Canadian Guidelines on Sexually Transmitted Infections

Cervicitis

August 2019

Public Health Agency of Canada
Agence de la santé publique du Canada

Canada

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

—Public Health Agency of Canada

Également disponible en français sous le titre :
Lignes directrices canadiennes sur les infections transmissibles sexuellement – Cervicite

To obtain additional information, please contact:
Public Health Agency of Canada
Address Locator 0900C2
Ottawa, ON K1A 0K9
Tel.: 613-957-2991
Toll free: 1-866-225-0709
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications@hc-sc.gc.ca

This publication can be made available in alternative formats upon request.

Publication date: August 2019

Cat.: HP40-1/2018E-2-PDF
ISBN: 978-0-660-42307-4
Pub.: 210707

Contents

1 Introduction

This guidance document is about the management of cervicitis.

1.1 Key information

Public health importance

Cervicitis is a common clinical finding that can be caused by a sexually transmitted infection (STI). The most common STI causes are *Chlamydia trachomatis* and *Neisseria gonorrhoeae;* however, these account for up to 25% of cases (depending on the population) and most cases are of unknown etiology. The true incidence and prevalence of cervicitis are unknown because of its varied causes and lack of agreement in the case definition.

Note: Untreated cervicitis can result in pelvic inflammatory disease (PID) that may lead to chronic pelvic pain and infertility. Cervicitis also increases HIV shedding at the cervical canal which may increase the risk of HIV transmission.

Screening

Cervicitis is an indication for STI screening in sexually active individuals.

Diagnostic testing

Patients with cervicitis should be tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* with a nucleic acid amplification test (NAAT) using a cervical swab. Vaginal swabs may also be used.

Testing for *Mycoplasma genitalium* is recommended in cases of persistent or recurrent cervicitis. Women with cervicitis should also be evaluated for bacterial vaginosis, trichomoniasis and herpes simplex virus (HSV) infection.

Treatment

Ceftriaxone 250 mg IM in a single dose in combination with **Azithromycin** 1 g PO in a single dose or **Doxycycline** 100 mg PO bid for 7 days
OR
Cefixime 800 mg PO in a single dose in combination with **Azithromycin** 1 g PO in a single dose or **Doxycycline** 100 mg PO bid for 7 days

Note: A test and wait approach (rather than empiric treatment) is appropriate if the patient is at low risk of STIs. This is because rates of antimicrobial resistance (AMR) are increasing and many cases are of unknown etiology.

Combination therapy is recommended for the empiric treatment of cervicitis due to ever-evolving AMR in *N. gonorrhoeae* and *M. genitalium*.

Follow-up
Follow-up will depend on etiology. Most patients treated for cervicitis do not require post-treatment follow-up unless there are recurrent or persistent symptoms. If an STI is suspected or confirmed, refer to the relevant guidelines for specific follow-up recommendations.

Partner notification
If an STI is suspected or confirmed, locate, evaluate and treat as appropriate all people who have had sexual contact with the index case within 60 days prior to symptom onset or date of specimen collection.

1.2 Definition

Since muco-purulent cervicitis was first described in 1984, there has been a lack of consensus about its definition in clinical and research studies. This has resulted in controversy about the interpretation and comparison of published studies.[1]

Various definitions or combinations of clinical findings have been used across studies. The use of microscopic Gram stain for the diagnosis of cervicitis lacks clinical usefulness[2], although this test is still done in some clinics.

The most consistent definition of cervicitis is: *the presence of purulent or mucopurulent exudate visible in the endocervical canal or easily induced/sustained bleeding or friability at the endocervical os (e.g. with insertion of a swab into the endocervix).*[1,3-5]

Note: This definition should be applied with caution during pregnancy.[6,7] Please refer to the section *Diagnosis during pregnancy* for more information.

The true incidence and prevalence of cervicitis are unknown because of its varied causes and lack of agreement in the case definition.

1.3 Etiology

There are many potential infectious causes for cervicitis and it may also be associated with non-infectious conditions.

