Approach to sexually transmitted infection testing for men who have sex with men

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Abstract

Objective To provide a guide on appropriate sexually transmitted infection (STI) testing for primary care providers to use with patients who identify as men who have sex with men (MSM).

Sources of information Canadian guidelines for STI testing and enteric and protozoan infections; Ontario guidelines for HIV screening and mpox; and US guidelines for STI testing.

Main message Across Canada rates of sexually transmitted bacterial, enteric, protozoan, and systemic infections—including HIV and mpox—have been steadily increasing among cisgender and transgender MSM. Despite often having similar clinical presentations, these infections have different incubation periods and testing approaches and must be ruled out effectively to guide diagnosis and treatment for MSM-identifying patients who present with symptoms of various conditions. Clinical information and screening recommendations, however, are often found in multiple guidelines rather than in a single source, thus further complicating these clinical encounters. This document provides a consolidated set of evidence and recommendations for STI testing in MSM.

Conclusion Testing approaches for STIs should be comprehensive and based on the patient's reported risk factors and clinical presentation. Where ongoing STI risk is identified and negative laboratory test results are received, MSM should also be counselled on recommendations for repeat screening and HIV prevention services, such as preexposure prophylaxis.

Editor's key points

- Sexually transmitted infections (STIs) are becoming increasingly complicated to identify based on clinical presentation, leading to potential sequelae of infection or missed or delayed diagnoses among men who have sex with men.
- Family physicians and other primary care providers provide essential services for STI testing, diagnosis, and management. Therefore, they should be aware of various clinical presentations and testing approaches available to rule out or confirm possible STI diagnoses in men who have sex with men.
- As part of STI management, family physicians should also be aware of recommendations for STI prevention, including indications for repeat testing and HIV preexposure prophylaxis.

Sexually transmitted infections (STIs) are an important public health concern in Canada. Primary and secondary prevention measures for STIs are essential to help reduce the incidence and prevalence of STIs, and family physicians and other primary health care providers have key roles to play in providing this care.[1] Among patient groups, men who have sex with men (MSM) face disproportionately high rates of STIs.[2] As clinicians who specialize in STIs and other infectious diseases and who provide services to MSM, we have witnessed the increasing complexity of STI diagnosis in this population as well as the complications that can arise when infections are missed and treatment is delayed. In this article we provide an overview of various clinical presentations and incubation periods for common STIs—including HIV—known to affect MSM.

Case description

A 34-year-old male patient requests testing for STIs. He reports 5 days of mild diarrhea with cramps and an incomplete sensation of evacuation. He has noted some blood when wiping. These symptoms started 2 days after his most recent sexual contact, which occurred during a visit to Ottawa, Ont. The patient reports having felt feverish for a few days. The review of systems is otherwise unremarkable, and the patient has no relevant past medical history.

The patient's most recent sexual contact was with a man who reported being HIV positive with an undetectable viral load. The patient knows nothing further about this partner. This encounter involved oral sex with oral-genital and oral-anal contact (given and received) and receptive anal sex. Condoms were not used. He reports that his penultimate sexual contact with someone different occurred 10 days before symptom onset and involved receptive anal sex.

On examination the patient's anal verge is erythematous. There are no lesions, discharge, or blood and no papules, pustules, ulcers, or chancres. The digital rectal examination does not reveal any masses, tenderness, or blood. Findings of examinations of the skin, oropharynx, cervical lymph nodes, genitals, and inguinal lymph nodes are unremarkable. The patient has proctocolitis and testing for infections outlined in **Table 1** is warranted to determine the cause of his symptoms.[1,3-8]

Sources of information

We reviewed guidelines from the Public Health Agency of Canada,[1,8] the US Centers for Disease Control and Prevention (CDC),[3] the Ontario Ministry of Health,[4] Health Canada,[5,6] and Public Health Ontario.[7,9]

