Epidemic syphilis among homosexually active men in Sydney

Fengyi Jin, Garrett P Prestage, Susan C Kippax, Catherine M Pell, Basil J Donovan, John M Kaldor, Andrew E Grulich
on behalf of the Australian–Thai HIV Vaccine Consortium

ABSTRACT

Objectives: To describe trends in the notification of infectious syphilis in New South Wales, the characteristics of homosexually active men recently notified with early syphilis, and the seroprevalence and incidence of syphilis, as well as associated risk factors, in a Sydney cohort of HIV-negative homosexually active men.

Design, setting and participants: Secondary analysis of New South Wales infectious syphilis surveillance data from 1998 to 2003; a case series of 57 homosexually active men diagnosed with early syphilis in inner Sydney from December 2002 to January 2004; and a prospective cohort study of syphilis among 1333 HIV-negative homosexually active men in Sydney recruited from June 2001 to December 2003.

Main outcome measures: Rates of notification of infectious syphilis in New South Wales and in areas of inner Sydney; behavioural and clinical features of men with syphilis in the case series; and incidence of syphilis and hazard ratios (HRs) associated with sexual behaviours in the cohort study.

Results: Infectious syphilis notifications in inner Sydney rose more than 10-fold (from 6 in 1999 to 162 in 2003), and the increase was confined to men. Of 57 men with early syphilis in the case series, 54% were HIV-positive and 32% reported no symptoms of syphilis. These 57 men were highly sexually active and likely to report recreational drug use. In the cohort study, 1292 men (97% of participants) consented to syphilis testing; the incidence of syphilis was 0.78 per 100 person-years, and risk factors included reporting unprotected anal intercourse with HIV-positive partners (HR, 5.31; 95% CI, 2.00–184.93) and insertive oral sex (HR, 4.55; 95% CI, 1.14–18.18).

Conclusion: Syphilis has been re-established among homosexually active men in Sydney, and HIV-positive men are over-represented. Frequent screening is needed in this population to curb the transmission of both syphilis and HIV.

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Syphilis is a sexually transmitted infection (STI) of considerable public health importance because of the serious consequences of congenital infection, its ability to cause neurological and cardiovascular disease in adults,[1] and its potential to increase the risk of transmission of HIV.[2]

The epidemiology of syphilis among homosexually active men in Australia,[3] as elsewhere,[4] has changed dramatically over the last 25 years. Up to the early 1980s, syphilis was extremely common,[5] but with the onset of the HIV/AIDS epidemic, there was a rapid decrease in the incidence of syphilis in homosexually active men in Australia[6] and other industrialised countries.[4] By the early 1990s, infectious syphilis was rare in Australian homosexually active men.[3,7]

Since the mid 1990s, increases in sexual risk behaviour have been reported in gay communities around the world.[8] Increases in the rate of diagnoses of STIs were reported soon after, and outbreaks of syphilis surfaced in other industrialised nations in the late 1990s.[9] Epidemics of syphilis have recently been reported in gay communities in the United States,[10-12] Canada,[13] and western Europe.[14-16] Here, we describe recent trends in syphilis among homosexually active men in New South Wales.

METHODS

Our investigation consisted of three separate components:

- routine New South Wales infectious syphilis surveillance data;
- a case series of homosexually active men diagnosed with early syphilis in inner Sydney; and
- data on seroprevalence and incidence of syphilis and associated risk factors in a cohort of HIV-negative homosexually active men in Sydney.

Syphilis surveillance

Syphilis is a notifiable disease in every state and territory in Australia.[17] In NSW, doctors and hospitals are required to notify cases of syphilis on clinical diagnosis, and pathology laboratories are required to report cases on the basis of serological or other evidence of infection. Data on infectious syphilis notifications (including primary, secondary and latent syphilis of less than one year's duration) from 1998 to 2003 were retrieved from NSW Health for analysis.

Enhanced surveillance was introduced by the Central Sydney Public Health Unit in 1999 and the South Eastern Sydney Public Health Unit in 2001 in response to international reports of increasing syphilis incidence among gay men. The aim of enhanced surveillance was to increase ascertainment of infectious syphilis among laboratory-notified cases, and to improve documentation of key clinical data such as the stage of disease and risk factors of infected patients. No data on sexual behaviour were collected. Data on infectious syphilis notifications in men from Central Sydney Area Health Service and South-Eastern Sydney Area Health Service between 1999 and 2003 were retrieved from those Area Health Services for analysis.

