Review CPD

A practical approach to the diagnosis and management of chlamydia and gonorrhea

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The 2 most frequent reportable bacterial sexually transmitted infections (STIs) worldwide and in Canada are those caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.[1,2] Rates of both infections have been increasing over the last decade despite public health efforts aimed at prevention, testing and treatment. In 2019, 139 389 cases of chlamydia and 35 443 cases of gonorrhea were reported in Canada, an increase of 33.1% and 181.7%, respectively, since 2010.[2] These increases may reflect improved diagnostics, increased screening and contact tracing or a true increase in incidence.[2]

Sexually transmitted infections have a substantial impact on affected individuals and communities. *Chlamydia trachomatis* and *N. gonorrhoeae* are commonly implicated pathogens in pelvic inflammatory disease and, if untreated, can lead to infertility.[3] Infection with a bacterial STI is associated with increased risk of HIV acquisition or transmission.[4] Perinatal transmission of *C. trachomatis* and *N. gonorrhoeae* can lead to ophthalmia neonatorum in infants, among other pathologies.[5] Treatment has become more challenging, given the increase in antimicrobial resistance in gonorrhea.[6]

We summarize the management of chlamydia and gonorrhea in primary care as health care providers work collectively toward the goal of decreasing the frequency of these infections and reducing associated morbidity through appropriate treatment. We draw on evidence from clinical practice guidelines, systematic reviews and meta-analyses (Box 1).

Box 1: Literature review

We conducted a targeted literature search of MEDLINE and Embase from inception to July 2022. Search terms included "*Chlamydia trachomatis*," "*Neisseria gonorrhoeae*," "sexually transmitted infection," "STI," "urethritis," "cervicitis," "pelvic inflammatory disease," "proctitis," "epididymitis," "diagnosis," "screening" and "treatment." We limited the search to articles in English. Our targeted search focused on identifying clinical practice guidelines, systematic reviews and meta-analyses, although we did not place any formal restriction on article type. We selected relevant articles, and manually reviewed their references for additional articles.

Key points

- The incidence of chlamydia and gonorrhea, 2 common sexually transmitted infections, is increasing.
- Annual asymptomatic screening for chlamydia and gonorrhea should be performed in all sexually active patients younger than 30 years, with more frequent screening for higher risk patients.
- Nucleic acid amplification testing for chlamydia and gonorrhea should be performed in both asymptomatic and symptomatic patients at sites of sexual exposure, guided by a careful sexual history.
- The treatment recommendations for chlamydia and gonorrhea are evolving and clinicians should follow local guidance.
- Antimicrobial resistance in gonorrhea is increasing; optimal treatment should be guided by principles of antimicrobial stewardship.

Why is taking a good sexual history important?

Taking a sexual history is essential to comprehensive care in patients presenting with STI symptoms and in asymptomatic people to assess for STI risk, determine the need for screening, address concerns and provide sexual health education.

Patients have reported wanting their health care provider to inquire about sexual health, but many face considerable barriers to self-disclosure of their sexual history.[7,8] Stigma is often associated with STIs. Providers conducting a sexual history should do so in a nonjudgmental, patient-centred and trauma-informed manner.[9] Syndemics theory describes how disease interacts with social constructs, which can help conceptualize how a person's unique social, cultural and health context influences how they access STI care.[10] Establishing the patient's pronouns, sexual orientation and gender identity is necessary to create an environment of respect and trust. The components of a sexual history can be remembered by the 5 Ps: partners, practices, protection, past history and pregnancy (Table 1).[11]

Table 1: Approach to taking a sexual history*[11]

Area	Examples of questions
Partners	• Are you currently having sex of any kind? • In the last 2 months, how many sexual partners have you had? • What is/are the genders of your sexual partners? • Do your partners have other sexual partners? What is/are their gender(s)?

Practices	• To offer the most appropriate testing, can you tell me more about what types of sex you have?
	• What parts of your body are involved when you have sex?
	  • Genital sex (penis in the vagina)
	  • Anal sex (penis in the anus)
	  • Oral sex (mouth on penis, vagina or anus)
	• How do you meet your sexual partners?
	• Have you or any of your partners used drugs?
	• Have you ever exchanged sex to meet your needs (money, housing, food etc.)?

