTAN: SPUTUM CULTURE CONVERSION AFTER 2 MONTHS

Authors:
A Ronnachit¹, A Khamraev², P du Cros³, J Greig³, T Pylypenko¹, Z Tigay², N Parpieva⁴, J Achar³

¹Médecins Sans Frontières, Nukus, Uzbekistan, ²Ministry of Health, Nukus, Uzbekistan, ³Médecins Sans Frontières UK, Manson Unit, London, United Kingdom, ⁴National Institute of TB and Pulmonology, Tashkent, Uzbekistan

Introduction: The shorter multi-drug resistant tuberculosis (MDR-TB) regimen has been recommended by the World Health Organisation (WHO) for eligible patients. However, little comparative data about its efficacy has been published. We compared 2-month culture-conversion status from a single-arm, prospective observational study of the shorter MDR-TB regimen (SR) with patients treated with WHO-approved conventional care (CC) under programmatic conditions in Uzbekistan, a country listed by the WHO as a high-burden MDR-TB country with high rates of second-line drug resistance.

Methods: SR data was compared with CC data from culture confirmed MDR-TB patients treated within the same TB program. Exclusion criteria included documented exposure to second-line drugs and second-line drug resistance. Multivariate-logistic regression was used to estimate associations between regimen and culture-conversion status after 2-months. Ethics approval was obtained.

Results: 241 CC and 88 SR patients were included. Patients treated with SR had an aOR of 1.91 (95%CI 1.08-3.38, p=0.026) of culture-conversion by 2-months compared with CC. Higher baseline sputum smear-positivity was negatively associated with culture-conversion, aOR 0.37 (95%CI 0.21-0.65, p<0.001) for scanty/1+, and 0.11 (95%CI 0.05-0.24, p <0.001) for 2+/3+. Poor adherence was negatively associated: aOR 0.42 (95%CI 0.21-0.83, p=0.013) with culture-conversion. A negative association with age was found, for every increasing year aOR 0.98 (95%CI 0.96-0.99, p=0.006).

Conclusion: There was an almost two-fold greater odds of culture-conversion by 2-months following treatment with the SR. Earlier culture-conversion has important infection-control and treatment implications, and use of SR may reduce transmission.

Disclosure of Interest Statement: The authors declare that there is no conflict of interest.
INITIAL PROGRAMMATIC EXPERIENCE OF BEDAQUILINE CONTAINING TREATMENT REGIMENS FOR DRUG-RESISTANT TUBERCULOSIS IN SOUTH FLY DISTRICT, WESTERN PROVINCE, PAPUA NEW GUINEA

Authors: Taune M1,2, Hiasihri S3, Huang K4, Ronnachit A4, Wallis P, Morris L3, Tugo O1, Dakulala P2, Bieb S2, John L2, Aia P2, Lavu E5, Coulter C6, Madjus S7, Innes A8, Islam T9, Chan G4, O'Brien D4, Graham S4, Majumdar S4

1Daru General Hospital, Western Province, PNG, 2National Department of Health PNG, 3Provincial Health Office, Western Province, PNG, 4Burnet Institute, Australia, 5Central Public Health Laboratory, PNG, 6Queensland Mycobacterial Reference Laboratory, Australia 7World Vision PNG, 8FHI 360 Asia Pacific Region, 9World Health Organisation, PNG.

Introduction: Treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) globally remain poor. The World Health Organization (WHO) for programmatic use has recently recommended Bedaquiline (BDQ), a novel drug for the treatment of MDR-TB. Daru Island, South Fly District (SFD), Western Province is the epicenter an outbreak of MDR-TB, including community transmission of extensively drug-resistant (XDR-TB) strains. Bedaquiline was introduced in the program in October 2015 and we describe the first programmatic use in PNG.

Methods: We conducted a cohort analysis using routine programmatic data for patients on BDQ-containing regimens enrolled from July 2015 to December 2016. Interim cohort outcomes (culture negative rate by month 6 of treatment) were assessed in patients with culture confirmed TB from 1 July 2015 to 30 June 2016. A core package of Active TB drug-safety monitoring and management (aDSM) was implemented.

Results: 21 patients received BDQ containing regimens. The median age was 36 years. 6 of 21 patients had microbiologically confirmed XDR TB. All patients are retained in care with no evidence of clinical or microbiological failure. In the interim cohort analysis (n=8), 7 (87.5%) patients on BDQ had a negative culture by month 6 of treatment, compared with 37 (44%) on non-BDQ containing regimens (n=85). A single serious adverse drug event was observed, unlikely related to Bdq.

Conclusion: Early experience with BDQ containing regimens in PNG demonstrates excellent interim treatment outcomes and a good safety profile and supports further scale up. New TB drugs with greater efficacy and better tolerability have the potential for great impact in the setting of a DR-TB outbreak and in routine use in resource-limited settings.

Disclosure of Interest Statement: No conflicts of interest to declare.
PREDICTORS FOR PNEUMOCOCCAL CONJUGATE VACCINATION (PCV) IN A LOW PCV COVERAGE SETTING IN THE EASTERN HIGHLANDS OF PAPUA NEW GUINEA

Authors:
Chan J1, Russell F1,2, Pomat W3, Sapura J3, Masiria G3, Kave J3, Ford R3, Kirarock W3, Kumani T3, Lehmann D4, Blyth CC4,5 on behalf of the PNG Aetiology Study Team

1 Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia
2 Centre for International Child Health- Dept. of Paediatrics, University of Melbourne, Melbourne, Australia
3 Infection and Immunity Unit, Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea
4 Telethon Kids Institute, University of Western Australia, Perth, Australia
5 School of Medicine, University of Western Australia, Perth, Australia.