Main message

Testing for gonorrhea and chlamydia. Between 2011 and 2019 rates of gonorrhea and chlamydia infections in Canada increased by 171% and 26%, respectively,[10] followed by decreases in 2020, likely due to decreased testing during the COVID-19 pandemic[10] rather than decreases in transmission. When testing MSM for gonorrhea and chlamydia, remember that most infections are identified in the pharynx and rectum. One study from Ottawa found 70% of gonorrhea and 65% of chlamydia infections in MSM were exclusively extragenital.[11] If practitioners order only urine testing, for every 3 gonorrhea infections identified, 7 would be missed.[11]

Gonorrhea and chlamydia testing should be done by nucleic acid amplification testing (NAAT), ruling out infection if results are negative. For cisgender MSM, first-catch urine specimens are recommended.[9] For asymptomatic transgender MSM with internal genitals (eg, vaginas, neovaginas, front holes), urine testing is noninferior to self- and clinician-collected swabs.[9] Symptomatic transgender MSM should undergo physical examination with clinician-collected specimens. Extragenital (pharynx and rectum) testing is indicated for all MSM.[1,3,9] With proper instructions, patients can self-collect pharyngeal and rectal swabs with sensitivity results equal to those of clinician-collected swabs.[12] Rectal specimens that are positive for chlamydia should undergo additional polymerase chain reaction (PCR) testing to rule out lymphogranuloma venereum. Chlamydia subtyping should also occur when patients present with suggestive symptoms,[1] including genital ulcerations or inguinal buboes. Patients with any PCR-based specimen that is positive for gonorrhea should be recalled for repeat testing by culture. This can be done at the time of treatment. Due to increasing rates of drug-resistant gonorrhea seen internationally,[13] collecting cultures and obtaining antimicrobial sensitivity data is prudent. Treated patients should return in 4 to 7 days for repeat testing as test of cure by culture. The US CDC suggests testing MSM every 3 to 6 months for gonorrhea and chlamydia.[3]

Testing for syphilis. Between 2011 and 2019 the incidence of infectious syphilis increased by 389% in Canada, with ongoing increases noted during the COVID-19 pandemic despite reduced testing.[10] Consistently, gay and bisexual men and other MSM account for most new diagnoses, although rates in recent years have been increasing among those who identify as heterosexual males and females with corresponding increases in congenital infections.[14]

Testing is done primarily via blood. Patients with a chancre may present prior to seroconversion and have a negative blood test result (sensitivity is 75% in the primary stage).[15] In such instances, testing should be repeated in 2 to 4 weeks to rule out infection. If there is clinical suspicion of syphilis, empirical treatment with 2.4 million units of benzathine penicillin G given intramuscularly should not be withheld while awaiting results; patients who are allergic to β-lactam medications can be prescribed 100 mg tablets of doxycycline taken orally twice daily for 14 days.[1] Patients with secondary syphilis (systemic symptoms such as rash, lymphadenopathy, and fever) will have a positive test result at presentation. Clinicians should bear in mind that once a patient has positive test results, the syphilis screen result remains positive for life. Serology will therefore identify historical infections. Repeat infections and response to treatment are based on changes in the rapid plasma reagin titre.[1,3,15] Patients who are contacts of people who are newly diagnosed with infectious syphilis should receive empirical treatment and have serology testing done at presentation (irrespective of timing since sexual contacts) and repeated 4 weeks after the contact of concern, if results are negative.[1,3,15] Although not routinely available, syphilis testing can involve direct testing of material from lesions (eg, direct fluorescent antibody testing, PCR), which can identify some primary infections before seroconversion,[1,3] but this can be performed only if lesions are present.[3,15] Interpretation of syphilis test results can be facilitated using a 2019 publication that 2 authors of this article (P.O.B. and P.M.) published in *BMJ*.[15] Although no clear evidence guides screening recommendations, Canadian and US guidelines advise MSM who are sexually active with more than 1 partner to be tested for syphilis every 3 to 6 months.[1,3]

Table 1. Differential diagnosis considerations for male patient described in case presentation

