with ST-3672 (n=22) predominant. At the bivariate level, infection with ST-3672 was associated with younger age (62% of those infected were 15–19 years old, p=0.002), and chlamydia co-infection (67% vs 37%, p=0.012). In multivariable analysis, age group remained significant, while an interaction between inner-core residency and chlamydia co-infection was detected. Case-contact networks were highly-fragmented, consisting mainly of dyads and triads. Of 85 components, the largest component included 6 nodes, while 61% were dyads. CUG testing indicated in-degree centralization was lower than expected (p<0.05). Genotyping combined with case-contact data increased the potential size and geographic reach of each component. Of potential components found after incorporating subtypes, 32% (10/33) were dyadic, with the largest component consisting of 45 nodes.
Conclusion Molecular data revealed connections that were not apparent from case-contact investigations alone, leading to more cases potentially linked together, and over a wider geographic area. A handful of subtypes were responsible for the majority of infections. Early identification of dominant subtypes may potentially curtail transmission of NG.
Disclosure No significant relationships.

P688 RECENT INCREASES IN RATES OF GONORRHEA IN TORONTO, ONTARIO, 2012–2018

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10.1136/sextrans-2019-sti.754

Background In Toronto, gonorrhea is the second most commonly reported sexually transmitted infection, after chlamydia. From 2000 to 2012, rates of gonorrhea in Toronto were stable, ranging from 56/100,000 to 72/100,000. However, rates started to rise in 2013. In 2018, rates increased by 37% from 2017, the largest observed annual increase since 2000, reaching a high of 158/100,000. This study aimed to describe gonorrhea trends in Toronto between 2012 and 2018.
Methods Data for gonorrhea cases reported between 2012 and 2018 were extracted from the integrated Public Health Information System on January 29 2019. Analyses were conducted in SAS 9.4.
Results In 2018, 4,549 gonorrhea cases were reported in Toronto, 135% higher than 1,939 cases (71/100,000) reported in 2012. The increase was driven by a rise in reports among males, increasing by 192% while females increased by 24%; males comprised 81% of cases in 2018. Males most commonly reported engaging in sex with men (MSM), and the proportion with this risk factor increased from 55% in 2012 to 69% in 2018. Conversely, the proportion of males reporting sex with women declined from 25% in 2012 to 17% in 2018. Females in 2018 most commonly reported not using a condom (77%) in the last sexual encounter, slightly higher than 2012 (71%). In 2018, 38% of cases (44% of males, 9% of females) had rectum and/or pharyngeal gonorrhea, higher than 20% of cases in 2017.
Conclusion The rising rates in gonorrhea, particularly among MSM, may be due to changes in screening guidelines in 2013 that included extragenital screening of gonorrhea. In April 2018, both rectal and pharyngeal specimens were approved for Nucleic Acid Amplification Testing in Ontario, potentially playing a role in the additional increase in 2018. This study demonstrates that it is important that physicians continue to screen for extragenital gonorrhea among MSM.
Disclosure No significant relationships.

P689 TURNING GONORRHEA AGAINST HIV: LATENT HIV 'SHOCK-AND-KILL' USING A GONOCOCCAL-DERIVED METABOLITE

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10.1136/sextrans-2019-sti.755

Background Clinical studies have long indicated that a pathological synergy exists between *Neisseria gonorrhoeae*and HIV, with gonococcal infection increasing HIV transmission between HIV serodiscordant sexual partners. In trying to understand this association, we discovered that *N. gonorrhoeae* liberate a small molecule that stimulates HIV replication from latently infected CD4+ T cells. This led to our discovery that heptose phosphate (HP)-containing metabolites, 7-carbon phospho-sugars not produced by animals, serve as a molecular cue that bacteria are present in the tissues and elicit an NF-κB-dependent transcriptional response. Based upon these observations, this study aims to test the hypothesis that HP can function both to (i) drive the virus from latency and (ii) stimulate the antiviral response to work in synergy with available highly active antiretroviral therapies to cure HIV infection.
Methods We have used a combination of cell line and primary human leukocyte-based models to test the effect of natural and synthetic analogues of HP to stimulate HIV from latency, both alone and in combination with potential latency reversing agents, and to understand their effect of HPs on different leukocytic populations that have potential to either promote or inhibit HIV infection.
Results We show that HP has a superior combination of HIV latency reversal without toxicity often evident with conventional LRAs, and HP activity synergizes with other LRAs such that these can be administered at lower concentrations. Finally, we observed that HP stimulates primary human leukocytic responses with anti-viral potential.
Conclusion Our findings suggest that HP-based agonists are a novel LRA capable of both driving HIV from latency and stimulating immune responses so as to help control the infection. By virtue of its synergy with other LRAs and clinically available anti-retroviral agents, this represents an enticing new avenue in ongoing efforts to develop a cure for established HIV infection.
Disclosure No significant relationships.

P690 ESTABLISHMENT OF THE GONORRHEA MOUSE MODEL FOR PRE-CLINICAL TESTING OF ANTIBIOTICS THAT FOLLOW THE PK DRIVER FAUC/MIC

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10.1136/sextrans-2019-sti.756

Background New antibiotics for gonorrhea are needed due to the emergence of resistance to extended-spectrum cephalosporins in *Neisseria gonorrhoeae* (*Ng*). We recently established the 17β-estradiol mouse model of gonococcal lower genital tract

infection for testing antibiotics that utilize free time above MIC as the pharmacokinetic (PK) driver to predict efficacy. We further established the mouse model for antibiotic testing by defining the *in vivo* efficacy of ciprofloxacin (CIP), an antibiotic that uses the free area under the curve over MIC (*f*AUC/MIC).

