O03.3 THE EUROPEAN GONOCOCCAL ANTIMICROBIAL SURVEILLANCE PROGRAMME FINDINGS 2017

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Background The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) annually investigates antimicrobial susceptibility data for *Neisseria gonorrhoeae* with patient epidemiological data to monitor current and emerging trends in antimicrobial resistance (AMR) across Europe. Susceptibility to ceftriaxone and azithromycin, currently recommended for combination treatment in the European management guideline, has decreased in the past; regular surveillance of AMR is crucial. We present the main Euro-GASP findings from 2017.
Methods Agar dilution and minimum inhibitory concentration (MIC) gradient strip tests were used to determine the antimicrobial susceptibility to cefixime, ceftriaxone and azithromycin (using EUCAST breakpoints) of 3248 *N. gonorrhoeae* isolates collected in 2017 from 27 countries across the European Union/European Economic Area (EU/EEA). Significance of changes in resistance compared to 2016 was analysed using Z-tests.
Results There were no isolates with ceftriaxone resistance (MIC>0.125 mg/L) (zero in 2016), 7.5% of isolates were azithromycin resistant (MIC>0.5 mg/L) (7.5% in 2016; p=0.93) and cefixime resistance (MIC>0.125 mg/L) was observed in 1.9% of isolates (2.1% in 2016; p=0.53). Seven isolates from four countries displayed high-level azithromycin resistance (MIC≥256 mg/L), which is the same number as observed in 2016, although in different countries (five countries in 2016). Ceftriaxone MICs for 28 isolates (0.9%) were 0.125 mg/L (on the resistance breakpoint) which is double the number observed in 2016 (14 isolates, 0.5%) although this increase is not statistically significant (p=0.33). Of the 28 isolates on the ceftriaxone resistance breakpoint, four showed intermediate susceptibility to azithromycin.
Conclusion Ceftriaxone, azithromycin and cefixime resistance levels remained stable compared with 2016. However, the current azithromycin resistance rate of 7.5% and the number of isolates on the resistance breakpoint for ceftriaxone threaten the effectiveness of the currently recommended European therapeutic regimen of ceftriaxone 500 mg plus azithromycin 2 g. Continued surveillance is essential together with, ultimately, development of new effective antimicrobials.
Disclosure No significant relationships.

O03.4 MODELLING INTERVENTION STRATEGIES FOR PREVENTING SPREAD OF EXTENSIVELY DRUG RESISTANT GONORRHOEA STRAINS AMONG AUSTRALIAN MSM

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Background Recent reports from Australia and the UK of extensively drug resistant (XDR) gonorrhoea strains, have increased concerns over remaining treatment options. Outbreak-type responses to detection of such strains may help to delay wider emergence of such resistance but lack a clear evidence base as to their effect. Here, we use mathematical models to assess the potential impact of outbreak response strategies in a high-incidence population of Australian men who have sex with men (MSM) with gonorrhoea.
Methods We developed an individual-based, anatomical site-specific model of gonorrhoea transmission in Australian MSM. The model was calibrated to available site-specific prevalence and incidence data with respect to the per-act transmission probabilities for four types of sexual practice. As pharyngeal importations were most difficult to control, we focused on these in estimating the probability of elimination of an imported XDR strain. We considered various combinations of contact tracing and screening interventions, with results for each scenario based on 5000 simulations.
Results At current levels of gonorrhoea screening in Australian MSM, we predict persistence of secondary spread at 5 years post-importation in just under 20% of simulations. If all infected regular partners of index patients are traced and treated, this persistence probability declines to ~8%, and further to ~4% and 0.04%, respectively, if 20% and 50% of all casual partners in the last two months are traced and treated. Alternatively, If the screening rate is increased to the level recommended in STI management guidelines, the probability of persistence after 5 years is ~9.7%. When combined with treatment of regular partners, this probability is reduced to <0.01%.
Conclusion This study suggests that contact tracing and screening rate can separately play an important role in responding to outbreaks of XDR gonorrhoea, and in combination these strategies may have the potential to prevent domestic establishment of such strains.
Disclosure No significant relationships.

O03.5 UTILITY OF REAL-TIME WHOLE GENOME SEQUENCING IN PARTNER NOTIFICATION AND CONTROL OF *NEISSERIA GONORRHOEAE* INFECTION

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Background Gonorrhoea is a sexually transmitted infection of global public health concern. We investigated whole genome sequencing (WGS) as a partner notification (PN) tool in gonorrhoea management.
Methods Between May-November 2018, all *N. gonorrhoeae* isolated from patients attending Leeds Sexual Health, UK, underwent WGS. Sequences were compared with historical isolates from Leeds, 2016 onwards. Reports listing sequences within 20 single nucleotide polymorphisms (SNPs) were issued to clinicians. Patient and PN data were reviewed; numbers of traceable and untraceable partners were determined. Reports were reviewed to confirm WGS links between traceable partners and to identify possible links for untraceable partners, as determined by a transmission nomogram and epidemiological match (gender, sexual orientation, onset of symptoms, and other identifiers e.g. name). Clusters of cases within 20 SNPs were examined for patterns.
Results Overall 380 isolates from 377 cases were successfully sequenced. Traceable partners were found in 244 cases. 147

cases had at least one traceable contact with confirmed attendance, and 122 had contacts testing positive. WGS confirmed links between traceable contacts in 82 cases. Reasons for unconfirmed links include contacts testing elsewhere and testing NAAT positive, culture negative. Untraceable contacts were reported in 157 cases; WGS provided possible links in 83, with confirmation in only six, given inherent information unavailability. Cases were grouped into 123 clusters, with eight containing >10 patients. Examination of clusters highlighted gaps in partner finding, including clusters containing heterosexual females with identical strains but no male; heterosexual males with identical strains who reported female sex worker contact; confirmed instances of partner underreporting; and 35 cases with multiple partners but no genetically related case.

