Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition

What's New?

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This article highlights the changes that have occurred during the revision process of the 1998 Canadian STD Guidelines. The complete *Canadian Guidelines on Sexually Transmitted Infections, 2006 edition* and the companion document, *Quick Reference: Canadian STI Guidelines* are available on the web in HTML and PDF format at the following website: **www.publichealth.gc.ca/sti**. Hard copies may be available from your local public health office.

Test your knowledge - **True or False?**

1. A nucleic acid amplification test (NAAT) can differentiate between LGV and non-LGV serovars of *Chlamydia trachomatis*.
2. The use of quinolones is always recommended as the preferred treatment for gonorrhea that was not acquired in an Asian country.
3. NAAT is the recommended method of testing for gonorrhea, whether using cervical or urethral swabbing.
4. There is no contraindication for the treatment of external genital warts.
5. Syphilis is only a concern for immigrant populations.

Answers: All are false

Under the coordination of the Public Health Agency of Canada (PHAC), an Expert Working Group (EWG) on sexually transmitted infections (STI) was convened with members from across Canada whose expertise lie in the fields of medicine, nursing, laboratory science, health promotion, public health and research. The EWG and STI experts from across the country voluntarily participated as authors and reviewers to update the 1998 Canadian STD Guidelines. The 2006 edition of the Canadian STI Guidelines provide evidence-based recommendations for the prevention, diagnosis, treatment and management of STI in Canada (Table I).

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Table I. Summary of Levels of Recommendation and Quality of Evidence Indicators

- Each of the 27 chapters underwent a minimum of four rounds of expert review, three rounds within the expert working group (EWG) and one round with at least two external reviewers.
- Final approval of each chapter was required by each member of the EWG before the chapter was considered complete.
- Each treatment recommendation in the guidelines has a quality of evidence and strength of recommendation indicator according to a combination of the methodologies from the US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care, as outlined below.

Level

A	Good evidence to support the recommendation (benefit substantially outweighs harm)
B	Fair evidence to support the recommendation (benefit outweighs harm)
C	Fair evidence, but not strong enough to justify a general recommendation
D	Fair evidence that the treatment is ineffective (or harm outweighs benefit)
I	Insufficient evidence (lacking, poor quality, conflicting)

Quality

I	Evidence from at least one randomized, controlled trial
II	Evidence from at least one clinical trial without randomization (cohort, case-control, time-series, dramatic results in uncontrolled experiment)
III	Expert opinion

Changes to the Content of the Old Guidelines

Chapters have been added to the Specific Populations section including Men Who Have Sex With Men (MSM)/Women Who Have Sex With Women (WSW), Substance Use, Immigrants and Refugees, and Inmates and Offenders. In addition to these new chapters, changes in content were made for all chapters of the guidelines. This article outlines some of the changes with highlights from the treatment recommendations.

Lymphogranuloma venereum (LGV)

Given the recent emergence of LGV in Canada[2] and internationally[3], a chapter has been added on this infection. Table II outlines the LGV treatment recommendations for individuals infected with LGV and their partners. Diagnosis of LGV can be difficult given that some of the symptoms can be present with other STI and other infections or conditions. In Canada, outbreaks of LGV have been found primarily among MSM, with initial symptoms being proctitis or inguinal/femoral lymphadenopathy. Culture and nucleic acid amplification tests (NAAT) do not differentiate between LGV and non-LGV serovars, and positive serology results are suggestive of LGV infection but only in the

presence of elevated titres (microimmunofluorescence [MIF] ≥1:256 or complement fixation [CF] ≥1:64). A positive laboratory result by one of these methods requires confirmatory testing using one or two LGV specific tests (restriction fragment length polymorphism [RFLP] or DNA sequencing). For suspected cases of LGV both swab (for NAAT or culture) and sera (for MIF or CF) samples should be submitted for laboratory testing. Suspected cases should be treated empirically for LGV while awaiting test results and given the high rates of co-infection, counselling and testing for other STI, including HIV, hepatitis B and hepatitis C is also recommended. Enhanced surveillance efforts for LGV are underway to help determine the epidemiology of this infection in Canada. It is important to promptly notify your local public health authorities of any suspected cases of LGV. The surveillance protocol and survey instrument are available on the PHAC website at: http://www.phac-aspc.gc.ca/publicat/lgv/index.html (English) and http://www.phac-aspc.gc.ca/publicat/lgv/index_f.html (French).

LGV has been found primarily among men who have sex with men, with initial symptoms being proctitis or inguinal/femoral lymphadenopathy.

