P666 INCREASED RESISTANCE TO EXTENDED-SPECTRUM CEPHALOSPORINS IN *NEISSERIA GONORRHOEAE* ISOLATES IN NANJING, CHINA (2013–2018)

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Background The aim of this study is to monitor the trend in antimicrobial resistance in *Neisseria gonorrhoeae* in Nanjing, China. Gonococcal strains isolated during 2015–2018 were examined for susceptibility to seven antibiotics and compared with results from 2013–14 (Antimicrob Agents Chemother, 2018)

Methods 1173 gonococcal strains were isolated from men with urethritis; n=789 (2015–18), compared with n=384 (2013–14). MICs for seven antibiotics were determined by agar dilution method. Criteria for decreased susceptibility to ceftriaxone (MIC≥0.125 mg/L) and cefixime (MIC≥0.25 mg/L) were defined by WHO. Using CLSI and EUCAST (for azithromycin only) criteria, the following MIC breakpoints were used to ascertain resistance: ≥128 mg/L, spectinomycin; ≥2 mg/L, penicillin and tetracycline and ≥1 mg/L, ciprofloxacin and azithromycin. Resistance determinants were investigated using WGS of two isolates which were resistant to both ceftriaxone and cefixime.

Results The percentage of isolates with decreased susceptibility to ceftriaxone rose from 9.9% in 2013–14 to 23% in 2016 and decreased to 16.7% in 2018 (P=0.01). The percentage of isolates with decreased susceptibility to cefixime rose from 0.3% (2013–14) to 15.7% in 2016 and decreased to 13.7% in 2018 (P<0.0001). 38 isolates displayed MIC≥0.5 mg/L for cefixime, among them 26.3%(10) belonged to ST5308 and one isolate to ST1407 NG-MAST types. Two isolates that exhibited MIC=1 mg/L for ceftriaxone and MIC=2 mg/L for cefixime were detected in 2017 and 2018, respectively. Each possessed mosaic penA-60.001 gene (the same as FC428 isolated in Japan). Azithromycin resistance decreased from 32.3% (2013–14) to 15.2% (2018) and high-level azithromycin resistance (MIC ≥256 mg/L) decreased from 10.4% (2013–14) to 3.4% (2018) (P<0.001). All 1173 isolates were susceptible to spectinomycin, but resistant to ciprofloxacin. 81.3% isolates were resistant to penicillin and 84.8% to tetracycline.

Conclusion The proportion of *N. gonorrhoeae* isolates with decreased susceptibility to extended-spectrum cephalosporins increased significantly from 2013 to 2018. Ceftriaxone-resistant strain has emerged in Nanjing, China.

Disclosure No significant relationships.

P667 GUIDING *NEISSERIA GONORRHOEAE* MANAGEMENT BY MOLECULAR DETECTION OF CIPROFLOXACIN RESISTANCE BY SPEEDX RESISTANCEPLUS GC ASSAY

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Background There is a growing concern due to the emergence of multi-drug resistance developed in *Neisseria gonorrhoeae*. A rapid molecular test could provide antimicrobial susceptibility knowledge prior to start of treatment and decrease the turnaround time from current culture methods (7 days). The aim was to evaluate the clinical performance of the ResistancePlus GC assay (SpeeDx) compared to the in-house PCR and antimicrobial susceptibility results for ciprofloxacin.

Methods Antimicrobial susceptibility data was captured on all GC culture positives from 2015–2017 in Scotland. A gyrA real-time PCR was used to detect for ciprofloxacin resistance in *N. gonorrhoeae*. In this study 168 samples were selected from a range of sites (Cervical/vaginal, Rectal, Urine or Throat). Results were compared to susceptibility results of cultures isolated from the same patient episode (within 14 days). The culture isolates displayed a range of MICs with 84 susceptible and 84 resistant to ciprofloxacin.

Results Ciprofloxacin resistance was seen in 420/1338 episodes (31.4%) in 2017. The ResistancePlus GC assay was able to detect *N. gonorrhoeae* in all of the samples (100%) and *gyrA* in 164/168 samples (97.6%).The 4 samples with *gyrA* undetected had high Ct's (≥35) in a 2nd line real-time PCR for *porA*. In total 162/164 *gyrA* results matched the phenotype of a culture isolate taken from the same episode (98.7%). Further analysis showed that performing the assay on the discrepant culture isolates matched the phenotype result.

Conclusion The ResistancePlus GC assay performed well on clinical samples and could offer ciprofloxacin susceptibility testing within 4 hours to a laboratory service. This would therefore allow for an alternative antibiotic to be prescribed. Modeling based on current episodes in Scotland could mean that ciprofloxacin would be able to be used in ≥50% of episodes which provides an exciting new approach to GC treatment.

Disclosure No significant relationships.

P668 TRANSFER OF HIGH-LEVEL MACROLIDE RESISTANCE IN *NEISSERIA GONORRHOEAE*

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Background Previous transformation experiments with *Neisseria gonorrhoeae* (Ng) have established that it is able to acquire high-level antibiotic resistance via transformation. We aimed to assess if a high-level ceftriaxone resistant Ng strain (WHO X) was able to acquire resistance to azithromycin (AZM) via this mechanism.

Methods A mid log phase culture of Ng WHO X (AZM MIC 0.25 µg/mL) was mixed with whole genomic DNA extracted from Ng WHO strain V (AZM ≥ 256 µg/mL). A concentration of 1,5x MIC of AZM was added as a stress factor for the selection of the resistance determinants. Control experiments were conducted by omitting the addition of AZM and/or DNA. Consecutively, the mixture was plated on blood agar plates and incubated at 36°C in a 6% CO_2 atmosphere. Of each blood agar plate 1 or 2 colonies were selected for E testing performed according to CLSI guidelines. Colonies growing alongside the E-test strip at the higher range of the MIC values were selected for further characterization, including whole genome sequencing, and to identify the acquired resistance mechanisms.

