Syphilis Outbreak among Men who Have Sex with Men, Tel Aviv, Israel, 2008–2009

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ABSTRACT: **Background:** Outbreaks of syphilis have been described among men who have sex with men (MSM) in many western urban communities in the last few years.

Objectives: To describe the first reported outbreak of syphilis among MSM in Israel within a decade of a constant increase in human immunodeficiency virus (HIV) prevalence.

Methods: All patients diagnosed with syphilis were contacted and asked about their sexual behavior, substance use and previous infections. All were tested for HIV and a phylogenetic analysis was performed.

Results: A total of 23 (59%) of all 39 male patients diagnosed with primary or secondary syphilis between August 2008 and August 2009 were interviewed. All were MSM and performed anal intercourse, while 13 (55%) reported unprotected anal intercourse. Most participants (21, 91%) practiced unprotected oral intercourse. Nine participants (39%) reported unprotected oral intercourse while using condoms during anal intercourse. Ten participants (43%) reported sexual contacts while traveling abroad in the previous few months. Most participants (96%) were co-infected with HIV, and 15 (68%) were already aware of their HIV infection. Fifteen (66%) reported the use of recreational drugs, alcohol, or both before or during sex. No common source or core transmitters were identified.

Conclusions: This syphilis outbreak included MSM who were co-infected with HIV and were characterized by risky sexual behavior including multiple partners, unprotected anal intercourse and substance use. Future targeted interventions should focus on HIV-infected MSM for secondary prevention.

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KEY WORDS: human immunodeficiency virus (HIV), Israel, men who have sex with men (MSM), sexually transmitted diseases, syphilis

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Following a gradual decline in the burden of syphilis starting in the late 1960s and until the late 1990s, a rise in incidence has been reported from many large cities in developed countries. Most of the outbreaks related to syphilis occurred in urban communities of men who have sex with men [1-8]. Risk factors recognized for syphilis infection in MSM are manifold [7-9]. They include multiple anonymous sexual partners [6,9], the increased popularity of the internet as a venue to search for sexual partners [2,10-12], previous diagnoses of sexually transmitted diseases [1,13], and the use of alcohol and other recreational drugs such as methamphetamines before or during sex [9,12-14]. Unprotected anal intercourse, especially the receptive positioning, is the main mode of acquiring infection with *Treponema pallidum* [1,13]. However, unprotected oral intercourse, generally perceived as "safer sex" practice in terms of HIV exposure, is an additional mode of acquisition of STD [1,3,5,10,13].

HIV infection is strongly associated with syphilis. In various reports, the rate of HIV and syphilis co-infection was as high as 50% [4-6,8,10,12,14]. This association between HIV and syphilis results from the common modes of transmission related to these STD, but also from the increase of unsafe sexual behavior among HIV-infected MSM, and from the greatly increased transmission of HIV in patients with ulcerative and inflammatory genital diseases such as syphilis.

This study describes the increase in the number of syphilis infections in MSM reported to the Tel Aviv Department of Public Health from August 2008 to August 2009, including the patients' demographic characteristics and behavioral determinants. The results will establish fundamentals for future interventions to prevent further transmissions of STD in the gay community of Tel Aviv, Israel.

MSM = men who have sex with men
STD = sexually transmitted diseases

SUBJECTS AND METHODS

Syphilis and HIV are reportable diseases in Israel, and physicians and laboratories are mandated to notify the health department of each diagnosis. The diagnosis of primary and secondary syphilis requires clinical manifestations and laboratory confirmation. Clinical manifestations included mainly, but not only, chancre or typical rash. The confirmatory serology tests include positive VDRL (Venereal Disease Research Laboratory) (Becton Dickenson, Shannon, Ireland) and positive TPHA (*Treponema pallidum* hemagglutination) (Axis Shield, Dundee, UK), or FTA (fluorescent treponemal antibody) (Bio-Marieux, Carponne, France).

