Sexually transmitted infections in adolescents: Maximizing opportunities for optimal care

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Sexually transmitted infections are a growing public health concern in Canada, with rates of *Chlamydia trachomatis* infection, gonorrhea and syphilis increasing among adolescents and young adults. The present practice point outlines epidemiology, risk factors, laboratory testing and management for *C trachomatis*, *Neisseria gonorrhoeae* and *Treponema pallidum*, with a lesser focus on HIV. The need for test-of-cure and indications for further investigations are also discussed. The importance of maximizing opportunities to screen for and treat sexually transmitted infections in this age group is highlighted.

Key Words: Chlamydia trachomatis; HIV; Neisseria gonorrhoeae; Test-of-cure; Treponema pallidum

Sexually transmitted infections (STIs) are a growing public health concern in Canada, where detection rates for *Chlamydia trachomatis* infection, syphilis and gonorrhea in adolescents and young adults have increased over the past decade.(1,2)

EPIDEMIOLOGY

C trachomatis (non-lymphogranuloma venereum serological variants), is the most frequently reported STI in Canada, predominantly affecting women 15 to 24 years of age and men 20 to 29 years of age. Approximately 50% of infants born vaginally to mothers with untreated chlamydia develop the infection. Only rarely has *C trachomatis* been described in infants delivered by Cesarean section.(3) Sexual abuse should be considered a possibility in prepubertal children with vaginal, urethral or rectal chlamydia infection. In addition to nucleic acid amplification testing (NAAT), cultures should be obtained when practical for medico-legal purposes.(4)

The transmission of *Neisseria gonorrhoeae* occurs during intimate contact such as sexual activity and the birth process. The possibility of transmission by household fomite exposure in prepubertal children has been suggested but is highly unlikely.(5) The possibility of sexual abuse must be considered when infection is acquired beyond the neonatal period.(6) Gonorrhea is more prevalent among young men 20 to 29 years of age, with rates increasing among men who have sex with men (MSM). However, rates among young women, notably in adolescents 15 to 19 years of age, have been increasing more rapidly than among men.(7) The number of female cases is likely to be underestimated because, unlike males, who tend to be symptomatic, females are often asymptomatic. Concurrent infection with *C trachomatis* is common.(6) Increasing gonococcal antimicrobial resistance has been observed both in Canada and globally.(8)

Treponema pallidum infection may be transmitted at any time during pregnancy or delivery.(9) However, the most commonly

Les infections transmises sexuellement chez les adolescents : maximiser les occasions de soins optimaux

Les infections transmises sexuellement sont une préoccupation croissante en santé publique au Canada. Les taux de l'infection par la *Chlamydia trachomatis*, la gonorrhée et la syphilis sont à la hausse chez les adolescents et les jeunes adultes. Le présent point de pratique expose l'épidémiologie, les facteurs de risque, les tests de laboratoire et la prise en charge de la *C trachomatis*, de la *Neisseria gonorrhoeae* et du *Treponema pallidum*, et aborde au passage le VIH. Les auteurs traitent de la nécessité du contrôle de guérison et des indications d'examen plus approfondis. Ils soulignent l'importance de maximiser les occasions de dépistage et de traiter les infections transmises sexuellement au sein de ce groupe d'âge.

affected groups are MSM 30 to 39 years of age, sex workers and their clients, and individuals who have acquired infection in endemic regions of the world. Many cities in Canada have become 'hot spots' for syphilis.

Rates of positive HIV tests vary across Canada. An increase in the national rate from 2000 to 2008 was followed by a downward trend in some regions.(10) The groups most commonly affected are MSM, individuals who have acquired infection via heterosexual contact, and injection drug users, with some variation in the relative proportions of these categories among provinces and territories.(10)

STI RISK FACTORS AND OPPORTUNITIES FOR ASSESSMENT

During routine and incidental medical visits, health care professionals should be asking young patients open-ended questions to elicit information about sexual history, STIs and associated risks. Because youth are not frequent users of the health care system, any visit is an opportunity for STI assessment.

Box 1 shows a list of behavioural and other factors associated with an increased risk of STIs.(1,11) When exploring risk factors, a clinician should take a simple, confidential, nonjudgmental approach and use language that can be easily understood by the patient.

