

SHORT REPORT

Is increased surveillance for asymptomatic syphilis in an HIV outpatient department worthwhile?

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Objectives: Syphilis outbreaks have recently been reported in the United Kingdom, some of which have included cohorts of HIV positive individuals. As a result we commenced 3 monthly screening of syphilis serology (STS) for HIV positive patients having routine follow up blood tests. We assessed if there was an increased number of individuals being screened and also whether the screening programme was diagnosing early cases of syphilis.

Methods: Data from a 1 year period following introduction of screening (May 2001) were analysed and compared with data from the same period last year. The case notes of patients with a positive VDRL were reviewed to establish, firstly, whether these represented new diagnoses and, secondly, whether patients were asymptomatic at the time of screening.

Results: 2670 patients had at least one CD4 count measured in the period (surrogate for patients having routine bloods). Of these, 2266 patients had STS performed (85%). 38 patients had a positive VDRL. Of these, 20 were confirmed as having early syphilis which was asymptomatic at the time of screening. Six asymptomatic cases were also confirmed with newly positive TPPAs and a negative VDRL. These 26 asymptomatic cases represent 29% of all cases of early syphilis diagnosed in our department and 50% of cases in the HIV positive cohort.

Conclusion: With intensive surveillance significant numbers of cases of asymptomatic early syphilis are being identified in a group of HIV individuals under routine follow up, at an earlier stage than would otherwise have been the case. This presents an opportunity to intervene not only to prevent clinical illness but also to institute infection control measures.

In the United Kingdom between 1996 and 2001, new diagnoses of infectious syphilis more than quadrupled from 122 cases to 715 cases.¹ This was largely due to a number of outbreaks predominantly in men who have sex with men (MSM) and were reported in Manchester and in the south east of England (Brighton and London areas).² The outbreaks included high numbers of HIV infected individuals.

In the monitoring of HIV infected individuals it has been recently recommended to perform syphilis serology 6 monthly.³ This screens both for recrudescence in those previously treated for syphilis and also for new infections. However in the context of a syphilis outbreak we felt increasing the frequency of monitoring to 3 monthly would potentially have two additional benefits. Firstly, testing syphilis serology at the time of regular HIV follow up visits would make this more routine and hence we would screen the population more effectively. Secondly, cases would likely be identified earlier and with treatment instituted, the period of infectivity consequently reduced. This would have a positive impact on one of the drivers of outbreaks.

As a result of these arguments, routine screening for syphilis was increased from yearly to 3 monthly in May 2001. The objectives of this study are to assess if there was an increase in the number of individuals being screened and also whether the screening programme was diagnosing early cases of syphilis.

METHODS

Syphilis serology was added to the routine computerised blood order sets used for HIV follow up care, so all individuals would have 3 monthly serology performed, unless this test was specifically deselected or blood tests were ordered individually, bypassing the order sets. Syphilis serology was performed using TPPA (Serodia) and VDRL (Oxoid carbon antigen).

In order to estimate the number having routine HIV follow up during this time we used the number having T cell subsets performed as a surrogate marker. We compared risk factors and demographics between those having serology performed and those in whom it was deselected.

We identified all cases with positive syphilis serology during a 1 year period between May 2001 and April 2002 from HIV positive individuals attending for routine care at the Kobler Clinic, Chelsea and Westminster Hospital, London. The notes of those individuals with newly positive serology and those in whom there was a fourfold or greater rise in VDRL titre were reviewed. Details on these individuals demographics, past history of syphilis, and HIV history were collected. In determining the number of cases with asymptomatic syphilis, individuals having syphilis serology performed because of clinical suspicion of syphilis were excluded.

Statistical analysis

All qualitative data are presented as numbers with proportions while quantitative data with Gaussian distributions are presented as means with standard deviation or medians with interquartile ranges when data were found to show skewed distribution.