Protection	• Do you and your partner(s) discuss STI prevention? • If you use prevention, what methods do you use? • How often do you use these methods (never, sometimes, all of the time)? • Have you received the human papillomavirus (HPV), hepatitis B (HBV) or hepatitis A (HAV) vaccine? • Have you ever used or considered using HIV pre-exposure prophylaxis (PrEP)?
Past history	• Have you ever been tested for STIs? • Have you ever been diagnosed and/or treated for an STI in the past? • Have any of your current or former partners ever been diagnosed or treated for an STI?
Pregnancy	• How important is it to you to prevent pregnancy? • Are you or your partner using contraception or any form of birth control?

Note: STI = sexually transmitted infection.
*Based on information contained in Reno H, Park I, Workowski K, et al. *A guide to taking a sexual history*. Atlanta: Centers for Disease Control and Prevention; reviewed 2022. Available: https://www.cdc.gov/std/treatment/SexualHistory.htm#

What are common clinical presentations?

Most chlamydia and gonorrhea infections cause no symptoms.[12] If symptoms develop, the incubation period for gonorrhea is 2–7 days, compared with 2–6 weeks for chlamydia.[13] Chlamydia and gonorrhea may have genital or extragenital symptoms, which are generally reflective of the site of infection. The clinical presentations of chlamydia and gonorrhea overlap, and they are usually clinically indistinguishable.

Genital symptoms

Urethritis is the most common syndrome in patients with a penis who are symptomatic. It is characterized by dysuria, urethral pruritis and discharge. Most cases of infectious urethritis are caused by *C. trachomatis* and *N. gonorrhoeae* or both. However, in almost half of cases of nongonococcal urethritis, no specific organism is identified despite extensive microbiological investigation (Box 2).[14]

Patients can develop acute epididymitis from chlamydia or gonorrhea, which is characterized by unilateral, posterior testicular pain and swelling, often accompanied by symptoms of urethritis. Among men younger than 35 years, *C. trachomatis* and *N. gonorrhoeae* are the most common causative organisms, but among older men and men who engage in insertive anal intercourse, causative agents can include enteric organisms like *Escherichia coli*.[15]

Although cervicitis is often asymptomatic, symptoms may occur and include abnormal vaginal discharge or intermenstrual bleeding.[16] Findings on physical examination include purulent endocervical discharge or sustained endocervical bleeding. Most cases of cervicitis have no identified cause. In as many as 25% of cases, *C. trachomatis* or *N. gonorrhoeae* is identified.[17] In around 15% of female patients, pelvic inflammatory disease can develop, characterized by abdominal or pelvic pain, dyspareunia or abnormal uterine bleeding, with findings of cervical motion or adnexal tenderness on physical examination.[18] Patients may have infertility as a consequence of pelvic inflammatory disease. An uncommon complication of pelvic inflammatory disease is Fitz–Hugh–Curtis syndrome, characterized by right upper quadrant pain related to inflammation of the liver capsule.[17]

Extragenital symptoms

Proctitis caused by chlamydia or gonorrhea may present with tenesmus, anorectal pain, bleeding and mucopurulent discharge. These infections typically occur in patients who engage in receptive anal sex, but can also be transmitted from the vagina to the anal canal.[19] *Chlamydia trachomatis*

Box 2: Infectious differential diagnosis of common clinical presentations of sexually transmitted infections

Urethritis

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- *Mycoplasma genitalium*
- *Trichomonas vaginalis*
- *Neisseria meningitidis*
- Hemophilus *spp.*
- Herpes simplex virus
- Adenovirus

Cervicitis

- *Chlamydia trachomatis*
- *Neisseria gonorrhoeae*
- *Trichomoniasis*
- Herpes simplex virus
- *Mycoplasma genitalium*
- Bacterial vaginosis

Proctitis

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis* (including lymphogranuloma venereum serovars)
- Syphilis
- Herpes simplex virus
- Mpox virus

Epididymitis

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- Enteric organisms (e.g., *Escherichia coli*)

and *N. gonorrhoeae* are the most commonly identified pathogens in cases of infectious proctitis.[20]

