Sexually Transmitted Diseases in Men Who Have Sex with Men: A Clinical Review

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Current Infectious Disease Reports 2003, **5:**135–144
Current Science Inc. ISSN 1523-3847

Increases in sexually transmitted diseases (STDs) among men who have sex with men (MSM) have coincided with recent increases in sexual risk behaviors across the United States and Europe. The identification of same-sex sexual risk behavior in men and the subsequent risk for certain bacterial and viral infections requires competency in taking a sexual history. Recent advances in the diagnosis and treatment of STDs have made STD management easier for physicians and patients and expanded the ability of a variety of health care professionals to participate in the management of STDs. This review focuses on recent developments in the epidemiology, pathogenesis, diagnosis, and management of common STDs in MSM.

Introduction

Men who have sex with men (MSM) are a diverse population defined by their sex and sexual behavior. The reliance on the patient report of sexual behavior challenges clinicians in identifying patients who might be at higher risk for certain viral and bacterial sexually transmitted diseases (STDs). Every patient evaluation should include a risk assessment for STDs that includes a nonjudgmental and direct ascertainment of sexual behaviors (Table 1). The type of sexual behavior must be delineated documenting insertive oral, receptive oral, insertive anal, receptive anal, or insertive vaginal sexual intercourse. Further description of oral-anal, anal-oral, digital-anal, or anal-digital practices should also be assessed for risk of enteric infections and hepatitis A. Even after direct questioning, many sexual behaviors are likely to remain hidden from the clinician, and continued probing and discussion of sexual activity will enhance the amount of information gathered and the ability of the clinician to provide appropriate preventive and diagnostic care.

One of the most dramatic changes in STDs in MSM has been in epidemiology. A significant reversal of declines in STD incidence occurred in the late 1980s through mid-1990s, with well-documented recent increases in syphilis, gonorrhea, and HIV. These increases in STD transmission parallel the reversal in AIDS morbidity and mortality with the advent of highly active antiretroviral therapy [1]. Decreases in condom use, increases in number of sexual partners, and changes in safer sex practices from oral sex to anal intercourse have been reported in MSM in major urban areas throughout the United States. Changes in community norms resulting from HIV treatment optimism and the improved physical well-being of HIV-infected persons are some associated factors [2•]. Contributing to these changes has been the advent of the Internet as a means to meet new sexual partners [3], the widespread recreational use of sex drugs like Viagra (Pfizer, New York, NY) (sildenafil citrate) or [4] methamphetamine [5,6], and the effect of direct-to-consumer HIV medication advertising mitigating the consequences of HIV/AIDS [7].

The recent publication of the Centers for Disease Control and Prevention (CDC) Treatment Guidelines for Sexually Transmitted Diseases in May 2002 offers a timely opportunity for a review of the epidemiology, clinical manifestations, and management of STDs in MSM [8••].

Bacterial Infections

Gonorrhea

Neisseria gonorrhoeae causes infections of the pharynx, urethra, and rectum (uncomplicated gonococcal infection), classically presenting as pharyngitis, urethritis, and proctitis, respectively. Asymptomatic infection with gonorrhea has been increasingly recognized as important, although the natural history of asymptomatic infections is largely unknown. Additional research in the pathogenesis of gonococcal infections might elucidate our current understanding of the duration of asymptomatic carriage, the rate at which asymptomatic infections become symptomatic, the sequelae of untreated asymptomatic infections, and the differences in bacterial load that might alter transmission.

Table 1. Sexual history taking in men who have sex with men

Obtaining an adequate sexual history is a continual process between the clinician and patient, guiding principles include
Ensuring confidentiality
Establishing trust and rapport
Maintaining nonjudgmental attitude
Asking open-ended questions
Examples include
"In order to take the best possible care of you, I need to ask a few questions about your sexual behaviors. Anything we discuss stays in this room."
"Are you sexually active?"
"Do you have sex with men, women, or both?"
"How many different people do you have sex with?"
"What types of sex do you have (eg, anal, oral, vaginal)?"
"What are ways you protect yourself from new sexually transmitted diseases, including HIV?"

Increases in rectal and urethral gonorrhea among MSM have been reported in Boston, Denver, Los Angeles, San Francisco, and Seattle since the mid-1990s in MSM aged 30 to 40 years and in those who are HIV infected [5,9–12,13•,14•]. In one study, risk factors for rectal gonorrhea included meeting partners on the Internet and methamphetamine use [5]. In other studies, researchers documented the high prevalence of asymptomatic pharyngeal gonorrhea by nucleic acid amplification testing (NAAT): 6% among MSM seeking anonymous HIV testing and 11% among MSM seen in an STD clinic in San Francisco [10,11].

