P653 MODELING THE IMPACT OF PARTIALLY EFFICACIOUS GONORRHEA VACCINES

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Background Gonorrhea is one of the most common sexually transmitted infections. Current control measures are inadequate and are threatened by the emergence of gonococcal antimicrobial resistance. This emerging challenge calls for a vaccine which will reduce the circulation and transmission of this infection, and thus emergence of drug-resistant strains in the population.
Methods A novel deterministic compartmental mathematical model of the heterosexual transmission of *Neisseria gonorrheae* was constructed to assess the impact of a pre-exposure (prophylactic) vaccine.
Results Catch-up vaccination with a prophylactic vaccine introduced in 2020, with vaccine efficacy in reducing susceptibility of 50% and vaccine coverage of 80% at 2030, reduced gonorrhea prevalence by 29% by 2030, 34% by 2040, and 37% by 2050. The number of vaccinations needed to avert one infection was 31 in 2030, 24 in 2040, and 13 in 2050. Through age group prioritization, the number of vaccinations needed to avert one infection (in 2030) ranged from 24 for the 15–19 years age group, to 50 for the 45–49 age group. Through risk group prioritization (also in 2030), prioritizing the highest sexual risk group (such as female sex workers) was most effective with only 1 vaccination needed per infection averted. Meanwhile, for the lowest sexual risk group (general population), 110 vaccinations were needed per infection averted.
Conclusion Even a partially efficacious gonorrhea vaccine can considerably reduce the prevalence of infection. Vaccine effectiveness is optimized by targeting high sexual risk groups and young individuals.
Disclosure No significant relationships.

P654 CLONAL SPREAD OF AZITHROMYCIN RESISTANT *NEISSERIA GONORRHOEAE* IN CANADA, 2014–2017

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Background *Neisseria gonorrhoeae* have acquired resistance to many antimicrobials including third generation cephalosporins and azithromycin, the current co-therapy recommended by the Canadian STI guidelines for gonorrhea treatment. Resistance to azithromycin and molecular sequence types were determined for *N. gonorrhoeae* circulating in Canada.
Methods From 2014–2017, *N. gonorrhoeae* isolates and data collected by Canadian provincial public health laboratories was submitted to the National Microbiology Laboratory (N=12,776) for *N. gonorrhoeae* multi-antigen sequence typing (NG-MAST) and azithromycin MIC determination (resistance MIC≥2.0 mg/L) by agar dilution, as described by the Clinical Laboratory Standards Institute.
Results Azithromycin resistance was identified in 3.3% (127/3,809), 4.7% (198/4,190), 7.2% (326/4,538) and 11.6% (616/5,290) of *N. gonorrhoeae* in 2014, 2015, 2016 and 2017, respectively, a significant increase between 2014–2017 ($p<0.001$). MICs ranged from 2-≥256 mg/L. The most common sequence types identified in the azithromycin resistant isolates include: 2014; ST10451 (n=40), ST10567 (n=38) and ST11765 (n=10); 2015; ST12302 (n=110), ST10451 (n=34) and ST9047 (n=23); 2016: ST12302 (n=240), ST15750 (n=27) and ST10451 (n=10); 2017; ST12302 (n=375), ST14698 (n=119) and ST15750 (n=17). ST12302 was newly recognized in 2015 and identified in only two provinces, Quebec and Ontario, but spread to Alberta (n=10) and British Columbia (n=16) in 2017. ST12302 is associated with low-level azithromycin resistance (MIC=2 mg/L). ST10451 emerged in 2014 in Quebec, Ontario and Alberta and was also identified in 2015–2017. ST10451 is related to ST1407 (differing by 1 bp) which is an internationally-recognized epidemic strain, harboring cephalosporin resistance.
Conclusion Azithromycin resistance in *N. gonorrhoeae* is established and spreading in Canada, increasing significantly between 2014 and 2017. This exceeds the 5% level at which the WHO states an antimicrobial should be reviewed as an appropriate treatment. Continued surveillance of antimicrobial susceptibilities and sequence types of *N. gonorrhoeae* is necessary to identify clusters, inform treatment guidelines and mitigate the impact of resistant gonorrhea.
Disclosure No significant relationships.

P655 MOLECULAR EPIDEMIOLOGY ASSOCIATED WITH RESISTANCE IN *NEISSERIA GONORRHOEAE* ISOLATES FROM SOUTH BRAZIL DURING 2008–2016

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Background *Neisseria gonorrhoeae* (NG) has an extraordinary ability to develop resistance to all antimicrobials used for its treatment. This study analysed molecular determinants of antimicrobial resistance and NG-MAST of 153 NG isolates collected at Florianopolis metropolitan area during 2008–2016.
Methods Minimal Inhibitory Concentration (MIC) was determined by agar dilution and the molecular epidemiology was evaluated by NG-MAST.
Results Resistance was observed to penicillin (PEN) (26.1%), tetracycline (TET) (41.2%), ciprofloxacin (CIP) (52.3%) and azithromycin (AZT) (5.2%). All isolates were susceptible to cefixime (CFX) and ceftriaxone (CRO). However, 8.5% of isolates had MIC=0.125 mg/L for CFX, one log below the resistance cut-off point (EUCAST). β-lactamase production was detected in 12.4% of isolates and one of them carried the $bla_{\text{TEM-135}}$ allele. The American or Dutch *tet*M gene were carried by 5.2% of the isolates. Mutations in the QRDR were observed in 87.5% of isolates resistant to CIP. NG-MAST showed 64 different sequence types (STs), including 19 novel STs. ST225, ST2992, ST1582, ST338, ST1407, ST2202 and ST6827 were most prevalent. G225 genogroup was associated with resistance to CIP ($p<0.001$), PEN ($p=0.016$) and TET

(p<0.001) whereas G1407 genogroup was associated with MIC=0.125 mg/L for CFX (p=0.001), resistance to CIP, PEN (p=0.016) and TET (p<0.001). Isolates that shared the same *tbp*B 29 allele were associated with resistance to AZT (p=0.008) and PEN (p=0.035). ST338 was associated with bla_{TEM-1} gene (p<0.001) and *tet*M (p=0.006), whereas the cluster sharing the same *tbp*B 137 allele was associated with *tet*M gene.