The true etiology of cervicitis often remains undetermined despite thorough investigation.[6]

- Most cases (61% to 83%) of cervicitis are of unknown etiology.[2,5]

The following findings have been reported regarding STI as a cause of cervicitis:

- Depending on the population being studied, *C. trachomatis* and/or *N. gonorrhoeae* may be detected in up to 25% of cases diagnosed with cervicitis.[6,8,9]
- There is an association between *Mycoplasma genitalium* and cervicitis.[10] One study found that women testing positive for *M. genitalium* had a 3.3 times higher risk of cervicitis.[11]

- *Trichomonas vaginalis* and herpes simplex virus (both HSV-1 and HSV-2) are associated with cervicitis.[6] Primary infections with HSV-1 or HSV-2 may cause diffuse erosive, hemorrhagic, vesicular, pustular or ulcerative lesions, usually with simultaneous involvement of the vulva.[6,12]
  Bacterial vaginosis, a polymicrobial clinical syndrome, may be associated with cervicitis. In two small studies, researchers found that treatment of bacterial vaginosis (BV) enhances the cure rate of cervicitis.[3,13]

1.3.1 Other possible infectious causes

Although a causal role has not been determined, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), adenoviruses and human T-cell lymphotropic virus (HTLV-1) have been isolated in secretions of women with cervical inflammation. [6, 8]

2 Prevention and control

2.1 General STBBI prevention and control

Case finding, education, counselling, partner notification and treatment are critical to control infection.

Healthcare providers should offer screening for other sexually transmitted and blood-borne infections (STBBIs) as part of their prevention and control strategies. Since many STBBIs are frequently asymptomatic and can lead to serious complications if left untreated, offer STBBI screening during the course of routine medical care, with special attention to those with risk factors. Normalizing screening in this way can reduce barriers to testing and the stigma associated with STBBI.

Integrate STBBI prevention strategies such as counselling, vaccination and education on preventive practices in client care. Motivational interviewing techniques may be used to identify barriers to prevention practices and the means to overcome them.

Offer vaccination for hepatitis B (HBV), hepatitis A (HAV) and human papillomavirus (HPV) as per the *Canadian Immunization Guide*.

Partner notification has public health benefits (e.g. disease surveillance and control) and reduces the risk of reinfection for the index case.

2.2 Specific prevention and control

Measures to control the transmission of the sexually transmitted organisms causing cervicitis include prevention, prompt diagnosis and appropriate treatment of the patient and their sexual partners. If an STI is suspected or confirmed, refer to the relevant chapter of the Guidelines for specific follow-up recommendations.

3 Clinical manifestations

People who are diagnosed with cervicitis can be asymptomatic. Symptoms may include:

- unusual vaginal discharge and/or
- vaginal bleeding during or after intercourse.

These symptoms may be seen with other conditions and are not diagnostic of cervicitis.

Note: Cervicitis may indicate upper-genital–tract infection and therefore those with a new episode of cervicitis should be assessed for signs of PID.

4 Assessment and diagnostic testing

4.1 Diagnostic testing

A speculum examination should be performed to evaluate the cervix and vaginal wall.

Note: Vaginal infections can cause symptoms that overlap with those of cervicitis. A diagnosis of vaginitis can be confirmed by laboratory testing of vaginal secretions to detect a change in vaginal flora consistent with BV, the parasite *T. vaginalis* and yeasts associated with vulvovaginal candidiasis.

- Measurement of vaginal pH may help determine the cause of the vaginal secretions

The following suggest cervicitis:

- Purulent or mucopurulent exudate from the endocervical canal
- Easily induced/sustained bleeding or friability at the endocervical os (e.g., with insertion of a swab into the os).

Clinical findings of cervicitis have low positive predictive value (PPV) for the diagnosis of *C. trachomatis* or *N. gonorrhoeae* infections.