The diagnosis of gonorrhea continues to be predominantly by culture, particularly for pharyngeal and rectal infections. A recent study in our program showed the superiority of NAAT over culture (sensitivity 93% vs 64%) in detecting pharyngeal infections [11]. Current studies document similar improvement in the detection of rectal gonococcal infections by NAAT. In many practice settings, simplified gonorrhea screening by NAAT on urine specimens has replaced culture and the need for urethral specimen collection, resulting in increases in the detection of asymptomatic infection. In urethritis, diagnosis by culture is often preferred because the discharge is readily accessible and the isolation of the organism allows for antimicrobial susceptibility testing. Antimicrobial susceptibility monitoring is a critical component of public health surveillance, which allows for timely and evidence-based therapeutic recommendations. Recently, reports have documented an increased prevalence of decreased susceptibility of gonococcal isolates to ciprofloxacin in Hawaii and California, resulting in changes in treatment recommendations from fluoroquinolones to third-generation cephalosporins like cefixime [12].

The recommended treatment for uncomplicated gonococcal infection is cefixime 400 mg orally as a single dose, ceftriaxone 125 mg intramuscularly as a single dose, or in regions where fluoroquinolone resistance has been documented to be less than 3%, ciprofloxacin 500 mg or levofloxacin 250 mg (or 500 mg) (Table 2). With these regimens, treatment success is about 95%; therefore, a follow-up test-of-cure is not necessary. In patients in whom coinfection with chlamydia has not been ruled out, chlamydia therapy is indicated. Recent data in MSM demonstrate a 15% chlamydial coinfection rate in gonococcal urethritis and proctitis [13•,14•,15]. Sexual partners within the previous 60 days of patients diagnosed with gonorrhea should be evaluated and treated for gonorrhea. In circumstances where it might be unlikely that sexual partners return for evaluation and treatment, patient-delivered partner therapy is recommended. Treatment of recent sexual partners prevents reinfection and might decrease continued transmission in the community.

Chlamydia

Chlamydia trachomatis causes infections of the pharynx, urethra, and rectum in MSM. Chlamydia is often an asymptomatic or minimally symptomatic infection. Recent data regarding rectal chlamydial infections in MSM [14•] document increases over the previous 5 years and a 10% prevalence of asymptomatic infection. Additionally, studies regarding MSM demonstrate that chlamydia might cause up to 20% of cases of nongonococcal urethritis (NGU), similar to the proportion of NGU attributable to chlamydia in heterosexual men [13•]. In asymptomatic populations of MSM undergoing urine screening for urethral chlamydial infection at anonymous HIV testing sites, 3% had chlamydial infection in San Francisco and 0.5% had chlamydial infection in Denver [10,16].

Before the advent of NAAT for the diagnosis of rectal chlamydial infection, the role of chlamydia in proctitis was underappreciated. One study using NAAT demonstrated that 17% of MSM attending an STD clinic with clinical proctitis had chlamydial infection [15]. Another recent study demonstrated that 20% of MSM with rectal symptoms were infected with chlamydia [17]. Comparison of NAAT versus culture identified six rectal specimens positive for chlamydia by NAAT and none by culture. In a research cohort of MSM, 4.2% had rectal chlamydia using the polymerase chain reaction (PCR) assay, whereas only 0.5% of this population had urethral chlamydia [18]. Another study in Seattle compared different methods of processing rectal specimens for the PCR assay and documented no differences by the means of specimen processing [19]. Other validation studies in individual

laboratories have confirmed the adequate performance of NAAT for the detection of rectal chlamydial infection.

To date, antimicrobial resistance has not been a substantial problem in the management of chlamydial infections. One reported case in 2000 documented chlamydia resistant to azithromycin, doxycycline, and ofloxacin, but the extent of resistance at the population level appears limited [20]. Routine surveillance for decreased antimicrobial susceptibility of chlamydia is not done, and monitoring relies on case reports. Because isolation of chlamydia depends on tissue culture that has been replaced by NAAT for routine testing, defining antimicrobial susceptibility largely depends on independent research laboratories and has not been a public health priority.