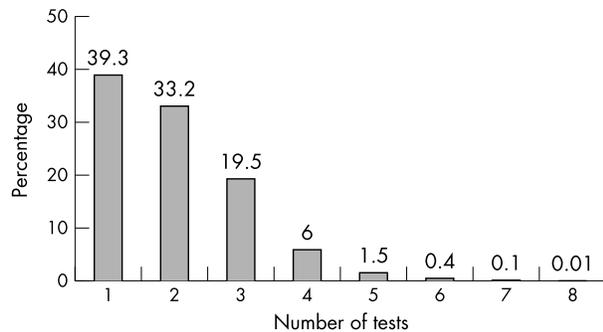
The determination of person days of follow up (PDFU) was calculated from first entry into the cohort to the time of first positive syphilis serology, or to the end of study period, or to the last recorded visit (or death date). Positive cases contribute only once to the analysis. The event rates were estimated using the Genmod procedure in *sas* version 8 with \log_{10} link with Poisson error distribution using natural logarithm transformed PDFU.

RESULTS

A total of 2670 patients had a CD4 count performed during the 12 month period of screening. Of these, 2266 (85%) had syphilis serology performed. This compares with 3% for the year preceding the study; 404 individuals did not have serology performed. For those having serology performed and those in whom it was deselected there was no difference in age, sex, ethnic origin, or sexuality between the two groups (table 1).

Table 1 Features of individuals who had syphilis serology performed compared to those who did not have serology

	Syphilis serology performed	Syphilis serology not performed	p Value
Number of individuals	2015	428	
Mean age	40.2 years	40.1 years	0.872
Percentage male	87.4%	88.4%	0.552
Percentage MSM	66.5%	72.1%	0.010
Mean CD4 count	370	368	0.876

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

A total of 4515 syphilis tests were taken on the 2266 patients who had serology performed. Figure 1 shows the percentage of individuals having one or more tests taken.

A total of 38 individuals had a positive VDRL. It was ascertained that nine were serofast from previously treated syphilis and seven had syphilis serology performed specifically because of the clinical suspicion of syphilis. Two patients were lost to follow up. The remaining 20 had asymptomatic early syphilis diagnosed as a result of routine screening. Details of these 20 individuals are given in table 2.

The median time since most recent syphilis serology was 6 months. For each 3 month period within the screening programme, the mean time since most recent syphilis serology became significantly less ($p=0.012$, Pearson's correlation coefficient).

Of note, eight of the 20 cases had a previous history of syphilis. In five of these individuals, their previous VDRL was negative, while in the remainder the diagnosis of early syphilis was made on the basis of a fourfold rise in the VDRL titre.

Of the 20, all but one was on antiretroviral therapy. Eight of them had detectable viral loads all at high levels, having had a recent viral load below level of detection on their current antiretroviral regimen. This rate of virological failure (37%) is significantly higher than the overall departmental rate of 17% ($p=0.03$, χ^2).

All have been treated for early syphilis. VDRL titres in these individuals have either fallen or become negative after treatment.

In all, 444 individuals with a negative VDRL had a positive TPPA. Most of these cases had treponemal tests previously documented as positive and a history of previous syphilis treatment. However, we assessed six cases as new cases of early asymptomatic individuals identified by screening, in whom there was no previous history of syphilis. Five were MSM and one was a heterosexual man.

None of these individuals had a previous history of syphilis or any known recent contact with syphilis. The time since their most recent syphilis serology was a mean of 4 months (range 2–6 months). All of these individuals had had at least one

Table 2 Twenty asymptomatic patients with early syphilis

Patient characteristic	Result
Age	36.6 years
Sex	
Male	20 (100%)
Sexuality	
Homosexual	20 (100%)
CDC classification	
AIDS	6 (30%)
Non AIDS	14 (70%)
Most recent CD4	371 cells range 286 to 465
Viral load	
Undetectable	12
Detectable	8
Range	11K to 157K
Time since most recent syphilis serology	
Median	6 months
Range	1–120 months
Mean May 01–July 01	78 months
Mean Aug 01–Oct 01	15 months
Mean Nov 01–Jan 02	8.3 months
Mean Feb 02–April 02	3.6 months
Previous history of syphilis	
Yes	8
No	12
Was last VDRL positive	
Yes	3
No	17
Known recent contact of syphilis	
Yes	0
No	20

negative serology during the screening programme. All cases were confirmed by a positive FTA.