Introduction: Pneumonia is the most important cause of childhood mortality and morbidity in Papua New Guinea (PNG). The 13-valent pneumococcal conjugate vaccine (PCV) was introduced to PNG in 2014 and in this study we describe PCV coverage over time and predictors for vaccination.

Methods: We completed a post-hoc analysis of vaccination coverage among children 2-59 months old, enrolled in a case-control study of pneumonia and meningitis. Cases were recruited at the Eastern Highlands Provincial Hospital and urban health clinics. Controls were recruited from the same villages as cases within an hour’s drive. Children were considered vaccinated if they had received two doses of PCV <12 months of age or one dose over 12 months of age. We calculated three-monthly rolling PCV coverage rates and determined predictors for vaccination using univariate and multivariate regression.

Results: Among the 1391 cases and controls enrolled from 2014-2015, PCV vaccination coverage started to increase from January 2015, reaching 30% coverage in December 2015 (figure 1). After adjustment, receipt of diphtheria-tetanus-pertussis vaccines was associated with an increased likelihood of PCV vaccination (aOR 9.3; 95% CI 5.8-14.8; p=0.000). In cases, distance from EHP hospital was also predictive of being vaccinated (aOR 3.0; 95% CI 1.2-7.4; p=0.02).

Figure 1: Three-month rolling vaccination coverage rate among cases and controls, Eastern Highlands Province, Papua New Guinea
Conclusion: PCV coverage remains low, however there is a trend towards increasing PCV coverage from 2015 onwards. Strategies to improve PCV coverage are required and should include programs targeting children from rural villages.

Disclosure of Interest Statement: This was an investigator-led study, funded by Pfizer Global and the PNG Institute of Medical Research
CONJUGATE PNEUMOCOCCAL VACCINATION AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION REDUCES INVASIVE PNEUMOCOCCAL DISEASE

Authors:
Roberts MB¹, Lewis I², Bak N¹

¹Infectious Diseases Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA
²Haematology Unit, Royal Adelaide Hospital and SA Pathology, Adelaide SA

Introduction: Immunosuppressed patients, especially haematopoietic stem cell transplant (HSCT) recipients, are particularly vulnerable to invasive pneumococcal disease (IPD) with reported rates between 3.81 and 22.5/1000 transplants. However, uptake of pneumococcal vaccination tends to be lower in the immunosuppressed, partly due to concerns of vaccine effectiveness. The Royal Adelaide Hospital (RAH) introduced protocolised conjugate pneumococcal vaccination (13vPCV) to all HSCT patients in 2010.

Methods: We conducted a retrospective study of all RAH HSCT patients from 2004 to 2015 to assess the impact of introduced 13vPCV on IPD incidence. Microbiological results from sterile sites for all HSCT patients in this period were reviewed for IPD. Individuals with IPD had clinical records evaluated for further data.

Results: Fourteen episodes of IPD occurred in twelve patients between 2004 and 2015. Twelve episodes occurred in the pre-2010 group who did not receive 13vPCV, 40% of serotyped isolates would have been covered by 13vPCV. Two episodes occurred in the post-2010 group who did receive 13vPCV, neither isolate serotype was covered by 13vPCV. In the equivalent period there were 936 HSCT, of which there was >90% enrolment and >90% vaccination protocol completion rates for surviving patients. There was a significant reduction in overall IPD rate from 28.4/1000 transplants pre-2010, to 3.6/1000 transplants in the post-2010 group. Similar reductions occurred in the autologous group from 25.5 to 2.8/1000 transplants and allogeneic group from 44.2 to 5.3/1000 transplants.

Conclusion: This is the first study to demonstrate the clinical effectiveness of 13vPCV in this cohort, highlighting its importance in preventing infectious complications of HSCT.

Disclosure of Interest Statement: No conflicts to disclose.
ROUTINE ERTAPENEM PROPHYLAXIS FOR TRANSRECTAL ULTRASOUND-GUIDED PROSTATE BIOPSY DOES NOT SELECT FOR CARBAPENEM-RESISTANT ORGANISMS: A PROSPECTIVE COHORT STUDY

Authors:
Bloomfield M1,2, Page M3, McLachlan A3, Studd R3, Blackmore T1,2

1 Department of Infection Services, Wellington Regional Hospital, Wellington, New Zealand, 2 Department of Microbiology, Wellington Southern Community Laboratories, Wellington, New Zealand, 3 Department of Urology, Wellington Regional Hospital, Wellington, New Zealand

Introduction: Post-transrectal ultrasound-guided prostate biopsy sepsis (PBS) is an increasing problem in this era of rising antibiotic resistance. Ertapenem prophylaxis has proven very effective at our institution for reducing this, however has raised local and regional antimicrobial stewardship concerns. This study investigated the possible selective effect of single dose ertapenem prophylaxis on faecal colonisation with carbapenem-resistant Enterobacteriaceae.

Methods: Patients had a rectal swab taken prior to receiving pre-biopsy ertapenem prophylaxis. A second swab was taken at follow-up 4-6 weeks later. Swabs were screened for carbapenem-resistant Enterobacteriaceae (CRE) using an enhanced Centers for Disease Control method. Pre-biopsy swabs were also screened for extended-spectrum and 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. Three cases (0.9%, 95%-CI 0.2-2.8%) of probable PBS were identified during the study period. None were bacteraemic or required ICU admission.