The recommended treatment of uncomplicated chlamydial infection is doxycycline 100 mg orally twice daily for 7 days or azithromycin 1 g orally once. Doxycycline is substantially less expensive than azithromycin, equally efficacious, and offers the patient a continuous reminder to abstain from sexual activity until treatment is completed. Azithromycin can be given under directly observed therapy to assure adherence, and because of its excellent safety profile, is easily amenable to give to patients to give to recent sexual partners, either through prescription or by directly providing additional doses. In an effort to augment the control of chlamydia in California, as of January 2001 state law authorized medical providers to dispense additional chlamydial therapy for partners of patients with chlamydial infection.

Syphilis

After being a common infection in MSM in the late 1970s, the prevalence of syphilis declined during the early AIDS epidemic to levels consistent with disease elimination by the mid-1990s [21]. The recent resurgence in sexual behaviors that increased STD transmission in MSM has lead to outbreaks of syphilis in Boston [22], Chicago [23], Los Angeles [24], New York [25], Philadelphia [26], San Francisco [27•], southern California [28], and Seattle [21,29]. Currently, in San Francisco, approximately two thirds of cases have occurred in HIV-positive men with a mean age of 38 years. Cases have been associated with venues such as bathhouses, sex clubs, adult bookstores, and meeting sites such as the Internet. Methamphetamine use has been associated with approximately 25% of cases. A recent survey in Chicago among MSM attending a community event documented that only approximately 25% of respondents knew that a rash was a symptom of syphilis, and 50% incorrectly identified urethral discharge as a symptom [30].

Substantial debate has occurred regarding how HIV infection affects the presentation and management of syphilis infection. Recent studies have documented that HIV-infected patients are more likely to present with multiple chancres and overlap of primary and secondary manifestations [31]. Since HIV-infected patients might be more likely to have a previous history of syphilis infection, these findings might be confounded by previous syphilis infection. Perhaps for the same reason serologic titers observed in HIV-infected patients have been higher at initial presentation and have had a slower decline [32]. Again, the role of previous syphilis infection in these observations has not been accounted for adequately.

Much has been made about the rate of neurosyphilis in HIV infection. A subanalysis from a large prospective study of syphilis diagnosis and management documented no difference in the rate of neurosyphilis detection, response to treatment, or clinical outcome at 1 year [32]. The short follow-up, however, limits these conclusions. More recent data indicate that advanced CD4 count might be associated with increased incidence of laboratory-defined neurosyphilis, but the clinical implications are unclear [33].

The diagnosis of syphilis in both HIV-uninfected and HIV-infected persons is reliably made by the use of dark field microscopy of exudates from primary or secondary lesions or serology. Both the rapid plasma reagin (RPR) and the venereal disease research laboratory (VDRL) tests are commercially available. Whereas the RPR might be slightly more sensitive, the VDRL is the only assay approved for testing of cerebrospinal fluid specimens. Early case reports suggesting the unreliable nature of syphilis serology in HIV-infected patients have not been substantiated. HIV-infected patients with syphilis should undergo close follow-up at 3, 6, 9, 12, and 24 months [8••]. A fourfold decline in titer at 6 months in patients with early infection and at 12 months in patients with late infection is usually consistent with adequate response to treatment.

The development of alternative therapies to penicillin are among the treatment advances for syphilis. Long-acting benzathine penicillin G is still the recommended standard therapy for the treatment of syphilis. The only recommended alternative therapy for penicillin-allergic patients is doxycycline. Data have shown that 1 g azithromycin is efficacious in the prevention of syphilis in persons exposed [34]. A recent pilot study has shown that a single dose of 2 g azithromycin is efficacious in the treatment of early syphilis [35]. Larger, more definitive studies are underway. Azithromycin offers the advantage of a noninjection antimicrobial and use in patient-delivered partner therapy. In addition, azithromycin-targeted mass chemoprophylaxis has been used to control syphilis in endemic and outbreak situations [36,37]. The use of treatments other than penicillin require close follow-up.