INFECTION	SYMPTOMS, INCUBATION PERIOD, AND MODE OF TRANSMISSION
Gonorrhea[1,3]	• Can cause infection of any mucosal membrane, including the genital tract, pharynx, and rectum • Urethritis may be asymptomatic but usually presents with dysuria and purulent discharge • Pharynx may serve as a reservoir and is typically asymptomatic; only rarely causes pharyngitis • Rectal infections may be asymptomatic but can cause localized inflammation with tenesmus and rectal discomfort and discharge; scant bleeding is possible • Incubation period: 2-7 d (range: 1-14 d) • Transmission: direct contact with infectious exudate
Chlamydia[1,3]	• Can cause infection of any mucosal membrane, including the genital tract, pharynx, or rectum • Urethritis may be asymptomatic but usually presents with dysuria and clear mucoid discharge • The pharynx may serve as a reservoir and is almost always asymptomatic • Rectal infections are often asymptomatic but can cause localized inflammation with rectal discomfort and discharge • The L serovar (lymphogranuloma venereum) can cause pronounced rectal symptoms including pain, tenesmus, bleeding and marked discharge; lower abdominal and low back pain from inflamed pelvic lymph nodes may also occur • Incubation period: 5-14 d (range: 1-6 wk) • Transmission: direct contact with infectious exudate
Syphilis[1,3]	• Initially causes a chancre (a shallow, indurated, typically painless ulcer); chancres can have surrounding edema; pain is possible • Chancres occur at the site of sexual contact and inoculation: penis, scrotum, lips, oral cavity, perianal region, or rectum • Rectal chancres would be difficult to see but could correspond with scant rectal bleeding and tenesmus • Incubation period: 3 wk (range: 3-90 d) • Transmission: direct contact with infectious lesions
Herpes simplex virus[1,3]	• Causes painful localized vesicles that rupture, leaving markedly tender ulcers with surrounding erythema and possible edema • First-episode herpes simplex outbreaks can cause fever • Typically occurs on the penis, scrotum, upper thighs, and perianal region • Rectal lesions will be difficult to see but can cause tenesmus, bleeding, and diarrhea • Incubation period: 6-8 d (range: 1-26 d) • Transmission: direct contact with infectious lesions
HIV[1,3,4]	• Acute HIV infection often causes mononucleosis-like symptoms • Seroconversion symptoms can include fever, chills, swollen lymph nodes, abdominal pain, sore throat, diarrhea, and rash • Incubation period: 2-6 wk • Transmission: direct contact with infectious bodily fluids
Mpox[5]	• Symptoms can range from localized clusters of to diffusely distributed ulcerated indurated lesions, which can be painful • Rectal mpox lesions can cause rectal pain, discharge, and bleeding; fevers are common with mpox infection, as is lymphadenopathy • Incubation period: 3-21 d • Transmission: direct contact with infectious lesions, mucosal surfaces, or fomites
Shigellosis (enteric infection)[6,7]	• Causes infection within the rectosigmoid colon, causing fever, abdominal cramps, and bloody mucoid diarrhea • Incubation period: 2 d (range: 1-7 d) • Transmission: oral-anal and oral-perineal contact
Escherichia coli, campylobacteriosis, salmonellosis, or yersiniosis (enteric infections)[7,8]	• Clinically indistinguishable infections causing varying degrees of abdominal pain, diarrhea (with or without blood or mucus), and possible fever • Incubation periods: range from 1-7 d • Transmission: oral-anal and oral-perineal contact
Cryptosporidiosis, cyclosporiasis, or giardiasis (protozoan infections)[7,8]	• Diarrhea, anorexia, abdominal cramps, bloating, and malaise • Incubation period: 7-14 d • Transmission: oral-anal and oral-perineal contact

Testing for herpes simplex virus (HSV). Herpes simplex virus, while often sexually transmitted, is not a reportable infection in all provinces and territories,[1] and therefore data on incidence and prevalence are not available. Using data from 2009 to 2011, researchers estimated the prevalence of HSV among Canadian adults to be 13.6%.[16]

Testing for HSV is used to confirm or rule out diagnosis in patients with suggestive anogenital lesions. Most commonly, HSV is identified by NAAT or viral culture.[1,3] A swab should be taken of an active lesion (unroofed vesicle or ulcer). Test sensitivity of viral cultures varies depending on duration of infection and type of lesion being sampled, ranging from 94% for vesicles to 87% for pustular lesions to 70% for ulcers.[1] Samples from healing or dried lesions are less likely to have positive results. Nucleic acid amplification testing is increasingly used for diagnosis and has sensitivity and specificity of 100%.[1] Blood tests have no role in the diagnosis of HSV.