Endocervical swabs should be collected for:

NAAT for the detection of *C. trachomatis* and *N. gonorrhoeae* (vaginal swabs or urine are also considered an appropriate specimen and are non-invasive, so testing is more acceptable). Culture (where available), for antimicrobial susceptibility testing prior to treatment, if *N. gonorrhoeae* is suspected.

Notes: Vaginal swabs for culture to detect *N. gonorrhoeae* are not recommended.[14]
Routine testing for *M. genitalium* is currently not recommended. Testing for *M. genitalium* is recommended **only** in cases of persistent or recurrent cervicitis. Refer to the *Management of persistent /recurrent symptomatic cervicitis* section for management considerations.
A bimanual examination should be performed to rule out PID. If PID is suspected, refer to the PID guidelines for recommendations.

Do not do a Pap test if cervical cancer is suspected[15]

- Pap smears have a low PPV when cancer is present and can alter the lesion which will interfere with results of subsequent colposcopy. Refer to a specialist for colposcopy if cancer is suspected and/or for assessment of any visible lesions on the cervix.

4.2 Diagnosis during pregnancy

Consult an expert as needed for the diagnosis of cervicitis during pregnancy.

Use caution when applying the usual clinical criteria for the diagnosis of cervicitis during pregnancy for the following reasons.

- The criteria for an accurate and precise diagnosis of cervicitis during pregnancy have not been established.[7] Changes to the gravid cervix make the clinical diagnosis more difficult.
- During pregnancy, increased cervical vascularity and edema, hyperplasia and hypertrophy of the cervical glands, are common.[16] Cervical mucus may also appear more viscid and cervical eversion may be exaggerated.

4.3 Screening considerations for other STBBIs

For patients with cervicitis at risk for STIs who are being evaluated or treated for *N. gonorrhoeae* and *C. trachomatis*, consider:

- Collecting vulvar or cervical swab of ulcerations or vesicles for culture and/or NAAT for HSV
- Obtaining a blood sample for serologic testing for syphilis
- Offering HIV counselling and testing as per the recommendations in the HIV Screening and Testing Guide

4.4 Differential Diagnosis

Diagnostic criteria are included in the Assessment and diagnostic testing section above. Cervical ectropion (or cervical eversion) is a particularly common finding in adolescents and may be misdiagnosed as cervicitis.[17,18]

The following non-infectious conditions can also cause cervicitis:

- Cancer
- Local irritation or allergic reactions from spermicides, lubricants, lotions, deodorants or douching[9,17]
- Contraceptive use[19]
- Inflammatory conditions such as Behcet's disease, sarcoidosis, erosive lichen planus and desquamative inflammatory vaginitis[4]

5 Management and treatment

5.1 When to treat

A "test and wait" approach (versus empiric treatment) may be best in certain circumstances.[5,20] This is because most cases of cervicitis are of unknown etiology and rates of AMR are increasing.

5.1.1 High risk for STI

Consider factors associated with increased risk of *C. trachomatis* and *N. gonorrhoeae* when deciding whether to treat cervicitis empirically (e.g. sexual partner with a known STI; sexually active and under 25 years of age; new sexual partner or multiple sexual partners). Studies report that 20 % to 24% of cases are associated with *N. gonorrhoeae* or *C. trachomatis* infection.[5,6,8,9]

- Cervicitis increases HIV shedding at the endocervical canal.[21,22] Treatment of cervicitis decreases the level of virus in cervical secretions and may therefore decrease risk of HIV transmission.[23,24]

If the individual is at risk for an STI, specifically at an increased risk for *C. trachomatis* or *N. gonorrhoeae* and follow-up is not assured, consider empiric treatment.

Note: If empiric treatment is provided, patients should be advised to abstain from unprotected intercourse for seven days after treatment begins and until treatment of their partner(s) is complete.

If the patient at is low risk for an STI, consider a test and wait approach.

- According to Lusk et al., there is growing support for pathogen-guided treatment whenever possible.[20]

5.2 Treatment

5.2.1 Empiric treatment

Combination therapy is recommended for the empiric treatment of cervicitis. This is due to ever-evolving AMR in STIs. Refer to the *Gonococcal infections guidelines* for medication-specific considerations about penicillin allergy and cross-reactivity with cephalosporins.