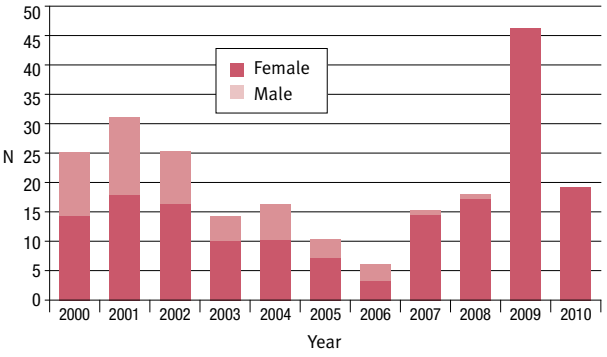
The health department conducts an epidemiological investigation following each reported case to detect the source of infection and to recommend testing for the recent sexual contacts of the infected individual. These investigations were performed by two physicians (T.B.N. and Z.M.) experienced with epidemiological work with the MSM community, by means of a face-to-face or phone interview. All syphilis cases reported to the Tel Aviv Department of Public Health were contacted and a semi-structured interview was performed, including demographic data, date of syphilis diagnosis, clinical manifestations upon diagnosis, sexual orientation and practices, HIV status, average monthly number of sexual partners, the number of sexual partners during the 3 months prior to the diagnosis of syphilis, type of sexual partners and general sexual practices including use of condoms, participation in group sex (defined as having sex with more than one partner at the same time), having sex outside Israel in the last year, use of alcohol or drugs, and previous STD diagnoses. In cases where the syphilis patient was infected with HIV, additional data were retrieved from patients' files in the AIDS clinic at the Tel Aviv Sourasky Medical Center, such as year of diagnosis, CD4 cell count and HIV viral load.

Blood samples obtained from study patients following their HIV diagnosis were analyzed retrospectively. HIV virus genotyping was carried out by the Trugene HIV-1 genotype kit (Siemens). Sequences LAV1HIV1, CM240AE, and U45016/C were used as reference to HIV-1 subtypes B, AE and C, respectively. Phylogenetic relationships among viral sequences were estimated using the maximum likelihood method. Epidemiological investigation and laboratory results were matched to identify social networks and to describe the dynamic of this outbreak.

The study was approved by the institutional review board at the Tel Aviv Medical Center. Anonymity of cases was fully maintained during the research.

The association between number of sexual partners and unprotected anal intercourse was calculated using independent two-tailed Student's *t*-test. In order to compare the study participants and those who were not interviewed a Student's *t*-test was performed for the ages of the participants and a two tailed chi-square test for their country of origin.

Figure 1. Annual number of males and females with primary and secondary syphilis patients reported in the Tel Aviv District, 2000–2010



RESULTS

The number of newly diagnosed primary and secondary syphilis in the Tel Aviv district had quadrupled from 10 in 2005 to 48 cases in 2009. The proportion of men among all the reported cases reached 100% [Figure 1]. Nine of 18 reported cases (50%) in 2008 and 46 of 48 (96%) in 2009 self-identified themselves as MSM.

Of the 39 MSM diagnosed with syphilis and reported to the Tel Aviv Department of Public Health between August 2008 and August 2009, 23 (59%) were interviewed; the other 16 (41%) could not be reached or refused to be interviewed. The age (34 ± 9.2 years) and place of birth (all born in Israel) were not statistically different from those who were interviewed ($P = 0.5$ and $P = 0.9$, respectively). Data retrieved from the interviews are detailed in Table 1. Important findings are given below:

Demographic data: The average age was 37 years. Twenty-one participants (91%) were born in Israel, and 2 immigrated from the former Soviet Union in 1991. The socioeconomic background varied, with 11 participants (50%) working in a profession that required an academic degree, and the rest employed in various small businesses or in temporary positions.

