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EXTRA-GENITAL CIPROFLOXACIN-RESISTANT *NEISSERIA GONORRHOEA* INFECTIONS AMONG SEXUAL-HEALTH CLINIC USERS IN LIMA, PERU

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Background The increasing prevalence of drug-resistant *Neisseria gonorrhoeae* (NG) infections has caused great concern. NG susceptibility to ciprofloxacin can be reliably predicted using a real-time polymerase chain reaction (PCR) assay for the determination of mutation at codon 91 of the gyrase A (*gyrA*) gene. Ciprofloxacin remains the empiric antimicrobial recommended to treat NG infections in Peru, however local data are limited regarding the prevalence of ciprofloxacin resistance.

Methods Clinical swab specimens from pharyngeal and rectal anatomic locations were collected quarterly between 2013 and 2016 from a cohort of men who have sex with men (MSM) and transgender women in Lima, Peru. NG detection was done using Aptima Combo 2 assay (Hologic Inc, USA). NG-Positive samples were selected for DNA extraction using High Pure PCR Template Preparation Kit (Roche Inc, USA). DNA was amplified using a probe-based Real-time PCR assay to determine point mutations at codon 91 of the *gyrA* gene.

Results Overall, 156 individuals had at least one sample that tested positive for NG by the Aptima assay, 61 (39%) of whom reported a previous sexually transmitted infection diagnosis and 50 (32%) were HIV-infected. Of the 80 participants with *gyrA* genotype results available, 67 (84%) had at least one sample with a *gyrA* mutant NG strain; also, 5 individuals alternated between wild type and mutant NG strain infections during follow up in the same anatomical site.

Conclusion We report the prevalence of individuals with extra-genital NG infections with a *gyrA* mutation conferring ciprofloxacin resistance. While most countries of the region recommend ceftriaxone for NG treatment, Peruvian guidelines need to be updated urgently given the high frequency of ciprofloxacin resistance. The use of molecular genetic markers may facilitate surveillance for antimicrobial resistance.

Disclosure No significant relationships.

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CELL ENVELOPE DAMAGE OF *N. GONORRHOEA* AFTER 15-MIN BETA-LACTAM EXPOSURE ENABLES RAPID ANTIMICROBIAL SUSCEPTIBILITY TESTING

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Background Designing diagnostic tools to perform phenotypic antimicrobial susceptibility testing (AST) at the point-of-care (POC) is a vital step in tackling the global threat of

antimicrobial resistance. Gonorrhea infections with resistance to the first-line dual therapy have already emerged, highlighting the impending threat of untreatable gonorrhea. A rapid, phenotypic AST could enable evidence-based (instead of empirical) therapy and improve surveillance. The focus of this work is to develop innovative strategies to measure the phenotypic antimicrobial susceptibility of *Neisseria gonorrhoeae* clinical isolates after just 15–30 min of exposure with an antibiotic. We focused on the duration of the exposure step because it remains the bottleneck for phenotypic AST with fastidious and slow-growing microorganisms.

Methods We selected nucleic acid readout because our long-term goals include building fully integrated POC devices that determine the phenotypic response to antibiotic of a specific pathogen rapidly. We have been developing rapid phenotypic ASTs based on quantification of nucleic-acid concentrations in antibiotic-exposed samples. We describe a new phenotypic AST that does not depend on the speed of DNA replication and applies to beta-lactams penicillin, ceftriaxone, and cefixime acting on clinical isolates of *N. gonorrhoeae* very rapidly.

Results Our assay had 100% categorical agreement with the gold-standard agar dilution AST when *N. gonorrhoeae* isolates were incubated for 15-min with penicillin, and 100% categorical agreement when incubated for 30 min with ceftriaxone and cefixime, and steps can be performed within 35 min measured from contrived urine samples exposed to penicillin.

Conclusion By designing techniques which allow us to rapidly determine the antibiotic phenotype, evidence-based prescription of antibiotics will become possible.

Disclosure No significant relationships.

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SHARP INCREASE OF CIPROFLOXACIN RESISTANCE OF *NEISSERIA GONORRHOEA* IN YAOUNDÉ, CAMEROON

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Background We hypothesize that in Yaoundé, Cameroon, the circulating *Neisseria gonorrhoeae* strains would have acquired resistance mechanisms to ciprofloxacin since the availability of the antibiotic under the form of a generic drug formulation in 2012.

Methods We conducted a retrospective study (2012–2017) using data collected at the Centre Pasteur du Cameroun. Antimicrobial susceptibility results of *N. gonorrhoeae* isolates were retrieved from the laboratory information system and the laboratory worksheets. We included results of the disk method for tetracycline, azithromycin, spectinomycin and the minimal inhibitory concentrations (MICs) obtained with the E-test method for penicillin, ceftriaxone and ciprofloxacin. Data on the beta-lactamase activity was included, if available. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints were applied.

