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

cefixime, ceftriaxone, azithromycin, ciprofloxacin and penicillin were defined according to EUCAST 4.0 standards.
Results Of 2115 isolates, 91.6% of isolates were from men. The most frequently tested materials among men were urethral (92.4%) and rectal swabs (3.8%), and among women mainly endocervical swabs (80.9%). Resistance to ceftriaxone (MIC ≥0.125 mg/L) occurred only sporadically (0–0.3%) during the entire observation period (2015 and 2018), while 1.0–2.1% of isolates were resistant to cefixime (MIC ≥0.125 mg/L). Proportion of isolates resistant to azithromycin (MIC ≥ 0.5 mg/L) was 11.4% (2014), 11.3% (2015), 4.3% (2016), 3.7% (2017), 9.4% (2018). 53.4–71.7% were resistant to ciprofloxacin, and 14.2–24.3.1% were resistant to penicillin.
Conclusion Resistance to ceftriaxone and to cefixime was low, whereas azithromycin resistance showed a discontinuous presentation with partly high levels during the observation period. Rates of ciprofloxacin and penicillin resistance were very high. According to the current national guidelines, ceftriaxone 1-2g IV and azithromycin 1,5g orally are usually used in dual therapy. Shortly revised national guidelines will state that use of azithromycin should be avoided if possible if a test of cure can be guaranteed and a susceptibility test is available. Continued surveillance of NG AMR remains relevant to ensure efficient disease management.
Disclosure No significant relationships.

P672 GENETIC PATHWAY TO HIGH LEVEL AZITHROMYCIN RESISTANCE IN *NEISSERIA GONORRHOEAE*

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Background The in-vitro genetic pathways to high-level azithromycin (AZM) resistance have hitherto not been established in *Neisseria gonorrhoeae* (Ng).
Methods A Ng morbidostat that dynamically increases AZM concentrations in response to Ng growth was built according to the protocol of Toprak et al. The reference strains Ng WHO-F and WHO-X were grown in 12 mL GC broth supplemented with IsoVitaleX™ (1%) and vancomycin, colistin, nystatin, trimethoprim selective supplement for 30 days in a 6% CO_2 environment at 36°C. Depending on the turbidity and growth of the culture, 1 mL of fresh medium or AZM was added to the culture vials after each cycle of 21 minutes. The experiment started with a concentration of 20x minimal inhibitory concentration (MIC) of AZM in the drug reservoir which was increased up to 320x MIC for both strains by the end of the experiment. Samples of the cultures were taken 2–3 times a week and MICs of AZM were determined using E-tests. Whole genome sequencing will be performed using Illumina MiSeq. All experiments were run in triplicate.
Results The initial MICs of WHO-F and WHO-X were 0,125 µg/mL and 0,25 µg/mL respectively. In the first week, the MICs of WHO-F and WHO-X increased approximately 24-fold for WHO-F and 48-fold for WHO-X. After 30 days, WHO-F and WHO-X had attained MICs of 96 µg/mL and ≥296 µg/mL, respectively. The genetic pathways to resistance will be analysed and presented.
Conclusion We were able to induce high level AZM resistance in Ng within 30 days of AZM exposure using our Ng morbidostat.
Disclosure No significant relationships.

P673 *IN-VITRO* ACTIVITY OF SMT-571 AND COMPARATORS AGAINST CLINICAL ISOLATES AND REFERENCE STRAINS OF *NEISSERIA GONORRHOEAE*

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Background The emergence and spread of multidrug resistance to antibiotics used to treat gonorrhoea has resulted in a dramatic loss of effective regimens for the condition. Currently, the extended spectrum cephalosporin, ceftriaxone, is the only viable monotherapy option available, however, resistance to this last line treatment is now emerging globally. Herein, we assessed the *in vitro* activity of a novel small molecule antimicrobial with a new mechanism of action, SMT-571, against a large collection of *N. gonorrhoeae* clinical isolates and reference strains including numerous MDR and XDR gonococcal isolates.
Methods MICs (mg/L) of SMT-571 were determined by agar dilution according to current CLSI guidelines. The MICs of ceftriaxone, cefixime, azithromycin, ciprofloxacin, spectinomycin, tetracycline, and ampicillin were determined using the Etest method (AB bioMérieux, Marcy l'Etoile, France).
Results SMT-571 showed potent *in vitro* activity against all the tested *N. gonorrhoeae* isolates (n=262) with MICs ranging from 0.064 to 0.125 mg/L, and the MIC50, MIC90 and modal MIC were all 0.125 mg/L. The compound was not influenced by pre-existing resistance mechanisms with no cross-resistance or correlation between the MICs of SMT-571 and comparator agents being observed.
Conclusion This study is the first broad evaluation of the *in vitro* activities of a new mechanism, novel small molecule antimicrobial for the treatment of gonorrhoea. SMT-571 demonstrated high *in vitro* activity against a large geographically, temporally and genetically diverse collection of clinical *N. gonorrhoeae* isolates and international reference strains, including various types of high-level resistant, MDR and XDR gonococcal isolates.
Disclosure No significant relationships.

P675 TWO RECENT CASES OF EXTENSIVELY DRUG-RESISTANT (XDR) GONORRHOEA IN THE UNITED KINGDOM LINKED TO A EUROPEAN PARTY DESTINATION

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Background The development of antimicrobial resistance (AMR) to macrolides and extended-spectrum cephalosporins (ESC) in *Neisseria gonorrhoeae* (NG), is a major public health