FOR EDITORIAL COMMENT, SEE PAGE 172. SEE ALSO PAGE 218.

National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, NSW.
Fengyi Jin, MPH, PhD Candidate; Garrett P Prestage, PhD, Senior Research Associate; John M Kaldor, PhD, Deputy Director; Andrew E Grulich, PhD, FAFPHM, Program Head.
National Centre in HIV Social Research, University of New South Wales, Sydney, NSW.
Susan C Kippax, PhD, Director.
Taylor Square Private Clinic, Sydney, NSW.
Catherine M Pell, MB BS, Senior Sexual Health Physician.
Sydney Sexual Health Centre, Sydney Hospital, Sydney, NSW.
Basil J Donovan, MD, FAChSHM, Director; and Professor, School of Public Health, University of Sydney.
Reprints will not be available from the authors. Correspondence: Mr Fengyi Jin, National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Level 2, 376 Victoria Street, Darlinghurst, NSW 2010. jjin@nchecr.unsw.edu.au

Case series of early syphilis in Sydney

From December 2002 to January 2004, homosexually active men who were diagnosed with early syphilis (primary, secondary and early latent syphilis) at three general practices and two sexual health centres in inner Sydney were invited to participate in this study. These clinics were chosen because surveillance data indicated that they diagnosed around half of all cases of syphilis in men in Sydney. Consenting patients were asked by their doctors to complete an anonymous self-administered questionnaire. Information collected included sexual behaviour, recreational drug use, HIV status, treatment-seeking behaviour, knowledge about syphilis and demographic factors.

Health in Men cohort study

The Health in Men (HIM) study is a community-based prospective cohort study of HIV incidence and associated factors conducted among HIV-negative homosexually active men in Sydney. The study commenced in 2001 and the methods have been described in detail elsewhere.[18] Briefly, homosexually active men are eligible for inclusion if they live in Sydney or participate regularly in its gay community, and if they tested HIV-negative at baseline. They were recruited from a variety of community-based sources from June 2001 to December 2003. All participants underwent an annual face-to-face interview, and an annual telephone interview at the midpoint between their face-to-face interviews. Interviews covered sexual behaviour and sexual identity, self-report of specific STIs, recreational drug use and demographic factors. At annual face-to-face interviews, HIM participants were offered syphilis testing. The screening test was an enzyme immunoassay (EIA; ICE Syphilis, Murex Biotech Ltd, Dartford, UK). Positive EIAs were confirmed with the *Treponema pallidum* particle-agglutination assay and fluorescent treponemal antibody absorption test. The rapid plasma reagin (RPR) test was used to assist clinical staging and to detect reinfection.

Ethical approval

The last two studies were approved by the Human Research Ethics Committee of the University of New South Wales. The case series study was also approved by the Human Research Ethics Committee at Central Sydney and South-Eastern Sydney Area Health Services.

Statistical analysis

Incident syphilis was defined as syphilis seroconversion or reinfection during the study. For the calculation of syphilis incidence, the date of syphilis acquisition was assumed to be the midpoint between the last negative test and the first positive test in the HIM study. Total person-years were calculated as the time from study entry to the date of acquisition, or last negative test in the HIM study for those who did not seroconvert or become reinfected with syphilis. Risk factors which seemed related to syphilis in the case series were examined using univariate Cox regression in STATA 8.0 (StataCorp LP, College Station, Tex, USA), and hazard ratios (HRs) were reported as the relative magnitude of risk factors. For ordered categorical variables such as age group and number of partners, *P* values for trend were reported. As this was largely a descriptive epidemiological analysis, power calculations were not performed.

