P636 HIGH DIVERSITY OF *NEISSERIA GONORRHOEAE* IN GERMANY REVEALED BY MOLECULAR TYPING USING NG-MAST (2014–17)

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Background *Neisseria gonorrhoeae* (NG) infections are not reportable in Germany. The Gonococcal Resistance Network (GORENET) is a laboratory network to monitor antimicrobial resistance (AMR) in Germany, linking data from sequence typing to epidemiological data. We described prevalence of gonococcal sequence types in Germany and associations to AMR to improve future treatment and prevention strategies.

Methods NG isolates collected between April 2014 and December 2017 were tested by E-test and sequence typed by NG multiantigen sequence typing (NG-MAST). For sequence typing, DNA was extracted and internal fragments of *porB* and *tbpB* were amplified by polymerase chain reaction. Fragments were sequenced by Sanger sequencing and evaluated using a global database (www.ng-mast.net). Genogroups were assigned to sequence types which shared one allele and exhibited ≥99% homogeneity in the other allele.

Results 1220 isolates were sequence typed (106 in 2014, 96 in 2015, 525 in 2016, and 495 in 2017). In total, we detected 422 different sequence types that grouped into 17 genogroups. Among the most prevalent genogroups were G2400 (6.8%), G1407 (6.8%), G5441 (6.2%), G25 (5.6%), G2992 (5.5%) and G10557 (5.3%). The multi-resistant G1407 and G2400 were most prevalent in 2014 (12.4% and 10.5%, respectively) and declined to 6.1% and 7.3% in 2017. Two new genogroups, G11461 (3.6%) and G17420 (2.1%), emerged showing high prevalence in 2017 and no association to extended-spectrum cephalosporin resistance. Furthermore, a novel genogroup-association with cefixime resistance and reduced cephalosporin susceptibility was identified.

Conclusion From 2014 to 2017 prevalence of G1407 declined and two novel extended-spectrum cephalosporin sensitive clones G11461 and G17420 seem to have replaced the multidrug resistance clone G1407. To verify these results, continuous testing with an increased number of isolates should be performed.

Disclosure No significant relationships.

P637 *NEISSERIA GONORRHOEAE* GENOMIC DIVERSITY IN HIGH RISK GROUPS IN SWITZERLAND

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Background *Neisseria gonorrhoeae* cases are increasing in Europe, with decreasing susceptibility to first line antibiotics. Whole genome sequencing (WGS) provides detailed information about gonococcal molecular epidemiology and prediction of antimicrobial resistance (AMR), especially if linked to epidemiological data. The aim of this study was to examine molecular, clinical and social epidemiological aspects of gonorrhoea infections in Switzerland.

Methods In 2015–2016, we cultured urethral, cervical, vaginal, rectal, and pharyngeal specimens from patients in three clinics predominantly attended by men who have sex with men (MSM) and female sex workers (FSW). MSM also completed a sexual behaviour questionnaire. Minimal inhibitory concentrations (MIC) were assessed by Etest, interpreted using EUCAST breakpoints except azithromycin (≥2 mg/L); WGS used an Illumina Miseq.

Results We sequenced 140 isolates from 116 participants, MSM (107, 92%, mean age 35.8 years) and FSW (6, 5%, mean age 25.3 years). Amongst MSM, 48/105 respondents (45.7%) reported recent sex abroad. Three patients (two MSM and one FSW) carried different strains at different body sites. The isolates show large genomic diversity, with 69 NG-MAST types and 37 MLST sequence types, largely embedded within characterised European Union clusters. NG-MAST 1407 was identified in n=4 isolates from two patients (FSW, not travel-associated and MSM, sex elsewhere in Europe). Mosaic *penA*XXXIV was seen in these isolates, and also in an NG-MAST 13488 from an MSM, which was also not travel associated. One isolate (heterosexual male, not travel-associated) with elevated cefixime MIC (0.19 µg/ml) carried a mosaic *penA*X in an NG-MAST 10557 background. Ciprofloxacin resistance was seen in these six isolates, and overall in 59/140 (42%), all containing GyrA mutations S91F and D95A/G/N.

Conclusion Switzerland has a high diversity of circulating gonorrhoea, generally related to European clusters. Multidrug resistant isolates were not identified in this study, but NG-MAST 1407 and *penA* mosaics, associated with elevated cephalosporin MICs, are circulating.

Disclosure No significant relationships.

P638 SURVEILLANCE OF GONOCOCCAL INFECTION TREATMENT FAILURES 2015–2018 IN QUÉBEC, CANADA

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Background Incident cases of gonococcal infection are increasing. Antibiotic resistance may compromise the effectiveness of treatment. In 2017, the proportion of azithromycin-resistant strains reached 31% in Quebec and a first strain non-susceptible to ceftriaxone and cefixime was detected.

Methods Since November 2014, public health departments are invited to report possible cases of treatment failures. Clinical and epidemiological information is collected using a standardized form for each report of gonococcal infection occurring <42 days after a previous episode in the same person. Antimicrobial susceptibility testing (AST) is conducted at the

provincial reference laboratory (Laboratoire de santé publique du Québec) and the NG-MAST typing is performed at the National Microbiology Laboratory. Cases are classified as retained (presence of all definition criteria) or suspected (not meeting all criteria but reinfection unlikely). Cases classifications are validated by a group of experts. Lack of re-exposure is based on the respondent's reported sexual history between the first treatment and the test of cure (TOC). Case definitions are consistent with those of Quebec and Canadian sentinel surveillance network for gonococcal infection.