Conclusion: Single dose ertapenem prophylaxis 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. It is highly effective prophylaxis for transrectal ultrasound-guided prostate biopsy. Ertapenem may, in the right setting, represent a useful prophylactic option for prevention of post-transrectal ultrasound-guided prostate biopsy sepsis.

Disclosure of Interest Statement: The study was funded by internal departmental funds allocated to research. No pharmaceutical or other industry grants were received in the development of this study.
IMPACT OF A DEDICATED POST-TRANSPLANT VACCINATION SERVICE ON COMPLIANCE RATES AT A LARGE AUSTRALIAN CANCER CENTRE

Authors:
Teh B¹,², Joyce T¹,³, Slavin M¹,²,⁴, Thursky K¹,²,⁴, Worth L¹,²,⁴

¹Department of Infectious Diseases, Peter MacCallum Cancer Centre, ²NHMRC Centre of Research Excellence, Infections in Cancer, ³Department of Haematology, Peter MacCallum Cancer Centre, ⁴Department of Medicine, University of Melbourne.

Introduction: Autologous haematopoietic stem cell transplantation (ASCT) results in impaired immunity to vaccine-preventable infections. Frequently, compliance with vaccination consensus guidelines is poor. We evaluated the impact of a dedicated vaccination service on post-transplant vaccination compliance with prevailing national immunisation guidelines.

Methods: A vaccination service for ASCT recipients was established at the Peter MacCallum Cancer Centre in March 2014, consisting of regular scheduled reviews, face-to-face education with nursing and medical staff and a vaccination schedule aligned with national guidelines. ASCT patients were retrospectively classified as ‘pre-clinic’ (Sept 2012-Sept 2013) or ‘post-clinic’ cohorts (Oct 2013-2014), according when the service became available. Uniform data were collated from clinical and pharmacy databases, including: type and timing of vaccine/s, number of cycles completed, and reasons for non-compliance with guidelines. Vaccination uptake and compliance in each cohort were compared.

Results: Post-clinic and pre-clinic cohorts consisted of 87 and 81 patients, respectively, with similar patient characteristics. The proportion commencing vaccination was not significantly different between groups (83.9% vs. 71.4%, p=0.12). Of 74 patients eligible for vaccination in post-clinic cohort only 1 patient lost to follow up (1.4%) whilst the loss to follow up rate was 6.3% in pre-clinic cohort. Of patients vaccinated, the proportion administered according to national guidelines was significantly higher in the clinic cohort (70.8% vs. 19.0%, p<0.01). More patients in this cohort completed all recommended vaccines (47.2% vs 32.8%, p=0.11).

Conclusion: Implementing a dedicated post-ASCT vaccination service increased compliance with national immunisation guidelines (vaccination uptake, timing of administration) with near complete vaccination coverage.

Disclosure of Interest Statement: No conflicts of interest for all authors.
HIGH BURDEN OF FIRST PRESENTATION AND RECURRENCE OF SEVERE LOWER LIMB BACTERIAL CELLULITIS: A LONGITUDINAL STUDY

Authors:
Rajakaruna G¹, Cannon J², Dyer J¹, Carapetis J²,³,⁴, Manning L¹,⁴

¹Fiona Stanley Hospital, ²Telethon Kids Institute WA, ³Perth Children's Hospital, ⁴University of Western Australia

Introduction: Lower limb bacterial cellulitis (LLBC) is a common and serious infection of skin and subcutaneous tissue. High rates of incidence, recurrence, morbidity and economic costs have been reported worldwide. Given the lack of good quality, contemporary data, we aimed to describe the epidemiology of first presentation, recurrence and excess mortality in Australian patients with LLBC.

Methods: The state-wide data-linkage system was used to extract records of adults presenting to Western Australian (WA) hospitals with first episode LLBC from January 2002 to December 2013. Incidence and recurrence rates were calculated and matched controls were used to describe excess mortality.

Results: Over 12 years, 43,410 LLBC episodes were reported in 36,276 patients. There was an annual increase in incidence (4.7% p.a.), with an overall incidence of 204.8 (95% CI 198.6-211.1) per 100,000 population in 2013. There were higher incidence rate ratios (IRR) in older patients aged 65-84 years (IRR 2.59 [2.50-2.69], P<0.001) and >85 years (IRR 7.04 [6.73-7.37], P<0.001) compared with 16-24 years. Males and Indigenous Australians also had higher IRR. There was significant seasonal variability with increased rates during summer. LLBC recurrence occurred in 4,598 (12.7%) patients, with increased risk in older patients, females and Indigenous Australians. When compared with matched controls, patients with LLBC had a higher mortality (P<0.0001).

Conclusion: There is a large and increasing burden of LLBC, especially amongst older Australians. Given the frequent recurrence, long term morbidity and association with increased mortality, efforts to reduce primary episodes and minimise the risk of recurrence should be a priority.

Disclosure of Interest Statement: This study was funded from internal funds held by the Department of Infectious Diseases at Fiona Stanley Hospital. No pharmaceutical grants were received in the development of this study.
A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL OF IBUPROFEN COMPARED WITH PLACEBO FOR UNCOMPLICATED CELLULITIS OF THE UPPER OR LOWER LIMB

Joshua S Davis¹,², Carol Mackrow³, Paula Binks¹, Wendy Fletcher³, Pascale Dettwiller⁴, Catherine Marshall³, Jane Day⁵, William Pratt⁵, Steven YC Tong¹,⁶

1. Global and Tropical Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, NT, Australia
2. Department of Infectious Diseases, John Hunter Hospital, Newcastle, NSW, Australia and the University of Newcastle
3. Hospital in the Home Program, Royal Darwin Hospital, Darwin, NT, Australia
4. Katherine Rural Clinical School, Flinders University, Katherine, NT
5. Hospital in the Home Program, Shoalhaven Hospital, Nowra, NSW, Australia
6. Victorian Infectious Diseases Service, the Royal Melbourne Hospital, and the University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia

Introduction: Cellulitis is a common skin and soft tissue infection resulting in substantial inflammation that may take weeks to resolve despite appropriate antibiotics. It is unclear whether the adjunctive use of non-steroidal anti-inflammatory drugs hastens the resolution of inflammation in patients with cellulitis.

