Clinical sciences oral session 1—Syphilis: enhanced approaches for detection & characterisation

**O3-S1.01 BRITISH OCULAR SYPHILIS STUDY (BOSS): NATIONAL SURVEILLANCE STUDY OF INTRAOCULAR INFLAMMATION SECONDARY TO INFECTIOUS SYPHILIS**

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**Background** Syphilis poses a significant public health problem. There has been a 1032% increase in the incidence of syphilis between 1999 and 2008 in the UK. There are currently no epidemiological studies looking at the incidence of ocular syphilis in the light of the outbreak. Ocular syphilis is a rare, but treatable if recognised early. The purpose of this study is to ascertain the incidence of intraocular syphilis in the UK and to characterise the clinical presentation patterns of ocular syphilis.

**Methods** A prospective study was conducted in the UK and Republic of Ireland, where cases of ocular syphilis were reported through the national reporting system (British Ocular Surveillance Unit) over an 18-month period from May 2009. Case definition was any adult patient who presented with intraocular inflammation and early infectious syphilis as evidenced by positive syphilis serology with (1) high titre RPR of >1:8 or (2) signs of secondary syphilis.

**Results** 35 new cases of ocular syphilis were reported (annual incidence 0.46 per million) with a mean age of 51.5 years (range 22–75 years). 86% were males; 88% were caucasians and 12% were Afro-Caribbean. The mean duration of symptoms was 1.0 month prior to presentation (range 2 days to 4 months). 46% of patients had bilateral involvement and the mean presenting logMAR visual acuity was 0.48 (20/60 Snellen; range −0.1 to −1.36). 54% had visual acuities of 20/40 Snellen or better at initial consultation. Presenting acuity was not influenced by duration of visual symptoms. Intraocular pressure on presentation was elevated in only one patient (27 mm Hg). Although 68.4% had an anterior uveitis (AU), isolated AU was rare (1 case). 63% had vitritis; 61% had a form of posterior uveitis, (60% retinitis, 56% vasculitis, 50% macular oedema, 28% choroiditis). 52% of cases had optic nerve involvement. Of males whose sexual orientation was ascertained 85% were MSM. Of patients whose HIV status was known, 71% were HIV positive.

**Conclusions** This study is the largest prospective series of ocular syphilis in the post-penicillin era providing up to date Western European incidence, demographic and clinical data. Syphilitic uveitis affects mainly adult males of all ages; majority were MSM or HIV positive. The uveitis is nonresponsive, posterior uveitis is common, and AU rarely presents in isolation. Clinician and public health awareness of ocular syphilis remains important.

**O3-S1.02 DECIPHERING THE CODE OF TREPONEMA PALLIDUM IN THE UK: IMPLICATIONS FOR TREATMENT AND PREVENTION**

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**Background** The efficacy and convenience of single-dose oral azithromycin meant it became the preferred treatment for syphilis in many countries and a suitable alternative to penicillin in many more. However, two point mutations (A2058G and A2059G) in the 23srRNA gene of *T. pallidum* (*T. pallidum*) have separately been shown to confer high-level macrolide resistance. Furthermore, molecular analyses of *T. pallidum* with an enhanced sub-typing method have revealed the existence of a number of strain types, which both persist over generations and may be associated with distinct clinical phenotypes.

**Methods** Following informed consent, whole EDTA blood and ulcer exudate absorbed onto filter paper Snostrips were collected from patients with any stage of syphilis in a London genito-urinary medicine clinic between 2006 and 2008. *T. pallidum* DNA was extracted and strain types and macrole resistance-associated mutations sought by: (1) PCR amplification of the 23srRNA gene and restriction fragment length polymorphism (RFLP) analysis following Mbo-II and BsaI digestion; (2) determination of the number of 60-base repeats within the ARF gene by PCR and agarose gel electrophoresis; (3) PCR amplification of the TPR gene family and RFLP analysis following MseI digestion; (4) sequence analysis of a section of the tp548 gene.

