Syphilis infection among homosexual men reporting contact with syphilis: a case control study

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ABSTRACT

Objective: High rates of syphilis have been reported among men who have sex with men (MSM) internationally. Guidelines recommend presumptive treatment of sexual contacts of individuals with syphilis at the point of care. The aim of this study was to determine the proportion who were infected with syphilis and the factors predictive of infection among men reporting contact with a man with syphilis.

Design: Contacts who were syphilis infected (cases) were compared with those who were uninfected (controls).

Setting: This study was conducted at the main public sexually transmitted diseases clinic in Victoria, Australia.

Participants: One hundred and seventy-two MSM presenting as sexual contacts of men with syphilis at a sexual health service in Melbourne, Australia, between July 2007 and October 2011 were assessed for syphilis.

Outcome measures: Proportion of MSM who are infected with syphilis and factors associated with infection.

Results: Of the 172 men who reported contact with syphilis, 26 (15%, 95% CI 10 to 20%) had syphilis. One man had primary syphilis, 4 had secondary syphilis, while the remaining 21 had early latent syphilis. Infection was associated with unprotected anal sex over the prior 3 months (adjusted OR 6.1, 95% CI 1.4 to 26.8).

Conclusions: One in seven sexual contacts of men with syphilis had syphilis. Most had early latent syphilis.

ARTICLE SUMMARY

Article focus
- The proportion who were infected with syphilis among men reporting contact with a man with syphilis.
- Factors predictive of syphilis infection among men reporting contact with a man with syphilis.

Key messages
- One in seven homosexual men who presented as contacts of syphilis had syphilis.
- Most had early latent infection.
- Contacts who reported recent unprotected anal sex were more likely to have syphilis.

Strengths and limitations of this study
- No previous studies have reported on the likelihood of syphilis infection among homosexual men presenting clinically as sexual contacts of men with syphilis.
- The men included were those who reported that a sexual partner had syphilis. We could not verify if the partner actually had syphilis.

INTRODUCTION

Over the last decade, high rates of infectious syphilis have been reported among men who have sex with men (MSM) internationally, with over-representation of cases occurring among HIV-positive MSM.1 Left untreated, syphilis can result in significant morbidity, including neurosyphilis, and further transmission of infection.1 Syphilis enhances the sexual transmission of HIV.2 This is concerning as MSM in many countries are also the primary risk group for HIV.1

MSM with infectious syphilis are often asymptomatic or have symptoms or signs that are not recognised as syphilis.3–5 Contact tracing and partner notification, where sexual contacts are notified that they may have been exposed to an infection to encourage them to access testing and treatment, have been cornerstones in the control of syphilis.6 Guidelines recommend presumptive treatment of sexual contacts of individuals with syphilis at the point of care because seroconversion—and therefore diagnosis and treatment—can be delayed, potentially resulting in further transmission.7

While there have been a number of previous studies that have examined the proportion of
partners of syphilis-infected individuals who are infected, there are no published data on the proportion of men who present to a clinical service as a sexual contact of a man with syphilis who are infected. The aim of this study was to determine the proportion who were infected with syphilis and the factors predictive of infection among men reporting contact with a man with syphilis.

METHODS

Design
Contacts who were syphilis infected (cases) were compared with those who were uninfected (controls).

Setting
This study was conducted at the main public sexually transmitted diseases clinic in Victoria, Australia. In June 2007, in order to study syphilis diagnoses among patients presenting as sexual contacts of syphilis-infected partners, any patient who presented as such was recorded as a syphilis contact on the centre's computer database. We extracted data on these contacts from the clinic database for all men who reported sex with men in the prior 12 months—from June 2007 to October 2011. The data included age, number of reported male sexual partners in the prior 3 and 12 months, reported condom use with anal intercourse, injecting drug use and HIV status. These data were routinely collected as part of clinical care and entered into the clinic's computer database at each consultation. Clinical information from the medical records and results of laboratory investigations were reviewed.

All men reporting sex with syphilis-infected men were serologically tested for syphilis using the rapid plasma reagin (RPR) test, Treponema pallidum enzyme immunoassay (EIA) and T. pallidum particle agglutination (TPPA). EIA for T. pallidum IgM was performed selectively by the testing laboratory. Contacts were offered treatment with benzathine penicillin at the initial visit. Men not known to be HIV positive were also tested for HIV.

The sample size calculation was based on the expected difference in the proportion of infected and uninfected men who never used condoms. Assuming 50% of infected men and 20% of uninfected men never used condoms, 22 cases and 110 controls were required for a study with 80% power and significance at 0.05. The \( \chi^2 \) test was used to compare categorical data and the Mann-Whitney U test for non-parametric data using SPSS version 20. Variables with a p value of <0.1 were entered into a logistic regression analysis. Ethical approval for this study was granted by the Alfred Hospital Human Research Ethics Committee.

RESULTS

During the study period 172 MSM presented to the centre reporting sexual contact with a syphilis-infected male partner. Twenty-six men or 15% (95% CI 10% to 20%) were syphilis infected. One man had primary syphilis (RPR 256), 4 had secondary syphilis (RPR range 64–512), while the remaining 21 had asymptomatic early latent infection (median RPR 4; range: non-reactive–256). All 22 men who had EIA for T. pallidum IgM performed had reactive IgM results.

The characteristics of the syphilis infected and uninfected men are compared in Table 1. Infection was associated with unprotected anal sex over the prior 3 months (adjusted odds ratio 6.1, 95% CI 1.4 to 26.8).