Nongonoccal urethritis/urethritis

Since chlamydia or gonorrhea is recovered in only approximately 40% of cases of urethritis in MSM, nongonoccocal, nonchlamydial urethritis (NGC/NCTU) is the most common diagnosis [13•]. Overall, NGC/NCTU in MSM is poorly studied and data can only be extrapolated from heterosexual populations. Because exposures in MSM are primarily oral or rectal, whereas in heterosexuals exposures are oral or vaginal, the limitations of these extrapolations are obvious. In heterosexual men, common etiologic agents recovered in NGC/NCTU include *Trichomonas vaginalis*,

Table 2. Treatment recommendations for common sexually transmitted diseases in men who have sex with men

Chlamydia
- Azithromycin 1 g PO once or doxycycline 100 mg PO bid x 7 d
- Alternate regimens: erythromycin base 500 mg PO qid x 7 d, or erythromycin ethylsuccinate 800 mg PO qid x 7 d, or ofloxacin 300 mg PO bid x 7 d, or levofloxacin 500 mg PO qd x 7d

Gonorrhea*
- Cefixime 400 mg PO once or ceftriaxone 125 mg IM once plus* a recommended regimen for chlamydia
- Alternate regimens: spectinomycin 2 g IM once, or ciprofloxacin 500 mg PO once, or ofloxacin 400 mg PO once, or levofloxacin 250 mg (or 500 mg) PO once plus* a recommended regimen for chlamydia or azithromycin 2 g PO

Nongonococcal urethritis†
- Azithromycin 1 g PO once or doxycycline 100 mg PO bid x 7 d
- Alternate regimens: erythromycin base 500 mg PO qid x 7 d, or erythromycin ethylsuccinate 800 mg PO qid x 7 d, or ofloxacin 300 mg PO bid x 7 d, or levofloxacin 500 PO qd x 7

Human papillomavirus
- External genital/perianal warts
  - Patient applied: podofilox 0.5% solution twice daily for 3 consecutive days followed by 4 days of no therapy x 4 weeks, or imiquimod 5% cream tiw x 12 weeks
  - Provider administered: liquid nitrogen or podophyllin resin 10%–25% in tincture of benzoin, or trichloroacetic acid or bichloroacetic acid 80%–90% each week until resolution
  - Alternative regimen: surgery or intralesional interferon
- Anal warts
  - Liquid nitrogen or trichloroacetic acid or bichloroacetic acid 80%–90%, or surgical removal

Herpes simplex virus‡
- First clinical episode of herpes
  - Acyclovir 400 mg PO tid x 7–10 d, or acyclovir 200 mg PO 5 x qd x 7–10 d, or famciclovir 250 mg PO tid x 7–10 d, or valacyclovir 1 g PO bid x 7–10 d
- Recurrent episodes
  - Acyclovir 200 mg PO 5 x d x 5 d, or acyclovir 400 mg PO tid x 5 d, or acyclovir 800 mg tid x 2 d, or famciclovir 125 mg bid x 5 d, or valacyclovir 500 mg PO bid x 3–5 d, or valacyclovir 1.0 g PO qd x 5 d
- Suppressive therapy
  - Acyclovir 400 mg PO bid, or famciclovir 250 mg PO bid, or valacyclovir 500 mg (or 1 g) PO qd
- In HIV infection§
  - Recurrent episodes
    - Acyclovir 400 mg 0O tid x 5–10 d, or acyclovir 200 mg PO qid x 5–10 d, or famciclovir 500 mg PO bid x 5–10 d, or valacyclovir 1.0 g PO bid x 5–10 d
  - Suppressive therapy
    - Acyclovir 400–800 mg PO bid-tid, or famciclovir 500 mg PO bid, or valacyclovir 500 mg PO bid

Hepatitis B virus
- Refer to gastroenterology or hepatology specialist

Syphilis
- Primary, secondary, and early latent
  - Benzathine penicillin G 2.4 MU IM once
  - Alternate regimens: azithromycin¶ 2 g PO once, or doxycycline¶ 100 mg PO bid x 2 weeks, or tetracycline¶ 500 mg PO qid x 2 weeks, or ceftriaxone¶ 1g IM/IV qd x 8–10 d
- Late latent and unknown duration
  - Benzathine penicillin G 7.2 MU administered as three doses of 2.4 MU IM at 1-week intervals
  - Alternate regimens: doxycycline 100 mg PO bid x 4 weeks or tetracycline 500 mg PO qid x 4 weeks
- Neurosyphilis**
  - Aqueous crystalline penicillin G 18–24 MU daily administered as 3–4 MU IV q 4 h x 10–14 d

*Cotreatment for chlamydia infection is indicated unless chlamydia infection has been ruled out using sensitive tests.
‡Testing for gonorrhea and chlamydia is recommended because a specific diagnosis might improve compliance and partner management.
‡Counseling about the natural history, atypical symptoms, asymptomatic shedding, and sexual transmission is an essential component of herpes management.
§If lesions persist or recur while receiving antiviral treatment, herpes simplex virus resistance should be suspected and a viral isolate should be obtained for sensitivity testing.
¶Because efficacy of these therapies has not been established and compliance with some of these regimens is difficult, close follow-up is essential. If compliance or follow-up cannot be ensured, then patient should be tested for hypersensitivity and, if needed, desensitized and treated with benzathine penicillin.
**One dose of 2.4 MU of benzathine penicillin G recommended at completion of neurosyphilis therapy.
bid—twice a day; IM—intramuscularly; IV—intravenously; PO—orally; qd—every day; qid—four times a day; tid—three times a day; tiw—three times a week.