Table II. Recommended treatment for LGV in Canada

- First Choice: Doxycycline 100 mg PO bid for 21 days *[B-II]*
- Alternative: Erythromycin 500 mg PO qid for 21 days* *[C-III]*
- Possible: Azithromycin 1g PO once weekly for three weeks† *[C-III]*

Treatment of sexual partners

Sexual partners from the last 60 days should be contacted, tested and treated as follows:

- Azithromycin 1g PO in a single dose *[C-III]*

OR

- Doxycycline 100mg PO bid for 7 days *[C-III]*

LGV= lymphogranuloma venereum

*Erythromycin dosage refers to the use of erythromycin base. Equivalent dosages of other formulations may be substituted. For pregnant women we must use erythromycin. However, the use of erythromycin estolate is contraindicated.

† While some experts believe azithromycin to be effective in the treatment of LGV, clinical data are lacking.

Aspiration of buboes may help symptomatically; however incision/drainage or excision of nodes is not helpful and may delay healing.

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Gonorrhea

An increased resistance to fluoroquinolones in some strains of *N. gonorrhoeæ* has resulted in changes to the recommended treatment for gonorrhea[4]. In Canada, the use of quinolones (i.e. ciprofloxacin and ofloxacin) is no longer recommended for treating gonorrhea-infected patients or their partners who are from, or are epidemiologically linked to areas reporting high rates of quinolone resistance (see Table III for recommendations). The use of quinolones should only be considered if other recommended treatments are not tolerated or available, and only in cases where patients are likely to return for follow up testing as test of cure is recommended to assess response to treatment.

Culture remains the recommended laboratory testing method for the diagnosis of gonorrhea. Culture is especially important under the following circumstances: child sexual abuse, sexual assault, clinical evaluation of pelvic inflammatory disease, treatment failure, infection acquired overseas or in regions with reported antimicrobial resistance. Antimicrobial susceptibility testing is suggested for all isolates and is required for all cases where test of cure results are positive and in all cases where there is treatment failure. Nucleic acid amplification testing (NAAT) of urine specimens may be useful for patients who are resistant to pelvic examination or urethral swabbing or who refuse testing. Using NAAT instead of culture is recommended when transport/storage conditions are not conducive to maintaining the viability of *N. gonorrhoeæ* (consult with your laboratory to determine appropriate methods of specimen collection and transportation). NAAT is approved for cervical and urethral swabs and urine specimens; certain types of NAAT are also approved for vaginal swabs. NAAT is not recommended for test of cure or for detection of possible re-infection less than 3 weeks following completion of treatment.

A rise in reported fluoroquinolone-resistant *N. gonorrhoeæ* resulted in changes to the recommended treatment for gonorrhea

Table III. Recommended treatment for youth and adults with urethral, endocervical, rectal or pharyngeal gonorrhea infection in Canada (except in pregnant and nursing women)

Preferred	Alternative ONLY if use of quinolones not recommended and cephalosporin allergy OR immediate/anaphylactic penicillin allergy
• Cefixime 400 mg PO in a single dose *[A-I]* OR • Ciprofloxacin 500 mg PO in a single dose* *[A-I]* OR • Ofloxacin 400 mg PO in a single dose* *[A-I]* OR • Ceftriaxone 125 mg IM in a single dose *[A-I]*	• Azithromycin 2 g PO in a single dose *[A-I]* OR • Spectinomycin 2 g IM in a single dose available only through the Special Access Program (SAP) *[A-I]*.
All regimens should be followed by empiric treatment for chlamydia: • Azithromycin 1 g PO in a single dose *[A-I]* OR • Doxycycline 100 mg PO bid for 7 days *[A-I]*	

***Caution**: Quinolones are not recommended if the case or contact are from, or are epidemiologically linked to any area with rates of quinolone-resistant *N gonorrhoeae* >3-5%: Asia, Pacific Islands (incl. Hawaii), India, Israel, Australia, United Kingdom; Regions of the United States (check with the U.S. Centers for Disease Control and Prevention for rates of quinolone resistance by geographic area); MSM with contact or epidemiologically linked to the United States; Areas in Canada experiencing high rates of quinolone resistance – current numbers provided by the National Microbiology Laboratory place Quebec, Ontario, Alberta and British Columbia above the 3% threshold for quinolone resistance. Please check with your local public health officials to learn about quinolone resistance in your area. For data on national quinolone resistance in Canada, please visit the Public Health Agency of Canada website (www.phac-aspc.gc.ca). When the use of quinolones are not recommended or in case of a cephalosporin allergy or immediate and/or anaphylactic reaction to penicillin, use Azithromycin, 2g PO in a single dose *[A-I]* or Spectinomycin, 2g IM in a single dose (available only through Special Access Program [SAP]) *[A-I]*.

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Chlamydia

The treatment recommendations for urethral, endocervical, and rectal chlamydia infections in youth and adults have been slightly modified from the ones in the 1998 STD Guidelines. Doxycycline, which was recommended in the past as an alternative to azithromycin treatment has now been added as a second preferred treatment option given evidence to support its efficacy (Table IV).