**Results** Forty-two of the 44 (95.5%) patients diagnosed with syphilis were male, of which 68.6% were MSM and 28/44 (63.6%) were HIV-1 infected. *T. pallidum* DNA was present in sufficient quantity and quality for analysis in 18/44 (40.9%), 23srRNA gene analysis revealed 6/18 (33.3%) wild-type sequences, 11/18 (61.1%) A2058G and 14/18 (77.8%) A2059G mutants. Full strain-typing was possible in 5 clinical samples (four were 14d/g and one was 14d/f), and partial typing in a further 7 (see Abstract O3-S1.02 table 1).

<table>
<thead>
<tr>
<th>Sample</th>
<th>Number of ARP gene repeats</th>
<th>TPR gene Mse-1 RFLP analysis</th>
<th>Tp548 gene sequence analysis</th>
<th>Final enhanced strain type</th>
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<td>1</td>
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<td>2</td>
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<td>14d/g</td>
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<td>−</td>
<td>F</td>
<td>−</td>
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<td>Positive control (Nichols)</td>
<td>14</td>
<td>−</td>
<td>A</td>
<td>14a/a</td>
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</table>

**Conclusions** The high frequency of *T. pallidum* macrolide resistance mutations described in the UK for the first time has clear implications for national treatment strategies. The majority of patients with syphilis were men, of which most were MSM and over half were HIV-1 positive. It is thought that transmission of *T. pallidum* within sexual networks has played a part in the resurgence of syphilis in the UK over the last decade and the predominance of the 14d/g subtype may reflect this. Alternative explanations are that this strain type is more virulent or has become endemic, as in the
case of the Scottish data that revealed 77% of syphilis cases there to be type 14d.

**O3-S1.03 PERFORMANCE OF REVERSE SEQUENCE SYPHILIS SCREENING IN JAMAICA**

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**Background** Algorithms for syphilis serologic testing traditionally have relied on screening with a non-treponemal test, such as Treponema pallidum particle agglutination (TP-PA). To reduce time, material and labour costs, many laboratories, including at the Comprehensive Health Centre in Kingston, Jamaica, have reversed the sequence testing first with a rapid treponemal test followed by non-treponemal testing of reactive sera.

**Methods** In a survey of STIs among men who have sex with men (MSM) in Jamaica, syphilis serologic testing is currently conducted using an initial rapid treponemal SD Bioline Syphilis 3.0 test followed by TRUST for reactive sera. Discordant sera that are Bioline-positive and TRUST-negative, or sera with TRUST titres < or = 8 undergo supplemental testing by TP-PA. SD Bioline was previously validated in the field and reference laboratory in Jamaica and is 95.2% sensitive and 95.3% specific compared to TP-PA. Here we report the results from sera obtained from 135 MSM in Kingston between December 2010 and February 2011.

**Results** Among 135 sera evaluated using the reverse syphilis screening sequence, 13 (9.6%) had a positive rapid treponemal test. Among these 13 reactive sera, 6 (46.2%) were nonreactive with TRUST. All discordant sera were also reactive by TP-PA, indicating that initial rapid testing did not produce false-positives in this setting. The proportion of discordant syphilis test results was similar among HIV+ and HIV- men. The prevalence of primary syphilis detected by concordant positive treponemal and non-treponemal tests in this survey was 5.2%, compared to 5.3% in a previous survey conducted in this population during 2007–2008 using the traditional screening sequence.

**Conclusions** The prevalence of primary syphilis among MSM in Kingston has not changed since the previous survey. In the current survey using the reverse screening sequence, nearly half of sera that were reactive with the treponemal test produced discordant results with the non-treponemal test. Such results are consistent with previous syphilis infection, treated or untreated, or early primary syphilis in which non-treponemal antibodies have yet to develop. Distinguishing these possibilities requires detailed history and clinical assessment in addition to serologic test results.

