

## SYPHILIS

# Increasing detection of asymptomatic syphilis in HIV patients

C E Cohen, A Winston, D Asboe, F Boag, S Mandalia, B Azadian, D A Hawkins

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**Background/objectives:** The burden of new syphilis diagnoses in London has mainly been in men who have sex with men (MSM), many of whom are co-infected with HIV. Our HIV unit introduced regular serological screening for syphilis during routine follow up care to detect patients who may be at risk of asymptomatic infection. We assessed if this remained an effective and necessary strategy in the second year since introduction.

**Methods:** All HIV outpatients with newly positive syphilis serology between 1 May 2002 and 30 April 2003 were identified using a prospectively collected database. Only patients who were asymptomatic at the time of screening were included (cohort B). They were compared to patients in the exact preceding year (cohort A).

**Results:** 2655 patients had at least one CD4 count measured in the period (surrogate marker for patients having routine follow up bloods), of whom 2389 (90%) had syphilis serology performed. 40 individuals were found to have early asymptomatic infection (two were re-infections), compared to 26 patients in cohort A. These 40 patients represented 36% of all patients with infectious syphilis treated within our department and 56% of those who were HIV positive. The event rate in cohort B was 7.3 per 1000 patient years (CI 5.2 to 9.9) compared to 2.8 (CI 1.8 to 4.0) in cohort A.

**Conclusion:** Routine screening is effective and has detected increasing numbers of HIV outpatients with early asymptomatic syphilis. Our department will continue this strategy for all HIV patients during their follow up care. We recommend that other units adopt similar initiatives that assist with regional control of the UK syphilis epidemic.

London's outbreak of infectious syphilis is the largest reported to date in the United Kingdom, with the burden of new diagnoses among men who have sex with men (MSM), many of whom are co-infected with HIV.<sup>1</sup> Enhanced laboratory surveillance of syphilis (ELSS) began in 2001 to coordinate national prevention and control of the infection.<sup>2</sup> Our HIV department responded by adding syphilis serology to computerised routine blood order sets and detected 26 HIV patients with early treponemal infection in the first year of use.<sup>3</sup> In light of evolving epidemiological data,<sup>4,5</sup> the objectives of this study were to assess our screening programme's effectiveness and continued necessity.

## METHODS

From our prospectively collected database at the Kobler Clinic, Chelsea and Westminster Hospital, we identified all HIV outpatients with newly positive syphilis serology or a fourfold or greater rise in VDRL titre, during a 1 year period between 1 May 2002 and 30 April 2003. In order to estimate the number of patients having routine HIV follow up blood

tests during this time, we used the number having T cell subsets performed as a surrogate marker.<sup>3</sup>

Only patients who were asymptomatic at the time of screening were included and known as cohort B. If patients were symptomatic or clinicians suspected syphilis at the time of screening, they were excluded. Patients found in the exact preceding year were known as cohort A. Syphilis screening was performed using TPPA (*Treponema pallidum* particle agglutination) and VDRL (veneral disease research laboratory) tests. FTA (fluorescent treponemal antibodies) were used for confirmation, if newly TPPA positive.

Qualitative data are presented as numbers with proportions. Quantitative data with Gaussian distributions are presented as means with standard deviations or medians with interquartile ranges (IQR) when data were found to show skewed distribution.

The determination of person days of follow up (PDFU) was calculated from first entry into the cohort to the time of first positive syphilis serology, or to the end of the study period, or to the last recorded visit (or death). Positive cases contribute only once to the analysis. The event rates were estimated using the Genmod procedure in SAS version 8 with log<sub>10</sub> link with Poisson error distribution using natural logarithm transformed PDFU.<sup>3</sup>

## RESULTS

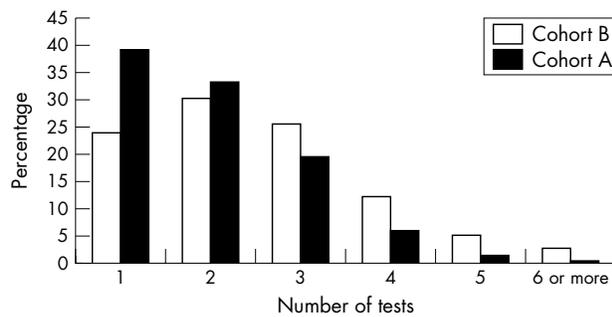
In all, 2655 patients had at least one CD4 count performed of whom 2389 (90%) had syphilis serology taken at the same time. This compares to 3% before routine screening introduction and 85% in the first year of use.

A total of 6081 syphilis tests were performed on these 2389 patients. The median time since most recent syphilis serology was 3 months (IQR 1.7–4.3) compared to 6 months in cohort A. When three or more samples were taken in the study period, a significantly higher proportion of cohort B was tested, compared to cohort A,  $p < 0.001$ ,  $\chi^2$  test—that is, cohort B were having more regular screening at routine outpatient visits (fig 1).

Of the 2389 HIV patients, 75 were VDRL positive. Six were excluded as initially diagnosed at our centre's genitourinary medicine (GUM) clinic, 18 were symptomatic, and 24 serofast from previously treated infection. However, 25 were newly VDRL positive and two patients had a more than fourfold increase in their VDRL titre as a result of re-infection (8 and 9 months later, respectively).

There were 455 individuals with a negative VDRL and positive TPPA; 19 were newly TPPA positive but six were symptomatic. The rest had previously documented treated treponemal infection with positive serological tests. This left 13 patients with new infection confirmed with FTA.