Methods: We conducted a double-blind randomised controlled trial comparing ibuprofen 400mg three times daily orally for five days with identical placebo in adults with uncomplicated cellulitis of the upper or lower limb, treated with intravenous cefazolin via an outpatient parenteral antibiotic treatment service at one of two Australian hospitals. Participants were assessed twice daily by a study nurse. The primary outcome measure was the proportion of patients with regression of inflammation 48 hours following the first effective dose of parenteral antibiotics. This trial was registered (ANZCTR 12611000515998).

Results: Fifty-one patients were enrolled; 48 had sufficient data available to be included in the modified intention to treat analysis. Inflammation had begun to regress at 48 hours in 20 participants (80%) in the ibuprofen group compared with 15 (65%) in the placebo group (Absolute risk difference +15% [95% CI -10% to +40%]), p>0.05). There was no significant difference in any of the secondary outcomes. Ibuprofen treatment appeared safe, with no patients developing renal impairment or necrotising fasciitis.

Conclusions: This trial demonstrated no significant benefit of adjunctive ibuprofen in adults with uncomplicated cellulitis. The trial was powered to detect a large effect, and hence it is unclear if the 15% absolute increase in the primary endpoint in the ibuprofen group was attributable to chance or not.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study and none of the authors have any conflicts of interest to declare.
ERTAPENEM FOR OSTEOARTICULAR INFECTIONS IN OBESE PATIENTS: A PHARMACOKINETIC STUDY OF PLASMA AND BONE CONCENTRATIONS

Authors:
Chambers J T¹, Page-Sharp M², Salman S³, Dyer J¹, Davis T³, Batty K T², Manning L³,⁴

¹ Department of Infectious Diseases, Fiona Stanley Hospital, Murdoch, Western Australia
² School of Pharmacy, Curtin University, Bentley, Western Australia
³ School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia
⁴ Harry Perkins Research Institute, Fiona Stanley Hospital, Murdoch, Western Australia

Introduction: Ertapenem is used off-label to treat osteoarticular infections, but there are few pharmacokinetic (PK) data to guide optimal dosing strategies or the probability of PK-pharmacodynamic target attainment (PTA) in this patient group who may be obese and/or frail with multiple co-morbidities.

Methods: Participants undergoing elective joint arthroplasty or lower limb and/or partial foot amputation received a dose of intravenous ertapenem prior to surgery, in addition to routine perioperative antibiotic prophylaxis. Plasma samples were collected at 8 time-points over 24 h and at least one bone sample per patient was collected at varying time-points post-infusion. Ertapenem concentrations in plasma and bone were measured using liquid-chromatography/mass-spectroscopy and analysed using non-linear mixed effects PK modelling.

Results: Plasma and bone concentrations were obtained from 10 participants. The final population PK model showed that a fat free body mass was the most appropriate body size adjustment. The model also demonstrated a strong effect of frailty on clearance with a doubling of plasma half-life in patients with moderate/severe frailty. Ertapenem equilibrated rapidly into bone, but concentrations were 40-fold higher in plasma and highly variable between individuals. Simulations demonstrated that the PTA for free plasma concentrations was ≤50% when the minimum inhibitory concentration (MIC) was ≥0.5mg/L. In bone, the PTA was ≤55% when the MIC was ≥0.25mg/L.

Conclusion: Local bone and free plasma concentrations appear adequate for osteoarticular infections where Enterobacteriaceae are the main causative pathogens, but for Staphylococcus spp., Bacteroides fragilis and Acinetobacter spp., standard dosing is unlikely to result in adequate PTA. Frailty may alter ertapenem PK.

Disclosure of Interest Statement: No pharmaceutical grants were received in the development of this study.
Introduction: Studies have demonstrated high rates of bacterial colonisation of hand-held mobile devices in hospital settings, but have not established a molecular epidemiological link between organisms colonising mobile devices and those causing disease in patients.

Methods: Over a 12-week period, all routine clinical isolates defined as multi-drug resistant (MDR) (MRSA, VRE and ESBL producing Enterobacteriaceae) were prospectively collected and stored. During the same time period, the mobile devices of all medical staff were swabbed. Swabs were cultured for resistant organisms, with identification by matrix-assisted laser desorption ionisation. Illumina whole genome sequencing was used to assess the genetic relatedness of MDR organisms found on phones and in clinical isolates.

Results: 90 MDR clinical isolates were collected from patients. A total of 45 mobile devices used by medical staff were swabbed. Of these, two phones cultured MRSA and one phone cultured A. baumannii. WGS was performed on the 17 MRSA and Acinetobacter isolates from phones and patient isolates. The two MRSA isolates from the phones were genetically similar, but were genetically different to all the clinical isolates. These two phones were spatio-temporally linked and came from the same 14-bed area of the ICU. All four MDR Acinetobacter isolates were genetically different.