**O3-S1.04 PERFORMANCE CHARACTERISTICS OF BIOPLEX 2200 SYPHILIS IgG AND LIASON TREPONEMA AUTOMATED ASSAYS FOR DETECTION OF ANTIBODIES TO TREPONEMA PALLIDUM**

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**Background** Serological testing continues to be a crucial tool for syphilis diagnosis and control. The commonly accepted syphilis screening algorithm is screening with non-treponemal tests such as RPR or VDRL, and confirming with treponemal tests such as TP-PA. Recently, automation has been introduced whereby serological screening using treponemal tests has resulted in reduced labour time and removal of the subjectivity associated with the traditional testing algorithm. The objective of this study was to compare the performance characteristics of two FDA approved automated tests, the BioRad BioPlex 2200 Syphilis IgG and the DiaSorin LIASON treponemal assays, with known predicate tests. The BioPlex 2200 syphilis IgG is a multiplex test that utilises three analytes (15-, 17-, & 47-kDa) to detect specific IgG antibodies, whereas the LIASON treponemal assay uses only one analyte (17 kDa) in a single step sandwich method to detect both syphilis IgG and IgM antibodies.

**Methods** A total of 1086 commercially obtained sera tested in this study consisted of: 450 from pregnant women, 409 from HIV positive individuals, and 111 from known syphilis patients of various disease stages. Characterised syphilis samples (n=140) were also obtained from the CDC serum repository. All samples were screened by the BioPlex IgG, Liaison, RPR and TP-PA tests. Any indeterminate results were repeated at least once.

**Results** Of the 1086 samples tested, the syphilis reactivities were the following: 551 (50.7%) by BioPlex IgG, 528 (48.6%) by LIASON, and 509 (46.9%) by TP-PA. The sensitivity and specificity when compared to TP-PA for LIASON was 98.5% and 93.0% respectively. The BioPlex IgG sensitivity and specificity when compared to TP-PA was 85.1% and 80% respectively. Overall, 443 (40.8%) samples were found to be reactive and 450 (41.4%) non reactive to both BioPlex and BioPlex IgG. All three tests agreed on 877 (81%) samples. On the 209 discordant samples TP-PA agreed with LIASON 85.2% (n=178), BioPlex 7.2% (n=15), but disagreed with both tests 7.7% (n=16).

**Conclusion** Both tests have high throughput, walk-away capability, and would be useful in low prevalence settings. There was good agreement between the LIASON and the BioPlex IgG in 895 (82%) samples (Cohen’s k=0.64). The LIASON had higher sensitivity most likely due to its detection of both IgG and IgM, while the BioPlex detected only IgG antibodies. Both tests show significant promise in the future of syphilis serology.

**O3-S1.05 QUALITY ASSURANCE OF SYPHILIS TESTING IN A RURAL HEALTH FACILITY USING DRIED TUBE SPECIMENS (DTS)**

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**Background** Assuring the quality of a diagnostic test is important in healthcare. For syphilis testing, this includes proficiency testing of previously well characterised serum samples by health workers blinded to the results of characterisation. As part of a study on the feasibility of using a Point of Care (POC) rapid test devise for syphilis testing in rural antenatal settings, proficiency testing material prepared in a referral laboratory using Dried Tube Specimens (DTS) was sent for testing by the nurses/midwives in these rural settings.

**Methods** Five well characterised DTS (one high RPR reactive, three low RPR reactives and one RPR non-reactive) were sent for on-site testing by the nurses/midwifes in these rural settings. Prepared in a referral laboratory using Dried Tube Specimens (DTS) was sent for testing by the nurses/midwifes in these rural settings.

**Results** Seven out of the eight facilities correctly reported results of the DTS for all the rounds. One facility however reported all specimens as negative at the first round. One-on-one training was provided for on-site testing in eight rural antenatal facilities in Eastern Ghana. Training of nurses/midwifes in reconstituting the DTS and their testing and reporting was previously carried out. An instruction leaflet was enclosed in each batch of the DTS. Four rounds of the testing were carried out at monthly intervals.

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