Jarisch–Herzheimer reaction was positively associated with treatment regimen prognosis ($p<0.05$).

Conclusion Our serological data demonstrate that this ceftriaxone regimen is more effective than the currently recommended benzathine penicillin regimen for early syphilis in non-pregnant, immunocompetent patients, especially for secondary syphilis.

LB1 – Late Breakers Oral Sesssion

LB1.1 INSIGHTS INTO THE EVOLUTION OF SYPHILIS SPIROCHETES WITHIN AT-RISK POPULATIONS: SEQUENCE VARIATION OF OUTER MEMBRANE PROTEIN β-BARREL DOMAINS IN CLINICAL SAMPLES

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10.1136/sextrans-2017-053264.102

Introduction Outer membrane proteins (OMPs) play critical roles in disease pathogenesis and are vaccinogens. Topologic characterisation of surface-exposed β-barrels of *Treponema pallidum* (*Tp*) Nichols rare OMPs enabled a novel strategy to assess sequence diversity and evolution of *Tp* in geographically diverse locations.

Methods Through early 2017, sequences encoding TprC (TP0117), TprD (TP0131), and BamA (TP0326) β-barrels were amplified from secondary syphilis patients from Cali (n=16) and swabs from patients in San Francisco (SF, n=6) and Czech Republic (CZ, n=9). Strains were assigned to the Nichols or SS14 clade based on *tp0548* and/or *tp0558* sequences.

Results 23 assignable CZ and Cali strains belonged to either the SS14 or Nichols clade (SS14 predominant), while all 6 SF strains belong to the SS14 clade. Sequence diversity at the three OMP loci was greatest in Cali, with evidence of recombination within *tprC* and *bamA* alleles, as well as between strains and clades at all 3 genetic loci. SF strains contained nearly identical sequences at all 3 genetic loci. The SS14 and Mexico A reference strains, both belonging to the SS14 clade, have identical *tprDs* (*tprD2*) but different *tprC* and *bamA* alleles. Mexico A *tprC*s were common at all three geographic locations, including Nichols clade strains from Cali. Mexico A *bamA*s were prevalent in Cali and SF, while CZ SS14 clades contained only SS14 *bamA*s. OMP sequences were obtained from all three loci in 7 of 8 Nichols clade strains. Of these 7, only 1 matched the Nichols reference strain, while the other 6 contained Mexico A alleles in at least 1 OMP locus. Of the 21 SS14 clade strains, 10 contained Mexico A alleles at all 3 loci; 2 contained Mexico A *trpCs* and Nichols *bamAs*; and 9 contained Mexico A *tprCs* and SS14 *bamAs*.

Conclusion OMP loci are evolving independently within *Tp*. Recombination of OMP sequences appears to be occurring between *Tp* strains and clades within patients. Mexico A OMP alleles are circulating widely among *Tp* strains. These findings have major ramifications for syphilis vaccine development.

LB1.2 WHAT IS THE STRENGTH OF EVIDENCE FOR HIV AND HPV INTERACTIONS? RESULTS FROM SYSTEMATIC REVIEWS AND META-ANALYSES OF LONGITUDINAL STUDIES

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10.1136/sextrans-2017-053264.103

Introduction We conducted two systematic reviews. Review 1 (R1) summarised evidence for the influence of HIV on HPV acquisition and clearance. Review 2 (R2) summarised the evidence for the influence of HPV on HIV acquisition. R1 is the first meta-analytic review to quantify the impact of HIV on HPV infection. R2 updates two earlier meta-analyses.

Methods Both reviews were conducted according to PRISMA and MOOSE guidelines. We searched PubMed and Embase up to January 2017 for longitudinal studies of HPV incidence and clearance rate by HIV status and of HIV incidence by HPV status. We derived pooled relative risk (RR) estimates using a random effect model and performed subgroup analyses to understand main sources of heterogeneity, examined dose-response relationship and produced funnel plots.