RESULTS

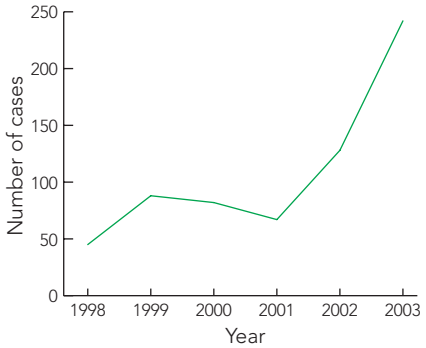
Surveillance data

Surveillance data in NSW showed a rapid increase in infectious syphilis notifications since around 2001 (Box 1). By 2003, they showed that nearly 90% of notifications of infectious syphilis in New South Wales were in men, 69% of whom lived in areas covered by the South-Eastern Sydney Area Health Service and Central Sydney Area Health Service. In these two inner-city area health services, the annual number of notified cases of infectious syphilis in men increased from 5 to 120 and from 1 to 42, respectively, between 1999 and 2003.

Case series of early syphilis in Sydney

Fifty-seven homosexually active men diagnosed with primary, secondary or early latent syphilis were recruited, representing just under half of all the men diagnosed with early syphilis in the same period in inner Sydney. Not all men answered every question. Their mean age was 39 years (range, 20–80 years). Fifty-four (96%) self-identified as gay or homosexual and 45 (80%) were inner-city residents. Thirty participants (54%) were HIV-positive. Fifty-two men (91%) reported oral sex with casual partners, and 29 (51%) reported that they believed they had contracted syphilis through oral sex. However, only 14 of these men (25% of all men) reported oral sex but no unprotected anal intercourse with casual partners in the last 6 months.

1 Infectious syphilis notifications in New South Wales 1998–2003



Source: New South Wales Health Department ◆

The most common reason that these men were having tests for syphilis was that they had symptoms (29 men; 51%), and 10 (18%) reported they were contacts of people with syphilis. However, 16 men (28%) reported that the test was part of their usual STI testing routine. The most commonly reported symptoms were a rash (42%) or a lesion such as an ulcer or sore (40%). Eighteen men (32%) reported no symptoms at all. Among the 39 who reported symptoms, 11 (29%) sought medical attention within a week of noticing symptoms, 12 (32%) did so within 1–2 weeks, and a further 9 (24%) were tested for syphilis within 3–4 weeks.

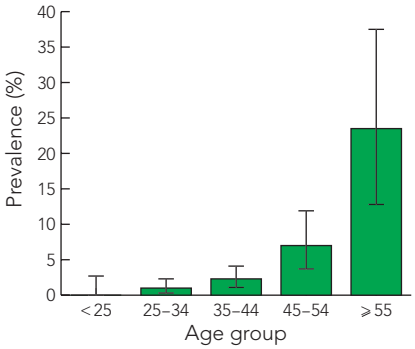
The men in the case series were very sexually active. During the previous 6 months, 35 (64%) reported more than 10 sexual partners, 11 (19%) reported having sex with somebody while overseas, and 29 (51%) reported having sex in Australia with somebody from overseas. They had sought sexual partners from a variety of venues; most commonly sex-on-premises venues, saunas and gay bars (65%, 58% and 58%, respectively).

These men were also likely to report recreational drug use. The most commonly reported drugs were amyl nitrite (77%), ecstasy (63%) and marijuana (58%). Injecting drug use in the last 6 months was reported by 10 men (18%). The most commonly injected drug was methamphetamine ("crystal"), reported by all 10.

Health in Men cohort study

By the end of 2003, 1333 HIV-negative men were recruited into the HIM study, and 1292 (97%) consented to syphilis testing. The mean age of those tested was 36.5 years (range, 18–75 years). Thirty-nine

2 Syphilis antibodies in the Health in Men cohort of HIV-negative homosexually active men



Error bars indicate 95% confidence intervals. Note: 79% of men seropositive to syphilis reported a past history of syphilis. ◆

(3%) were seropositive for syphilis at baseline, indicating previously treated (31 men; 79%) or previously undiagnosed (8; 21%) infection. Serological evidence of past syphilis increased markedly with age (Box 2). The mean age of seropositive men was 48.9 years (range, 32–69 years).

At least one annual face-to-face follow-up interview was attended by 794 men by the end of 2003 (median follow-up time, 1.1 years). Among these men, nine had confirmed incident syphilis (three of whom did not report being diagnosed in the past year), and no syphilis reinfections. The mean age of men with incident syphilis was 34.6 years (range, 22–44 years). The overall incidence rate was 0.78 per 100 person-years. None of the men with incident syphilis also acquired HIV infection during the study.

