What's new in management of sexually transmitted infections?

Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition

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In Canada, a steady increase in the incidence of all 3 reportable sexually transmitted infections (STIs), gonorrhea, chlamydia, and infectious syphilis, has been documented since 1997. The 1998 Canadian guidelines on sexually transmitted diseases[1] have recently been extensively revised. The new *Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition*[2] and companion *Quick Reference: Canadian Guidelines on Sexually Transmitted Infections* provide up-to-date evidence-based recommendations for prevention, diagnosis, treatment, and management of STIs. This article highlights some of the modifications introduced in the revised guidelines with a focus on changes in treatment and management recommendations.

At-risk populations

Recognizing that some vulnerable populations are disproportionately affected by STIs, have specific and unique sexual health considerations, and might present with STIs that are rare in the general population, new chapters focusing on these vulnerable populations have been added to the guidelines. These chapters address the specific needs of men who have sex with men (MSM) and women who have sex with women, immigrants and refugees, sex workers, and inmates and offenders. There is also a new chapter on substance use.

Gonorrhea

A steady rise in drug-resistant gonococcal infections has resulted in changes to the recommendations for management of gonorrhea. Reported quinolone resistance in Canada rose from 1% in the 1990s to 15.7% in 2005.[3] Regional variations in quinolone resistance range from 0 to 60% in Canada, with Quebec, Ontario, Alberta, and British Columbia most affected. Fluoroquinolones, such as ciprofloxacin, levofloxacin, and ofloxacin, are no longer recommended for treating patients or their contacts with links to areas reporting rates of resistance higher than 3% to 5%. Oral cefixime or injectable ceftriaxone should be first-line treatment for patients in those areas. Azithromycin or spectinomycin should be reserved for patients who are allergic to cephalosporin or who have serious anaphylactic reactions to penicillin. Test of cure is recommended when a quinolone is used.

Specimen collection and transportation procedures have been updated. Culture is the recommended diagnostic test because it allows for antibiotic resistance testing, but the Nucleic Acid Amplification Test (NAAT) can be used when transport or storage conditions are not ideal for culture or when patients are reluctant to undergo pelvic examination or urethral swabbing. Repeat gonorrhea testing is recommended 6 months after completion of treatment to detect reinfection.

Chlamydia

Screening at-risk groups and repeat screening for those infected 6 months after treatment is now recommended. The NAAT can be used for non-medicolegal testing of urine and of urethral, vaginal, or cervical specimens; however, it has not been evaluated adequately for use with throat or rectal specimens. There is now sufficient evidence to recommend either a single oral dose of azithromycin or a 1-week oral dose of doxycycline as the drugs of choice.

Syphilis

The elimination of infectious syphilis in Canada was identified as an imminent goal as recently as 1996. Rates have risen steadily since that time, however, due to ongoing regional outbreaks. In 2004, the national infectious syphilis rate was almost 9 times the 1997 rate (3.5 vs 0.4 per 100 000 people). Preliminary data for 2006 indicate a worsening of this trend, with a projected rate of 5.1/100 000.[4] Enhanced surveillance efforts across Canada have determined that infectious syphilis rates are highest among MSM, many of whom are also HIV-positive, highlighting the need for counseling regarding safer sexual practices, including the risks associated with unprotected oral sex.

During the past 5 years, outbreaks of syphilis have been reported in Canada and around the world, indicating a need for increased screening, especially in high-risk populations. In some jurisdictions, outbreaks have been reported in the heterosexual population. The rates of congenital syphilis have increased as well. These rates highlight the need for diligent prenatal screening and postnatal assessment. Pregnant women (or their partners) at high risk of syphilis and those living in areas

experiencing heterosexual syphilis outbreaks should have antenatal screening during the first trimester at 28 to 32 weeks and again at delivery. All infected pregnant women should be managed in conjunction with a maternal-fetal medicine specialist. All infants born to mothers with infectious syphilis should receive intensive clinical and laboratory follow-up in conjunction with a pediatric specialist. A high index of suspicion for congenital syphilis is required.

Benzathine penicillin G given intramuscularly is the treatment of choice for infectious and latent syphilis in adults, but to date it is available only through Health Canada's Special Access Program. Local public health departments can provide information on access requirements.