Results In R1, 37 publications comprising 25 independent study populations were included. The incidence of HPV (pooled crude RR [cRR]=1.55, 95% CI 1.29–1.88) and of high-risk (HR) HPV (pooled cRR=2.20, 95% CI 1.90–2.54) was doubled whereas HPV clearance rate (pooled cRR=0.53, 95% CI 0.42–0.67) and HR-HPV clearance (pooled cRR=0.69, 95% CI 0.57–0.83) was nearly halved among people living with HIV (PLHIV). HPV incidence when CD4 count ≤200 cells/μL among PLHIV was higher, but not statistically significant, than for CD4 >200 cells/μL (pooled cRR=6.65, 95% CI 2.98–14.85 vs 3.20, 95% CI 2.48–4.13). In R2, 14 publications comprising 11 independent study populations were included. HIV incidence was almost doubled in the presence of prevalent HPV infection (pooled cRR=1.91, 95% CI 1.38–2.65) and for HR-HPV (pooled cRR=1.63, 95% CI 1.26–2·09). Risk of HIV acquisition increased with the number of HPV types. Crude and adjusted pooled estimates were similar in both reviews. There was more evidence of publication bias in R2 than R1.

Conclusions The findings met most Bradford-Hill criteria for causation. Our results have clinical and public health relevance: HPV vaccination may benefit PLHIV and indirectly help to reduce HIV transmission. HIV prevention may also reduce HPV transmission.

LB1.3 ANTICIPATING RESISTANCE OF *MYCOPLASMA GENITALIUM* TO QUINOLONES AND MACROLIDES: NANJING, CHINA

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10.1136/sextrans-2017-053264.104

Introduction For treatment of *Mycoplasma genitalium* (Mg) infection, azithromycin is first line initial treatment but

persistent NGU caused by Mg may not respond to repeat azithromycin treatment; quinolones, in particular moxifloxcin, have been shown to be effective. The molecular epidemiology of mutations in macrolide- and quinolone-resistance determining regions (RDRs) of 23S rRNA, parC and gyrA genes remains unclear in China.

Methods From April 2011 to August 2015, male subjects with clinical and microscopic evidence of urethritis provided a first-voided urine specimen and the mgpA gene was partially amplified and sequenced to diagnose Mg infection. RDRs of the 23s rRNA, parC and gyrA genes were sequenced.

Results Among 1816 male-patients, the overall prevalence of *M. genitalium* was 19.7% (358/1816). *N. gonorrhoeae* prevalence was 46.6% (847/1816). Among 969 NGU-cases, prevalence of: *C. trachomatis* was 42.3% (409/968), *M. genitalium* 27.9% (271/969), *U. urealyticum* 21.3% (182/856), *T. vaginalis*1.8% (17/969) and *M. hominis* 0.7% (6/855). Based on data available from partial (5.4%) sequencing of the MgPa gene (mgpA) an evolutionary tree was constructed that divided the 358 *Mg* mgpA sequences into five major clusters. Among 358 *Mg* positive samples, successful sequencing was accomplished for: the 23s rRNA gene (341 specimens), the parC gene (344 specimens) and the gyrA gene (339 specimens). 88.9% (303/341) had mutations in 23s rRNA, 89.5% (308/344) had sense mutations in parC, and 12.4% (42/339) had sense mutations in gyrA.The most common single base pair mutation in the 23s rRNA gene was A2059G (211/303; 69.6%) followed by A2058G (60/303; 19.8%) and A2059T (30/303; 9.9%). The most common mutation in the parC gene was G248T (289/344; 84%) and in the gyrA gene G285A (22/339, 6.5%).

Conclusion The high mutation rate in 23s rRNA and parC in Mg strains in Nanjing are a harbinger of resistance to macrolides and quinolones that may follow. Molecular surveillance of indigenous strains of Mg is warranted to anticipate the development of antimicrobial resistance.