In univariate analyses, age was not related to incidence of syphilis in the cohort. Certain sexual behaviours were significantly associated with incident syphilis, including unprotected anal intercourse with HIV-positive partners, insertive oral sex with ejaculation with casual partners, as well as the number of partners in the last 6 months (Box 3). Men who reported seeking sexual partners through beats (public places where men seek out other men for sex) and telephone sex had an increased risk of acquiring syphilis. Use of individual recreational drugs was not related to risk of syphilis (data not shown), although reporting a history of either methamphetamine use or injecting drug use was associated with a non-significant elevation in risk (HR, 2.00; 95% CI, 0.50–8.01, and HR, 3.42; 95% CI, 0.43–27.43 respectively).

3 Risk factors for incident syphilis in the Health in Men study

	No. men	Person years	Incidence*	Hazard ratio	95% CI
Age (*P* trend = 0.262)					
< 25	1	68.52	1.46	1	—
25–34	3	405.85	0.74	0.53	0.06–5.11
35–44	5	415.85	1.20	0.90	0.10–7.68
45–54	0	212.70	0.00	na	na
⩾ 55	0	49.22	0.00	na	na
No. of partners in last 6 months (*P* trend = 0.028)					
⩽ 5	1	529.91	0.19	1	—
6–10	2	187.16	1.07	5.87	0.53–64.70
11–50	4	331.02	1.21	6.72	0.75–60.13
> 50	2	102.92	1.94	10.57	0.95–116.65
Unprotected anal intercourse					
By partner's HIV status (*P* trend = 0.005)					
None	1	391.93	0.26	1	—
HIV-negative partners only	2	403.61	0.50	1.89	0.17–20.79
HIV status of partners unknown	3	300.06	1.00	3.93	0.41–37.80
HIV-positive partners	3	56.54	5.31	19.22	2.00–184.93
By partner type (*P* = 0.466)					
None	1	391.93	0.26	1	—
With regular only	4	430.36	0.93	3.67	0.41–32.85
With casual only	2	176.47	1.13	4.18	0.38–46.15
With both	2	153.38	1.30	4.85	0.44–53.55
Insertive oral sex to ejaculation with casual partners (*P* = 0.026)					
No	3	725.82	0.41	1	—
Yes	6	324.30	1.85	4.55	1.14–18.18
Places where sexual partners were sought					
Internet (*P* = 0.769)					
No	4	592.50	0.67	1	—
Yes	5	559.64	0.89	1.22	0.33–4.55
Gay bar (*P* = 0.646)					
No	4	410.72	0.97	1	—
Yes	5	741.42	0.67	0.73	0.20–2.73
Beats† (*P* = 0.033)					
No	3	796.13	0.37	1	—
Yes	6	356.02	1.69	4.26	1.07–17.03
Sauna (*P* = 0.128)					
No	2	533.95	0.37	1	—
Yes	7	618.19	1.13	3.06	0.64–14.75
Other sex venues (*P* = 0.513)					
No	5	774.07	0.65	1	—
Yes	4	378.07	1.06	1.56	0.42–5.81
Telephone sex (*P* = 0.043)					
No	6	1055.2	0.57	1	—
Yes	3	96.93	3.09	5.06	1.25–20.43

* Per 100 person years. † Public places where men seek out other men for sex. na = not applicable. ◆

DISCUSSION

After more than a decade of extremely low rates of infection, syphilis has re-established itself among homosexually active men in Sydney, leading to a 10-fold increase in the number of infectious syphilis notifications in inner Sydney between 1999 and 2003. While concentrated among men who were HIV-positive,[19] the incidence rate of syphilis in those who were HIV-negative approached 1% per year.