Of the 146 uninfected men, 24 had serological results consistent with their history of past treated syphilis. Twenty of these men had repeat serology performed, with none experiencing an increase in RPR titre, suggesting re-infection with syphilis. Of the remaining 122 uninfected men, 56 (46%) had syphilis serology repeated, with the median duration between diagnosis and latest serological follow-up being 190 days (range 6–1033). None of these men experienced syphilis antibody seroconversion.

DISCUSSION

In this study, one in seven MSM who presented to a clinic reporting sexual contact with a syphilis-infected man had syphilis. Most men had early latent infection and were asymptomatic for syphilis. A significantly higher prevalence of syphilis was seen among men who did not use condoms with anal sex.

To our knowledge, there have only been four previously published studies that have aimed to determine the proportion of partners of individuals with early syphilis who were syphilis infected. Three of these studies, which were performed in the 1940s, did not include MSM. The prevalence of early syphilis in these studies of heterosexual couples ranged between 48.5% and 62.1%. In a study published in 1983, the prevalence of early syphilis among male contacts of men with primary or secondary syphilis was 49%. However, no sexual behavioural data were collected in this study, therefore as in the other three studies, the effect of frequency of sex and types of sexual contact—including condom use—on the prevalence of syphilis among contacts was not examined. Our study differs from these four earlier studies because the men included were those who presented to a sexually transmitted diseases clinic, as opposed to individuals who were actively traced as contacts of index cases.

There are a number of limitations to this study. First, the men included were those who reported that a sexual partner had syphilis. We could not verify if the partner actually had syphilis. It is possible some partners did not have syphilis, or if they did, were not infectious, potentially contributing to the lower rate among contacts in this study compared with the 49% seen by Schober et al, where all male index cases had confirmed primary or secondary syphilis. Second, as in the four previous studies, we do not know if the men in this study who
were syphilis infected were infected by, or transmitted infection to, their syphilis-infected male partner, or indeed if they were infected by a third individual. Third, while we collected sexual behavioural data on the men in our study, we were not able to specifically capture their sexual interactions with their reported syphilis contact nor could we determine the relative importance of oral sex or insertive versus receptive anal sex. It is possible that differences in frequency and type of sexual practices—including condom use—may have contributed to the difference in the prevalence between our study and that seen by Schober et al. Fourth, the proportion of contacts who are infected and stages of infection may differ in other settings, for example, depending on the degree and efficacy of partner notification undertaken for syphilis and on the prevalence of syphilis in the population. Ostensibly, effective partner notification would lead to more individuals with asymptomatic syphilis presenting for care.

Is the policy of routinely treating male partners of syphilis-infected men with benzathine penicillin warranted? In part, this depends on the cost effectiveness of this strategy, which needs to take into account the morbidity and further transmission that would arise from delayed or untreated infection. In our population, six men were treated for syphilis for every man who was infected. Economic modelling would be of interest but would be hampered by the scarcity of data on the likelihood of syphilis transmission between men, a subject that warrants further research.

### Table 1

**Characteristics of male sexual partners of men with syphilis: comparison of those with syphilis and those who were uninfected**

<table>
<thead>
<tr>
<th></th>
<th>Syphilis-infected men (n=26) no. (%)</th>
<th>Uninfected men (n=146) no. (%)</th>
<th>Odds ratio (95% CI) p Value</th>
<th>Adjusted odds ratio (95% CI) p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age</strong></td>
<td>34.5</td>
<td>33</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>No. of male partners in last 3 months*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>18† (69.2)</td>
<td>70 (47.9)</td>
<td>2.4 (1.0 to 6.0)</td>
<td>0.045</td>
</tr>
<tr>
<td>≥3</td>
<td>8 (30.8)</td>
<td>76 (52.1)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Condom use in last 3 months‡</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>10 (38.5)</td>
<td>14 (9.6)</td>
<td>5.2 (2.0 to 13.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever</td>
<td>16 (61.5)</td>
<td>116 (79.4)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No. of male partners in last 12 months*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–11</td>
<td>23 (88.5)</td>
<td>110 (75.3)</td>
<td>2.5 (0.7 to 8.9)</td>
<td>0.14</td>
</tr>
<tr>
<td>≥12</td>
<td>3 (11.5)</td>
<td>36 (24.7)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Condom use in last 12 months‡</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>5 (19.2)</td>
<td>10 (6.8)</td>
<td>3.0 (0.9 to 9.6)</td>
<td>0.058</td>
</tr>
<tr>
<td>Ever</td>
<td>21 (80.8)</td>
<td>125 (85.6)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Injecting drug use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>26 (100.0)</td>
<td>134 (91.8)</td>
<td>0.8 (0.7 to 0.9)</td>
<td>0.15</td>
</tr>
<tr>
<td>Ever</td>
<td>0 (0.0)</td>
<td>11 (7.5)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>HIV status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2 (7.7)</td>
<td>32 (21.9)</td>
<td>0.3 (0.1 to 1.3)</td>
<td>0.093</td>
</tr>
<tr>
<td>Negative</td>
<td>24 (92.3)</td>
<td>114 (78.1)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*The median number of male partners reported for the prior 3 and 12 months were 2 and 11 respectively.
†All 18 infected men had at least one partner in the prior 3 months.
‡Use of condoms ever included men who reported using condoms during anal sex sometimes or always. Anal sex included both insertive and receptive sex. Those who reported no anal sex were excluded from the analysis.

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