

Canadian Guidelines on Sexually Transmitted Infections

2016 Updates
Summary

April 2017



**TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP,
INNOVATION AND ACTION IN PUBLIC HEALTH.**

—Public Health Agency of Canada

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This document is intended to provide information to public health and clinical professionals and does not supersede any provincial/territorial legislative, regulatory, policy and practice requirements or professional guidelines that govern the practice of health professionals in their respective jurisdictions, whose recommendations may differ due to local epidemiology or context.

2016 Updates

This document outlines key content changes to the Canadian Guidelines on Sexually Transmitted Infections (CGSTI). This summary should be used in conjunction with the Guidelines until such time as the chapters are updated.

Health professionals are encouraged to regularly visit the [Complementary resources](#) on the CGSTI web page. Frequent additions are made to this page that supplements the content of the guidelines.

Azithromycin

Revised advisory statement^{1,2}

- There have been rare reports of QT prolongation and torsades de pointes in patients receiving therapeutic doses of azithromycin.
- Caution is required when treating patients with congenital or documented QT prolongation; with electrolyte disturbance, particularly in cases of hypokalemia and hypomagnesemia; or with clinically relevant bradycardia, cardiac arrhythmia or cardiac insufficiency.
- Caution is also required when treating patients currently receiving treatment with other active substances known to prolong the QT interval, such as antiarrhythmics of classes IA and III, antipsychotic agents, antidepressants and fluoroquinolones.
- Elderly patients may be more susceptible to drug-associated effects on the QT interval.

For further information, please refer to the [health advisory](#) issued by Health Canada.

Combination therapy for gonococcal infections

Timing of combination therapy

- Combination therapy (with a cephalosporin and a macrolide) is currently recommended for all cases of gonorrhoea. Ideally the 2 drugs should be administered concurrently. If they are not, the effectiveness of the treatment may be reduced.
- Based on the pharmacokinetics/pharmacodynamics of cephalosporins and macrolides, there is insufficient evidence to make recommendations related to the need to repeat treatment when the 2 medications are not given concurrently.
- Clinicians are encouraged to assess each case individually to guide their decision-making related to retreatment, and to consult an experienced colleague or infectious disease specialist as necessary.

Fluoroquinolones

Advisory statement

Although fluoroquinolones are generally well tolerated, there have been rare reports of disabling and persistent serious adverse reactions including tendinopathy, peripheral neuropathy, and central nervous system disorders in patients receiving therapeutic dosages of oral and injectable fluoroquinolones.

Refer to the Government of Canada [Recalls and safety alerts](#) website for further details, including information for healthcare professionals, and to the Health Canada [Safety Review](#) for a summary of the assessment of the potential risk of persistent and disabling side effects.

HIV management updates

Early initiation of antiretroviral therapy (ART)

- Treatment of HIV is a rapidly evolving and complex area, with changes in optimal therapy occurring as new research and evidence become available.
 - These advances in treatment have slowed the progression of the disease to such a degree that HIV infection is now understood to be a chronic and manageable condition, enabling people with HIV to live healthy, long, and active lives.
- Early diagnosis and initiation of antiretroviral therapy (ART) can lead to reduced morbidity and mortality associated with HIV infection and disease progression.
- Consultation with a colleague experienced in HIV/AIDS care or infectious diseases is recommended for the initiation of ART.
 - The goal of therapy is to suppress viral replication to the point where plasma HIV RNA is undetectable, with minimal patient toxicity.
 - There is emerging evidence pointing to the presence of benefits when ART is initiated as soon as the HIV diagnosis is confirmed, regardless of CD4 count.
 - The Association of Medical Microbiology and Infectious Disease Canada has developed a position statement "[The Use of Early Antiretroviral Therapy in HIV-infected Persons](#)" summarizing the benefits and risks to be considered.
 - Routine monitoring of CD4 lymphocyte count and plasma HIV RNA viral load is key in assessing the effectiveness of antiretroviral therapy.

Pre-exposure prophylaxis (PrEP)

- Antiretrovirals may be used in some circumstances to prevent HIV type 1 (HIV-1) infection, as part of a comprehensive risk-reduction program.
- Refer to the [Health Canada regulatory decision summary](#) for approved indications, benefits and risks related to PrEP.
- Care providers are strongly encouraged to consult with an infectious disease specialist or a colleague experienced in HIV care, to help guide the patient assessment to determine whether a benefit exists to initiate PrEP.

Post-exposure prophylaxis (PEP) following recent exposure

- Antiretrovirals may be used as PEP to help prevent HIV infection. PEP should be initiated **as soon as possible**, as it may be less effective if initiated more than 72 hours after exposure.
- In the event a patient presents soon after a high-risk exposure, care providers are strongly encouraged to consult with an infectious disease specialist, or a colleague experienced in HIV care, to help guide the patient assessment to determine whether a benefit exists to initiate PEP.
- The decision to initiate PEP for HIV infection is based on clinical judgment and should be made jointly with the exposed individual.