Our report has the strength of combining data from routine surveillance, a case series of infectious syphilis, and a cohort study of HIV-negative homosexually active men. The case series enrolled just under half of those men notified with infectious syphilis in the South-Eastern Sydney Area Health Service during the study period. Despite the breadth of these data, some limitations must be borne in mind. First, the case series did not have a control series. Rather, comparisons are possible with other socio-behavioural studies of gay men in Sydney,[20] and with the HIM cohort study. Second, the cohort study was only of HIV-negative gay men, and the overrepresentation of HIV-positive gay men in the case series suggests that the incidence in HIV-positive men is likely to be greater. Third, the fact that there were only nine incident cases of syphilis in the cohort limited the power of the study and precluded a multivariate analysis of risk factors.

In the HIM cohort of HIV-negative men, nearly one in four of those aged over 55 years tested positive to syphilis at baseline, indicating that infectious syphilis was previously very common in this population. Of a cohort of Sydney gay men recruited in 1984, 38% reported a history of syphilis.[5] By contrast, in men aged under 35 years in the HIM study, the prevalence of serological markers of syphilis was less than 1%, reflecting the dramatic reduction in syphilis transmission in the wake of the HIV/AIDS epidemic. This difference illustrates the potential for syphilis to become hyperendemic again in Australian gay men.

Nearly a third of participants with infectious syphilis in the case series reported no symptoms, and three of the nine men with incident syphilis cases in the HIM study did not report a syphilis diagnosis in the past year. A recent study conducted in a sexual health clinic in Greece reported that as many as 68% of people with infectious syphilis reported no symptoms.[21] Men with asymptomatic syphilis or symptomatic but undiagnosed syphilis could be an important source of ongoing transmission, pointing to the importance of screening in high-risk populations like sexually active gay men. Both the Australian chapter of Sexual Health Medicine and the Centers for Disease Control and Prevention (CDC) in the United States have recently recommended that homosexually active men should be tested for syphilis at least annually.[22,23]

Our results suggest that syphilis is transmitted through oral sex frequently — about a quarter of men in the case series believed they had been infected through this route, and reported no unprotected anal intercourse with casual partners in the last 6 months. In the HIM study, insertive oral sex with casual partners was also significantly associated with incident syphilis. Other studies have also reported syphilis transmission by oral sex.[24,25]

Our data suggest that targeted screening may need to be more frequent among some groups of homosexually active men, particularly those with HIV infection. This should be coupled with community education to aid recognition of symptoms and raise awareness that asymptomatic syphilis is common, and practices such as oral sex, which are considered safe in terms of HIV transmission, are not effective for preventing syphilis transmission. The predominance of anonymous sexual partners is likely to limit the effectiveness of contact tracing as a public health approach in this population.

Our case series and cohort study have established some important risk factors for syphilis. First, men in the case series were much more likely to report being HIV-positive than in other studies of gay men in Sydney, in which around 15%–20% of men report they are HIV-positive.[26] In syphilis epidemics in other industrialised countries, a similar overrepresentation of HIV-positive men has been reported.[27] Second, a variety of sexual practices were strongly related to increased risk of syphilis, including having more partners, reporting looking for sexual partners at beats and by telephone sex, reporting unprotected anal intercourse with casual partners or with HIV-positive partners, and reporting insertive oral sex with casual partners. Third, men in the case series were more likely to report using a variety of recreational drugs and more likely to report injecting drug use than community-based samples of gay men in Sydney,[20] although, in the cohort study, the relationship was not statistically significant.

The fact that the risk factors for syphilis that we have described are broadly similar to risk factors for HIV is of concern. The ulcers caused by syphilis may potentially increase susceptibility to and transmissibility of HIV,[2] and cotransmission of HIV and syphilis has been described.[28] Syphilis may upregulate expression of the HIV chemokine coreceptor (CCR5) on monocytes, and thereby increase HIV susceptibility independent of ulcer formation.[29] In this way, the re-establishment of syphilis in this community may pose an additional threat to HIV control.

In conclusion, the Sydney gay community is experiencing a resurgence of syphilis, and HIV-positive homosexually active men are over-represented. Surveillance data from Victoria indicate that a similar outbreak of syphilis in men is beginning in Melbourne,[30] while Brisbane may have been spared to date.[31] As with other STIs of increasing incidence — including gonorrhoea, chlamydia, and HIV[30] — it is probably only a matter of time before urban gay communities throughout Australia are affected.

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COMPETING INTERESTS

None identified.

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