Conclusion: To the authors' knowledge, this is the first study to assess the molecular epidemiological link between MDR organisms found on mobile devices and those from patients. Despite MDR organisms being able to colonise physician mobile devices, these organisms were genetically different to those seen in patient isolates during the same time period.

Figure 1. MRSA dendrogram
Disclosure of Interest Statement:
There are no disclosures of interest to declare from any contributor to this research project.
POSTEXPOSURE IMMUNOPROPHYLAXIS USING THE HUMAN MONOCLONAL ANTIBODY m102.4 FOLLOWING HUMAN EXPOSURE TO EQUINE HENDRA VIRUS INFECTION

Authors:

Introduction: Hendra virus is associated with a significant mortality rate in both equine and human hosts. Human exposure to infected horse respiratory secretions or blood products carries a high risk of infection. There is no established medical therapy to treat or prevent this disease in humans. The human monoclonal antibody m102·4 has been shown to be an effective postexposure prophylactic agent in animal models, for both Hendra and Nipah virus.

Methods: Retrospective data was collected from ten patients with high level exposure to Hendra virus who received m102.4. The data collected included patient demographics, drug pharmacokinetic data, adverse reactions and serology/biochemical data from a time period between 2014 to 2016.

Results: We describe ten cases where humans with high level exposure to Hendra virus have received m102·4. All of these patients remained disease free without clinical or serological evidence of Hendra virus infection. There were minimal associated adverse reactions.

Conclusion: The human monoclonal antibody m102·4 may play a role in preventing Hendra virus infection in humans. This is concordant with the data demonstrated in animal models and highlights the potential role for preventing and treating both Hendra and Nipah virus infection in humans.

Disclosure of Interest Statement: No conflicts of interest to declare.
AN INTEGRATED FIRST-IN-HUMAN STUDY OF THE NOVEL LONG-ACTING ANTIMALARIAL DSM265 DEMONSTRATES A FAVOURABLE SAFETY AND TOLERABILITY PROFILE, AND PREDICTS A CLINICALLY EFFICACIOUS DOSE FOR TREATMENT OF FALCIPARUM MALARIA

Authors:
McCarthy JS1,4, Lotharius J2, Rückle T2, Chalon S2, Phillips MA3, Elliott S4, Sekuloski S1, Griffin P1,4, Ng CL5, Fidock DA5, Marquart L1, Williams NS3, Gobeau N2, Bebrevska L2, Rosario M6, Marsh K7, Möhrle JJ2

1QIMR Berghofer MRI; 2Medicines for Malaria Venture; 3University of Texas Southwestern Medical Center, Dallas, TX, USA; 4Q-Pharm Pty Ltd, Herston, Australia; 5Columbia University, NY, NY, USA; 6Takeda Pharmaceuticals; 7AbbVie, Chicago, IL, USA.

Introduction: DSM265 is a novel antimalarial that selectively inhibits Plasmodium dihydroorotate dehydrogenase (DHODH), an enzyme essential for pyrimidine biosynthesis. In this first-in-human study, we investigated its safety, tolerability and pharmacokinetics, and tested its in vivo activity against P. falciparum.

Methods: Part 1 was a single ascending dose (25–1200 mg), double-blind, randomised, placebo-controlled study; part 2 was an induced blood-stage malaria (IBSM), open-label, randomised, active-comparator controlled study, where participants were inoculated with P. falciparum and treated with a single dose of DSM265 (150 mg) or mefloquine (10 mg/kg).

Results: In part 1, 73 participants were enrolled (DSM265, n=55; placebo, n=18). In part 2, nine participants were enrolled (DSM265, n=7; mefloquine, n=2). DSM265 showed a good safety profile, with no drug-related serious or severe adverse events. The most common drug-related adverse event was headache. The mean plasma C\text{max} ranged between 1.3 and 34.8 \mu g/mL across doses tested; median T\text{max} was between 1.5 and 4 h; mean elimination half-life was 86 - 118 h. The DSM265 (150 mg) parasite reduction ratio was 1.55 (95% CI 1.42-1.67), with a corresponding parasite clearance half-life of 9.4 h (95% CI 8.7-10.2). The median MIC in blood was 1.04 \mu g/mL (range 0.55-1.50), resulting in a predicted single efficacious dose of 340 mg.

Conclusion: This is the first report of an integrated Phase 1 and IBSM study in antimalarial drug development. Its good safety profile, long elimination half-life and antimalarial effect support its development as partner drug in a single-dose antimalarial combination treatment.

Disclosure of Interest Statement: This study was funded by the Global Health Innovation and Technology Fund, Bill & Melinda Gates Foundation, Wellcome Trust, UK Department of International Development.
A NOVEL ASSAY TO ASSESS IMMUNE COMPROMISE AND RISK OF INFECTION POST HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Authors:
Douglas AP\textsuperscript{1,5}, Yu J\textsuperscript{2,4}, Szer J\textsuperscript{3,4}, Ritchie D\textsuperscript{3,4}, Slavin MA\textsuperscript{1,4,5}, Sasadeusz J\textsuperscript{1,4}, Visvanathan K\textsuperscript{2,4}

1. Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Australia
2. Immunology Research Centre, St Vincent’s Hospital, Melbourne, Australia
3. Department of Clinical Haematology and Bone Marrow Transplant Service, Royal Melbourne Hospital, Melbourne, Australia
4. University of Melbourne, Melbourne, Australia
5. Peter MacCallum Cancer Centre, Melbourne, Australia

Introduction: Managing immunosuppression in patients post allogeneic haematopoietic stem cell transplantation (alloHSCT) is challenging. Excessive immunosuppression can be complicated by infection, while inadequate immunosuppression can result in graft versus host disease (GVHD). An accurate method to assess immune status in the setting of HSCT is lacking. Unlike other commercially available assays which assess the adaptive immune response alone, QuantiFERON Monitor\textsuperscript{®} (QFM) measures interferon-gamma (IFN-\gamma) release from whole blood following incubation with both innate (R848) and adaptive (CD3 antibody) immune stimulants.

