P648 FACTORS ASSOCIATED WITH *NEISSERIA GONORRHOEAE* AZITHROMYCIN RESISTANCE IN THE QUEBEC SENTINEL NETWORK, 2015–2017

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Background *N. gonorrhoeae* azithromycin resistance (MIC $\geq$ 2 mg/L) increased from 1.7% to 30.9% between 2013 and 2017 in Quebec, Canada. The Quebec sentinel network aims to 1) maintain a sufficient number of cultures for antimicrobial resistance surveillance; 2) link antimicrobial susceptibility surveillance to epidemiological and clinical information; and 3) monitor treatment failures. We herein examine the associations between *N. gonorrhoeae* azithromycin resistance and epidemiological/clinical characteristics.

Methods Three regions participated: Montréal (two clinics recruiting mostly men having sex with men (MSM)), Montérégie (22 clinics recruiting mostly heterosexuals) and Nunavik (participated only in 2016, recruited mainly heterosexual Inuit people). One strain per year, per individual was selected. When data was presented for 2015–2017 (2015 was incomplete), the most recent strain per individual was considered. Proportions were compared using chi-square tests.

Results Between September 2015 and December 2017, 68% of episodes (840/1240) had a culture performed and 571 strains were obtained, including all duplicates. This analysis includes 190 strains in 2016, 270 strains in 2017 and 469 strains for 2015–2017. Most isolates were collected in MSM (349/469; 76%). Sampling sites were urethra (329/469; 70.2%), rectum (90/469; 19.2%) and pharynx (50/469; 10.7%). Azithromycin resistance was significantly higher in MSM (25.5% vs 9.2% in heterosexuals, p<0.001), in cases who reported previous gonorrhea (27.3% vs 15.3%, p=0.004), syphilis (29.5% vs 19.8%, p=0.045), HIV (31.8% vs 20.1%, p=0.035) and who reported a sex partner outside Quebec in 2016 (36.7% vs 16.8%, p=0.021), but this difference was not maintained in 2017 (21.2% vs 21.7%, p=0.951). No significant difference was observed with regard to age, number of sex partners, anatomical site and presence of symptoms.

Conclusion Recommendations to perform cultures appear to be well implemented (70% of episodes). Azithromycin resistance seems to be well established in Quebec with a possible declining contribution of travel-acquired resistant infection.

Disclosure No significant relationships.

P649 VARIATIONS IN TIME TO CLINICAL PRESENTATION FOR PATIENTS WITH UNCOMPLICATED GENITAL GONORRHOEA

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Background Current high rates of gonorrhoea highlight a need for rapid effective treatment. Specifically, reducing the duration between onset of symptoms and presentation for clinical care can prevent the onward transmission of infection and the development of sequelae. We sought to evaluate variation in time to presentation (TTP).

Methods Participants were recruited from 14 clinics across England into the gentamicin for the treatment of gonorrhoea (GToG) trial between October 2014 and November 2016. Demographic, behavioural, and clinical data were analysed from participants presenting with genital discharge and/or dysuria who tested positive for *Neisseria gonorrhoeae* using a nucleic acid amplification test.

Results 316 participants (269 men) with a median age of 27.6 years (range 16.3–68.4) were included. 194 (61%) were Caucasian, 29 (9%) Black African, 27 (9%) Asian and 66 (21%) of other ethnicities. Median TTP was 4 days (range 1–252) with participants reporting genital discharge (297/316 [94%]), dysuria (251/316 [79%]), genital discharge and dysuria (232/316 [73%]) and 76/316 (24%) additional concurrent symptoms (e.g. rectal bleeding, genital itching). TTP was longer than a week in 24% of participants. Age was inversely correlated with TTP ($r_s = -0.276$; $P = 0.01$) and TTP was longer in women compared to men (median 14 vs 3 days; $P<0.001$), and in those with other symptoms (median 7 vs 3 days; $P<0.001$). Sexual behaviours comprising same sex partner, higher number of partners, or casual/one-off relationships were associated ($P<0.05$) with shorter TTP. TTP was also shorter ($P<0.05$) in those with a history of previous gonorrhoea, but not previous chlamydia or history of HIV testing. TTP did not vary ($P\geq0.05$) by ethnicity, chlamydia co-infection, amount of discharge, or reported condom use.

Conclusion Specific demographic, behavioural and clinical factors were associated with TTP in individuals with symptomatic gonorrhoea. Detailed knowledge of these factors can be used to prioritise and optimise gonorrhoea management and prevention.

Disclosure No significant relationships.

P650 RANDOMIZED CLINICAL TRIAL COMPARING GENTAMICIN+AZITHROMYCIN VS. CEFTRIAXONE + AZITHROMYCIN FOR RECTAL AND PHARYNGEAL GONORRHEA

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Background Dual therapy including ceftriaxone plus azithromycin is currently the recommended first-line gonorrhea treatment internationally. However, for gonorrhea cases where ceftriaxone or other extended-spectrum cephalosporin can not be administered (e.g., cephalosporin resistance, allergy, or unavailability), the therapeutic options are very limited. In a previous randomized controlled clinical trial (RCT) by Kirkcaldy et al. (Clin Infect Dis. 2014), gentamicin 240 mg plus azithromycin 2 g showed 100% microbiological cure for uncomplicated gonorrhoea. However, only 10 pharyngeal infections and one rectal infection were examined. We further evaluated the efficacy and tolerability of gentamicin+azithromycin for treatment of uncomplicated rectal and pharyngeal gonorrhea.