**Abbreviations:** ELSS, enhanced laboratory surveillance of syphilis; FTA, fluorescent treponemal antibodies; GUM, genitourinary medicine; IQR, interquartile range; MSM, men who have sex with men; PDFU, person days of follow up; TPPA, *Treponema pallidum* particle agglutination; VDRL, veneral disease research laboratory



**Figure 1** Percentage of individuals having one or more syphilis serology tests performed.

Thus, 40 individuals in cohort B (27 in the VDRL group and 13 in the TPPA group) were found with asymptomatic infection at the time of screening compared to 26 in cohort A (20 and six patients respectively). Table 1 shows the demographics of cohort B who had a mean age of 40 years and were mostly white MSM; 28 (70%) were treated with benzathine penicillin, 10 (25%) with doxycycline and two received treatment elsewhere following diagnosis in the Kobler Clinic. VDRL titres have either fallen or become negative after therapy, as in cohort A.

Of those receiving antiretrovirals, three were failing their current regimen and five had recently stopped a failing combination. This failure rate of 25.8% in cohort B was not significantly different from that found in cohort A (37%),  $p = 0.409$ , or significantly higher than the overall departmental rate of 17%,  $\chi^2$  test,  $p = 0.273$  (table 1).

During the study period, 112 patients were treated for early syphilis in our GUM department—John Hunter Clinic. This represented a 27% increase compared to the preceding year. Of these patients, 71 (63%) were HIV positive and 41 (37%) HIV negative/unknown status. The 40 asymptomatic patients in cohort B represent 36% of the patients treated for syphilis and 56% cases in the HIV group (29%  $p = 0.357$ ,  $\chi^2$  test, and 50%  $p = 0.486$ ,  $\chi^2$  test, in cohort A respectively).

These data give an event rate of 7.3 per 1000 patient years (CI: 5.2 to 9.9) in cohort B compared to 2.8 (CI 1.8 to 4.0) in cohort A. This is significantly higher than the preceding year,  $p < 0.05$ . Both figures are comparable because they are standardised for 1 year of patient follow up. It shows that routine screening in its second year of use is

**Table 1** Forty asymptomatic patients with early syphilis

Patient characteristics	Result
Mean age	40 years
Sex	39 (97.5%) male
Sexual orientation	38 (95.0%) MSM
Ethnicity	35 (87.5%) white 4 (10.0%) Afro-Caribbean 1 (2.5%) other
CDC classification	
AIDS	14 (35.0%)
Non-AIDS	26 (65.0%)
Most recent CD4	Median 402 cells (IQR 284–554)
Viral load	
Undetectable <50 copies/ml	23 patients (57.5%)
Detectable >50 copies/ml	17 patients (42.5%)
Range	Median 23 710 copies/ml (IQR 6513–61 091)
Antiretroviral naïve	9 patients (22.5%)
On antiretrovirals	31 patients (77.5%)
Failing current regimen	3 patients (9.7%)
Stopped failing combination	5 patients (16.1%)

**Table 2** The phases of the phase specific model<sup>5 10 11</sup>

Phase	Description
I	Epidemic growth period: start of invasion of the host population
II	Hyperendemic phase: absence of controls
III	Decline phase: control starts to take effect
IV	Endemic phase: steady state with established control techniques
V	Elimination phase: eradication not necessarily possible

detecting increasing numbers of patients with newly acquired syphilis.

## DISCUSSION

Studies show a return to unsafe sexual practices among some high risk MSM groups, with increasing levels of partner change and availability of more diverse social and sexual networks using the internet.<sup>6 7</sup> This behaviour was implicated in cohort B using ELSS information where the majority of sexual contacts were untraceable, placing limitations on outbreak control.

Our unit has now introduced a separate sexual health clinic within the HIV outpatient department. This has facilitated rapid screening, diagnosis, and treatment of sexually transmitted infections and improved access to a range of services. It has provided an opportunity for promoting greater awareness around the association between ease of syphilis transmission and oral sex and the fact that syphilis may increase the likelihood of HIV transmission and drug resistant variants.<sup>3 6 8 9</sup> The large number of MSM in cohort B may reflect the Kobler Clinic cohort, which comprises 72% MSM and is not necessarily representative of asymptomatic syphilis groups identified through screening elsewhere.

It is encouraging to learn that other centres within the United Kingdom have adopted similar screening initiatives to our own for their HIV cohorts. Our effective strategy has detected increasing numbers of asymptomatic patients using 3 monthly screening. It has prevented 40 HIV positive individuals developing the unpleasant clinical sequelae of syphilis and shortened their period of infectiousness. The phase specific model used for epidemic characterisation illustrates that we remain in the initial stages for a foreseeable period and our unit will maintain increased surveillance until there is elimination but not necessarily eradication of syphilis and a return to phase V.<sup>5 10 11</sup> (table 2). We recommend continuation of routine syphilis screening for HIV outpatients within the United Kingdom when attending for follow up care.

## Key messages

- Regular routine syphilis screening for HIV outpatients is an effective initiative for detecting asymptomatic infection
- In its second year, the programme has detected increasing numbers of HIV patients with newly acquired infection
- Identifying patients earlier can assist in controlling the UK syphilis epidemic
- The majority of diagnoses were in MSM, which has provided an opportunity for targeted prevention strategies within this group

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## CONTRIBUTORS

CC collected data and wrote paper; AW and FB contributed to writing paper; DA conceived study, study design, and contributed to writing paper; SM, statistical analysis of data; BA, laboratory collaboration and contributed to writing paper; DH, study design and contributed to writing paper.

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