The lymphogranuloma venereum (LGV) serovars (L1, L2, L3) of *C. trachomatis* can cause invasive infections that preferentially affect lymphatic tissue. Lymphogranuloma venereum can present as small painless ulcers or painful hemorrhagic proctitis, with complications including anal fistulae and strictures.[21] In the last 2 decades, LGV has emerged as an important cause of proctitis among men who have sex with men (MSM) in North America and Europe.[22]

Oropharyngeal infections with gonorrhea are commonly asymptomatic, although patients can present with sore throat, pharyngeal exudate or cervical lymphadenitis.[23] Chlamydia is not an important cause of pharyngitis.[24]

Although uncommon, gonorrhea infection can cause bacteremia, leading to septic arthritis or disseminated gonococcal infection, with tenosynovitis, dermatitis or polyarthralgias.[23] Reactive arthritis — characterized by polyarthritis, conjunctivitis or uveitis, and urethritis or cervicitis — can occur after an infection with chlamydia or gonorrhea, although chlamydia is the more common inciting infection.[25]

Who should be screened for infection?

Opportunistic screening is critical in identifying asymptomatic chlamydia and gonorrhea infections. The Canadian Task Force on Preventive Health Care recommends annual opportunistic screening for chlamydia and gonorrhea in all sexually active people younger than 30 years.[26] Although based on low-quality evidence, an opportunistic approach to screening is likely to increase the number of STIs diagnosed and destigmatize sexual health conversations.

More frequent screening should be offered to people at higher risk of acquiring STIs, although little evidence exists to guide the optimal frequency of screening. Among MSM, current guidance suggests, at minimum, anatomic site-based screening for chlamydia and gonorrhea annually.[13,24] More frequent screening (i.e., every 3–6 months) is recommended for at-risk people of any gender within groups who may be disproportionately affected by STIs, including those taking HIV pre-exposure prophylaxis (PrEP), those who have recently had an STI, those living with HIV or those with multiple sexual partners.[13,24,27] One cohort study of 557 MSM and transgender women taking HIV PrEP found that semiannual STI screening would have led to delayed diagnosis in more than 30% of patients with chlamydia or gonorrhea, compared with quarterly screening.[28] Pregnant patients should be screened at their first prenatal visit, with rescreening in the third trimester if they initially test positive for or are at ongoing risk of STIs.[13,24]

Clinicians should determine appropriate anatomic sites for screening based on information from the sexual history, although they should consider screening extragenital sites (i.e., rectum and oropharynx), even in the absence of either reported symptoms or sexual exposures. Studies of people attending STI clinics have found that a considerable proportion of STIs are missed when STI testing is conducted only for patients with reported symptoms or on sites with known exposure, or when testing includes only urine.[29,30] Testing for gender-diverse patients will depend on their specific anatomy.

How should patients be tested?

In asymptomatic patients, approaches to sample collection for nucleic acid amplification testing (NAAT) for chlamydia and gonorrhea include a first-void urine (first 10–20 mL, any time of day, at least 1 hour since previous void) or vaginal swab; other options include a urethral or cervical swab (Table 2). In patients with a vagina, a vaginal swab is preferred over first-void urine, as urine testing may detect 10% fewer infections.[31] Those with a neovagina or gender-affirming penile reconstruction should provide a urine sample for NAAT. Extragenital testing options include a pharyngeal or rectal swab for chlamydia and gonorrhea NAAT. In symptomatic patients, first-void urine and swabs of sites of reported symptoms should be collected for chlamydia and gonorrhea NAAT, and for gonorrhea culture and sensitivity testing. Patient-collected swabs are acceptable, as studies have shown equivalence between self- and clinician-collected oral, vaginal and rectal swabs for chlamydia and gonorrhea

Table 2: Testing for chlamydia and gonorrhea

Site	Approach for asymptomatic patients or screening	Approach for symptomatic patients
Penile urethra	• First-void urine for NAAT for chlamydia and gonorrhea	• Urethral swab for gonorrhea culture and sensitivity testing, and first-void urine for NAAT for chlamydia and gonorrhea
Cervix or vagina*	• Vaginal swab (preferred), cervical swab or first-void urine for NAAT for chlamydia and gonorrhea	• Cervical swab for gonorrhea culture and sensitivity testing, and for NAAT for chlamydia and gonorrhea, or • Vaginal swab for gonorrhea culture and sensitivity testing, and for NAAT for chlamydia and gonorrhea, or • First-void urine for NAAT for chlamydia and gonorrhea
Throat	• Throat swab for NAAT for chlamydia and gonorrhea	• Throat swab for gonorrhea culture and sensitivity testing, and for NAAT for chlamydia and gonorrhea
Rectum	• Rectal swab for NAAT for chlamydia and gonorrhea	• Rectal swab for gonorrhea culture and sensitivity testing, and for NAAT for chlamydia and gonorrhea