Table 2. Treatment recommendations for common sexually transmitted diseases in men who have sex with men *(Continued)*

Alternate regimens: procaine penicillin G 2.4 MU IM qd x 10–14 d plus probenecid 500 mg PO qid x 10–14 d or ceftriaxone¶ 2 g IM/IV qd x 10–14 d
Enteric infections
Amebiasis
Metronidazole 750 mg PO tid x 10 d followed by either iodoquinol 650 mg PO tid x 21 d or paromomycin 500 mg PO tid x 7 d
Giardiasis
Metronidazole 250 mg PO tid x 5 d or paromomycin 500 mg tid x 7 d
Shigellosis
Ciprofloxacin 500 mg PO bid x 3 d or other fluoroquinolones
Cryptosporidiosis
Supportive treatment should be administered including fluid and electrolyte replacement and antimotility agents
Paromomycin 500 mg PO qid x 14 d, or nitazoxanide 500 mg PO bid x 3 d, or azithromycin 1200 mg qd x 21–28 d
Parasites
Pubic lice
Permethrin 1% cream applied to affected area and rinsed off in 10 minutes or pyrethrins and piperonyl butoxide applied to the affected area and washed off in 10 minutes
Scabies
Permethrin cream 5% applied from neck down and washed off after 8–12 h
Alternate regimen: lindane 1% applied from neck down and washed off after 8–12 h

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‡Counseling about the natural history, atypical symptoms, asymptomatic shedding, and sexual transmission is an essential component of herpes management.
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Mycoplasma genitalium, *Ureaplasma urealyticum*, herpes simplex viruses, adenoviruses, *Streptococcus* species, *Haemophilus* species, and anaerobes. The most recent studies have implicated *M. genitalium* in heterosexuals with NGC/NCTU, but the role this agent plays in MSM is unknown [38]. Noninfectious etiologies of NGU should also be considered, such as inflammatory reactions to urethrally inserted drugs like cocaine, chemicals in lubricants like nonoxynol-9, devices like metal urethral dilators used in certain sex play, postcatheterization after medical procedures, and immunologically mediated conditions like Reiter's syndrome.

Although most causes of NGC/NCTU are not specifically determined, most cases respond to traditional therapy for NGU: doxycycline 100 mg orally twice a day for 7 days or azithromycin 1 g orally once. After 7 days, a small proportion of patients might present with persistent symptoms. These patients should be re-evaluated for urethritis with microscopic examination of urethral discharge or urine sediment, be questioned about treatment adherence, be assessed for the possibility of reinfection, and be retreated with a different antimicrobial effective against NGU. Persistent urethritis after retreatment warrants referral to a urologist, along with metronidazole for possible *T. vaginalis* or anaerobes.

Viral Infections

Herpes

With the recent advent of type-specific serologic assays for the determination of herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2) antibody and the role that genital and rectal herpes infections play in HIV transmission, a renewed interest has developed in the epidemiology of HSV among MSM. Recent studies have documented higher prevalence levels of HSV-2 antibody in MSM compared with heterosexual men (31% vs 18%) [39], and a higher proportion of initial genital herpes infections attributable to HSV-1 infection among MSM compared with women and heterosexual men (47% vs 21% vs 15%, respectively) [40]. In one study in Canada, 54% of genital herpes infections were attributable to HSV-1 [41], whereas in San Francisco approximately 30% of genital herpes infections among MSM STD clinic attendees were attributable to HSV-1 [42].