Sexual orientation and practices: Nineteen participants (83%) identified themselves as gay and 4 (17%) as bisexual. Most participants had more than one sexual partner per month (averaging 3), while during the 3 months prior to the syphilis diagnosis, participants reported having up to 70 sexual partners, averaging 11. All the study participants performed anal sex, and almost all of them (96%) performed receptive anal sex. Only 10 participants (45%) reported constant condom use during anal sex, while the rest either used condoms irregularly or did not use them at all. Those who reported unprotected anal intercourse (N=13) had a greater number of sexual partners in the last month than those who did not (N=10) (4.2 and 2.1, respectively, $P = 0.29$). Two individuals (9%) performed vaginal

Table 1. Characteristics of individuals diagnosed with primary and secondary syphilis in Tel Aviv, Israel, August 2008–August 2009

Total no. of patients		23
Average age (yrs, range)		36 (23–62)
Place of birth	Israel Former Soviet Union	21 (91%) 2 (9%)
Sexual orientation	Gays Bisexuals	19 (83%) 4 (17%)
Sexual practices	Average and median no. of sexual partners per month (range)	Average 3 Median 2 (1–10)
	Average and median no. of sexual partners in the 2 months prior to syphilis presentation (range)	Average 8 Median 4 (1–70)
	Anal sex Insertive Receptive Both	23 (100%) 1 (4%) 8 (35%) 14 (61%)
	Constant use of condom during anal sex (N=23)	10 (43%)
	Constant use of condom during vaginal sex (N=2)	2 (100%)
	Constant use of condom during oral sex (N=21)	0 (0%)
	Group sex	4 (17%)
	Sex while traveling overseas*	10 (43%)
Substance use	None "Poppers" Alcohol Cannabis Cathinone derivatives 3,4 methylenedioxymethamphetamine (MDMA) Ketamine Cocaine Amphetamines Gamma hydroxybutyrate (GHB)	4 (17%) 15 (65%) 8 (35%) 11 (48%) 10 (43%) 6 (26%) 3 (13%) 3 (13%) 1 (4%) 1 (4%)
HIV status and treatment and previous STD	HIV positive at presentation Past diagnosis of HIV on presentation with syphilis Average CD4 count, cells/mm^3 (range) Use of antiretroviral drugs Previous STD	22 (96%) 15 (68%) 438 (248–817) 9 (60%) 13 (57%)
Clinical presentation of syphilis	Primary syphilis (genital, anal or oral ulcers) Secondary syphilis (fever, rash, lymphadenopathy) Mixed findings of primary and secondary syphilis at presentation	2 (9%) 16 (70%) 5 (22%)

*Having sex with a non-Israeli partner while abroad

sex; both used condoms regularly with their concurrent female partners, but one of them used condoms irregularly during anal sex with his male partners. Almost all participants (N=21, 91%) practiced fellatio, and none of them used condoms during the oral intercourse. Nine (39%) participants reported unprotected oral intercourse, but regularly used condoms during anal or vaginal intercourse. Four patients (17%) participated in group sex during the 3 months prior to the diagnosis of syphilis. None of the participants was engaged in a monogamous sexual relationship. Ten participants (43%) reported they had sex with non-Israeli partners while traveling to other countries in the previous few months prior to their syphilis diagnosis. The locations for these encounters included Berlin (three participants), Frankfurt, Madrid, New York, Montreal, Chicago, Paris, Moldova and Thailand (one each).

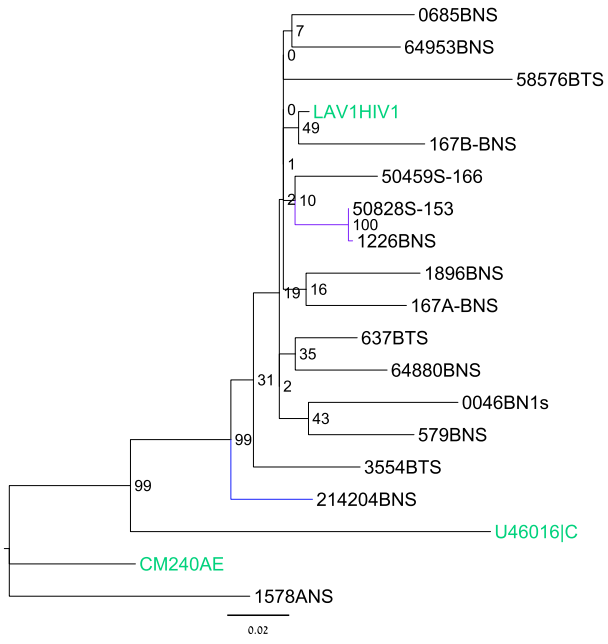
HIV status and prior STD: Almost all participants (96%) were co-infected with HIV; 15 (68%) were already aware of their HIV infection, while 7 (32%) were newly diagnosed with HIV at their presentation with syphilis. Of the 15 known cases of HIV, 9 (60%) reported unprotected anal intercourse. Thirteen participants (57%) had a prior diagnosis of STD (excluding HIV) or related symptoms. These included pediculosis pubis (N=7), urethritis (N=4), anal herpes (N=2), condyloma (N=3), and hepatitis B (N=2).

