Published in final edited form as:

Sex Transm Dis. 2018 September ; 45(9) : S38–S41. doi:10.1097/OLQ.0000000000000815.

Old pathogen, new challenges: a narrative review of the multi-level drivers of syphilis increasing in American men who have sex with men

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Abstract

Since the turn of the current century, syphilis incidence and prevalence have been increasing more rapidly among men who have sex with men (MSM) than any other U.S. subpopulation, exceeding their previously high rates in the 1970's and 1980's, prior to the AIDS epidemic. The reasons for these trends are multi-factorial and complex, involving individual behavioral, socio-cultural, structural and biological factors, which will be reviewed in this paper. MSM tend to have more sexual partners than heterosexuals, and engage in practices (e.g. anal sex) that are highly efficient for syphilis transmission, and non-detection of primary chancres. In the era of highly active antiretroviral therapy rendering adherent patients non-infectious and the use of pre-exposure prophylaxis, there is substantially less concern about HIV transmission and acquisition among MSM, resulting in higher levels of condomless sex. The increased concentration of syphilis among Black MSM is partially related to assortative mixing, i.e. Black MSM being more likely to have other Black sex partners, as well as decreased access to preventive services and treatment due to economic marginalization, Societal rejection and discrimination may also potentiate factors that may increase sexual risks resulting in syphilis, e.g. depression and substance use. The anticipation of experiencing homophobic discrimination in health care settings may lead many sexually active MSM to delay needed screening and treatment, thus being infectious to partners for longer periods of time than other populations. To effectively control the syphilis epidemic among MSM, scaling up a combination of programs, ranging from enhanced community education to training clinicians and health care systems to provide culturally competent care, will be necessary.

Epidemiology

The number of Primary and Secondary syphilis (P&S) cases reported to the Centers for Disease Control & Prevention (CDC) have increased dramatically since the beginning of the new century, with MSM accounting for 58% of primary and secondary syphilis cases in the United States in 2016 (1,2). These rates reflect a dramatic increase in the prevalence of syphilis in American MSM over the past decade (3,4), which exceeded the the previously record high rates seen in the 1970's and 1980's among MSM, prior to the advent of the

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Conflicts of Interest: No other conflicts are declared.

AIDS epidemic. The increased detection of syphilis appears to be a global phenomenon, with reports from Europe (5,6), other developed countries (7,8), and Latin America (9) noting similar trends. Among 44 U.S. states reporting information on the sex of intimate partners for more than 70% of male cases, the overall rate of P&S syphilis among all men (aged ≥ 18 years) in the United States in 2015 was 309.0 per 100,000 among MSM compared to 2.9 among men who reported sex with women only (MSW) (2). The disparity in syphilis rates between MSM and MSW reflects multiple factors, including the increased number of sexual partners among some MSM compared to most MSW, assortative mixing among MSM (i.e. only having MSM partners, concentrating the spread of infection within the subpopulation) and biological susceptibility (see below). The syphilis epidemic in American MSM is characterized by marked racial disparities. Among 11,359 cases of P&S syphilis among MSM with known race/ethnicity in 2014, 40.3% were among white MSM and 32.2% were among black MSM (4). Although more cases were diagnosed among white MSM, the national rates of P&S syphilis diagnoses were 168.4 per 100,000 for white MSM and 583.9 per 100,000 for black MSM. Regional rates suggested syphilis was most prevalent in the South at 602 per 100,000 for Black MSM, with rates were consistently higher among black MSM in each region compared to white MSM (3,4). However, even in jurisdictions with relatively fewer Black MSM, syphilis incidence among MSM, particularly HIV-infected MSM, have reached unprecedented levels, e.g. between 2.5 and 4% annual incidence in Seattle (10).

The reasons for the current increases in syphilis among American MSM are diverse and include social, behavioral, biological, and epidemiological factors, not of all them are unique to the U.S. epidemic. However, some issues are specific to the American context, particularly the disproportionate syphilis burden among Black MSM. The multifactorial etiology of increasing syphilis rates among MSM means that ultimate control will require diverse approaches that address key drivers of this persistent epidemic. Some of the most salient features will be reviewed below.