SCREENING FOR STIs

Comprehensive Canadian guidelines for STI screening have been published.(1) The decision to screen is based on risk factors and symptoms, both genital and systemic, always recognizing that rectal and pharyngeal gonococcal infections are often asymptomatic. Test types and specimen requirements should be discussed with the local laboratory before collection (Tables 1 and 2). Ideally, all of a patient's sexual contacts should be identified, tested and treated appropriately, although ensuring full disclosure and follow-up in

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BOX 1**Which adolescents should be screened for sexually transmitted infections?**

Adolescents whose history includes one or more of the following features are considered at increased risk of acquiring a sexually transmitted infection (STI):

In females:

All who are sexually active or are victims of sexual assault or abuse

In males:

- If their history suggests sexual contact with person(s) with a known STI
- A previous STI
- Being a patient of an STI clinic previously
- A new sexual partner or >2 sexual partners within the past year
- Injection drug use and/or other substance use, such as alcohol or chemicals (eg, pot, cocaine, ecstasy, crystal meth), especially if associated with sexual activity
- Unsafe sexual practices (ie, unprotected sex [oral, genital or anal]; sexual activities with risk of blood exchange [ie, sadomasochism, sharing sex toys])
- Anonymous sexual partnering (ie, meeting on the Internet, in a bathhouse, or at a rave)
- Sex workers and their clients
- 'Survival sex' (ie, exchanging sex for money, drugs, shelter or food)
- Street involvement or homelessness
- Time in a detention facility
- Experience of sexual assault or abuse

Adapted from reference 1

individuals with multiple sexual partners is challenging. Local public health units can assist in this process.

Chlamydia: All sexually active females <25 years of age should be screened at least annually, with additional screening being considered for individuals with new or multiple sexual partners. Sexually active males of any age who have risk factors for *C trachomatis* (Box 1) should be screened. After treatment, screening should be repeated every six months if the risk of reinfection persists.(12,13) NAAT is the most sensitive and specific test for *C trachomatis*. First-catch void urine, vaginal (including self-collected), endocervical or urethral specimens are all suitable for NAAT testing.(14,15) Recent evidence suggests that a midstream urine specimen would be adequate but first catch is preferred.(16) Serological testing should not be used for diagnostic purposes due to cross-reactivity and the associated difficulty of interpreting test results. A noninvasive screening specimen (eg, urine) can be obtained if the patient is asymptomatic and has no risk factors or indications for a pelvic examination. A culture of cervical or urethral specimens remains the test of choice for medico-legal purposes, but it is a less sensitive test than NAAT.(17)

Test-of-cure (TOC) using NAAT three to four weeks after completion of therapy is recommended for prepubertal individuals. TOC is recommended in postpubertal patients when compliance is uncertain, an alternative treatment was used, re-exposure is likely or an adolescent is pregnant.(18)

Gonorrhea: Screening should occur in the same groups as for chlamydial disease. First-catch urine is recommended for screening asymptomatic individuals, particularly when urethral and cervical samples are not practical. Pharyngeal specimens should be obtained

TABLE 1
What screening tests should be used to detect sexually transmitted infections?

Infection	Screening tests/samples	Follow-up testing
Chlamydia	NAAT is the most sensitive and specific test. Can be performed on urine, urethral swabs, vaginal or cervical swabs* A culture of cervical or urethral specimen is the test of choice for medico-legal cases (eg, child abuse). Confirmation by NAAT using a different set of primers or DNA sequencing may be used Serology should not be used for diagnosis	Test-of-cure 3 to 4 weeks after treatment: If compliance is uncertain If second-line or alternative treatment was used If re-exposure risk is high In the pregnant adolescent In prepubertal children
Syphilis	Serology remains the usual diagnostic test unless the patient has lesions compatible with syphilis Treponemal-specific EIA is a more sensitive screening test than nontreponemal tests; however, testing algorithms vary across jurisdictions If treponemal-specific assay is positive, a second treponemal test is usually required	Follow-up testing depends on the nature of infection, as follows: Primary, secondary, early latent infection: Repeat serology at 1, 3, 6 and 12 months after treatment Late latent: Repeat serology 12 and 24 months after treatment
Gonorrhea	NAAT can be used to detect gonorrhea from urine, and urethral, vaginal and cervical swabs in symptomatic and asymptomatic individuals* NAAT is the only method available in some jurisdictions Culture allows for antimicrobial susceptibility testing and should be performed if a patient does not promptly respond to therapy, given concerns regarding antimicrobial resistance Cultures should be submitted for asymptomatic or symptomatic MSM, who have an increased incidence of antibiotic resistance For rectal and pharyngeal testing, discuss preferred specimens with the testing laboratory Culture preferred for throat specimens For medico-legal purposes, a positive result obtained from NAATs should be confirmed using culture or a different set of primers, or by DNA sequencing techniques	Test-of-cure (culture 3 to 4 days post-treatment or NAAT 3 to 4 weeks later) if: Second-line or alternative treatment was used Antimicrobial resistance is a factor Compliance is uncertain Re-exposure risk is high An adolescent is pregnant Previous treatment failure Pharyngeal or rectal infection A child is prepubertal Signs, symptoms persist post-treatment
HIV	Serum EIA is initial screening test Western Blot or other confirmatory test is then performed Screen all patients seeking evaluation and treatment for sexually transmitted infections Ensure appropriate counselling	EIA antibodies may be detected at 3 weeks with fourth-generation HIV antibody screening tests, but can take up to 6 months with older tests. Follow-up testing should be planned when an initial test is negative after a known exposure