Use of substances: Fifteen (66%) participants reported the use of recreational drugs, alcohol, or both, before or during sex. Four additional participants reported using volatile amyl nitrate (poppers) during sex but no other drugs, leaving only four participants who did not use substances.

Clinical presentation of syphilis: The detailed description of the clinical presentation of our study participants is presented elsewhere [15]. The clinical presentation was of primary syphilis with genital ulcers only (N=2, 9%), secondary syphilis, with mainly fever, rash and lymphadenopathy but without genital ulcers (N=16, 70%), or a mixed presentation of both (N=5, 22%). Uncommon manifestations included uveitis (one patient) and lip ulcer (one patient). The patient who had a lip ulcer reported unprotected anal and oral intercourse.

Social network: Phylogenetic analysis did not identify any tight clusters among the different HIV viruses and suggested that most likely they are not from the same source [Figure 2]. Two of the

Figure 2. Phylogenetic analysis of HIV samples from study participants



patients, however, recorded 50459S-166 and 1226BNS clustered together with a bootstrap of 100, suggesting a possible closer contact. Epidemiological investigation did not identify significant contact between the cases.

DISCUSSION

Since the start of the new millennium, outbreaks of syphilis have been reported in large urban communities of MSM. Tel Aviv, the largest metropolitan city in Israel, hosts the largest community of MSM. Its liberal atmosphere and tolerability of sexual minorities as well as the option to remain anonymous in a big city enabled the rise of an openly gay community [16]. It was only a matter of time until an epidemic of syphilis, which until now had been reported in other urban areas in developed countries [17], would affect this community. An outbreak was therefore expected due to recent reports of the international transfer of HIV among MSM between developed countries.

Only limited data on syphilis in Israel have been published in the last few years [18]. These included seropositivity for infectious syphilis in 1.3% of female sex workers in the Tel Aviv area [19] and prevalence rates of 0.3% and 0.7% in 3223 heterosexual males and 993 gays, respectively, who visited the Tel Aviv STD clinic between 2002 and 2008 (Z. Mor, personal communication). A high rate of syphilis co-infection was reported in HIV-positive patients residing in northern Israel (27%). Nevertheless, this patient population consisted of mainly Jewish Ethiopian immigrants, among whom MSM practices are presently uncommon [20].

This study describes an outbreak of syphilis in the Tel Aviv district, affecting almost exclusively MSM. The cases described were born in Israel or immigrated two decades ago and, consistent with previous reports, had a high number of sexual partners, a high prevalence of past STD and frequently used alcohol or recreational drugs in association with sexual acts. None of the participants had been in a monogamous relationship when they presented with syphilis. More than 40% of the patients reported sexual intercourse while traveling outside Israel, in cities known to have a high burden of syphilis in the MSM communities, e.g., Berlin, New York [5], among others. This fact leads to the assumption that some of the infections were imported.