HIV screening and testing: general principles

Approach to testing

- Care providers are strongly encouraged to tailor testing approaches to meet the needs of their patients in order to reduce barriers to HIV testing.
 - For more information on reported barriers and recommendations to address them, refer to the [HIV Screening and Testing Guide](#) and to the [Canada Communicable Disease Report, Volume 41-12](#)
- In-depth behaviour-based risk assessments and extensive pre- and post-test counselling are not requirements for offering an HIV test. **An assessment that the individual understands how HIV is transmitted, the implications of testing (advantages and disadvantages), and how to interpret the test results is sufficient.**
 - Verbal consent is sufficient to proceed with HIV testing.
- For occasions when patients may not be able to accurately estimate their risk, the [HIV Screening and Testing Guide](#), Appendix B, includes more detailed guidance for providers on conducting rapid risk assessments.

Who to test

- It is recommended that the consideration and discussion of HIV testing be made a component of routine medical care in order to normalize HIV testing.
 - In general, care providers should take an active approach to HIV testing, offering HIV testing to clients whether or not clients have asked for a test.
- In addition, there may be circumstances where HIV screening/testing is indicated based on patient history.

HIV testing is clinically indicated and should be done routinely in the following circumstances:

- an individual has symptoms and signs of HIV infection;
- an individual has an illness associated with a weakened immune system;
- an individual is diagnosed with tuberculosis (active or latent infection);
- a woman is pregnant or planning a pregnancy; and partner(s) as appropriate.

HIV testing should be offered/provided to an individual who:

- has an identified [risk factor for HIV infection](#) or is at [risk for other STIs](#);
- requests an HIV test;
- is sexually active but has not been tested for HIV;
- reports unprotected anal or vaginal intercourse or the use of shared drug equipment with a partner whose HIV status is positive or unknown;
- is a victim of sexual assault.

Risk factors

The presence of a concomitant sexually transmitted infection (STI) has been found to affect HIV transmission. STIs increase susceptibility to HIV by a factor of 2 to 4 and increase its transmissibility 2 to 3 times.

- Diagnosing and treating STIs in those at risk for HIV could reduce the risk of acquisition of HIV. Similarly, diagnosing and treating STIs in those infected with HIV could reduce their risk of transmitting HIV to an uninfected partner.

HIV risk factors

- Use of shared drug equipment
- Unprotected anal or vaginal intercourse
- Multiple or anonymous sexual partnering
- For men, a history of sex with other men
- Diagnosis of other STIs, hepatitis B or C, tuberculosis, or other infections known to be associated with HIV infection
- Sexual activity or use of shared drug equipment with someone from regions where HIV is endemic
- Originating from a region where HIV is endemic
- Occupational exposure in the healthcare setting (e.g., needlestick injury)
- Receipt of blood or blood products in regions where HIV is endemic
- Receipt of blood or blood products in Canada prior to November 1985

A full list of additional STI risk factors can be found in the [Primary Care and Sexually Transmitted Infections](#) chapter.

Mycoplasma genitalium

Persistent PID

- In patients who have completed treatment for PID and have persistent symptoms, consideration should be given to *M. genitalium* and *T. vaginalis* as possible causative organisms.
- *M. genitalium* testing is not widely available in Canada.
 - Consult your local laboratory concerning the availability of testing.
 - Testing is offered through the National Microbiology Lab (NML). Clinicians should consult the NML [Guide to Services: Streptococcus and STI Unit](#) for information on specimen collection and transportation requirements.
 - If testing is done and results are positive, treat for *M. genitalium* using **moxifloxacin** 400 mg PO once daily for 14 days.^{3,4}
 - If testing is not a viable option, empiric treatment using moxifloxacin should be considered.

Persistent or recurrent urethritis

If clinically indicated, consider:

- repeating urethral specimens for Gram stain (where available) and culture for *N. gonorrhoeae*;
- repeating first void urine (FVU) to test for *N. gonorrhoeae*, *C. trachomatis* (if initially negative);
- obtaining a urethral specimen for herpes simplex virus culture;
- consulting a urologist, an infectious disease specialist or an experienced colleague.

In patients who have completed treatment for urethritis and have persistent symptoms, consideration should be given to *M. genitalium* and *T. vaginalis* as possible causative organisms.

- FVU specimens can be tested for *M. genitalium* and *T. vaginalis* using NAAT.