Genital herpes infections cause a substantial amount of morbidity in MSM, with symptoms ranging from recurrent itchiness, redness, or burning sensation, to blisters and sores and genital neuropathic pain. These manifestations can involve the penis, scrotum, perineal area, anus, or rectum. Definitive diagnosis is often difficult because it requires isolation by culture of HSV from the affected area. Most

laboratories will routinely identify the subtype using direct fluorescent type-specific antibody if HSV is isolated in a clinical specimen. Serologic testing might be helpful to rule out infection because the seropositivity of HSV-1 and HSV-2 in the general population is about 70% and 22%, respectively [43]. A negative antibody test for both subtypes thus makes infection unlikely. Recent data demonstrate that asymptomatic viral shedding is common in HSV-2-infected MSM, similar to previous data in women, occurring in more than 50% of men an average of 1 day a month [44,45•].

The most important recent advances in the treatment of genital HSV have been the US Food and Drug Administration (FDA) approval of valacyclovir, 500 mg orally twice daily for 3 days for recurrent infections, and the recent demonstration of the efficacy of acyclovir, 800 mg orally three times per day for 2 days [46]. Clinicians can prescribe valacyclovir as a 1-g scored dose and direct their patients to split the tablet. The average wholesale cost of three 1-g tablets of valacyclovir is similar to the cost of the recommended dosage of generic acyclovir for recurrent infections (400 mg orally twice a day for 5 days).

Hepatitis A, B, and C

Viral hepatitis infections are a major concern for MSM because both hepatitis A virus (HAV) and hepatitis B virus (HBV) are sexually transmitted via oral-anal sex and anal intercourse. Current Centers for Disease Control and Prevention (CDC) guidelines for preventive care in MSM recommend routine vaccination against HAV and HBV, though vaccination coverage of this population is low [47]. The recently FDA-approved combination HAV/HBV vaccine provides a simpler delivery system for vaccination; it is given over several months in three separate doses. Various vaccination schedules of 0, 1, 4 months and 0, 2, 6 months have been documented to be equally immunogenic, and data demonstrate that even after one dose more than 50% of patients have demonstrable seroprotection. HAV is most often a self-limited infection with rare fatalities. The morbidity, however, can be substantial, and recently HAV immunization in MSM has been shown to be cost saving [48].

Treatment for chronic active hepatitis B is evolving. Recent clinical data indicate that therapy with antiviral agents such as lamuvidine 100 mg orally every day and interferon-α 10,000,000 U subcutaneously three times per week can suppress viral replication in 30% to 40% of patients. The recent FDA approval of the drug adefovir, 10 mg every day, is a promising new addition to treatment options for chronic HBV.

Hepatitis C virus (HCV) was once thought to be an important infection for MSM, since population-based prevalence data indicated a higher risk of infection than in the general population [49]. More recent data accounting for previous injection drug use reveals that MSM might not be at an increased risk, and the sexual transmission of HCV is rare [50]. Since coinfection with HAV or HBV may accelerate the course of HCV, it is imperative that persons with HCV receive immunizations for HAV and HBV [51].

Human papillomavirus and anogenital warts

There are more than 70 oncogenic and nononcogenic subtypes of human papillomavirus (HPV) associated with sexual transmission. In MSM, these infections can cause asymptomatic infection, external genital warts, internal rectal warts, and anal carcinoma. Exposure to HPV through sexual activity is common, and population-based prevalence studies document that more than 80% of sexually active persons have been exposed to HPV. A clear relationship exists between the number of sexual partners and increased prevalence of HPV and increased number of HPV subtypes.

External genital warts are a common reason why MSM present for clinical care and evaluation. Men may present with warts on various areas of the penis and anus. Anal condylomata acuminata should be a clinical cue to receptive anal sex and should prompt further discussion of risk behaviors and appropriate screening. Most external genital warts can be adequately diagnosed by visual inspection, but if the diagnosis is uncertain, biopsy may be indicated.

Patients might also complain of internal rectal warts either self-diagnosed or diagnosed by a sexual partner. It is not our current practice to treat these warts unless there is rectal obstruction or substantial bleeding.

Treatment for external genital warts includes provider- or patient-applied therapy such as liquid nitrogen, podophyllin 25%, trichloroacetic acid, imiquimod 5%, or podofilox gel. Patient-applied topical applications appear more efficacious on mucosal sites and other areas that are less keratinized. One advantage of imiquimod 5% is that it might be associated with a reduced recurrence rate because it activates host immunologic mechanisms to clear infection rather than simply ablate the wart [52].