*Data adapted from references 1, 8, 18. EIA Enzyme immunoassay; NAAT Nucleic acid amplification testing. *Discuss specimen selection to ensure that the NAAT is validated for the specimen to be collected and the patient being tested. For example, NAAT testing has not been validated for children ≤12 years of age and for medico-legal specimens.*

when there is a history of oral sex, and rectal samples if there is a history of receptive anal intercourse. Cultures provide the best opportunity for determining the resistance pattern of the isolate. Culture with susceptibility testing is particularly important given the emerging antimicrobial resistance of *N gonorrhoeae*, and should always be performed in the following circumstances, if possible: when the sexual abuse of children (rectal, pharyngeal, vaginal) is suspected; in sexual assault cases; when treatment failure is presumed; in evaluating pelvic inflammatory disease; in symptomatic MSM; and when infection is believed to have been acquired overseas or in an area of recognized antimicrobial resistance.(1)

NAAT testing can be used in place of culture to detect gonorrhea but does not provide antibiotic susceptibility information. NAAT is validated for urine, urethral and cervical samples. NAATs validated for these sites can also detect rectal and oropharyngeal infections, but are currently not licensed in Canada for this purpose. However, clinicians should consult regularly with their regional laboratories because recommendations change over time. For example, NAAT testing has not been validated for children ≤ 12 years of age and for medico-legal specimens.

In light of the rising rates of gonococcal resistance to cephalosporins and azithromycin and resulting treatment failures, combination therapy for gonorrhea is recommended. When indicated, TOC should be performed, using culture if possible. All prepubertal children with *N gonorrhoeae* require routine TOC by culture performed three to seven days post-treatment. In some jurisdictions, NAAT testing is used two to three weeks post-treatment when a culture cannot be obtained because NAAT remains positive much longer than a culture after adequate therapy.(18) TOC is also recommended if the following contexts apply:(18) a second-line or alternative treatment is used; antimicrobial resistance is suspected; high re-exposure risks exist; an adolescent is pregnant; a previous treatment has failed; or pharyngeal infection signs or symptoms persist following treatment.

It has also been suggested that if clinicians or health departments are concerned about local cephalosporin resistance, a period of routine TOC surveillance for all gonorrhea cases should be considered.(19)

Repeat screening using NAAT testing six months after completing therapy is recommended for individuals at risk for reinfection.(20,21) Cotreatment for chlamydia is indicated for all patients with proven gonorrhea, even if chlamydia is not detected.