Conclusion This study showed high rates of resistance to PEN, TET and CIP associated with persistence and dissemination of gonococcal strains resistant to CIP and plasmid resistance to PEN and TET. Despite the high resistance profile to CIP, the treatment recommended to the south region of Brazil was the association of CIP-AZT until 2017, when the national recommendation changed it to CRO-AZT.

Disclosure No significant relationships.

P656 GYRA AND PARC MUTATIONS IN FLUOROQUINOLONE-RESISTANT *NEISSERIA GONORRHOEAE* ISOLATES FROM KENYA

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Background Phenotypic fluoroquinolone resistance was first reported in Western Kenya in 2009 and later in Coastal Kenya and Nairobi. Until recently gonococcal fluoroquinolone resistance mechanisms in Kenya had not been elucidated. The aim of this paper is to analyze mutations in both GyrA and ParC responsible for elevated fluoroquinolone MICs in *Neisseria gonorrhoeae* (GC) isolated from heterosexual individuals from different locations in Kenya.

Methods Antimicrobial Susceptibility Tests were done on 84 GC in an ongoing STI surveillance program. Of the 84 isolates, 22 resistant to two or more classes of antimicrobials were chosen for analysis. Antimicrobial susceptibility tests were done using E-test and the results were interpreted with reference to European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards. The isolates were sub-cultured and whole genomes sequenced using Illumina platform. Reads were assembled *de novo* using Velvet, and mutations in the GC Quinolone Resistant Determining Regions identified using Bioedit sequence alignment editor. Single Nucleotide Polymorphism based phylogeny was inferred using RaxML.

Results Double GyrA mutations; S91F and D95G/D95A were identified in 20 isolates. Of these 20 isolates, 14 had an additional E91G ParC mutation and significantly higher ciprofloxacin MICs (p=0.0044*). On the contrary, norfloxacin MICs of isolates expressing both GyrA and ParC QRDR mutations were not significantly high (p=0.82) compared to MICs of isolates expressing GyrA mutations alone. No single GyrA mutation was found in the analyzed isolates, and no isolate contained a ParC mutation without the simultaneous presence of double GyrA mutations. Maximum likelihood tree clustered the 22 isolates into 6 distinct clades.

Conclusion Simultaneous presence of mutations in ParC and GyrA has been reported to increase gonococcal fluoroquinolone resistance from different regions in the world. Our findings indicate that GyrAS91F, D95G/D95A and ParC E91G amino acid substitutions mediate high fluoroquinolone resistance in the analyzed Kenyan GC.

Disclosure No significant relationships.

P657 HIGH AZITHROMYCIN RESISTANCE AND DECREASING CEFTRIAXONE SUSCEPTIBILITY IN *NEISSERIA GONORRHOEAE* IN SHENZHEN (2010–2017), CHINA

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Background Emergence and development of resistance in *Neisseria gonorrhoeae* (NG) to antibiotics has become a major public health problem worldwide. The aim of our study was to determine the antimicrobial susceptibility, especially ceftriaxone and azithromycin, and molecular epidemiological typing of NG isolates in Shenzhen, China.

Methods A total of 1,282 NG isolates were collected from Shenzhen, between 2010 and 2017. The minimum inhibitory concentrations (MICs) of NG isolates were determined by the agar dilution method. Resistance to azithromycin (AZM-R) was defined as MIC $\geq$1.0 mg/L, and decreased susceptibility to ceftriaxone (CRO^D) was defined as MIC $\geq$0.125 mg/L. Isolates were genotyped using *Neisseria gonorrhoeae* multi-antigen sequence typing (NG-MAST).

Results Among the isolates, 5.0% showed CRO^D, 17.3% was AZM-R and 1.3% was both CRO^D and AZM-R. Increasing ceftriaxone MICs was found from 2010–2014 to 2015–2017 [ridit value: 0.585; 95% confidence interval (95%CI): 0.559–0.611], but not for CRO^D and AZM-R. The proportions of isolates resistant to ciprofloxacin (97.4%, increasing from 96.6% in 2010–2014 to 98.8% in 2015–2017) and penicillin (68.2%, increasing from 60.6% in 2013–2014 to 73.5% in 2015–2017) were increasing, but PPNG was decreased. All isolates were susceptible to spectinomycin. Genogroup 5308 was inversely association associated with AZM-R; the corresponding odds ratio (95%CI) was: 0.098 (0.013–0.747).

Conclusion The founding of increasing ceftriaxone MICs over the time and high proportions of AZM-R in Shenzhen region calls for reevaluation dual therapy. Timely and efficient surveillance with isolates characterization and changes of susceptibility over time is essential.

Disclosure No significant relationships.