- *M. genitalium* testing is not widely available in Canada.
 - Consult your local laboratory concerning the availability of testing.
 - Testing is offered through the National Microbiology Lab (NML). Clinicians should consult the NML [Guide to Services: Streptococcus and STI Unit](#) for information on specimen collection and transportation requirements.
 - If testing is done and results are positive, treat for *M. genitalium* using **moxifloxacin** 400 mg PO once daily for 7 days.⁵⁻⁷
 - If testing is not a viable option, empiric treatment using moxifloxacin should be considered.

Syphilis

These revised treatment recommendations replace those in Table 3 of the Syphilis chapter.

Treatment of early syphilis (primary, secondary, early latent [< 1 yr. duration])

Non-pregnant adults and youth⁸⁻¹³

Preferred

- Benzathine penicillin G 2.4 million units IM as a single dose [A-II for all individuals]

Note:

- Limited data exist to definitively guide management decisions in HIV infected individuals with early syphilis.
 - Based on the serologic response to treatment, the available data suggest that the treatment of HIV-infected patients with early syphilis should be similar to those who are HIV negative.

Pregnant adults and youth

Preferred

- Benzathine penicillin G 2.4 million units IM as a single dose [B-II]

OR

- Benzathine penicillin G 2.4 million units IM as a single dose weekly for 2 doses [C-III]

Considerations

- A single dose of benzathine penicillin G is effective in most cases of early syphilis.
- Some experts recommend that primary, secondary and early latent cases be treated with two doses of benzathine penicillin G 2.4 million units 1 week apart, particularly in the third trimester, due to:
 - difficulty in accurately staging cases of syphilis;
 - physiological changes in pregnancy that may alter the pharmacokinetics of penicillin and reduce plasma penicillin levels;
 - limited data suggesting a possible benefit to additional therapy.
- The efficacy of additional doses in preventing fetal syphilis is not known.
- Treatment failures have been reported with:
 - delay from time of infection to treatment;

- infection acquired in the third trimester;
- high VDRL/RPR titres ($\geq 1:32$ dilutions).
- There is no satisfactory alternative to penicillin for the treatment of syphilis in pregnancy; insufficient data exist to recommend alternative regimens (including ceftriaxone^{8,14} and macrolides⁸).
- In pregnant women with a history of IgE mediated reactions to penicillin, penicillin desensitization is recommended, followed by treatment with penicillin [A-III].
- Infants born to mothers who may have been sub optimally treated or who have a suboptimal response to treatment should be assessed for the possibility of congenital syphilis.
 - Refer to Table 4 in the Canadian Paediatric Society’s practice point entitled [Congenital syphilis: No longer just of historical interest](#), for information related to the management of infants born to women with reactive treponemal tests (TTs) during pregnancy.

Screening for neuro-syphilis in asymptomatic adults and youth co-infected with HIV¹⁵⁻¹⁹

These revised recommendations for indications for CSF examination in HIV-positive patients should replace the guidance that is currently found in the *Cerebrospinal fluid* section of the Syphilis chapter.

- All patients with HIV and syphilis should have a detailed neurological evaluation.
- All co-infected individuals should also have close serologic and clinical follow-up post-treatment.
- Most HIV-positive individuals will respond appropriately to single dose benzathine penicillin G for early syphilis.

CSF abnormalities in HIV-positive patients

- CSF abnormalities (e.g. elevated WBC and elevated protein) are common in persons with HIV, even without syphilis.
 - The significance of these findings is unclear in patients without neurologic symptoms or signs.
- While some studies have reported CSF abnormalities in patients with CD4 ≤ 350 cells/ μ L and VDRL/RPR $\geq 1:32$ dilutions, CSF examination has not been associated with improved outcomes if the neurologic evaluation is normal.
- Some experts recommend CSF examination in persons with CD4 ≤ 350 cells/ μ L and VDRL/RPR $\geq 1:32$ dilutions but this remains controversial.

Criteria for CSF examination in HIV-positive patients

- In patients with suspected/confirmed syphilis, criteria for CSF examination include the following:
 - presence of neurologic (including ocular and otic/auditory) symptoms or signs;
 - treated syphilis with suboptimal decline in VDRL/RPR titre.
- CSF examination may also be considered in patients with VDRL/RPR $\geq 1:32$ dilutions and/or CD4 ≤ 350 cells/ μ L.

- Routine CSF examination is not recommended in late latent syphilis unless other criteria for CSF examination are met.