Syphilis: All pregnant adolescents should be screened for syphilis early in pregnancy and, ideally, again at delivery. Individuals at high risk for syphilis may also be screened at 28 to 32 weeks' gestation or at more regular intervals (eg, monthly) if at very high risk (eg, ongoing sex trade work in an area experiencing an outbreak of infectious syphilis).(4) Nontreponemal tests (such as rapid plasma reagin [RPR]) may yield false-negative results in early cases of primary syphilis. Enzyme immunoassays (EIAs) may provide a more sensitive screening test for syphilis. Due to specificity concerns, if the treponemal-specific EIA is positive, a second treponemal confirmatory test is required (eg, *T pallidum* particle agglutination assay [TP-PA], microhemagglutination assay [MHA-TP], fluorescent treponemal antibody absorption [FTA-ABS], or the INNO-LIA assay).(22)

Follow-up RPR testing is recommended after the treatment of all stages of syphilis with a reactive RPR. This testing should be performed at one, three, six and 12 months after treatment of infectious cases and at 12 and 24 months in late latent cases.(18)

HIV: Education about HIV prevention and testing is an essential part of routine health care of adolescents. In addition to testing, appropriate counselling should be arranged and an appropriate

TABLE 2
What samples should be collected based on clinical syndromes?

Clinical syndrome	Samples/screening tests
Asymptomatic males with risk factors as per Box 1	First-catch urine or Urethral swab for <i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> Serology for: Syphilis HIV Other serological tests to consider: Hepatitis A (particularly with oral-anal contact) Hepatitis B (if no history of vaccine) Hepatitis C (particularly in an injection drug user)
Asymptomatic females with risk factors as per Box 1	First-catch urine or Vaginal swab for <i>C trachomatis</i> , <i>N gonorrhoeae</i> * Serology for: Syphilis HIV Other testing to consider: Hepatitis A serology (particularly with oral-anal contact) Hepatitis B serology (if no history of vaccine) Hepatitis C serology (particularly in an injection drug user)
Males with symptoms of urethritis	Urethral swab for Gram stain and culture for gonorrhea (NAAT may also be used where available) AND First-catch urine for <i>C trachomatis</i> (NAAT)
Women with symptoms of cervicitis	Vaginal or cervical swab for Gram stain, <i>N gonorrhoeae</i> culture and <i>C trachomatis</i> (NAAT or culture) Swab of cervical lesions (if present) for herpes simplex virus Vaginal swab for wet-mount
Suspected pharyngeal gonococcal infection	Swab the posterior pharynx and the tonsillar crypts Use the swab to directly inoculate the appropriate culture medium, or place it in a transport medium
Symptoms of vaginitis	Collect pooled vaginal secretions, if present If no vaginal secretions are present, swab the vaginal wall in the posterior fornix to prepare a smear or place the swab in a transport medium Wet-mount and Gram stain smears are useful in the diagnosis of microbial vulvovaginitis, candidiasis, bacterial vaginosis and trichomonas. Because of the low sensitivity of direct microscopy, culture or polymerase chain reaction may also be used, where available, for trichomonas Collection of vaginal specimens from adolescents is usually performed as part of a speculum examination Vaginal-wash specimens are preferred, especially in prepubertal girls. If not possible, use swabs moistened with water Use very thin swabs in young children

Data adapted from reference 1. *Vaginal swabs may be self- or clinician-collected. Cervical swabs may be used if a pelvic examination is performed. NAAT Nucleic acid amplification testing

antiretroviral treatment strategy implemented.(23-25) This level of care should continue through the transition into adult care. (26-29)

KEY ISSUES IN MANAGING STIs

Choosing antimicrobial agents

The Canadian Paediatric Society supports treatment guidelines set out in the Public Health Agency of Canada's Canadian guidelines on sexually transmitted infections;(1) these regimens (Table 3) are

TABLE 3
Recommended treatment of uncomplicated gonococcal infection in children and youth*

	Children/youth ≥9 years of age	Children <9 years of age
Anogenital infections (urethral, endocervical, vaginal, rectal)		
Preferred treatment	Ceftriaxone 250 mg IM in a single dose PLUS azithromycin 1 g PO in a single dose [†] OR Cefixime 800 mg PO in a single dose PLUS azithromycin 1 g PO in a single dose [†]	Ceftriaxone 50 mg/kg IM up to 250 mg in a single dose PLUS azithromycin 20 mg/kg (maximum dose of 1 g) PO in a single dose OR Cefixime 8 mg/kg PO BID x 2 doses (maximum 400 mg per dose) PLUS azithromycin
Alternative treatment	Spectinomycin 2 g IM in a single dose (available only through Health Canada's Special Access Programme) PLUS azithromycin 1 g PO in a single dose [†] OR Azithromycin 2 g PO in a single dose [§]	Spectinomycin 40 mg/kg IM in a single dose (maximum dose of 2 g) (available only through SAP) PLUS azithromycin 20 mg/kg (maximum dose of 1 g) PO in a single dose
Pharyngeal infection		
Preferred treatment	Ceftriaxone 250 mg IM in a single dose PLUS azithromycin 1 g PO in a single dose [†]	Ceftriaxone 50 mg/kg IM up to 250 mg in a single dose PLUS azithromycin 20 mg/kg (maximum dose of 1 g) PO in a single dose
Alternative treatment	Cefixime 800 mg PO in a single dose PLUS azithromycin 1 g PO in a single dose [†] OR Azithromycin 2 g PO in a single dose [§]	Cefixime 8 mg/kg PO BID x 2 doses [†] (maximum 400 mg per dose) PLUS azithromycin 20 mg/kg (maximum dose of 1 g) PO in a single dose