Results The MIC for AZM of WHO strain X increased to greater than 256 µg/ml. There was no change in the MICs of Ng in the control experiments. Whole genome sequencing results will be presented demonstrating the pathways to resistance.

Conclusion *Neisseria gonorrhoeae* is able to rapidly acquire high level macrolide resistance in the presence of both DNA of AZM highly resistant NG strains and AZM.
Disclosure No significant relationships.

P669 CLINICALLY ISOLATED THIAMINE AUXOTROPHS OF *NEISSERIA GONORRHOEAE* INDICATE INCREASED SUSCEPTIBILITY TO HOST INNATE DEFENSES

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Background Thiamine pyrophosphate (TPP) is an important metabolite that affects many metabolic pathways within the cell.) Thiamine (thi) auxotrophs of *Neisseria gonorrhoeae* (Gc) that could not grow without TPP or other thiamine derivatives were isolated from patients in the 1970's, but the effect of thi auxotrophy on Gc pathogenesis is not known. We recently demonstrated that a genetically defined Gc mutant that cannot biosynthesize TPP is more susceptible to killing by neutrophils, cationic antimicrobial peptides (CAMPs), and reactive oxygen species (ROS) in vitro, and attenuated for experimental infection of mice that have a neutrophil response to infection. Here we investigated the susceptibility of five recently isolated TPP auxotrophs to paraquat, an inducer of ROS and CAMPs as a first step towards understanding the consequence of thi auxotrophy during human infection.
Methods Eighty-nine Gc isolates in the USUHS Gc Resistance and Reference Repository isolated between 2014 and 2017 were screened for the capacity to grow on medium without TPP. Auxotrophs were tested for susceptibility to paraquat and colistin (polymyxin E) using standard methods.
Results Five thi auxotrophs were identified among the 89 isolates tested (5.6%). Four of the auxotrophs exhibited increased susceptibility to paraquat and colistin compared to a wild-type Gc strain. Auxotroph 4097, in contrast, showed a ~2-fold greater resistance to 0.0195 mM of paraquat and colistin compared to a wild-type Gc strain, suggesting this isolate may carry a compensatory mutation(s).
Conclusion We conclude that clinically isolated thi auxotrophs are more susceptible to ROS and CAMPS. We hypothesize that these isolates may have a lesser ability to withstand oxygen-dependent and independent effectors of the host inflammatory response and that selection for compensatory mutations during infection may be one mechanism by which thi auxotrophs remain in circulation. Analysis of WGS data is underway to identify the genetic basis of thi auxotrophy and possible compensatory mutations.
Disclosure No significant relationships.t

P670 INTERNATIONALLY DISSEMINATED CEFTRIAXONE-RESISTANT *NEISSERIA GONORRHOEAE* STRAIN FOUND IN CHINA

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Background Ceftriaxone has been used to treat gonorrhea in China for more than one decade, but an increasing level of decreased susceptibility or clinical resistance to ceftriaxone has been found. Moreover, the international spread ceftriaxone-resistant clones has been recognized as a threat to effective control of gonorrhea. We now describe an imported ceftriaxone-resistant *N. gonorrhoeae* strain isolated in China, 2016.
Methods The isolate was collected in 2016. The antimicrobial susceptibility to ceftriaxone (CRO), cefixime (CFM), azithromycin (AZM), spectinomycin (SPT) and ciprofloxacin (CIP) was determined using the agar dilution method in reference lab at National Center for STD Control. A combination of molecular epidemiological methods including *N. gonorrhoeae* multiantigen sequence typing (NG-MAST), multi-locus sequence typing (MLST) and *N. gonorrhoeae* sequence typing for antimicrobial resistance (NG-STAR) was used to determine characteristics and resistant determinants of this isolate.
Results The strain was resistant to CRO (MIC 0.5 mg/L), CFM (MIC 1 mg/L), TET (4 mg/L) and CIP (≥32 mg/L), but susceptible to AZM (0.25 mg/L) and SPT (16 mg/L). The MLST type was ST1903, and NG-MAST type was ST3435. The NG-STAR type was ST233, which contains a type 60 mosaic penA allele, –35A Del in the mtrR promoter, G120K-A121D in PorB, L421P in PonA, S91F-D95A in GyrA, S87R in ParC, and wild-type 23srRNA.
Conclusion We identified a ceftriaxone-resistant *N. gonorrhoeae* strain which has sustainably transmitted worldwide for more than 3 years. The epidemiological and molecular typing data drew an integral transmission chain of this clone from Japan to China, and then disseminated globally. These findings indicate an imported risk of resistant clones in China and also call for an enhanced global gonococcal antimicrobial surveillance to track the emergence and dissemination of resistant strains for timely control the spread.
Disclosure No significant relationships.

P671 DISTRIBUTION OF ANTIMICROBIAL RESISTANCE IN *NEISSERIA GONORRHOEAE* – 5 YEARS OF GERMAN GONOCOCCAL RESISTANCE NETWORK (GORENET)

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Background The widespread antimicrobial resistance (AMR) of *Neisseria gonorrhoeae* (NG) is a serious problem for the treatment of gonorrhoea. Because NG infections are not reportable in Germany, only limited data on disease epidemiology and antimicrobial susceptibility patterns are available. The Gonococcal Resistance Network (GORENET) monitors trends of NG AMR in Germany and links this to epidemiological data and NG multiantigen sequence typing (NG-MAST) data to guide treatment algorithms and target future prevention strategies.
Methods Between April 2014 and December 2018, NG isolates and data on patient-related information were collected from laboratories nationwide and centralized susceptibility testing using E-test was performed. Susceptibility results for