Methods: Whole blood samples were prospectively collected from alloHSCTs at conditioning and days 10, 30, 60, 90, 120 and 180 and assayed by the QFM test. IFN-\gamma levels were plotted against time post alloHSCT and correlated to episodes of infection and GVHD.

Results: 40 patients were enrolled in the study (68\% male; median age 47 years; 33\% myeloablative, 67\% reduced intensity conditioning). IFN-\gamma levels rose steadily over the first 180 days post transplantation and there was a trend between those with and without acute or chronic GVHD although this did not reach statistical significance. IFN-\gamma levels were statistically significantly lower in those with active infection compared to those without (p=0.028 using logistic regression with IFN-\gamma as a continuous variable).

Conclusion: Immune function, as measured by the QFM assay, appears to steadily increase over the first 180 days post alloHSCT. Lower IFN-\gamma levels correlated with risk of infection. This assay is promising as a means to monitor immune recovery and predict risk of infection and hence tailor immunosuppression and prophylaxis accordingly.

Disclosure of Interest Statement: No conflicts to disclose.
DEVELOPMENT OF A MOBILE LABORATORY FOR SUDDEN ONSET DISASTERS

Authors:
Marr I¹, Baird RW², Quilty S³, Coatsworth N⁴

¹National Critical Care and Trauma Response Centre, Level 8 Royal Darwin Hospital, NT, Australia, ²Territory Pathology, Royal Darwin Hospital, Darwin, Australia, ³Department of Medicine, Katherine District Hospital, Katherine, Australia, ⁴Infectious Disease Unit, The Canberra Hospital, Canberra, Australia.

Introduction: Sudden onset disasters (SOD) require a rapid medical response to limit ongoing death and injury. As part of Australia’s preparedness, the National Critical care and Trauma Response centre is equipped to deploy a surgical field hospital to both national and international disasters. We developed a mobile field laboratory to enhance the clinical services offered in SOD.

Objectives: Design and trial a mobile laboratory unit for use in Sudden Onset Disasters (SOD) that meets a WHO Emergency Medical Team (EMT) 2 standard.

Methods: Using RT-PCR FilmArray®, iSTAT®, HemoCue301®, HemoCueWBC® and portable microscopy a mobile laboratory was developed with field appropriate standard operating procedures meeting ISO guidelines. A 12 day deployment to a remote Northern Territory Hospital (Katherine) with limited laboratory capacity tested functionality and reproducibility of results with validation against current NATA accredited results.

Results: Over the study period 11 RT-PCR FilmArray multiplex tests provided 9 positive and 3 negatives, including blood culture (n=4), gastrointestinal (n=4), respiratory multiplex screens (n=3). All results were confirmed with NATA standardised testing. There were 20 WBC HemoCue and HemoCue301 tests performed, with non-significant differences (p>0.05) on each parameter when compared to Sysmex XN 550. iSTAT tests were run in parallel against Vitros 250 showing non-significant differences for CHEM4 (n=10), CG8 (n=10) and TnI (n=5) cards, p>0.05.

Conclusions: This small pilot trial shows a EMT2 mobile field laboratory can provide reproducible results when compared to NATA accredited testing in an isolated Northern Territory location.

Disclosure of Interest Statement: Nothing to disclose.
A SMARTPHONE-BASED SYSTEM FOR MEASURING AND SUPPORTING ADHERENCE TO MEDICATION

Authors:
Molton JS1,2, Pang Y1, Wang ZC2, Qiu BQ2, Wu P2, Rahman-Shepherd A1, Ooi WT2, Paton NI1,2

1 National University Health System, Singapore, 2 National University of Singapore

Introduction: Suboptimal adherence for infectious diseases such as tuberculosis (TB) results in poor clinical outcomes and ongoing infectivity. Directly Observed Therapy (DOT) has a number of limitations. We aimed to develop and evaluate a smartphone-based system to facilitate remotely observed therapy rather than in-person observation.

Methods: We developed an integrated smartphone and web-based system to provide medication reminders and facilitate video recording of pill ingestion, for upload and later review.

We evaluated the system in a single arm, prospective study. Healthy volunteers age ≥21 were instructed to take a supplement pill once, twice or three-times a day, for 2 months, and to video each pill taking episode using the system. Adherence was measured by the smartphone system and by pill count.

Additionally we developed face and image recognition modules to automate the verification process, and a conditional cash transfer module to encourage adherence by rewarding successful video uptake with small cash incentives.

Results: 42 eligible participants were recruited (median age 24). Overall median estimated participant adherence by MIST was 90.0%, similar to that obtained by pill count (93.8%). There was a good relationship between adherence as measured by the system and by pill count (Spearmans rs 0.66, p<0.001).

Conclusions: We have demonstrated the feasibility, acceptability and accuracy of a smartphone-based adherence support and monitoring system that has applicability for infectious diseases such as TB and HIV.