*Based on national guidelines. Clinicians are also advised to consult local guidelines, which may differ based on local epidemiology and antimicrobial resistance. The above is based on the Canadian Sexually Transmitted Infection (STI) Guidelines, available at: www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-2-eng.php. **Jurisdiction-specific recommendations:** Clinicians should also consult provincial/territorial guidelines for treatment of gonorrhea because there are differences in preferred treatment based on region-specific epidemiology and resistance profiles for *Neisseria gonorrhoeae*, with ceftriaxone as the preferred treatment for all forms of gonococcal infection. **Neonates (birth to one month of age):** The recommended dose of ceftriaxone is 25 mg/kg to 50 mg/kg (maximum 125 mg). **Routine combination therapy with a macrolide in young infants is not recommended** due to the association with pyloric stenosis. Testing should be performed for chlamydia and, if results are positive, treatment should be initiated. **Alternate combination therapy:** [†]Azithromycin 1 g orally (PO) is preferred over the alternative of doxycycline 100 mg PO twice per day (BID) for seven days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a seven-day treatment regimen. Doxycycline is contraindicated in pregnant and breastfeeding women and in children <9 years of age. **Azithromycin monotherapy:** [§]Azithromycin 2 g PO in a single dose should only be considered as an alternate treatment option if there is a history of severe allergy to cephalosporins. There is a risk of treatment failure when using azithromycin monotherapy for the treatment of gonorrhea in settings of emerging azithromycin resistance. There are also significant gastrointestinal side effects associated with high-dose azithromycin. IM Intramuscular

described in detail at www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-2-eng.php. Clinicians should always consult this resource and any local public health guidelines for emerging trends and related treatment strategies. The increase in cases of quinolone-resistant gonorrhea(1) and, more recently, a rising number of isolates with reduced susceptibility to cefixime and ceftriaxone, with associated treatment failures, are cause for concern.(8) These emerging data have resulted in changes to preferred treatments in some jurisdictions.(30,31)

General issues

Specific primary and secondary prevention strategies are known to decrease the risk for STIs. Clinicians should be mindful of, and counsel on, contextual issues that can impact treatment:

- Primary prevention measures include vaccination against hepatitis B virus and human papillomavirus, condom use and behavioural change.
- Effective secondary preventive strategies include partner notification, and treatment and screening for STIs in asymptomatic young adults.
- Providing education and management strategies for the partners of individuals with STIs are essential for infection control and patient well-being.
- The STIs noted above are reportable diseases, and clinicians should be familiar with the reporting process for their area and comply in a timely fashion. Public health authorities can assist with contact tracing when indicated.
- Directly observed therapy is important to improve compliance with antimicrobial treatment of STIs among adolescents.

- Check for the presence of multiple STIs, including HIV, because the same risk factors are shared by different STIs.
- TOC is recommended for prepubertal children with *N gonorrhoeae* and/or chlamydia infections.
- Retesting at six months is indicated for adolescents and adults with *N gonorrhoeae* and/or chlamydia because the risk for reinfection is a major concern in this age group.

Recommended resources:

- Public Health Agency of Canada. Centre for Communicable Diseases and Infection Control. Canadian guidelines on sexually transmitted infections: The evergreen edition. 2010: www.phac-aspc.gc.ca/std-mts/sti-its/guide-lignesdir-eng.php.
- Toronto Public Health STI Treatment Reference Guide: www.toronto.ca/health/professionals/communicable_diseases/pdf/sti_treatment_ref.pdf.

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