Table IV. Recommended treatment for adults with urethral, endocervical, rectal or conjunctival chlamydia infection (except in pregnant and nursing women)

Preferred	Alternative
• Doxycycline 100 mg PO bid for 7 days *[A-I]* OR • Azithromycin 1 g PO in a single dose if poor compliance is expected* *[A-I]*	• Ofloxacin 300 mg PO bid for 7 days *[B-II]* OR • Erythromycin 2 g/day PO in divided doses for 7 days† *[B-II]* OR • Erythromycin 1 g/day PO in divided doses for 14 days† *[B-I]*

* If vomiting occurs more than one hour post administration, a repeat dose is not required.
† Erythromycin dosages refer to the use of erythromycin base. Equivalent dosages of other formulations may be substituted (with the exception of the estolate formulation which is contraindicated in pregnancy). If erythromycin has been used for treatment, test of cure should be performed 3 to 4 weeks after completion of therapy.

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Syphilis

Over the last three years, outbreaks of syphilis have been reported both in Canada and worldwide resulting in a need for increased screening, especially among high risk populations. Screening for syphilis involves the use of non-treponemal tests (NTT), for example Venereal Disease Research Laboratory (VDRL), followed by confirmatory treponemal tests if the NTT is reactive. In patients with suspected primary syphilis or late latent syphilis, the NTT may be non-reactive in which case it is appropriate to add a treponemal test to the initial screen, or in the case of primary syphilis, to repeat the NTT after 2-4 weeks. In regions experiencing outbreaks of syphilis it may be appropriate to screen at baseline with both non-treponemal and treponemal tests. The revised guidelines provide a new guide for the interpretation of serological tests for syphilis (Figure V). Benzathine penicillin G is still the treatment of choice. It is available only through provincial/territorial Ministries of Health which obtain the drug from non-Canadian pharmaceutical companies through Health Canada's Special Access Program (SAP).

Table V. Interpretation of serologic tests for syphilis

Non-Treponemal Test: RPR, VDRL	Treponemal Test: TP-PA	Treponemal Test: FTA-ABS	Most likely condition
Non-reactive	Non-reactive	Reactive	Primary syphilis with compatible history/clinical findings
Reactive (Dilutions can vary)	Reactive	Reactive	• Infectious syphilis (primary, secondary, early latent), especially if titre > 1:8 OR • Old treated syphilis (especially if titre < 1:8) OR • Follow-up of treated syphilis OR • In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America) or bejel
Non-reactive	Reactive	Reactive	• Usually treated syphilis OR • Late latent of unknown duration if no history of confirmed treatment OR • In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America) or bejel OR • Early infection (primary syphilis)
Reactive	Non-reactive	Non-reactive	Biological false positive* (repeat in 3-4 weeks)

FTA-ABS= fluorescent treponemal antibody absorbtion test
RPR= rapid plasma reagin
TP-PA= *T. pallidum* particle agglutination
VDRL= Venereal Disease Research Laboratory
*Some causes of false positive serologic tests for syphilis include certain collagen vascular diseases, pregnancy and injection drug use.

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Genital Herpes

As summarized in Table VI, treatment for genital herpes is recommended for clinically significant symptoms. In addition to the recommendations listed below, the recommended treatment for severe primary episodes is: infused IV acyclovir 5 mg/kg over 60 minutes every 8 hours *[A-I]*, with step down to oral therapy when clinical improvement has occurred. To be effective, treatment needs to be started as early as possible during the development of a recurrent lesion - preferably fewer than 6 hours (famciclovir) *[B-I]* to 12 hours (valacyclovir) *[B-I]* after the first symptoms appear. Suppressive therapy is intended for patients with frequently recurring genital herpes, generally for those with recurrences at least every 2 months or 6 times per year. For patients with fewer recurrences, episodic therapy is recommended (Table VI). For pregnant women, treatment with acyclovir has been shown to be effective in reducing recurrences, asymptomatic shedding, and the need for cesarean section, but does not completely eliminate maternal-to-child transmission of herpes simplex virus (HSV).