LB1.4 IMPROVED OUTCOMES FOLLOWING RESISTANCE-GUIDED TREATMENT OF *MYCOPLASMA GENITALIUM* INFECTION

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10.1136/sextrans-2017-053264.105

Introduction Resistance to 1 st (azithromycin) and 2nd line (moxifloxacin) therapy in *Mycoplasma genitalium* (MG) now exceeds 50% and 15%, respectively, in the Asia-Pacific region. New approaches to achieve high levels of cure and minimise resistance are urgently needed. We evaluated a novel strategy of switching from azithromycin to doxycycline for MG-associated syndromes and using resistance-guided therapy, with sitafloxacin for macrolide-resistant infections.

Methods From July 2016 Melbourne Sexual Health Centre switched from azithromycin to doxycycline 100 mg twice daily 7 days for non-gonococcal urethritis/cervicitis/proctitis. Cases were tested for MG and macrolide-resistance mutations (MRM) by PCR (ResistancePlus MG test, SpeeDx Pty Ltd). After doxycycline, MG-positive cases without MRM received 2.5g azithromycin (1g then 500 mg daily for 3 days) and MRM-positive cases received sitafloxacin 100 mg twice daily for 7 days. Retest for microbiologic cure and standardised assessment of adherence, side-effects and post-diagnosis sexual contact occurred 14–90 days after the second antibiotic. Those reporting condomless sex or sex with an incompletely treated partner were excluded.

Results Of 162 evaluable MG infections (35 women, 42 heterosexual men, 85 homosexual men, median age 29) diagnosed to 9 March 2017, MRM were detected in 116 [71.6% (95% confidence interval (CI) 64.0–78.4). Microbiologic cure occurred in: 44 of 46 infections without MRM, treated with doxycycline then azithromcyin [95.7% (95%CI 85.2–99.5)] and in 107 of 116 infections with MRM treated with doxycycline then sitafloxacin [92.2% (95%CI 85.8–96.4)]. Mean fall in $\log_{10}$ bacterial load (on doxycycline prior to the 2nd antibiotic, n=17) was 2.9, p<0.01. Sitafloxacin was associated with diarrhoea (8.6%) and tendon/joint pain (6.0%). Five (3.1%) patients missed >20% of doses of any antibiotic.

Conclusion Switching from azithromycin to doxycycline for presumptive treatment of STI syndromes, and use of resistance-guided therapy cured >92% of MG infections in the context of high levels of antimicrobial resistance.

LB1.5 THE EFFICACY AND SAFETY OF GENTAMICIN FOR THE TREATMENT OF GENITAL, PHARYNGEAL AND RECTAL GONORRHOEA: A RANDOMISED CONTROLLED TRIAL

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10.1136/sextrans-2017-053264.106

Introduction Gentamicin is effective against *N. gonorrhoeae in vitro* and systematic reviews have reported cure rates of 62%–98% but the quality of studies was low and there are few data on pharyngeal or rectal infections. A recent large non comparative trial reported a cure rate of 100% when gentamicin was combined with 2g oral azithromycin, but a high incidence of gastrointestinal adverse effects limited tolerability and few extra-genital infections were included. The aim of this study was to evaluate the efficacy and safety of gentamicin versus ceftriaxone, each combined with 1g of azithromycin, for the treatment of gonorrhoea.

Methods A multi-centre, blinded, randomised controlled trial in participants with genital, pharyngeal or rectal gonorrhoea who received either gentamicin 240 mg or ceftriaxone 500 mg (each as a single intramuscular injection). The diagnosis of gonorrhoea was based on a positive nucleic acid amplification test (NAAT) or gram stained smear on microscopy. The primary endpoint was microbiological cure based on NAAT two weeks after treatment. The trial had 90% power to detect non-inferiority with a lower CI for an absolute risk difference of 5%. Data collection was completed in March 2017.

Results 720 patients from 14 sexual health clinics in England were randomised to receive ceftriaxone (n=362) or gentamicin (n=358). Baseline characteristics of the two groups were well balanced. 306 participants randomised to ceftriaxone (85%) and 292 randomised to gentamicin (82%) had primary outcome data available. 98% (299/306) and 91% (267/292) of participants randomised respectively had clearance of