Pelvic inflammatory disease

The updated guidelines reflect new evidence for treatment of pelvic inflammatory disease (PID) for both inpatients and outpatients. Changes in management reflect the need to control acute infection while preventing long-term sequelae, such as infertility, ectopic pregnancy, and chronic pelvic pain. Recommended treatment regimens for PID must provide empiric broad-spectrum coverage for likely etiologic agents and take into consideration the polymicrobial nature of the disease. Regimens must provide coverage for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Gram-negative facultative bacteria, and streptococci. Anaerobic coverage should be considered, but whether elimination of anaerobes from the upper tract is necessary remains to be seen, even though anaerobes are detected in most patients with PID.

Oral cefixime is no longer recommended for outpatient management of PID. Injectable ceftriaxone is the preferred treatment.

Epididymitis

Determining the possible etiologic agent of epididymitis should be based on evaluation of patients' risk and their likelihood of having acquired an STI. Recommendations for treatment of epididymitis have changed to reflect current evidence. The recommended treatment regimen for epididymitis most likely caused by a chlamydial or gonococcal infection is doxycycline plus ceftriaxone or ciprofloxacin (unless contraindicated or not recommended due to quinolone resistance) and for epididymitis most likely caused by enteric organisms is ofloxacin.

Lymphogranuloma venereum

Outbreaks of lymphogranuloma venereum (LGV) have been reported in many European countries and in North America among MSM. These outbreaks have been characterized by high rates of co-infection with HIV and syphilis. Because of LGV's recent emergence in Canada, a national surveillance system was initiated in February 2005 by the Public Health Agency of Canada in partnership with provincial and Territorial programs to determine the epidemiology of this infection in Canada. A new chapter has been added to the 2006 *Canadian Guidelines on Sexually Transmitted Infections* outlining recommendations for diagnosis, prevention, and treatment of LGV.

Diagnosis of LGV can be difficult given that symptoms overlap with those of other STIs and other infections and conditions. Culture and NAATs do not differentiate between LGV and non-LGV serovars, so positive results of either test require additional LGV-specific confirmatory testing. Patients should be treated empirically for LGV while awaiting test results. Due to issues of cross-reactivity and difficulty with interpretation, serology testing should not be used for diagnostic purposes in the absence of culture or NAAT. Given the high rates of co-infection, counseling and testing for other STIs, including HIV, hepatitis B, and hepatitis C, is also recommended for suspected cases.

Human papillomavirus

Shortly after publication of the 2006 *Canadian Guidelines on Sexually Transmitted Infections*, a quadrivalent vaccine against human papillomavirus (HPV) types 6, 11, 16, and 18 was approved for prevention of HPV infection in Canada. The National Advisory Committee on Immunization's statement and recommendations for use of the vaccine followed shortly after.[5] The potential protection against specific types of cancer (cervical, vaginal, vulvar; 70%) preinvasive lesions of the cervix, and external genital warts (90%) is substantial. Vaccine does not provide complete protection against cervical cancer, so it is important to continue cervical cancer screening.

The 2006 publication of the STIs guidelines describes both office-based and self-administered treatments for genital and perianal warts. All medications produce local side effects that can be alleviated by decreasing the intensity of treatment; none of the treatments should be used for cervical, meatal, vaginal, or anal lesions. Another drug, imiquimod can be used as a primary treatment for HPV and for resistant refractory cases. Its safety and effectiveness for pregnant women are unknown, so it is contraindicated during pregnancy.

Genital ulcer disease and herpes simplex virus

The incidence of herpes simplex virus (HSV) types 1 and 2 is unknown for Canada, although limited provincial and Territorial data are available. The natural history of HSV infection is now better understood than a decade ago. All patients presenting with genital ulcers should be tested for HSV and syphilis. Suspected cases of genital herpes that have never been laboratory confirmed should undergo laboratory testing, as clinical diagnosis is often unreliable, and the infection carries lifelong consequences.

Parenteral therapy (acyclovir) is recommended for severe primary disease with conversion to oral therapy when substantial improvement has occurred. For recurrent episodes, treatment should be started as early as possible during development of a recurrent lesion.

Suppressive therapy is indicated for frequently recurring genital herpes (at least every 2 months or more than 6 times per year). For patients with fewer recurrences, episodic therapy is recommended. For pregnant women, treatment with acyclovir starting at 36 weeks' gestation has been shown to reduce recurrent disease, asymptomatic shedding, and the need for cesarean section, but not to eliminate mother-to-child transmission of HSV.

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The new *Canadian Guidelines on Sexually Transmitted Infections, 2006 Edition* and companion *Quick Reference: Canadian Guidelines on Sexually Transmitted Infections* are available on the Public Health Agency of Canada's website at **http://www.phac-aspc.gc.ca/std-mts/sti_2006/sti_intro2006_e.html**.