Results Between November 2014 and December 2018, 44 cases of possible treatment failures were reported. After exclusion of 9 cases, 35 were analysed (25 classified as retained and 10 as suspected). There were 10 women, 24 men (68% MSM) and one trans person. Pharynx was identified as site of treatment failure for 14 cases (40%). AST were available for 23 cases (66%): 78% were resistant to ciprofloxacin and 43% to azithromycin. All strains were susceptible to cephalosporins, but one strain showed reduced susceptibility to cefixime. Eleven cases (31%) received azithromycin monotherapy as initial therapy.

Conclusion Treatment failure exist and is not always related to documented resistance. This analysis probably underestimates the real extent of treatment failures since it requires TOC that are not systematically collected. Reinfection cannot be completely excluded.

Disclosure No significant relationships.

P639 MOLECULAR MARKERS TO PREDICT CEFIXIME DECREASED SUSCEPTIBILITY OF *NEISSERIA GONORRHOEAE*: A GLOBAL REVIEW

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Background In the last two decades, there have been numerous reports worldwide of *Neisseria gonorrhoeae* (NG) infections with clinical treatment failure to cefixime. Mutation in multiple NG genes including *pen*A, *mtr*R, *pil*Q, *pen*B, and *pon*A, have been associated with cefixime decreased susceptibility and resistance, however, no single mutation has been identified as necessary or sufficient.

Methods We performed a systematic review of all PubMed-published articles from 01/01/1995 to 11/01/2018 that reported molecular characteristics of decreased susceptibility of NG to cefixime. We summarized the findings and made suggestions for the development of a molecular-based NG assay to predict cefixime susceptibility. Based on clinical outcome data, we defined a minimum inhibitory concentration (MIC) $\geq$ 0.12ug/mL as the cutoff for decreased susceptibility to cefixime. For a wild-type (non-mutated) sequence comparison, we used the *pen*A peptide sequence of NG reference strain M32091.

Results We found 74 articles, of which we excluded 49 due to incomplete information. Among the 25 articles included, there were 415 reported NG strains with reduced susceptibility to cefixime from 22 countries. Two types of *pen*A alterations accounted for 99.5% (413/415) of strains with decreased susceptibility to cefixime: (1) mosaic *pen*A, which can be identified by mutations at amino acid position 375–377 or (2) non-mosaic *pen*A but with at least one critical amino acid substation at position 501, 542, or 551. The other two strains with MIC $\geq$ 0.125 μg/mL were found in Spain in 2013 with a non-mosaic *pen*A sequence but no alteration at amino acid position 501, 542 or 551.

Conclusion We conducted a systematic review of published reports of over 400 NG strains with decreased susceptibility to cefixime. We identified a combination of sequences in the mosaic and non-mosaic regions of the *pen*A gene that if wild-type (non-mutated) may serve as reliable and sensitive markers to predict cefixime susceptibility globally.

Disclosure No significant relationships.

P640 TARGETING MURI PROTEIN TO COMBAT DRUG RESISTANCE IN *NEISSERIA GONORRHOEAE* USING HOMOLOGY MODELING AND DRUG DOCKING STUDIES

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Background *Neisseria gonorrhoeae*, a causative agent of gonorrhea, has developed resistance to most of the drugs and hence aptly declared as 'Superbug'. Glutamate racemase (MurI) considered as an important drug target. Therefore, identification of novel drugs for the treatment of gonorrhea is urgently required.

Methods The amino acid sequence of MurI of *Neisseria gonorrhoeae* (YP_208550) was retrieved from NCBI. Based on query coverage, e-score and percentage similarity, 3OUT (glutamate racemase from Francisella tularensis) was selected as template after PDB BLAST, homology model was generated by Modeller programme of Discovery Studio 4.0.Best model was selected based on DOPE score and PDF energy score and further verified by Verify-3D protocol and Ramachandran Plot. Receptor binding site was identified after superimposition of template structure and modelled structure and the co-crystalized ligand of the template was docked into the modeled MurI structure. Based on docking score, best pose was selected and receptor-ligand pharmacophore model was generated.

Results The best homology model generated was selected based on the verify score of 107.93 from Verify 3D program of Discovery Studio 4.0. Validation of the selected model by Ramachandran plot showed214 residues (91.8%) fall in most favored region. RMSD of 0.2475 A0was generated by superimposition of query and template structures. Quality factorof 84% for the protein models was obtained using ERRAT.Six pharmacophores were generated using best docking pose between D-glutamate and MurI. These were subjected to virtual screening with DrugBank database.586 hits so obtained were filtered by fit value of 3.51which resulted in268 hits. These 268 hits were further subjected to Lipinski and veber filter followed by ADMET, gave 73 hits. These were subjected to energy minimization and docking to obtain the best hits.

Conclusion The study identifies potential compounds that interact with active site of MurI protein, opening new avenues for the treatment option against multidrug resistant strains.

Disclosure No significant relationships.