004.5 COMPARISON OF THE CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF NEONATAL HERPES INFECTIONS CAUSED BY HERPES SIMPLEX VIRUS TYPE 1 AND TYPE 2; FINDINGS FROM A POPULATION-BASED SURVEILLANCE SYSTEM, 2006–2012

doi:10.1136/sextrans-2013-051184.0105

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Background The epidemiology of neonatal herpes infection (nHSV) is changing as herpes simplex virus type 1 (HSV-1) is an increasingly common cause of genital herpes. Few sources of population-based data for nHSV exist; nHSV has been a notifiable disease in New York City (NYC) since 2006.

Methods To compare the clinical and demographic characteristics of nHSV due to HSV-1 and herpes simplex virus type 2 (HSV-2), we used standard case investigation forms to abstract infant inpatient/outpatient medical records, and maternal labour and delivery records for babies ≤ 60 days of age diagnosed with laboratory-confirmed herpes infection and reported in NYC during 2006–2012. Disease syndromes were grouped as invasive (disseminated/central nervous system infection/death) versus localised (skin/eye/mucous membrane infection,). Cases lacking liver function test results, or lumbar puncture were excluded from analyses of disease syndrome. Bivariate analyses compared clinical and demographic characteristics by viral type.

Results There were 91 cases reported (HSV-1, 40; HSV-2, 36; untyped, 15). Among 76 cases with viral typing, the majority (53%; 40/76) were HSV-1. There were no statistically significant differences by viral type for any variables examined: age ≤ 7 days at presentation (HSV-1, 59% versus HSV-2, 41%), fever (HSV-1, 38% versus HSV-2, 46%), vesicles (HSV-1, 46% versus HSV-2, 53%), invasive disease (HSV-1, 53% versus HSV-2, 70%), case fatality rate (HSV-1, 18% versus HSV-2, 19%), maternal history of genital herpes (HSV-1, 20% versus HSV-2, 20%), maternal genital lesions at delivery (HSV-1, 8% versus HSV-2, 3%), vaginal delivery (HSV-1, 69% versus HSV-2, 61%), white non-Hispanic maternal race/ethnicity (HSV-1, 26% versus HSV-2, 12%), maternal age < 20 (HSV-1, 15% versus HSV-2, 27%).

Conclusions Neonatal herpes infections due to HSV-1 and HSV-2 have a similar presentation, and death rate. To prevent nHSV, candidate HSV vaccines will need to protect against HSV-1, as well as HSV-2 infection in women.

004.6 *MYCOPLASMA GENITALIUM* - IS IT A PATHOGEN IN ACUTE PELVIC INFLAMMATORY DISEASE (PID)?

doi:10.1136/sextrans-2013-051184.0106

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Background PID is a polymicrobial infectious condition of the female upper genital tract. *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT), long considered the predominant organisms involved in the pathogenesis of PID, are identified in fewer than half of U.S women diagnosed with acute PID. *Mycoplasma genitalium* (MG) is associated with male urethritis and some evidence suggests an association with other STD syndromes including cervicitis and PID. Our objective was to examine the association between MG and acute PID.

Methods The ACE Trial is a randomised double-blind study evaluating the value of anaerobic therapy for acute PID. At enrollment, specimens were collected from the cervix and endometrium for testing for GC, CT and MG by transcription-mediated amplification. Histology was performed on endometrial tissue. Identification of cervical and endometrial organisms was correlated with endometritis.

Results Among the 125 women diagnosed with acute PID, twenty two percent (n = 27) tested positive for *M. genitalium*, while CT, GC and bacterial vaginosis were present in 14%, 7% and 54%, respectively. Forty six women (37%) had histologic endometritis. Histologic endometritis was more common among those having cervical infections with GC, CT or MG than uninfected women (66% vs. 24%, $p < 0.001$). Among women with endometritis, GC, CT and MG were present in 17%, 30% and 36%, respectively. Endometritis was present in 71% (20/28) of women with endometrial GC, CT or MG. Endometrial identification of GC (100% vs. 34%, $p < 0.05$), CT (77% vs. 32%, $p < 0.01$) and MG (64% vs. 33%, $p < 0.05$) were each independently associated with endometritis.