The majority of syphilis patients in this study were co-infected with HIV (96%), a rate higher than reported for similar communities in developed countries [4-6,8,10,12,14]. This high rate is alarming, as syphilis can facilitate both the transmission and the acquisition of HIV [3]. Several aspects of this association should be noted. First is the change in sexual behavior among HIV-infected individuals. The effective antiviral therapy for HIV may have led to exaggerated optimism and thus more risky sexual practices among HIV-positive and negative persons alike [17,21]. As a result, a more common practice of unprotected anal intercourse was recorded in both HIV-infected (60%) and uninfected individuals (50%) in our study. HIV and syphilis co-infection was found to be more likely in HIV-positive patients receiving antiretroviral treatment and having an undetectable HIV viral load than in HIV-positive untreated controls [2,3,5], suggesting optimism about AIDS treatment. Second is the sexual behavior of HIV-positive individuals. In contrast to the reaction of the MSM community to HIV at the beginning of the epidemic, when safer sex, limiting the number of partners, and abstinence, were common among HIV-infected individuals, in recent years more MSM with HIV infection practice intentional unprotected anal intercourse ("barebacking") [4], mainly with persons of similar HIV status ("sero-sorting"). Although this practice can decrease HIV spread to HIV-negative partners, it may increase the risk of acquiring other STDs or drug-resistant HIV strains. Our report supports this phenomenon, with a 60% rate of unprotected anal intercourse among the participants who had known HIV infection prior to syphilis diagnosis. The high rate of co-infection also supports routine screening for STD in HIV-positive patients, as was suggested in Israel in the past, and recommended by a U.S. advisory committee on HIV and STD prevention [22]. Third is the common practice of unprotected oral intercourse. This was practiced by both HIV-positive and negative persons, and is generally perceived as "safe sex" in terms of HIV transmission and risk reduction among MSM. While generally assumed that it can rarely lead to HIV transmission, unprotected oral intercourse is an additional route of spread for syphilis and other STDs. We received reports that 21 (91%) of our participants did practice unprotected anal intercourse, while 9 (39%) used condoms concomitantly during anal intercourse. Fourth is substance use during sexual intercourse, which is a recognized risk factor as it may affect decision-making and result in risky sexual behavior [23]. Drug use is also strongly related to online sex and STD/HIV transmission risk, as "party and play" is a common nickname to describe an electronic personal profile in gay-oriented internet sites. The association between unprotected anal intercourse and substance use was also found in a recent online study performed in Israel [24]. Our study showed substance use in 83% of participants.

Contact tracing has been a challenge for the health practitioners involved, since most of the participants were either reluctant to disclose personal details of their sexual partners or did not know their contacts due to the anonymous nature of their relationship. Those who could communicate with their contacts were asked to convey this information directly to the sexual partners; the other contacts were notified by a health officer from the health department. Some countries have also faced difficulties in contact tracing of MSM infected with syphilis as compared to heterosexuals, such as Canada [14] and the UK (London) where only 4% of contacts of MSM were traced [4]. Nevertheless, our impression is that there was no single common source for this outbreak, but a sporadic occurrence of syphilis among multiple sexual networks related to unsafe

sex practices. A similar pattern was described among MSM in Sheffield, UK, where a "starburst" occurrence of cases was reported, unlike a spread from a possibly traceable origin in the heterosexual cases that had a single or a core source [25]. Phylogenetic analysis of HIV from the patients did not support a common source and did not identify core transmitters, including the cases that were newly diagnosed with HIV.

The limitations of this study include the relatively small sample size and the reluctance of some participants to provide information about their sexual partners. Although a reporting bias is expected in interviews that include intimate information about sexual practices, the data collected in this current descriptive study present a clear impression of sexual habits and practices of MSM diagnosed with syphilis in Israel. Also, a difference may be found in interview techniques between the two interviewers.

A significant decrease in the number of reported syphilis cases in Tel Aviv was noted in 2010 (19 patients vs. 49 in 2009). This decline in the outbreak might be explained by heightened awareness among the MSM community and especially among those living with HIV. This awareness may be related to the prompt investigation, discussions with the patients, and media publicity.

In summary, this study describes the first outbreak of primary and secondary syphilis among MSM in Tel Aviv, which affected the gay community in Israel. Most of the cases were concomitantly infected with HIV and were characterized by risky sexual behavior, including multiple partners, unprotected anal intercourse and substance use.

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"Legend – a lie that has attained the dignity of age"

Henry Louis Mencken (1880-1956), American journalist, essayist, magazine editor, satirist and acerbic critic