Testing for HIV. The rate of HIV diagnoses in Canada remained fairly stable between 2011 and 2020, and MSM continue to account for nearly half of incident infections.[17] Among MSM, those with ongoing risk factors for HIV acquisition should be offered HIV preexposure prophylaxis (PrEP) (**Table 2**).[18] In a study conducted in Kenya and Uganda involving HIV-serodiscordant male and female couples, providing PrEP to uninfected partners was associated with a 96% reduction in HIV incidence[19]; cumulative evidence indicates this reduction is greater than 99%. A study conducted in Ottawa suggests the use of PrEP may help curb the number and rate of new HIV diagnoses at the population level.[20]

For patients presenting after known or possible exposure to HIV, testing should be done at presentation and repeated at 3 weeks and 6 weeks after exposure.[4] Patients who present within 72 hours of exposure should be referred to a local emergency department for consideration of post-exposure prophylaxis (PEP). Fourth-generation antigen and antibody tests can rule in new infections as early as 17 days from acquisition and rule out infection after 6 weeks.[4] Third-generation antibody tests, including point-of-care tests, have a testing window period of 12 weeks.[4] Patients presenting with seroconversion-like symptoms (ie, mononucleosis-like) or chronic infection (eg, chronic weight loss, persistent nontender lymphadenopathy, recurrent thrush) should also be tested.[1,3,4] Ontario testing guidelines recommend annual testing for MSM "even when they report consistently using risk reduction practices—as gaps in protection may occur."[4] Testing for HIV is recommended every 3 months for MSM who report recurring condomless sex with more than 1 partner.

In 2020 Health Canada approved HIV self-testing.[21] Self-tests can be purchased from the manufacturer or from pharmacies, or they can be obtained for free from GetaKit (**https://getakit.ca**), a project led by 2 of the authors of this article (P.O.B. and L.O.) at the University of Ottawa, which provides such self-tests to persons with risk factors across Ontario.[22] In 2023 Health Canada approved a point-of-care combination syphilis and HIV test with an overall sensitivity of 76.7% and specificity of 99.8%.[23-25] The sensitivity of this point-of-care test for syphilis drops to 28.4% for persons with nonreactive rapid plasma reagin results, signalling that this test

Table 2. HIV preexposure prophylaxis recommendations

STEP	APPROACH
Assessments at baseline	• History and examination: signs and symptoms of HIV seroconversion and medication use • Blood tests: HIV, syphilis, hepatitis B virus (and hepatitis C virus, as indicated), β-hCG levels (when indicated), creatinine level • Urine NAAT: gonorrhea, chlamydia • Extragenital NAAT: oropharynx, rectum
Assessments at 1 mo	HIV test, creatinine level
Initial prescription[18]	• 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate taken orally daily for 30 d (for males, females, transgender individuals) Or: • 200 mg of emtricitabine and 25 mg of tenofovir alafenamide fumarate taken orally daily for 30 d (for MSM only)
Monitoring every 3 mo	• History and examination: signs and symptoms of HIV seroconversion and medication use • Blood: HIV test, syphilis test, creatinine level • Urine NAAT: gonorrhea, chlamydia • Extragenital NAAT: oropharynx, rectum
Ongoing prescription[18]	• 200 mg of emtricitabine and 300 mg of tenofovir disoproxil fumarate taken orally daily for 90 d (for males, females, transgender individuals) Or: • 200 mg of emtricitabine and 25 mg of tenofovir alafenamide fumarate taken orally daily for 90 d (for MSM only)

hCG—human chorionic gonadotropin, MSM—men who have sex with men, NAAT—nucleic acid amplification test.

cannot rule out early or late infections.[25] This test is also only a screen and cannot be used in persons with prior syphilis infections, as these antibodies persist after a first infection. While this test may be useful in outreach settings or when follow-up is challenging, the performance limitations of this device hinder its usefulness in clinical settings and may provide a false sense of security in people at higher risk. Serology testing should always be used in conjunction with this point-of-care device.