Conclusion *Mycoplasma genitalium* is identified in 22% of women diagnosed with acute PID. Similar to CT and GC, the presence of MG in the endometrium is highly associated with endometritis among women diagnosed with PID. This study suggests that *M. genitalium* may play an important role in the pathogenesis of PID.

O.05 - Molecular analysis of STI pathogens and their environments

005.1 HIGH GRADE ANAL INTRAEPITHELIAL NEOPLASIA: ONE VIRUS, ONE LESION

doi:10.1136/sextrans-2013-051184.0107

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Ba**ckground** Prevention and treatment of anal intraepithelial neoplasia (AIN) in HIV+ men who have sex with men (MSM) is subject of discussion. Knowledge on causative HPV types is crucial in understanding AIN and in vaccination studies. However, data on AIN-specific HPV are limited and whole tissue sections (WTS) often show multiple HPV infections.

In this study, we analysed whether WTS and subsequent laser capture micro-dissection (LCM) with HPV PCR genotyping accurately detects type-specific HPV DNA in individual areas of high grade (HG)AIN.

Methods 31 WTS with HGAIN of 21 HIV+ MSM were analysed by the SPF10 PCR/LiPA25 (version 1) HPV genotyping system. In case of multiple HPV types, PCR was repeated in selected areas of AIN, isolated by LCM.

Results WTS PCR showed a single HPV type in 17 (55%). In the remaining 14 WTS sections with multiple HPV types, PCR was repeated in LCM-isolated dysplastic areas (median: 4 per WTS). In 12 of 14 these samples, the number of HPV types could be reduced to single HPV types within discrete areas of a lesion, resulting in a total of 29 (17+12), in which (components of) HGAIN show a singe HPV type. HPV 16 was found in 14/29 (48%), HPV 18 in 3 and HPV 58 in 3. The remaining HPV types that could be linked to a lesional area were HPV 26, 31, 35, 39, 52, 53, 54, 59, 67, 68/73, 74, 91 and one indeterminate HPV type.

Conclusion WTS PCR and subsequent LCM PCR is accurate in detecting lesion specific HPV types in AIN and it seems that 94% of the AIN-lesions (on macroscopic or microscopic level) are caused by a single HPV type. Apart from HPV 16, the predominant type, a wide range of other HPV types are responsible for HGAIN, which has consequences for vaccination development.

005.2 MEASURING SYPHILIS: QUANTITATIVE PCR CAN BE USED TO MONITOR TREATMENT RESPONSE

doi:10.1136/sextrans-2013-051184.0108

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Background The humoral response to *Treponema pallidum* (*T. pallidum*), which causes syphilis, is divided into 'non-specific' anti-lipid and specific anti-treponemal protein antibodies. A four-fold reduction in anti-lipid antibodies is used to diagnose cure, which can take six or more months.

Quantitative PCR (qPCR) can measure *T. pallidum* DNA copies in blood and ulcer samples. Bacteraemia is more common and of higher load in early disease.

We present a pilot study monitoring the early treatment response in patients with infectious syphilis by qPCR.

Methods Patients with symptomatic primary or secondary disease were admitted to hospital and following baseline sampling were treated with 2.4 M units of benzathine penicillin. Whole blood was collected into EDTA and Tempus RNA preservation tubes and the ulcer sampled using a philtre paper strip every four hours for *T. pallidum* DNA (*tpp047* gene) and RNA (*16S rRNA*) quantification. Sampling ended when two consecutive PCRs were negative. Standard serological follow-up was performed.

Results Three men were recruited (two secondary, one primary). All were homosexual and two were HIV-1 infected.

Blood DNA quantification and clearance: A mean peak-level of 1611(range 1212) *tpp047* copies/ml was detected and mean half-life for clearance (t½ clearance) was 7.89 hours (range 5.34). Blood RNA: Mean peak-level 8829(range 20366) *16SrRNA* copies/ml blood; (t½ clearance) 5.24 hours (range 0.78). Ulcer DNA 1.14×10^5 copies/strip and RNA 4.35×10^7 copies/strip with a t½ (clearance) of 1.67 and 3.76 hours, respectively. *T. pallidum* nucleic acids were undetectable in all samples after 56 hours.

All patients had serology consistent with disease stage at baseline and cure at one month.

Conclusions

- *T. pallidum* qPCR presents a novel and quick way of monitoring early syphilis treatment efficacy. Both DNA and RNA may be suitable targets to measure bacterial clearance from blood and ulcer exudates.
- Ulcers may be non-infectious as soon as 56 hours post-treatment.