Note: NAAT = nucleic acid amplification test.
*For patients with a neovagina, a first-void urine is the preferred screening test. In symptomatic patients, efforts should be made to conduct gonorrhea culture and sensitivity testing, as well as NAAT for chlamydia and gonorrhea. When culture and sensitivity testing is not possible, either a cervical or vaginal swab for NAAT or a first-void urine is appropriate.

testing.[32,33] Self-collection may also improve uptake of STI screening.[13,24]

Clinicians should refer to their local microbiology laboratories for recommendations on collection and transport protocols in their region. First-void urine can be collected in a sterile urine container for chlamydia and gonorrhea NAAT. The swabs contained within chlamydia and gonorrhea NAAT kits can be used on the cervix, urethra, vagina, throat or rectum; swabs from these sites can also be sent for gonorrhea culture. Bacterial culture for chlamydia is not routinely performed in Canada.[13]

Genotyping of LGV serovars can be requested if a patient presents with a syndrome consistent with LGV.[13] Some Canadian jurisdictions will automatically test all positive rectal chlamydia swabs for LGV serovars. However, it is important to indicate suspicion for LGV on laboratory requisitions, as automatic LGV testing is not universal, and nonrectal specimens (e.g., genital ulcers) are not automatically tested.

How should patients be treated?

Gonorrhea

Treatment of gonorrhea is challenging, as it readily develops antimicrobial resistance, and guidelines are not congruent in their recommendations. The Canadian STI guideline recommends dual therapy with ceftriaxone or cefixime, plus azithromycin or doxycycline (Table 3).[13] The STI treatment guideline from the United States Centers for Disease Control and Prevention (CDC) increased the previously recommended ceftriaxone dose (Table 3).[24] The CDC also recommended against dual therapy based on increasing antimicrobial resistance, and concern for impacts on the microbiome and selective pressure on other pathogens.[24] It is likely that this approach will be adopted by guidelines from other jurisdictions in the future. If monotherapy with ceftriaxone is used, an increased dose of ceftriaxone is recommended, compared with that used in dual therapy (Table 3).[24] Currently, given varying recommendations, clinicians should follow local guidance, which will be based on resistance patterns in their area.

Chlamydia

The Canadian STI guideline recommends doxycycline or azithromycin as the first-line (preferred) treatment for chlamydia,[13] whereas the CDC recommends doxycycline as first-line treatment, with azithromycin as a second-line (alternate) regimen (Table 3).[24] The preference for doxycycline is based on a systematic review and meta-analysis comparing treatment with azithromycin and doxycycline for chlamydia, which found that treatment failed more often with azithromycin, particularly among men with rectal chlamydia.[34,35] Thus, doxycycline is the preferred agent for treating rectal chlamydia. If adherence to therapy is a concern, single-dose azithromycin may be preferred. For pregnant patients, azithromycin is the first-line treatment.[13] For patients with suspected or confirmed LGV, treatment with doxycycline should be continued for 21 days.[13]

Other treatment considerations

Given the potential complexity of cases and the evolving treatment landscape, providers should consult with an expert in STI management when necessary. All patients being treated for chlamydia or gonorrhea should be strongly advised to abstain from sexual activity for 7 days after treatment and until all partners have been treated.[13] Sexual partners from the previous 60 days should be tested and treated, or offered expedited partner treatment (i.e., clinicians can provide empiric treatment for the patient to give to their partner), which has been found to reduce the rates of recurrent or persistent infection.[36] Details around indications and timing of tests of cure are discussed in Table 3. Tests of cure and repeat screening recommendations are often not followed, although they remain important for the appropriate care of the patient and to decrease transmission.[37]

