

S11 - Molecular aspects of antimicrobial resistant *Neisseria gonorrhoeae*

S11.1 REAL-TIME PCR DETECTION OF *N. GONORRHOEAE* RESISTANCE: WHERE ARE WE NOW?

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Ongoing emergence and spread of *Neisseria gonorrhoeae* antimicrobial resistance is of global concern and was recently designated an “urgent threat” by the United States Centres for Disease Control and Prevention. Australia is not immune to the *N. gonorrhoeae* resistance problem as highlighted by the first report of a ceftriaxone-resistant strain from Australia in 2014. Enhancing antimicrobial resistance (AMR) surveillance strategies to advance detection of gonococcal AMR is a priority. Whilst bacterial culture-based methods remain the most definitive means of assessing *N. gonorrhoeae* AMR, there has been decreasing availability of cultured isolates for AMR susceptibility testing owing to increased use of nucleic acid amplification test (NAAT)-based methods for gonorrhoea diagnosis. Molecular AMR surveillance tools have the potential to overcome these problems. In particular, polymerase chain reaction (PCR)-based methods targeting key genetic markers of resistance can facilitate rapid, more intense sampling, for *N. gonorrhoeae* strains of public health importance following NAAT-based diagnosis. This presentation will discuss the development of real-time PCR methods for *N. gonorrhoeae* AMR detection and in doing so will highlight potential technical obstacles that may impinge upon assay design and performance.

S11.2 EFFLUX PUMPS IN *NEISSERIA GONORRHOEAE* – CAUSE OF RESISTANCE AND TARGETS FOR THERAPEUTICS AND VACCINE?

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Neisseria gonorrhoeae is the cause of the sexually transmitted infection termed gonorrhoea, which afflicts over 100 million people worldwide each year. Since the mid-1940s, beginning with the availability of penicillin (Pen), antibiotic therapy has been the mainstay for curing infection and halting the spread of the gonococcus in the community. Unfortunately, gonococci developed resistance to Pen and many other antibiotics that were brought into clinical practice to counter act the growing problem of Pen (and other antibiotics) resistance. With the recent emergence of strains expressing resistance to the third-generation cephalosporins (cefixime and ceftriaxone) or other important antibiotics (macrolides and fluoroquinolones) there is considerable fear that without new antibiotics, gonorrhoea will become more difficult to treat; indeed, some have warned of the possibility of untreatable infections. In order to address this public health crisis of antibiotic resistant gonococci, it is essential that new bacterial targets are identified so as to facilitate the development of novel therapeutic drugs. I will discuss the role of the MtrC-MtrD-MtrE efflux pump in the development of gonococcal resistance to antibiotics and host-derived antimicrobials (e.g., cationic antimicrobial peptides). These phenotypes are

augmented in gonococcal strains that have mutations that result in enhanced transcription of the *mtrCDE* efflux pump gene complex. I will provide evidence that this efflux pump is critical for the ability of gonococci to resist certain antibiotics as well as surviving during infection. Against this background, I will propose that this pump offers new targets for drug development (efflux pump inhibitors) and vaccine development to combat antibiotic resistant gonococcal strains and to prevent infections.

S11.3 USE OF WHOLE GENOME SEQUENCING TO DETERMINE THE PROBABILITY OF ANTIMICROBIAL RESISTANCE IN *NEISSERIA GONORRHOEAE*

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Neisseria gonorrhoeae has demonstrated remarkable ability to rapidly develop antimicrobial resistance to each antimicrobial class used for therapy including the currently recommended class of antimicrobials, the cephalosporins. Emerging resistance to cephalosporins will severely complicate treatment of gonorrhoea. Advanced Molecular Detection approaches, such as whole genome sequencing to determine mechanisms of resistance, have the potential to advance our understanding of gonorrhoea. To date, we have sequenced >1,000 genomes from *N. gonorrhoeae* isolates with elevated cefixime or azithromycin minimum inhibitory concentrations (MICs) or resistance to previously recommended antimicrobials, and isolates collected from multiple geographic sites to accomplish the following objectives: (1) to identify mutations that confer antimicrobial resistance or increased MICs; (2) to inform the development of molecular assays for resistance determinants through insights gleaned from WG from which point-of-care assays for resistance markers will be developed. Such assays will change the paradigm of gonorrhoea treatment. Use of real-time results on the presence or absence of resistance determinants will allow clinicians to personalise treatment for patients, and prevent inadvertent use of agents that are no longer routinely recommended because of resistance. Such assays can also substantially expand the reach of surveillance of antimicrobial resistance and allow public health officials to rapidly detect and respond to outbreaks of resistant strains; and (3) to develop and maintain a microbial library, a web-accessible and searchable database that will include bacterial and viral genomic sequences and associated meta-data, such as basic de-identified demographic characteristics of patients and phenotypic susceptibility data. In the long term, knowledge of the genetic mechanisms responsible for resistance or decreased susceptibility in *N. gonorrhoeae* gained from sequencing may translate into the identification or development of new therapeutic agents.

S12 – Sexual health issues for Indigenous youth in Australia and New Zealand

Indigenous peoples worldwide suffer disproportionately poor sexual and reproductive health. This symposium will describe the sexual and reproductive health issues for Indigenous youth in Australia and New Zealand. Given that both Indigenous populations are demographically young in age compared to other ethnic groups, they require strategies that address their unique developmental and cultural needs. We will draw on data from