Current Expert Working Group activities

Under revision

- *Herpes Simplex Virus* (HSV) chapter
- *Syphilis* chapter

Coming soon

- Public release of a new *Cervicitis* chapter
- Public release of a new *Mycoplasma genitalium* chapter

References

- (1) Ray WA, Murray KT, Hall K, Arbogast PG, Stein CM. Azithromycin and the risk of cardiovascular death. *N Engl J Med* 2012 May 17;366(20):1881-1890.
- (2) Mosholder AD, Mathew J, Alexander JJ, Smith H, Nambiar S. Cardiovascular risks with azithromycin and other antibacterial drugs. *N Engl J Med* 2013 May 2;368(18):1665-1668.
- (3) Heystek M, Ross JDC. A randomized double-blind comparison of moxifloxacin and doxycycline/metronidazole/ciprofloxacin in the treatment of acute, uncomplicated pelvic inflammatory disease. *Int J STD AIDS* 2009;20(10):690-695.
- (4) Ross JDC, Cronjé HS, Paszkowski T, Rakoczi I, Vildaite D, Kureishi A, et al. Moxifloxacin versus ofloxacin plus metronidazole in uncomplicated pelvic inflammatory disease: results of a multicentre, double blind, randomised trial. *Sex Transm Infect* 2006;82(6):446-451.
- (5) Bradshaw CS, Chen MY, Fairley CK. Persistence of *Mycoplasma genitalium* following azithromycin therapy. *PLoS One* 2008;3(11):e3618.
- (6) Bradshaw CS, Jensen JS, Tabrizi SN, Read TR, Garland SM, Hopkins CA, et al. Azithromycin failure in *Mycoplasma genitalium* urethritis. *Emerg Infect Dis* 2006 Jul;12(7):1149-1152.
- (7) Walker J, Fairley CK, Bradshaw CS, Tabrizi SN, Twin J, Chen MY, et al. *Mycoplasma genitalium* incidence, organism load, and treatment failure in a cohort of young Australian women. *Clin Infect Dis* 2013;56:1094-1100.
- (8) Clement ME, Okeke NL, Hicks CB. Treatment of syphilis: a systematic review. *JAMA* 2014 Nov 12;312(18):1905-1917.
- (9) Ganesan A, Mesner O, Okulicz JF, O'Bryan T, Deiss RG, Lalani T, et al. A single dose of benzathine penicillin G is as effective as multiple doses of benzathine penicillin G for the treatment of HIV-infected persons with early syphilis. *Clin Infect Dis* 2015 Feb 15;60(4):653-660.
- (10) Cousins DE, Taylor M, Lee V. The outcome of treatment of early syphilis with different benzathine penicillin regimens in HIV-infected and -uninfected patients. *Int J STD AIDS* 2012 Sep;23(9):632-634.
- (11) Knaute DF, Graf N, Lautenschlager S, Weber R, Bosshard PP. Serological response to treatment of syphilis according to disease stage and HIV status. *Clin Infect Dis* 2012 Dec;55(12):1615-1622.
- (12) Tittes J, Aichelburg MC, Antoniewicz L, Geusau A. Enhanced therapy for primary and secondary syphilis: a longitudinal retrospective analysis of cure rates and associated factors. *Int J STD AIDS* 2013 Sep;24(9):703-711.
- (13) Niragira O, Ha S, Pogany L, Singh A. Benzathine penicillin G for the management of early syphilis among HIV co-infected persons: A systematic review. *Canada communicable disease report = Releve des maladies transmissibles au Canada* 2016 February 4;42(2):30-36.
- (14) Zhou P, Gu Z, Xu J, Wang X, Liao K. A study evaluating ceftriaxone as a treatment agent for primary and secondary syphilis in pregnancy. *Sex Transm Dis* 2005 Aug;32(8):495-498.
- (15) Golden MR, Marra CM, Holmes KK. Update on syphilis: resurgence of an old problem. *JAMA* 2003 Sep 17;290(11):1510-1514.
- (16) Ghanem KG, Moore RD, Rompalo AM, Erbelding EJ, Zenilman JM, Gebo KA. Neurosyphilis in a clinical cohort of HIV-1-infected patients. *AIDS* 2008 Jun 19;22(10):1145-1151.
- (17) Ghanem KG, Moore RD, Rompalo AM, Erbelding EJ, Zenilman JM, Gebo KA. Lumbar Puncture in HIV-Infected Patients with Syphilis and No Neurologic Symptoms. *Clinical Infectious Diseases* 2009 March 15;48(6):816-821.

- (18) Ghanem KG, Moore RD, Rompalo AM, Erbelding EJ, Zenilman JM, Gebo KA. Antiretroviral Therapy Is Associated with Reduced Serologic Failure Rates for Syphilis among HIV-Infected Patients. *Clinical Infectious Diseases* 2008 July 15;47(2):258-265.
- (19) Dumaresq J, Langevin S, Gagnon S, Serhir B, Deligne B, Tremblay C, et al. Clinical prediction and diagnosis of neurosyphilis in HIV-infected patients with early Syphilis. *J Clin Microbiol* 2013 Dec;51(12):4060-4066.