Testing for mpox. In May 2022 a global mpox outbreak occurred, and more than 1500 diagnoses have been made in Canada since then; 1255 (83%) of these infections were recorded in Ontario and Quebec.[26] Nearly all cases were among MSM and, uniquely, this outbreak was associated with sexual transmission.[5,26]

For patients with a rash or lesions, a direct swab of the lesions, lesion fluid, or material (crust, scab) is recommended.[27] Considering the high viral concentration in these specimens and test sensitivity of approximately 90%,[27] other mpox testing methods are not indicated when skin lesions are present. For lesions in the oral cavity, throat, anus, or rectum, swabs of the nasopharynx and rectum are recommended. In patients in whom mpox is suspected (eg, contacts, prodromal symptoms) but skin lesions are not evident and in patients for whom adequate samples cannot be obtained from skin lesions, a nasopharyngeal or throat swab and blood test are recommended.[27] While these tests may be less sensitive than lesion swabs (ie, 60% to 70% for nasopharyngeal test, 40% to 50% for blood test),[27] they may help identify patients with asymptomatic mpox infections.

Testing for enteric bacteria and protozoa. Outbreaks of *Shigella* infection (shigellosis) among MSM have been reported with approximately 50% of isolates having antibiotic resistance and increasing numbers being extensively drug resistant.[28,29] While antibiotics can reduce symptom course and severity, shigellosis usually resolves without treatment within 5 to 7 days.[6,28,29] Antibiotics are usually recommended only for severe disease, including for bacteremia. The primary testing method for *Shigella* and other enteric bacteria (**Table 1**)[1,3-8] is stool culture from patient-collected samples.[29] Patients should be given vials containing stool transport media and instructed to add fresh stool to the vial. Antimicrobial resistance testing is conducted on specimens with positive test results[28] and is important to ensuring adequate therapeutic coverage, if treatment is indicated.

Giardia species are enteric protozoa transmitted through contaminated food and water and by oral-anal contact.[8,30] Symptoms include diarrhea with steatorrhea, abdominal cramps and bloating, flatulence, nausea, and malaise.[8,30] *Cryptosporidium* species can cause diarrhea, ranging from scant to voluminous, with associated nausea and crampy abdominal pain.[8] Testing for intestinal protozoa is by direct microscopic examination, although NAAT is becoming common. Patients should be provided with vials containing ova and parasite transport media and instructed to add fresh stool to the vial. In low-prevalence settings at least 2 or 3 separate samples should be collected.[31]

For all enteric infections, testing is indicated only when symptoms are present.

Case resolution

Laboratory test results were received confirming the diagnoses of non–lymphogranuloma venereum rectal chlamydia and shigellosis. Results were negative for rectal gonorrhea, pharyngeal chlamydia, and gonorrhea; HIV, syphilis, and mpox serology; HSV and rectal mpox PCR; and enteric and protozoan stool samples. The patient was treated for rectal chlamydia with 100 mg of oral doxycycline twice daily for 7 days[1] and counselled on hydration and shigellosis symptom monitoring. The patient was initiated on PrEP and advised to continue monitoring per guidelines.[18] We also offered doxycycline PEP, which consists of a single 200 mg dose, preferably within 24 hours but not more than 72 hours after sex; this intervention has been shown in 2 US studies[32,33] to reduce the risk of chlamydia and syphilis infection by about 70%; the effect on gonorrhea varied, possibly due to local resistance patterns. The US CDC recommends doxycycline PEP for MSM who have been diagnosed with an STI within the preceding 12 months.[34] See **Tables 3** and **4** for a summary of recommendations.[1,3-7,15,18,27,33]