005.3 MORE THAN MEETS THE EYE: A MOLECULAR PHYLOGENETIC ANALYSIS REVEALS IMPORTANCE OF NOVEL BACTERIA IN BACTERIAL VAGINOSIS (BV)

doi:10.1136/sextrans-2013-051184.0109

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Background BV is a highly prevalent dysbiotic condition associated with adverse reproductive and health outcomes in women. BV is marked by loss of certain lactobacilli and acquisition of complex communities of anaerobic bacteria. Gram stain is the gold standard for diagnosis, wherein the abundances of four bacterial morphotypes are assessed; Lactobacillus, Gardnerella, Bacteroides and Mobiluncus. Newly described uncultivated bacteria are highly specific for BV, but no studies have investigated the association between these bacteria and Gram stain morphotypes.

Methods We examined the association of bacteria detected by broad-range 16S-rRNA gene PCR/pyrosequencing with bacterial morphotypes detected in Gram stains from 220 women with and without BV. We also used species-specific quantitative PCR and fluorescence in situ hybridization (FISH) methods to document concentrations of two bacteria with curved rod morphologies: *Mobiluncus* species and the uncultivated BV-associated bacterium-1 (BVAB1).

Results We provide evidence that curved Gram-negative rods designated Mobiluncus morphotypes by Gram stain are more likely BVAB1. Rank abundance plots of vaginal bacteria in women with curved rods (Nugent 9–10) showed that BVAB1 was the dominant bacterium (26%), while relative abundance of *Mobiluncus* was only 0.2%. BVAB1 sequence reads were also associated with Mobiluncus morphotypes ($p = 7.4E-06$). Among women with Nugent scores 9–10, the mean concentration of BVAB1 DNA was 2-log units greater than *Mobiluncus* ($p < 0.001$). FISH analyses also revealed that among women with Nugent scores of 10, the mean number of BVAB1 cells was greater than *Mobiluncus* cells ($p < 0.001$). In addition, we noted that *Prevotella* and *Porphyromonas* spp. are significantly associated with the Bacteroides morphotype, whereas *Bacteroides* species are rare.

Conclusions Gram stain morphotype designations for BV need revision to account for novel vaginal bacteria. These findings have major implications for studies using Gram stains as a proxy to describe the vaginal microbiota.

005.4 ASSOCIATION BETWEEN CHLAMYDIA TRACHOMATIS GENITAL INFECTION AND THE VAGINAL MICROBIOME

doi:10.1136/sextrans-2013-051184.0110

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Background *Chlamydia trachomatis* (CT) genital infection is one of the most widespread sexually transmitted infections (STIs). It is thought that certain types of vaginal microbiota are better able to prevent STIs, however, very little is known about the relationships between species and genomic composition of the vaginal microbiome and risk of infection. Information about these can be used to advance prevention strategies for STIs. We sought to characterise the vaginal microbiome at the time of diagnosis and after treatment of CT infection.

Methods 101 women with CT genital infection were recruited to a longitudinal study in Baltimore, MD. Participants were treated at diagnosis and returned for clinical visits every 3 months for 9 months, at which times the vaginal microbiota was determined using 16S rRNA analysis. We further applied high-throughput metagenomics to characterise the genomic makeup of the vaginal microbiome.

Results The average age of participants was 19.3 (range 14–28) and 92% were African-American. During CT infection, comprehensive surveys of the vaginal microbiota demonstrated two distinct community state types characterised by: (1) a complex assemblage of strict anaerobes with low proportions of *Lactobacillus* spp. (60% of samples) or (2) a high relative abundance of *Lactobacillus iners*-dominated communities (37% of samples). Metagenomic evaluation suggested unique characteristics of the genomes of the dominant species in these communities (i.e., *L. iners, Gardnerella vaginalis*). *L. iners* appeared more genetically diverse than other *Lactobacillus* species.

Conclusions Complex communities of strict anaerobes with low proportions of *Lactobacillus* or specific *L. iners* genome types represented a hallmark of the chlamydia-infected state in this population. Some *L. iners* may be better suited to adapt to diverse environments while others may be contributing factors to an at-risk microbiome. In the era of personalised medicine, future work will enhance our ability to intervene and establish a protective vaginal microbiome.