Results Over the years *N. gonorrhoeae* isolates showed resistance towards all tested antibiotics: the MICs of ciprofloxacin shifted to higher concentrations (with MIC₉₀ of 6 mg/l in 2013 to 32 mg/l in 2017) and 84% of the tested strains were resistant in 2017; resistance to penicillin was highest in 2016 (91%) and overall mainly plasmid mediated; the highest MIC values of 1 and 1.5 mg/l for ceftriaxone were detected in 2017 in 2 isolates; a total of 7 and 8 isolates resistant to

ceftriaxone and spectinomycin, respectively, were detected over the time period; 7% of the isolates was resistant to azithromycin in both 2013 and 2015; a high percentage (mean: 59%) of resistance to tetracycline was observed over the whole period. Overall, 42% of the isolates were resistant to three or more antimicrobials.

Conclusion A sharp increase in ciprofloxacin resistance of *N. gonorrhoeae* was detected, requiring the revision of the current Cameroonian treatment guidelines recommending ciprofloxacin. In addition, multidrug resistant *N. gonorrhoeae* strains are present in Yaoundé, Cameroon. A national surveillance program to monitor the antimicrobial susceptibility at national level should be installed and supported.

Disclosure No significant relationships.

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IN VITRO EVALUATION OF GEOTIDACIN, AN ORAL ANTIMICROBIAL AGAINST MULTIDRUG-RESISTANT MYCOPLASMA GENITALIUM

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Background *Mycoplasma genitalium* has rapidly developed resistance to first-line azithromycin and second-line moxifloxacin. Third-line pristinamycin is difficult to source and only 80% effective. Consequently, there is an urgent need for alternative therapies, and to protect new antimicrobials against development and/or spread of resistance. Resistance-guided therapy and combination with other antimicrobials are important tools. Geotidacin is a novel, first-in-class triazaacenaphthylene topoisomerase II inhibitor inhibiting DNA replication by a mechanism distinct from fluoroquinolones. Limited studies have shown activity against fluoroquinolone susceptible *M. genitalium* strains

Methods We determined the geotidacin minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) in 54 *M. genitalium* isolates by the Vero-cell culture method. Macrolide resistance was present in 31 isolates, fluoroquinolone resistance in 18 (33%) isolates; 17 had dual resistance. Synergy testing was performed for geotidacin and doxycycline by checkerboard titration for four macrolide or dual resistant isolates.

Results Geotidacin was active against all 54 *M. genitalium* isolates with median and modal MIC of 0.125 mg/L and MIC₉₀ at 0.25 mg/L (range ≤0.016–0.5 mg/L). No difference in MIC between macrolide resistant and susceptible isolates ($p=0.24$) or between fluoroquinolone and dual-resistant and susceptible isolates ($p=0.2$) was demonstrated. Geotidacin MBC was available for 45 *M. genitalium* isolates with a median MIC of 0.064 and a median MBC of 0.125 mg/L and all isolates had ≤4 fold difference between MIC and MBC suggesting bactericidal effect. Checkerboard titrations showed synergistic or additive effect with a Fractional Inhibitory Concentration Index (ΣFIC) of 0.5 for two isolates (one macrolide resistant and one dual resistant) and additive effect (ΣFIC at

0.62 and 0.75) for a macrolide and a dual resistant isolate, respectively.

Conclusion Geotidacin warrants further evaluation in clinical treatment trials for *M. genitalium*. Combination therapy with doxycycline should be clinically studied to assess effect and potential protection against development and/or spread of resistance.

Disclosure No significant relationships.

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RAPID SEQUENCE TYPING FOR ANTIMICROBIAL RESISTANCE SURVEILLANCE IN NEISSERIA GONORRHOEA USING WHOLE GENOME SEQUENCING

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Background The *Neisseria gonorrhoeae* (NG) genome changes by ~4 single nucleotide polymorphisms (SNP) per genome per year, information which is considered when predicting sexual networks using next generation sequencing to type circulating gonococcal strains. Oxford Nanopore Technologies' MinION provides opportunities for rapid "run-until" sequencing until a target coverage is achieved. We assessed MinION capacity to rapidly predict NG whole-genome strain type, from patients attending a London sexual health clinic, as an aid to rapid turn-around antimicrobial resistance (AMR) surveillance.

Methods One-directional MinION sequencing using bar-coded DNA library preparations from 44 well characterised NG isolates, prospectively collected from clinic, were run on MinION flow cells (version R9.2; three per flow cell) and Illumina MiSeq platform as a comparator. To determine shortest run-time to accurately predict strain type, MinION sequences at various time points and genome coverages were placed on a phylogenetic tree consisting of the same isolates sequenced on the MiSeq platform, clustered with a large European NG reference collection (Euro-GASP).

Results Total library preparation time was approximately one hour per flow cell. Whole genome coverage for MinION sequences varied per isolate as sequencing proceeded at different rates. In 44 isolates, 90 minutes of MinION sequencing produced a median coverage of 21-fold, and was sufficient for 30/44(68%) isolates to achieve <4 SNP differences compared to the corresponding MiSeq sequence. Estimated median SNP distance between the platforms at 90 minutes (of MinION sequencing) was 1.9 SNPs (IQR: 0.4–5.9).

Conclusion MinION sequencing enabled the placement of the majority of NG sequences onto the correct location on a reference tree after 90 minutes of sequencing, suggesting that such a method, particularly with newer iterations of the technology and library preparation protocols, might support early identification of sexual networks that support transmission, as well NG AMR surveillance.

Disclosure No significant relationships.