Methods A non-inferiority, open-label, single center RCT was conducted in Prague, Czech Republic. Patients, 18–75 years of age, diagnosed with uncomplicated rectal or pharyngeal gonorrhea by nucleic acid amplification test (NAAT) (GeneProof®) were randomized to treatment with gentamicin 240 mg intramuscularly plus azithromycin 2 g orally or ceftriaxone 500 g intramuscularly plus azithromycin 2 g orally. The primary outcome was negative culture and negative NAAT, i.e., one week and three weeks, respectively, after treatment.
Results Both clinical and microbiological cure was achieved by 100% of patients in the gentamicin+azithromycin arm (n=68; 40 rectal, 14 pharyngeal, and 14 infections in both localizations) and ceftriaxone+azithromycin arm (n=66; 36 rectal, 14 pharyngeal, and 16 infections in both localizations). Administration of gentamicin was significantly less painful than ceftriaxone according to the visual analog score ($p<0.001$). Gastrointestinal adverse events were slightly more common in ceftriaxone arm (50.0%) than in gentamicin arm (41.2%), but in most (64%) cases they were mild.
Conclusion Both gentamicin+azithromycin and ceftriaxone +azithromycin were 100% effective for treatment of rectal and pharyngeal gonorrhea. Gentamicin 240 mg plus azithromycin 2 g appears to be an effective alternative for treatment of both urogenital and extragenital gonorrhea in case of ceftriaxone resistance, allergy, or unavailability.
Disclosure No significant relationships.

P651 ELUCIDATING THE EFFECT OF ESCULETIN AGAINST GLUTAMATE RACEMASE – A NOVEL DRUG TARGET OF *NEISSERIA GONORRHOEAE*

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Background *Neisseria gonorrhoeae* (NG) is a sexually transmitted pathogen infecting both men and women. In spite of a number of antibiotics, gonorrhea (also known as "The Clap"), remains a frequently reported STI and is an important cause of pelvic inflammatory disease and infertility. Due to resistance to most of the currently used drugs, *NG* has been named as 'Superbug' posing a serious threat to gonorrhoea treatment worldwide. Therefore, there is an urgent need to find novel drug targets and to develop new antibacterial agents.
Methods Using system biology to identify potential drug targets and the known inhibitors/drugs against homologous proteins, we identified a novel drug target, namely glutamate racemase (GR). This enzyme is involved in the early phase of peptidoglycan biosynthesis in both gram positive and gram negative bacteria. As protein-ligand interactions play a key role in structure-based drug design, we screened natural compounds for binding to NG-GR by carrying out docking studies, shortlisted the best docked compounds and evaluated them for their functional, structural and antibacterial activity.
Results The computational analysis showed that the coumarin derivative-esculetin exhibited best binding affinity among all the tested compounds. Characterization of the biophysical properties of purified recombinant GR using circular dichroism, in the absence and presence of esculetin, indicated a change in protein conformation in the presence of esculetin. This change is the protein structure was associated with a concomitant inhibition of racemization activity of recombinant GR. Esculetin also inhibited the growth of the bacteria in culture both in time and concentration dependent manner.
Conclusion In conclusion, these observations could provide impetus for further research in this direction. Better understanding of antibacterial mechanisms of esculetin will help in establishing lead molecules for the treatment of gonococcal infections.
Disclosure No significant relationships.

P652 USE OF SPECIMENS SUBMITTED FOR *NEISSERIA GONORRHOEAE* MOLECULAR TESTING TO ENHANCE SURVEILLANCE IN A CANADIAN ARCTIC TERRITORY

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Background Surveillance for antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (NG) is critical to monitor trends and to inform treatment guidelines for NG. In Nunavut (NU), a Canadian Arctic territory, culture for NG is not possible due to environmental conditions which affect organism viability. Specimens submitted for nucleic acid amplification tests (NAAT) are routinely used to screen for NG and have the potential to provide important surveillance information with additional testing.
Methods In January, 2018, Nunavut commenced submission of Roche-Cobas NG positive NAAT specimens to the National Microbiology Laboratory (Winnipeg, Canada). Samples were sequenced using *Neisseria gonorrhoeae* multi-antigen sequence typing (NG-MAST). Real-time (RT-) PCR assays were used to detect single nucleotide polymorphisms (SNPs) in genes associated with ciprofloxacin resistance (gyrA, parC) and azithromycin resistance (23S rRNA).
Results From January to September, 2018, 257 samples were submitted to NML. 229 samples were typeable and 21 different NG-MAST STs were identified, of which approximately half are unique to NU. The most prevalent ST was ST16840 (34.5%, 79/229) which is associated with ciprofloxacin resistance and is closely related to ST 10451, a common sequence type identified across Canada. 28.5% (66/229) were ST5985, a common ST circulating in Canada and is associated with tetracycline resistance. Fully susceptible ST 4637 represented 10.5% (24/229) specimens. Of 216 specimens, 92 were predicted to be ciprofloxacin resistant and of 218 specimens; less than five samples were predicted to be azithromycin resistant.
Conclusion Data from Nunavut, a Canadian Arctic region where the collection of NG culture is not feasible, support the use of NAAT positive NG specimens to provide enhanced surveillance to monitor the types of NG circulating in a community and ensure that currently recommended therapies are appropriate. Future surveillance initiatives linking the samples to epidemiologic data has the potential to support additional public health interventions in at-risk populations.
Disclosure No significant relationships.