Methods Lower genital tract infection with *Ng* strain FA1090 was established in female mice using published methods for two days, after which increasing oral doses of CIP (or controls) were administered (n = 10–20 mice/group) and infection was quantified for 8 days. Plasma drug levels from uninfected mice were measured after administration of similar doses of CIP, and PK parameters (modeled using WinNonlin software) were correlated with observed efficacy.

Results Single oral doses ranging from 5 to 60 mg/kg CIP showed significant activity against strain FA1090, with the highest doses (15, 30, and 60 mg/kg) clearing 100% of infections within 8 days; these correspond to predicted *f*AUC/MICs of 66–264. The 60 mg/kg dose cleared infection in all mice within 48 h, which we defined previously as the endpoint in the model that best correlates with *in vivo* exposures required for successful CRO/CFX treatment regimens.

Conclusion The gonorrhea mouse model shows a dose-dependent response for CIP against a CIP^S strain with a dose of 60 mg/kg required to clear infection in 48 hrs. PK modeling suggests that achieving exposures necessary for effective treatment of CIPR strains (mic ≥1 μg/ml) would be challenging. These data that establish PK/PD correlations for CIP - with a *f*AUC/MIC driver- further strengthens the usefulness of this mouse model to test novel antimicrobial compounds against gonorrhea.

Disclosure No significant relationships.

P691 WIDESPREAD USE OF HIGH-DOSE CEFTRIAXONE THERAPY FOR UNCOMPLICATED GONORRHEA WITHOUT REPORTED CEFTRIAXONE TREATMENT FAILURE

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10.1136/sextrans-2019-sti.757

Background Antimicrobial resistance (AMR) to *N. gonorrhoeae* has emerged for each of the antibiotics following their introduction into clinical practice recommended as first-line therapies. To improve rational and effective clinical antibiotic treatment, we analyzed the prescription patterns of antibiotics and its therapeutic effect in the treatment of uncomplicated gonorrhea in China.

Methods We obtained data from a follow-up multicenter-surveillance program. Multinomial logistic regression analyses were conducted to explore the associations between demographic/clinical variables with the levels of sensitivity to ceftriaxone and prescription of high-dose ceftriaxone.

Results In this study, 1686 patients infected with *N. gonorrhoeae* were recruited in a surveillance network during the period of 1 January 2013 through 31 December 2017 in 7 hospitals distributed in 5 provinces. The prevalence of isolates with decreased susceptibility to ceftriaxone was 9.8% (131/1333), fluctuating between 5.6%~12.1%. Injectable ceftriaxone was chosen as the first-line treatment among 83.1% patients, and most of them (72.7%,1018/1401) received more than 1000 mg dosage. Patients who were infected with gonorrhea or infected with other STDs before (AOR 1.611 95%CI [1.103–2.352]; AOR 2.329 95%CI [1.553–3.494]) or who used already antibiotics for this infection (AOR 1.597, 95%CI [1.04–2.452]) were associated with higher prescribed ceftriaxone dosage prescribed. All of the patients recruited in this study were cured regardless of the isolates' susceptibility to ceftriaxone or the dosage of ceftriaxone they received.

Conclusion No ceftriaxone failure treatment for uncomplicated gonorrhea were reported in China, however, high-dose ceftriaxone were widely used in China, its impacts needs further studies.

Disclosure No significant relationships.

P692 GENTAMICIN SUSCEPTIBILITY TO *NEISSERIA GONORRHOEAE* IN MALAWI AFTER TWENTY-FIVE YEARS OF SUSTAINED USE

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10.1136/sextrans-2019-sti.758

Background Gentamicin has been used exclusively for the treatment of *Neisseria gonorrhoeae* (GC) in Malawi, since 1993. Previous gentamicin susceptibility testing in 1993, 1996 and 2007, showed ≥95% susceptibility by both agar dilution and E-test. However, clinical cure rates 1–2 weeks following treatment, have been in the 90% range. We are in the process of repeating this assessment to inform treatment guidelines.

Methods We are enrolling HIV-infected men presenting with acute urethritis at the sexually transmitted infections (STI) clinic at Bwaila District Hospital in Lilongwe, Malawi. All participants provide urethral swabs for STI etiologic testing, and are treated syndromically per Malawian standard of care, with gentamicin 240 mg IM, doxycycline 100 mg, BID for 7 days, and metronidazole 2g single dose. Patients are seen one week post-treatment for repeat clinical exam and GC culture. All specimens with a positive GC culture are tested locally for gentamicin susceptibility via E-test. E-test inhibition with ranges from 0-4, 4-16, and ≥16 are categorized as high, moderate, and low susceptibility, respectively. Clinical cure is determined by genital examination.

Results 42 men with gonococcal urethritis have been enrolled to date. Baseline gentamicin E-test results: high susceptibility: 0-1: 21%; 1-2: 60%; 2-4: 19%; moderate or low susceptibility ≥4: 0%. 37/42 men (88%) returned for follow-up. 4/37 (11%) were culture positive for GC, including 2 (5%) symptomatic men. 3/4 (75%) of the week one E-test results were in the high susceptibility range, and 1/4 (25%) was in the low susceptibility range (≥16).