Table VI. Recommended treatment for herpes simplex virus (HSV) in Canada

First episode	**Recurrent episodes**	**Suppressive therapy**
• Acyclovir 200 mg PO 5 times/day for 5-10 days *[A-I]* OR • Famciclovir 250 mg tid for 5 days *[A-I]* OR • Valacyclovir 1000 mg bid for 10 days *[A-I]*	• Valacyclovir 500 mg bid for 3 days *[B-I]* OR • Valacyclovir 1 g daily for 3 days *[B-I]* OR • Famciclovir 125 mg bid for 5 days *[B-I]* OR • Acyclovir 200 mg 5 times/day for 5 days *[C-I]*	**Non-pregnant women**: • Acyclovir 200 mg 3 -5 times daily *[A-I]* OR • Acyclovir 400 mg bid *[A-I]* OR • Famciclovir 250 mg bid *[A-I]* OR • Valacyclovir 500 mg daily *[A-I]* (for patients with nine or fewer recurrences per year) OR • Valacyclovir 1000 mg daily *[A-I]* (for patients with more than nine recurrences per year) **Pregnant women:** • Acyclovir 200 mg qid *[A-I]* OR • Acyclovir 400 mg tid *[A-I]*

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Human papillomavirus (HPV) Infections

The revised Canadian STI guidelines contain new recommendations for self-administered treatment of external genital warts for men and women (Table VII). All treatments are associated with local skin reactions which can be managed by decreasing the intensity of the treatment. Efficacy rates are difficult to determine due to lack of uniformity in clinical trials. Even though the recurrence rate is high (60%), the podofilox/podophyllotoxin 0.5% solution is more efficacious, more stable and is associated with fewer side-effects than the podophyllin treatment carried out in the medical office. In Canada, this product is available in two brands, Wartec™ and Condyline™; both contain the same medication, however, the former comes with a plastic applicator and the latter with a cotton swab. This product should not be used by pregnant women or by women who are not using a highly effective and reliable method of contraception. In addition these treatments should not be used for cervical, meatal, vaginal or anal condyloma.

Imiquimod (Aldara™) can be used as a first line treatment for HPV as well as for refractory cases. Recurrence rates (10%) with this product are lower than those for all other types of treatment. Imiquimod acts as an immune modulator. It is not considered to be safe for use during pregnancy and should not be used by pregnant women.

For HPV, all treatments of external genital warts are associated with skin reactions which can be managed by decreasing the intensity of the treatment. Efficacy rates are hard to determine due to lack of uniformity in the clinical trials.

Table VII. Recommendation for self-treatment of external genital warts (except during pregnancy)

• Self-application of a podofilox/podophyllotoxin 0.5% solution (Wartec™, Condyline™) under the direction of a physician. Apply to warts every 12 hours for 3 consecutive days of each week, avoiding surrounding skin. The cycle can be repeated for up to 6 weeks with the total dose per day not to exceed 0.5 mL *[A-I]*.
• Imiquimod (Aldara™) self-application, 3 times a week, for up to 16 weeks. Leave at least one day between applications. Wash off after 6-8 hours *[A-I]*.

Source: Public Health Agency of Canada. *Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition.* Ottawa, ON: Public Health Agency of Canada, 2006. © Reproduced and adapted with the permission of Public Works and Government Services Canada.

Epididymitis

Finally, a recent review of the latest data has resulted in significant changes to the recommended treatment for Epididymitis (see Table VIII).

Table VIII. Canadian treatment recommendations for epididymitis

Epididymitis caused by chlamydial or gonococcal infections • Ceftriaxone 250 mg IM in a single dose *[A-I]* OR • Ciprofloxacin 500 mg PO in a single dose *[A-I]* (unless not recommended due to quinolone resistance – see Table III for gonococcal infections recommendations) PLUS • Doxycycline 100 mg PO bid for 10-14 days *[A-I]*
Epididymitis caused by enteric organisms • Ofloxacin 200 mg PO bid for 14 days *[A-I]*

N.B. Cefixime is no longer a recommended treatment.

Source: Public Health Agency of Canada. *Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition*. Ottawa, ON: Public Health Agency of Canada, 2006. © Reproduced and adapted with the permission of Public Works and Government Services Canada.

This article outlines only a small proportion of the recommendations outlined in the Canadian Guidelines on Sexually Transmitted Infections 2006 Edition. You can access more information on these Guidelines at the following website: http://www.phac-aspc.gc.ca/std-mts/sti_2006/sti_intro2006_e.html (English) or http://www.phac-aspc.gc.ca/std-mts/sti_2006/sti_intro2006_f.html (French).

References

1. Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition. In Press, 2006.
2. Kropp RY, Wong T on behalf of the Canadian LGV Working Group. Emergence of lymphogranuloma venereum in Canada. *CMAJ* 2005; 172 (13): 1674-6.
3. van de Laar MJW, Fenton KA, Ison C, on behalf of the ESSTI network. Update on the European lymphogranuloma venereum epidemic among men who have sex with men. *Eurosurveillance* 2005; 10 (6).
4. Mann J, Kropp R, Wong T, Venne S, Rowmanowski B; Expert Working Group for the Canadian STI Guidelines. Gonorrhea treatment guidelines in Canada: 2004 update. *CMAJ* 2004; 171 (11): 1345-6.

Note: Complete references for all diagnosis, treatment, and management recommendations for each infection listed in this article are found in the *Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition*.
www.publichealth.gc.ca/sti