Conclusion WGS has the potential to improve gonorrhoea PN and control by identifying new links and clusters with significant gaps in partner finding, where PN can be enhanced. Its utility will improve with larger databases.

Disclosure No significant relationships.

O03.6 VAGINAL BACTERIA AND RISK OF INCIDENT AND PERSISTENT INFECTION WITH HIGH RISK SUB-TYPES OF HUMAN PAPILLOMAVIRUS

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Background Certain vaginal bacteria may increase women's risk for infection with high risk sub-types of human papilloma virus (hrHPV). The role of vaginal bacteria in hrHPV persistence is less well studied. We assessed associations between vaginal bacteria and hrHPV acquisition and persistence among Kenyan women in the placebo arm of the Preventing Vaginal Infections trial.

Methods Nonpregnant, HIV-uninfected women aged 18–45 from Kenya and the United States were enrolled in a randomized trial of periodic presumptive treatment to reduce vaginal infections over 12 months. Genital fluid specimens collected at enrollment and every 2 months thereafter were tested for 14 hrHPV types using the Hologic APTIMA HPV assay. Quantitative PCR targeting the 16S rRNA gene from ten bacteria was used to measure bacterial concentrations in vaginal swabs. Multivariate multinomial logistic regression and multistate Markov models restricted to Kenyan placebo participants were used to assess associations between log10-transformed bacterial concentrations (categorized in tertiles) and hrHPV acquisition and persistence.

Results Among the 84 Kenyan placebo participants, hrHPV was detected in 79/563 specimens (14%), with 16 episodes of persistent hrHPV (detection in ≥2 consecutive specimens; median duration was 6 months). Controlling for age, hormonal contraceptive use, and condom use, *Lactobacillus jensenii* concentration was positively associated with hrHPV incidence (adjusted odds ratio (aOR)=1.57; 95% CI 1.07–2.30); and *Atopobium vaginae* (aOR=1.40; 95% CI 1.02–1.93), *Megasphaera* species (aOR=1.39; 95% CI 1.03–1.88), and *Mageeibacillus indolicus* (aOR=1.48; 95% CI 1.09, 2.02) concentrations were positively associated with hrHPV persistence. BV (Nugent score ≥7) was not significantly associated with hrHPV incidence or persistence. Multistate Markov models did not indicate that bacterial concentrations were associated with transitions between HPV detection states.

Conclusion These findings suggest that higher concentrations of certain vaginal bacteria may increase risk of hrHPV incidence and persistence. Future work with more frequent sampling could provide additional insight into factors associated with hrHPV persistence.

Disclosure No significant relationships.

O04 – ANTIMICROBIAL RESISTANCE IN STI PATHOGENS

Monday, July 15, 2019 4:15 PM – 5:45 PM

O04.1 NOVEL PATHWAY TO CEFTRIAXONE RESISTANCE IN CLINICAL ISOLATES OF *N. GONORRHOEAE* VIA POINT MUTATIONS IN THE RNA POLYMERASE

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Background Widespread antimicrobial resistance in *Neisseria gonorrhoeae* has limited the effective treatment options. Cephalosporins remain one of the few classes of antibiotics recommended for gonococcal infections, but reduced susceptibility to the third-generation cephalosporins, including ceftriaxone, has emerged. Most reduced susceptibility to ceftriaxone is caused by an alternative *penA*(PBP2) allele. However, the isolates with the among the highest level cephalosporin resistance identified in the US lack this allele and other penA resistance mutations, raising the possibility of cephalosporin resistance not mediated directly through penA.

Methods To identify the genetic basis of resistance in these isolates, we employed an undirected transformation strategy, and used molecular microbiology and genetics methods to investigate the mechanism of resistance.

Results Here, we show that resistance to ESCs has arisen in clinical isolates multiple times through distinct mutations in the RNA polymerase components rpoB and rpoD. The resistance caused by these changes is not a general tolerance response: these mutations neither changed the growth rate *in vitro*nor altered susceptibility to other classes of antibiotics (including penicillin). These mutations result in large variations in transcription, including in genes coding for penicillin binding proteins (increase in PBP1, decrease in PBPs 3 and 4) and pilus pore. We show that increases in PBP1 protein levels contribute to the rise in CRO MIC, likely through replacement of inhibited PBP2 activity, though other factors are needed to recapitulate the resistance seen in the clinical isolates with rpoB and rpoD mutations.

Conclusion Pathways to extended spectrum cephalosporin resistance do not require alterations to penA (PBP2) and can arise through mutations in components of the RNA polymerase holoenzyme. Additional pathways to cephalosporin