Conclusion

Over the past several years we have seen advances in HIV treatment and prevention. Preexposure prophylaxis, which is more than 99% effective in preventing HIV infection when taken as prescribed,[35,36] has allowed MSM to explore sexuality in the absence of condom use.[37] With this, however, we may anticipate an increase in other STIs, including infectious proctitis. Clinicians should be alert for compatible signs and symptoms and keep both recently identified STIs in mind, such as mpox, as well as more familiar infections. Clinicians should also remember that many STIs can be asymptomatic and screening at all anatomic sites (genital tract, pharynx, rectum)[11] is recommended every 3 to 6 months for MSM who are sexually active with more than 1 partner.[1,3] Finally, empirical treatment should be offered to MSM who are sexual contacts of individuals diagnosed with STIs and to those with compatible clinical manifestations, and consideration should be given to doxycycline PEP for MSM with STI diagnoses.

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Table 3. How and when to test for sexually transmitted infections in men who have sex with men

INFECTION	HOW TO TEST	WHEN TO TEST	CONSIDERATIONS
Gonorrhea or chlamydia[1,3]	• First-catch urine	At presentation	• Sensitivity: 97%-100%
	• Swabs: -Pharynx -Internal genitals, front holes, neovaginas -Rectum	At presentation	• Use NAAT • Sensitivities: 96%-100% • Testing can be done immediately after exposure
Syphilis[1,3,15]	• Serology	• At presentation • ≥4 wk from potential exposure • Repeat every 3 mo if ongoing risk	• EIA screen, with or without RPR and TPPA assay • Sensitivity: -75% in primary infection -98%-100% in secondary infection
	• DFA or PCR test	At presentation when lesions are present	• Sensitivity: 73%-100% • Can detect only in primary and secondary infection
Herpes simplex virus[1,3]	Swabs	At presentation	• Sensitivity: -94% for vesicles -87% for pustular lesions -70% for ulcers • Sensitivity decreases as time from onset to specimen collection increases
HIV[1,4]	Serology	• At presentation • ≥6 wk from potential exposure • Repeat every 3 mo if ongoing risk	• Fourth-generation antigen and antibody test • Sensitivity: 99.9%
Mpox[5,27]	• Swabs: -Lesions -Pharynx -Rectum	At presentation	• Sensitivity: -85%-90% for lesions -60%-70% for pharynx -40%-50% for serology • Swab pharynx only when asymptomatic contact or lesions cannot be swabbed
	• Serology	At presentation	• Sensitivity: 40%-50% • Do serology only when asymptomatic contact or lesions cannot be swabbed
Enteric bacteria and protozoa[6,7]	• Culture for enteric organisms • Ova and parasite test for protozoa	At presentation	• Test only if symptomatic • 2-3 ova and parasite test specimens are required in low-prevalence settings

DFA—direct fluorescent antibody, EIA—enzyme immunoassay, NAAT—nucleic acid amplification test, PCR—polymerase chain reaction, RPR—rapid plasma reagin, TPPA—*Treponema pallidum* passive particle agglutination.

Table 4. Infection prevention strategies (beyond condom use) for men who have sex with men

INFECTION	PREVENTION STRATEGIES
Gonorrhea or chlamydia[3,33]	Doxycycline PEP
Syphilis[3,33]	Doxycycline PEP
Herpes simplex virus[1]	Suppressive therapy for persons with diagnosed infection and >6 outbreaks per year
HIV[18]	• PrEP • PEP (must be initiated ideally within 24 h of exposure, up to a maximum of 72 h after exposure)
Mpox[5]	Vaccination
Enteric bacteria and protozoa[6,7]	• Dental dams • Handwashing

PEP—post-exposure prophylaxis, PrEP—preexposure prophylaxis.

Contributors
All authors contributed to conducting the literature review and interpretation and to preparing the manuscript for submission.

Competing interests
None declared

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