Table 3: Treatment of chlamydia and gonorrhea

Pathogen	Canadian guideline[13]	CDC guideline[24]	Test of cure	Follow-up
Chlamydia trachomatis	**Preferred treatment** • Doxycycline (100 mg orally, twice daily for 7 d) or azithromycin (1 g orally, once) • LGV: doxycycline (100 mg orally, twice daily for 21 d) **Alternative treatment** • Levofloxacin (500 mg orally, daily for 7 d) **Treatment for pregnant patients*** • Azithromycin (1 g orally, once)	**First-line treatment** • Doxycycline (100 mg orally, twice daily for 7 d) • LGV: doxycycline (100 mg orally, twice daily for 21 d) **Second-line treatment** • Azithromycin (1 g orally, once) or levofloxacin (500 mg orally, daily for 7 d) **Treatment for pregnant patients*** • Azithromycin (1 g orally, once) (preferred), or amoxicillin (500 mg orally, 3 times daily for 7 d)	**Indications** • Suspected treatment failure • Suspected poor adherence • Nonpreferred regimen used • Pregnancy **Approach** • Swab for NAAT for chlamydia and gonorrhea 4 wk after therapy completed	• Re-screen 3 mo after treatment completed
Neisseria gonorrhoeae	**Preferred treatment** • Ceftriaxone (250 mg IM, once) and azithromycin (1 g orally, once), or • Cefixime (800 mg orally, once) and azithromycin (1 g orally, once); this is considered an alternative regimen for pharyngeal infections and treatment of MSM **Alternative treatment** • Ceftriaxone (250 mg IM, once) or cefixime (800 mg orally, once), and doxycycline (100 mg orally, twice daily for 7 d), or • Azithromycin (2 g orally, once) and gentamicin (240 mg IM, once); this regimen should be considered only if severe allergy or documented resistance to cephalosporins **Treatment for pregnant patients*** • Ceftriaxone (250 mg IM, once) or cefixime (800 mg orally, once), and azithromycin (1 g orally, once)	**First-line treatment** • Ceftriaxone (500 mg IM, once, if patient weighs < 150 kg; 1 g IM, once, if patient weighs > 150 kg) **Second-line treatment** • Cefixime (800 mg orally, once) or gentamicin (240 mg IM, once), and azithromycin (2 g orally, once) **Treatment for pregnant patients*** Same as above	Consider for all positive sites **Indications** • Suspected treatment failure • Suspected poor adherence • Nonpreferred regimen used • Pregnancy • Pharyngeal infection • Documented antimicrobial resistance **Approach** • Swab for gonorrhea culture and sensitivity test 3–7 d after treatment (preferred) or swab for NAAT for chlamydia and gonorrhea 4 wk after treatment	Re-screen 3 mo after treatment completed

Note: CDC = Centers for Disease Control and Prevention, IM = intramuscularly, MSM = men who have sex with men, NAAT = nucleic acid amplification test.
*Doxycycline is contraindicated in pregnancy.

What about antimicrobial resistance?

Globally and in Canada, rates of antimicrobial resistance in *N. gonorrhoeae* are increasing, with decreasing susceptibility to cephalosporins and azithromycin.[6,38] In Canada, between 2012 and 2016, the proportion of multidrug resistant *N. gonorrhoeae* increased from 6.2% to 8.9%, with most isolates identified in Ontario and Quebec.[39] Actions that clinicians can take to combat antimicrobial resistance are to perform gonorrhea culture and sensitivity testing when possible to limit unnecessary antimicrobial use, and to forgo dual therapy for gonorrhea when chlamydia is excluded. Whether the widespread discontinuation of dual therapy for gonorrhea would negatively affect clinical outcomes or prevent antimicrobial resistance has not yet been established, however. Treatment can be delayed until test results are available in situations where reliable patient follow-up is likely. In cases of confirmed or suspected multidrug-resistant *N. gonorrhoeae*, clinicians should consider consulting an expert in the management of STIs.

Conclusion

Chlamydia and gonorrhea are the most common bacterial STIs in Canada, and their incidence is increasing.[2] Most infections are asymptomatic, which highlights the importance of routine screening for people who are sexually active.[26] Screening and diagnostic testing in symptomatic patients should be guided by a comprehensive sexual health history, which also provides an opportunity for patient education around sexual health. However, the optimal screening frequency in different populations remains unclear. With increasing rates of antimicrobial resistance, treatment should be guided by adherence to the principles of antimicrobial stewardship.

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