Socio-behavioral issues

Historically, MSM have tended to have more partners than heterosexual men, and have been more likely to engage in concurrent relationships (11). In recent decades there has been a tendency towards decreased condom use (12), which may reflect the relaxing of safer sex norms in an era when HIV is no longer perceived to be a fatal disease, and other STDs have been increasingly perceived to be as treatable, preventable, or inconsequential. However, the explanation for MSM having multiple condomless sexual partners may have longer-standing antecedents. Throughout human history, until recently, MSM have generally grown up in non-affirming societies, and as they have matured they have had to contend with the knowledge that their sexual preferences were not societally acceptable (13–15). This has led to high rates of internalized stigma, resulting in elevated rates of depression, general anxiety disorder, and other behavioral health challenges for which MSM tend to have much higher prevalence than do demographically matched heterosexual males (16–20). Perhaps to mitigate the psychological trauma that they may feel, the use of recreational drugs among MSM has been common, with higher rates of specific substance use, e.g. poppers, marijuana, alcohol, and stimulants, than among heterosexual males (21, 22). The

phenomenon of “chem-sex” has been associated with high rates of syphilis acquisition and transmission as well as HIV and other sexually transmitted infections (23–25). Early childhood violence/victimization may potentiate the likelihood of ongoing sexual risk taking, substance abuse, and increased STD/HIV risk (25, 26). The frequent co-occurrence of these behavioral adversities in MSM create a syndemic (27,28), requiring preventive interventions that address co-prevalent factors.

Bio-behavioral Issues

Although insertive and receptive anal intercourse are the most efficient ways to transmit HIV, and syphilis (29–31), receptive or insertive oral sex (fellatio) may also transmit syphilis while not transmitting HIV (32). The practice of oral sex has been more prevalent among MSM before and during the HIV/AIDS era, but the rates of oral sex compared to anal sex have increased in many settings as a safer sex practice in order to decrease the risk posed by anal intercourse (30, 33). In addition to the efficiency of oral sex in transmitting syphilis, HIV itself may be a driver of the efficiency of syphilis transmission (34). Individuals who are HIV-infected and acquire syphilis are more likely to transmit syphilis to their partners. Moreover, the practice of serosorting (preferentially choosing partners of the same HIV serostatus) may have helped to concentrate the syphilis epidemic among HIV-infected men who have sex with men (35–38). The hyper-concentration of syphilis among HIV-infected individuals could abate as the rationale for serosorting becomes less necessary, given that HIV infected individuals may feel that they won’t transmit HIV to their partners if they are virologically suppressed on antiretroviral therapy when engaging in condomless sex (39), and high risk HIV-uninfected individuals can avail themselves of pre-exposure prophylaxis (PrEP) (40–42). Thus, HIV-uninfected individuals, who previously had a lower prevalence of syphilis, may now be in more frequent contact with HIV-infected individuals with a higher prevalence of syphilis (43). More recently, the growth of sexualized internet-based social media has been a facilitator of syphilis transmission, given the newfound ease in meeting sex partners on line (43–46).

Systemic and structural issues

Many of the phenomena that have led to the growth of syphilis among American MSM are not unique to the United States, and the ease of travel, in addition to the use of the Internet to meet partners, has helped to further globalize the syphilis epidemic in MSM. However, one of the distinguishing characteristics of the U.S. syphilis epidemic is the disproportionate disease burden among black MSM (2,3). Multiple studies have indicated that black MSM do not have more sexual partners than MSM of other races or ethnicities, but are more likely to be HIV positive and more likely to engage in assortative mixing (47). That is to say, they are more likely to choose partners within their own racial community, thereby hyper concentrating the HIV epidemic. Moreover, black MSM like other African Americans may often be economically disenfranchised and therefore less likely to access health services in a timely manner (48). Black MSM may have also experienced racism and other micro-aggressions and be less likely to access healthcare in settings they do not feel are culturally sensitive (49, 50). Thus, the U.S. syphilis epidemic is potentiated by health disparities that

are unique to the U.S., and which require more intensive social attention if the goal of “syphilis elimination” is to be achieved.