During this 12 month time period a total of 88 cases of early syphilis have been treated in St Stephen's Centre (in addition to the Kobler Clinic, this includes the John Hunter Sexual Health Clinic); 36 cases (41%) were in HIV negative individuals and 52 cases (59%) were in HIV positive individuals.

The 26 asymptomatic cases with early syphilis diagnosed via the screening programme represents 29% of all cases of early syphilis and 50% of cases in the HIV positive cohort.

These data give an event rate per 1000 patient years of 2.82. Looking at the event rate for each 3 month period during the 12 months, the rate has risen showing that the screening programme is picking up increasing numbers of new cases.

DISCUSSION

Incorporating syphilis serology on computer order sets has improved syphilis testing in this population by 27-fold. The screening has detected a significant number of new cases of asymptomatic syphilis and has detected 50% of cases of syphilis in HIV infected individuals. Some of these diagnosis have been made at a very early stage of infection. This early diagnosis is demonstrated in the group with the positive TPPA only, presumably being diagnosed before VDRL conversion.

It has been argued that effective sexually transmitted infection (STI) prevention programmes, by shortening the duration of infectiousness of an STI, drive up the rate of partner change needed to maintain a reproductive rate above one.⁴ In this screening programme we are diagnosing and treating a significant proportion of our early syphilis cohort earlier than presentation would be if symptomatic disease was allowed to develop, thereby reducing the infectious period of disease.

This early diagnosis also reduces the number of individuals experiencing the unpleasant symptoms of early infectious syphilis and provides a unique opportunity for contact tracing, patient education, and screening for concomitant STIs.

Sexual transmission of HIV, including via oral sex, may be increased in the presence of other STIs.^{5,6} The recent syphilis outbreak has included mainly MSM and large numbers of HIV positive individuals. In this group oral sex may be practised as a form of "safer sex," where the risk of HIV transmission was traditionally thought to be lower. Recent data have revealed a strong association between unprotected oral sex and syphilis infection.⁷ In our cohort seven of the individuals were failing current antiretroviral therapy with high serum HIV viral loads. This syphilis screening programme may prevent HIV transmission and transmission of drug resistant HIV variants. It is interesting to note that the virological success rate on antiretroviral therapy in this group is significantly lower than the current success rate in our unit.

Should the routine screening for syphilis in asymptomatic individuals be every 3 months or less frequently? We suggest 3 monthly screening is appropriate for the following reasons.

Firstly, in this group CD4 lymphocyte counts and HIV RNA viral loads are being performed every 3 months hence screening for syphilis fits into routine follow up.

Secondly, in our cohort we are continuing to identify a significant number of cases towards the end of the first year of screening and in those who have had a negative syphilis serology 3 months previously. The mean time since most recent syphilis serology has fallen significantly throughout the year of screening to 3.6 months in the last quarter. In view of this we would argue that if the screening was done on a less frequent basis a significant number of individuals would have had early syphilis for more than 3 months, if they did not become symptomatic, before a diagnosis was made.

We do acknowledge that this observed diagnosis rate is in a central London clinic, in an area of the United Kingdom currently acknowledged to have a syphilis outbreak. Three monthly screening may be less crucial in areas with a lower current incidence.

Conflict of interest: None.

CONTRIBUTORS

AW collected data and wrote paper; DH, design of study and contributed to writing paper; SM, analysis of results and statistics; FB,

Key messages

- (1) Increased surveillance for asymptomatic syphilis has detected 50% cases of syphilis in HIV infected individuals under routine follow up
- (2) With increasing numbers of early syphilis being reported, 3 monthly syphilis serology allows detection of some cases of at a very early stage
- (3) By detecting syphilis at an earlier stage, the duration of infectiousness is reduced, an important factor in infection prevention programmes

contributed to writing paper; BA, interpretation of results and laboratory collaboration; DA, conceived study, design of study and contributed to writing paper

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