Previous studies have documented the relation between oncogenic subtypes of HPV and anal carcinoma. These studies have led some experts to recommend routine anal pap smears as a means to reduce the rate of anal carcinoma in MSM [53]. The current rate of anal carcinoma at 50 cases per 100,000 MSM per year is similar to the rate of cervical carcinoma before the implementation of cervical carcinoma screening programs. Whereas HIV-infected persons might have higher rates of abnormal anal pap smears, the effect of highly active antiretroviral therapy (HAART) on the reversion of abnormal anal pap smears is currently under study. Because HIV-infected patients are living longer, one might expect the incidence of anal carcinoma to increase in this population if HAART has no effect. Anal carcinoma is a treatable albeit not curable condition with substantial treatment-associated morbidity. A controlled trial of a monovalent human papillomavirus type 16 (HPV-16) vaccine demonstrated efficacy in reducing the incidence of both HPV-16 infection and HPV-16-related cervical cancer in women [54]. Additional research is needed to demonstrate

if HPV-16 vaccination in MSM would have a similar effect on reducing the incidence of anal carcinoma.

Parasitic/Enteric Infections

Since the original seminal paper describing enteric infections in MSM by Quinn *et al.* [55], a few reports have contributed to the clinical epidemiology of these infections. *Giardia lamblia*, *Entamoeba histolytica*, *Shigella* species, and *Cryptosporidium parvum* are important causes of gastroenteritis, particularly colitis characterized by cramping, tenesmus, and diarrhea in the former three and voluminous, loose, watery diarrhea in the latter. Recent studies have documented continued population-based outbreaks of shigellosis in MSM related to oral-anal or digital-anal contact [56,57].

Bacterial stool culture for enteric pathogens and ova and parasitic examination with *Giardia* antigen testing of stool should be performed on MSM presenting with abdominal pain and diarrhea. Whereas one stool specimen might be sufficient to rule in infection, three stool specimens collected on different days are usually required to obtain adequate sensitivity to rule out infection. Giardiasis is treated with metronidazole 250 mg three times a day for 5 days, whereas amebiasis is treated with 500 mg three times a day for 10 days. Amebiasis treatment is followed by treatment with a luminal agent like paromomycin or iodoquinol for 7 to 21 days to eradicate amebic cysts. Successful therapy for cryptosporidiosis is limited, and most infections in immunocompetent hosts resolve without treatment. Treatment with supportive care includes fluid and electrolyte replacement along with an antimotility agent. Recent reports of treatment include the use of paromomycin and azithromycin, alone or in combination with other antibiotics. Nitazoxanide, a broad-spectrum antihelminthic drug, is effective in reducing clinical symptoms and oocyte shedding in cryptosporidiosis [58].

Shigella and other bacterial causes of gastroenteritis are also important to rule out. Shigellosis often presents in MSM as abdominal pain and diarrhea with or without blood. Diagnosis is by stool culture and treatment is with a fluoroquinolone antibiotic for 3 days. Recent reports of *Shigella* species resistant to trimethroprim-sulfamethoxazole and ampicillin make these antimicrobials less useful in routine management [56,59].

Parasites (Crabs, Scabies)

Pubic lice (*Pthirus pubis*) and scabies (*Sarcoptes scabei*) are commonly encountered in clinical practice. Symptoms of pubic lice include itching in the pubic area and often patient identification of lice or nits on the hair shaft. Diagnosis is made by visual inspection and identification of the lice or by finding small red macules in the skin around the hair follicules. Treatment is with several different topical shampoos, including permethrin (1%) cream, pyrethrins, or piperonyl butoxide applied to the affected area.

Scabies can cause more morbidity than pubic lice. Often patients complain of itching around the waist, wrist, and in the webbed area between the fingers. Raised papular lesions can also occur on the scrotum or penis, mimicking secondary syphilitic lesions or epidermoid cysts. Often warmth exacerbates the symptoms such that patients complain of worse itching at night associated with being under the bed covers or after a hot shower.

The diagnosis of scabies is made by history and physical findings. Rarely, lesions can be scraped and mite or mite feces identified by microscopy under oil immersion. Treatment is with permethrin cream 5% applied overnight. Rare complications include seizures. Some experts recommend repeat treatment at 1 week.

HIV and Sexually Transmitted Diseases

Over the previous decade substantial evidence has described the relation between STDs and HIV transmission. Early epidemiologic studies documented increased risk for HIV acquisition among those with ulcerative STDs [60]. Intervention studies demonstrated that STD control reduced HIV transmission [61], and biologic data demonstrated increased local HIV viral replication in anatomic sites with concurrent bacterial STDs [62]. Over the previous year, studies have further elucidated the role that immunologic mechanisms, including local cytokine production, might play in increasing HIV viral replication after induction by bacterial infection [63]. Current studies in our program are beginning to help researchers understand what effect incident STDs, in particular syphilis, might have on HIV viral replication, immune activation, and disease progression in HIV-infected patients.