Disclosure of Interest Statement: This study was funded by National University of Singapore. No pharmaceutical grants were received in the development of this study. All authors declare no conflicts of interest.
IMPLEMENTING MOBILE HEALTH FOR TUBERCULOSIS CARE IN SYDNEY: EXPERIENCE WITH VIDEO DIRECTLY OBSERVED THERAPY

Authors:
Chapman, S1 Holzman, S2,3, Rios KC2,4, Shah, M2

1 Western Sydney University, New South Wales, Sydney, Australia
2 Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
3 Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
4 emocha Mobile Health, Inc., Baltimore, Maryland, USA

Introduction: Tuberculosis (TB) remains a disease of public health interest in Australia, with over 1,300 cases annually. Directly observed therapy (DOT) remains the standard of care in New South Wales, but is logistically challenging and resource intensive for patients and providers. Video-based DOT represents a promising potential alternative methodology to ensure high rates of treatment adherence and completion. We evaluated an asynchronous video-DOT application, miDOT, that allows patients to securely record and transmit videos of themselves taking medication to a secure website, where providers can view and verify adherence at their convenience.

Methods: We conducted a prospective implementation study of video-DOT at the Parramatta Chest Clinic in Western Sydney. All TB patients were eligible, and were enrolled at the discretion of the TB clinic providers. Upon enrollment, participants utilized the video-DOT system to document adherence to treatment. The primary outcome was percentage of total doses that were verified by observation (i.e. DOT), comparing the time period before (i.e. in-person DOT) and after enrollment (i.e. miDOT).

Results: 19 participants uploaded 1389 videos documenting treatment (mean 73 videos/person, most frequently with daily dosing schedule). The proportion of observed (i.e. verified in-person, or uploaded video) treatment doses increased from a median of 66% (IQR 56%-73%) prior to enrollment (pre-miDOT period) to a median of 95% using miDOT (IQR 90%-98%, p=0.0003).

Conclusion: Asynchronous video-DOT is an effective tool for expanding capacity to perform DOT in TB clinics, with high adherence. Additional research is needed to evaluate generalizability of findings in Australia.

Disclosure of Interest Statement: Maunank Shah is the inventor of the miDOT system, which is licensed to emocha Mobile Health Inc. Katrina Rios is an employee of emocha mobile health Inc. emocha Mobile Health provided the miDOT system without charge to the Paramatta Chest Clinic for the duration of the study and had no role in the study design, data collection or analysis. Scott Chapman (PI) has no conflicts and provided oversight of the study and data abstraction. Samuel Holzman has no conflicts to disclose and led data analysis.
AN EVIDENCE-BASED APPROACH TO UNDERSTANDING THE TRANSMISSION CYCLE AND RISKS OF COXIELLA BURNETTI INFECTION IN COMPANION ANIMALS

Authors:
Bosward KL¹, Norris JM¹

¹ Sydney School of Veterinary Science (SSVS), Faculty of Science, University of Sydney

Introduction: Confirmed cases of Q fever in veterinary personnel in small animal practice and companion animal handlers such as cat breeders have illustrated that cats and dogs, especially periparturient ones, can be a source of transmission. Determining the extent of this risk to humans and the source of transmission to companion animals is vital and requires a multifaceted approach.

Methods: Studies at SSVS have included cross-sectional surveys of knowledge attitudes and practices of cat breeders, veterinarians, veterinary nurses; seroprevalence studies in cats and dogs from a range of subpopulations (pet, breeding, feral/stray, camp dogs in remote Indigenous communities); and molecular studies of raw milk and pet meat to determine the presence of C.burnetti DNA.

Results: Cat breeders and veterinary nurses in Australia reported low levels of knowledge and awareness of Q fever disease and vaccination, resulting in a poor vaccination rates. Seroprevalence studies showed increased evidence of prior/current infection in breeding cats and camp dogs in indigenous communities. Pilot studies investigating the potential sources of C.burnetii in raw pet meat and unpasteurized ‘cosmetic bath’ milk has found modest concentrations of C. burnetii DNA in bulk-tank samples of unpasteurised ‘cosmetic bath’ milk collected from health food stores and raw meat containing kangaroo from pet food distributors.

Conclusion: Further carefully constructed cross-sectional and multi-disciplined studies with an open mind and attention to detail are required to follow our research leads to date in this complex area, if we are to truly understand the cycle of transmission of C.burnetii in animals and humans.

Disclosure of Interest Statement: The authors have been funded by Australian Companion Animal Health Foundation, NH&MRC and the Canine Research Fund. No pharmaceutical grants were received in the development of these studies.
Introduction: Rheumatic heart disease (RHD) causes significant morbidity and mortality in school aged children in Timor-Leste, but its prevalence has not been evaluated or described. We conducted the first echocardiography-based screening study to determine the prevalence of RHD in school-aged Timorese children.

Methods: School students were enrolled from schools in Dili (urban) and Ermera (rural) districts in Timor-Leste, using opt-out consent. Demographic and anthropometric data were collected and all students had a limited echocardiogram looking for evidence of RHD. RHD was classified as borderline or definite, according to World Heart Federation criteria. Patients with RHD were entered into a register for ongoing secondary prophylaxis, with the first dose of benzathine penicillin G administered on the day of the study.

Results: 1413 children were screened; 739 (52%) were girls and the median age was 12 years (range 4-24). The prevalence of definite RHD was 1.8% and borderline 1.6% (total 3.4%). Borderline or definite RHD was more common in Ermera than Dili though the difference was not statistically significant (4.1% vs 2.2%; p=0.07). Definite RHD was more prevalent in girls than boys (2.8% vs 0.7%; p<0.01). Congenital heart disease was identified in 20 children (1.4%). Of the 26 definite RHD cases, 23 (88%) received education and a first dose of BPG during the study.