Syphilis in the ART for prevention era

The recognition that effective antiretroviral treatment renders HIV-infected individuals functionally non-infectious and the more recent demonstration of the efficacy of PrEP has been associated with increased condomless sex in MSM (40–42, 51–53). Thus, individuals can be protected from retroviral transmission or acquisition, while being highly susceptible to acquiring and transmitting syphilis. Individuals who use antiretrovirals for prevention may be more likely to play part of a syphilis transmission chain, since their choice to use HIV preventive medication may signal a desire not to use condoms. Although the rise of syphilis has antedated the demonstration of the efficacy of PrEP (1–3), several recent studies have shown that individuals who are using PrEP have a high likelihood of acquiring syphilis (40–42, 51, 53). Although it has been speculated that antiretrovirals could increase susceptibility to syphilis through a biological mechanism, an analysis of incident syphilis cases in the iPrEX MSM PrEP study found that the rates of syphilis acquisition were comparable in the placebo group as among those who were receiving the active medication (54). Thus the interaction of PrEP and syphilis reflects behavioral and epidemiologic realities, rather than a direct biological effect.

While concerns have been raised about the role of PrEP in decreasing condom use, and potentiating risk compensation because of decreased worries about HIV acquisition (50), HIV-uninfected individuals who are not using PrEP are of even greater concern, since incident syphilis is a harbinger of increased likelihood of acquiring HIV (55). Thus, rather than focusing on syphilis as a negative consequence of PrEP, incident syphilis among HIV-uninfected, high-risk MSM is an indication for those individuals who may most benefit from PrEP, and a reason for frequent syphilis screening for those using PrEP. Quarterly STD testing of PrEP users may allow for earlier identification and treatment of incident syphilis cases, allowing for prompt partner notification and fewer onward transmissions..

Syphilis, MSM and the healthcare system

The dramatic increases in syphilis among MSM are a cause for concern among clinicians and public health officials. The rise syphilis among MSM could possibly be associated with increasing rates of congenital syphilis in the progeny of female partners (1). For MSM themselves and their partners, there are increasing reports of neurological and physiological complications of syphilis in both HIV-infected and HIV-uninfected individuals (56, 57). Thus, it is particularly important for clinicians to be attentive to identifying syphilis in order to provide optimal health services for patients who may be at greatest risk. Part of the challenge to controlling the MSM syphilis epidemic is that sexual and gender minority patients may not feel comfortable disclosing their same-sex attraction behavior to their primary providers (57–60), underscoring the need for healthcare providers to be trained to provide culturally competent care for their sexual and gender minority patients. Some MSM, particularly those from racial and ethnic minority communities, may not be comfortable

working with partner notification services, because of concerns about stigma and cultural insensitivity. The common recurrence of syphilis among some MSM underscores the need for effective partner notification services (61). Fortunately, over the past decade, more attention has been focused on sexual and gender minority health (62), and an increasing array of tools have been developed to assist providers in the provision of culturally-informed care (e.g. www.lgbthealtheducation.org) (63). As clinicians become more capable to provide culturally competent care for MSM patients, they will be able to screen and counsel individuals whom they might not otherwise have thought to be at risk for syphilis.

It is very unlikely in the current era of HIV treatment as prevention and pre-exposure prophylaxis that the rise in syphilis and other sexually transmitted diseases will result in increasing use of condoms by all MSM, though increased community education may motivate some to use condoms for STD prevention. Thus, the utilization of traditional clinical and public health tools, i.e. patient education, frequent routine screening of at-risk individuals (61), prompt initiation of treatment, and partner notification services will be the mainstays efforts to curtail the further spread of syphilis among MSM for the near future.

Acknowledgments

Sources of Funding: This work was funded in part by the Harvard Center for AIDS Research (P30 AI06354). Dr. Mayer is also supported by NIAID contract HHSN2722013000121 (“Sexually transmitted Infections Clinical Trials Group”).

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Summary

The reasons for the increase in syphilis in MSM are multi-factorial and complex, involving individual behavioral, socio-cultural, structural and biological factors, which will be reviewed in this paper.