Because most of the studies on STD and HIV interactions have been conducted in the primarily heterosexual epidemic in Africa, there are limited data regarding MSM. Because most HIV infections in MSM are acquired through receptive anal intercourse, the role of rectal gonococcal infections has been most studied. One study documented a threefold increased risk for HIV seroconversion in MSM with rectal gonorrhea [64]. A second more recent study documented that gonococcal infection increases the risk of recent HIV infection by a similar magnitude [65]. Data regarding rectal chlamydial or herpes infection also document increased risk of HIV seroconversion, but intervention studies and biologic studies are lacking.

Prevention of Sexually Transmitted Diseases in Men Who Have Sex with Men

Prevention of STDs in MSM can take two basic approaches: primary or secondary. Primary prevention focuses on decreasing the exposure of MSM to infection through promotion of partner reduction, increased condom usage, oral sex, and nonpenetrative sex play. Primary prevention was successfully adopted by MSM in the mid- and late 1980s. These behavioral changes resulted in profound declines in the incidence

of new STDs and HIV. One of the public health consequences of successful HIV therapy, however, has been a reversal in safer sex practices, in particular for HIV-infected MSM. A substantial proportion of this population has abandoned primary prevention strategies. Thus, secondary prevention focused on increased health care seeking behavior, increased screening, early detection of infection, treatment, and partner-treatment are strategies that intervention programs and affected communities have embraced. During the AIDS epidemic, as STDs declined, many MSM lost their basic knowledge of STD signs and symptoms, STD transmission, and the value of routine screening. Now with noninvasive accurate and even self-collected screening tests for gonorrhea and chlamydia, MSM and their providers can screen for these infections and treat early, thereby reducing the duration of infection and the subsequent prevalence. With reductions in prevalence, declines in incidence should follow.

Several groups, including the California STD Controllers' Association, the Seattle-King County STD Program, and CDC, have promulgated screening recommendations for STDs in HIV-infected MSM and MSM in general [66•,67••]. The following screening tests should be performed at least annually or more often based on the number of new sexual partners for sexually active MSM: 1) HIV serology, if HIV-negative or not previously tested; 2) syphilis serology by VDRL or RPR; 3) urine nucleic acid amplification test for gonorrhea; 4) urine nucleic acid amplification test for chlamydia; 5) pharyngeal nucleic acid amplification test or culture for gonorrhea in men with oral-genital exposure; 6) rectal gonorrhea and chlamydia nucleic acid amplification test or culture in men who have had receptive anal intercourse; and 7) vaccination against HAV and HBV. Prevaccination serologic testing might be cost effective in MSM, among whom the prevalence of HAV and HBV infection is likely to be high (> 25%). More frequent STD screening (*eg*, at 3- to 6-month intervals) might be indicated for MSM at highest risk (*eg*, those who acknowledge having multiple anonymous partners or having sex in conjunction with illicit drug use, and patients whose sex partners participate in these activities). Screening tests usually are indicated regardless of a patient's history of consistent use of condoms for insertive or receptive anal intercourse. Providers also should be knowledgeable about the common manifestations of symptomatic STDs in MSM (*eg*, urethral discharge; dysuria; anorectal symptoms, such as pain, pruritis, discharge, and bleeding; genital or anorectal ulcers; other mucocutaneous lesions; lymphadenopathy; and skin rash). If these symptoms are present, providers should perform appropriate diagnostic tests. Forthcoming guidelines from the Infectious Disease Society of America and the Department of Health and Human Services echo these recommendations in HIV-infected persons in care.

Conclusions

Sexually transmitted disease management in MSM requires the expert clinician to be conversant with risk assessment, the clinical presentation, and current diagnosis of certain infections, and to be familiar with new therapeutic agents. Successful STD care of MSM can be achieved because many infections are easily diagnosed and curable with simple single-dose therapy. The current challenges lie in effecting risk reduction and optimizing preventive care in a cost-effective manner. New molecular-based diagnostic studies will offer insights into the etiology of several clinical syndromes, but the basis of care will always rely on the same critical components of medicine: listening and talking to patients.

Acknowledgment

The authors would like to acknowledge Stephen Forte for his assistance in preparation of the manuscript.

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