Conclusion: RHD is prevalent in Timor-Leste, with some of the highest rates observed in the world. Girls are affected more commonly than boys. Community engagement is essential to ongoing follow up and effective delivery of secondary prophylaxis.

Disclosure of Interest Statement: This study was sponsored by East Timor Hearts Fund, Menzies School of Health Research and RhEACH, Telethon Kids Institute. In-country partners include Bairo Pite Clinic and St John of God Healthcare Timor-Leste. A donation of LA-Bicillin for treatment of children with rheumatic heart disease was made by Pfizer. Pfizer has no role in the design, implementation or analysis of the study.
RESPONDING TO THE OUTBREAK OF DRUG-RESISTANT TUBERCULOSIS IN DARU, SOUTH FLY DISTRICT, WESTERN PROVINCE, PNG

Authors: Majumdar S1, Chan G1, Adepojibi T1, Lawson J1, Wallis P1, Huang K1, Ronnachit A1, Wallis A1, O’Brien D1, Graham S1,

1Burnet Institute, Melbourne, Australia.

Introduction: There is a major outbreak of drug-resistant tuberculosis (DR-TB) that is having a devastating effect on the population of the South Fly District (SFD) of the Western Province of Papua New Guinea (PNG) with the majority of cases resident on Daru Island. The local epidemic is characterised by high rates of primary transmission of DR-TB, with a population incidence among the highest ever recorded (503 per 100 000 in 2016). Operational research (OR) to test interventions and innovations that will increase the efficiency of the response is needed.

In 2014, the Government of PNG convened an emergency response taskforce for DR-TB hotspots, with significant support from the Australian government. The Burnet Institute’s Reducing the Impact of Drug-Resistant TB (RID-TB) in Western Province supports the design and implementation of an effective SFD TB program, working in partnership with the Provincial Health Office (PHO), Daru General Hospital (DGH), the National Department of Health (NDoH), World Vision PNG and the World Health Organisation.

Significant progress has been made by the SFD TB program and partners since 2014 through health and community systems strengthening that has resulted in an improvement in case detection and treatment outcomes for all forms of TB. Through the Tropical Disease Research Regional Collaboration Initiative (TDRRCI), Burnet will partner with PNG institutions to develop an OR framework using the Structured Operational Research Training (SORT-IT) model. This session will provide an outline of the response, progress, and challenges and describe the SORT-IT model.

Disclosure of Interest Statement: The RID-TB Project is funded by the Australian Government’s Department of Foreign Affairs and Trade. No other relevant disclosures.
USING NASOPHARYNGEAL CARRIAGE SURVEILLANCE IN CHILDREN HOSPITALISED WITH ACUTE RESPIRATORY INFECTION TO DETERMINE THE PNEUMOCOCCAL CONJUGATE VACCINE COVERAGE REQUIRED FOR INDIRECT IMMUNITY

Authors:

1 Pneumococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia.
2 Department of Paediatrics, University of Melbourne, Melbourne, Australia.
3 National Immunization Programme, Ministry of Health, Vientiane, Lao PDR.
4 Ministry of Health, Ulaanbaatar, Mongolia.
5 School of Medicine, University of Western Australia, Perth, Australia.
6 Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea.
7 Wellcome Trust Research Unit, Lao-Oxford-Mahosot Hospital, Vientiane, Lao PDR.
8 Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, United Kingdom.
9 World Health Organization, Vientiane, Lao PDR.
10 Institute for Infection and Immunity, St George's- University of London, London, United Kingdom.
11 BUGS Bioscience, London Bioscience Innovation Centre, London, United Kingdom.
12 Regional Office for the Western Pacific, World Health Organization, Manila, Philippines.
13 Telethon Kids Institute, University of Western Australia, Perth, Australia.
14 Centre for International Child Health- Dept. of Paediatrics, The University of Melbourne, Melbourne, Australia.
15 International Child Health, Menzies School of Health Research, Darwin, Australia.
16 Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom.
17 Department of Microbiology and Immunology, University of Melbourne, Melbourne, Australia.
18 Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom.

Introduction: Pneumococcal conjugate vaccines (PCVs) prevent disease through direct protection of vaccinated individuals, and indirect protection by reducing nasopharyngeal (NP) carriage and transmission of vaccine-type pneumococci. While the indirect effects of PCV vaccination are well described, the PCV coverage required to achieve the indirect effects is unknown. We will determine this using hospital-based NP pneumococcal carriage surveillance.

Methods: Surveillance includes children aged 2-59 months admitted to participating hospitals at three sites with acute respiratory tract infection. Thirteen-valent PCV (PCV13) status is obtained from written records. An NP swab is collected according to standard methods and examined by lytA qPCR, with positives serotyped by microarray. PCV13 coverage is determined using administrative data or community survey.

Results: In Lao PDR, Papua New Guinea, and Mongolia, we have recruited 973, 204, and 240 children, respectively. For each site, we will present monthly PCV13 carriage rates. In Laos PDR, where PCV13 coverage is <50%, PCV13 carriage rates are declining among vaccinated children (direct effects) but not unvaccinated children (indirect effects, figure 1).
Data will also be pooled across sites to examine relationships between PCV13 coverage and carriage.

**Conclusion:** As PCV13 coverage increases, we hypothesise that PCV13 carriage to decline in vaccinated and unvaccinated individuals. These results will inform vaccine policy makers about the PCV coverage required to maximise the effects of PCV.

**Disclosure of Interest Statement:** This study received funding from the Bill and Melinda Gates Foundation. No pharmaceutical grants were received in the development of this study.