Consider the following when selecting the second therapeutic agent (doxycycline or azithromycin) for empiric combination therapy of cervicitis:

Azithromycin

- Azithromycin combination therapy regimens are effective against *N. gonorrhoeae* and *C. trachomatis*; however, resistance of *N. gonorrhoeae* to azithromycin is increasing

- Escalating macrolide resistance has been observed in *M. genitalium*, which may be a causative organism of cervicitis[11,25]
- Single dose azithromycin may select for macrolide resistance in *M. genitalium*[26]

Note: Azithromycin may be preferred if the patient is unlikely to comply with a multiday treatment regimen.

There have been reports of QT prolongation in patients receiving therapeutic doses of azithromycin. Please refer to the *Health Advisory* issued by Health Canada about azithromycin and risk of cardiovascular complications and death.

Doxycycline

- Effective for treating chlamydial infections
- There are high rates of resistance to tetracycline in *N. gonorrhoeae* in Canada
- Treatment failure may occur in cases of gonococcal cervicitis.
- If gonococcal infection is confirmed, a test of cure from all positive sites should be done.
- Doxycycline is contraindicated in pregnancy and breastfeeding
- Tetracycline resistance is seen frequently in *M. genitalium*[27] however, if used to treat chlamydia, tetracycline is unlikely to select for further macrolide resistance in *M. genitalium*[28]

5.2.2 Treatment regimens

Refer to the complete product monograph for prescribing information including contraindications and adverse reactions.

Ceftriaxone 250 mg IM in a single dose [C-III] in combination with Azithromycin 1 g PO in a single dose [C-III] or Doxycycline 100mg PO bid for 7 days [C-III]
OR
Cefixime 800 mg PO in a single dose [C-III] in combination with Azithromycin 1 g PO in a single dose [C-III] or Doxycycline 100mg PO bid for 7 days [C-III]

Note: Encourage patients to use condoms consistently and correctly, as this may reduce cervicitis risk.[2]

Refer to the alternative treatment options for *N. gonorrhoeae* if any of the above therapies are contraindicated.

5.2.3 Management of persistent/recurrent symptomatic cervicitis

Patients with persistent/recurrent symptoms should be evaluated for the following:

- Re-exposure to an untreated partner
- Acquisition of an infection from a new partner

- Non-adherence to treatment
- The presence of antimicrobial-resistant organisms (e.g. *N. gonorrhoeae*)
- Infection with other pathogens (e.g. *T.vaginalis* / change in vaginal flora consistent with BV, HSV, CMV, adenoviruses and HTLV-1) - if not already done.

Consider *M. genitalium* as a possible cause in patients with persistent symptoms following empiric treatment for cervicitis, when pre-treatment NAAT tests are negative for chlamydia and gonorrhea or follow-up test of cure is negative.

- If available , collect cervical swabs for NAAT testing for *M. genitalium*
- If not previously done , collect cervical swabs for NAAT testing for *T. vaginalis*
- If testing is done and results are positive, treat for *M. genitalium* as per the recommendations in the *Mycoplasma genitalium* guidelines
- If testing is not a viable option, consider empiric treatment.

Repeated or prolonged administration of antibiotic therapy for persistent symptomatic cervicitis is not recommended because of limited evidence of effectiveness.

If cause remains undiagnosed, consider referral to an experienced colleague, or biopsy if clinically indicated.

6 Follow-up

Follow-up depends on etiology.

Patients treated for cervicitis do not usually require post-treatment follow-up unless there are recurrent or persistent symptoms. If an STI is confirmed, refer to the relevant chapter of the Guidelines for the specific follow-up recommendations.

7 Reporting and partner notification

7.1 National/provincial/territorial notification

Cervicitis is not a reportable condition in most jurisdictions, but may be caused by infections (e.g. *C. trachomatis, N. gonorrhoeae*) that are reportable by laboratories and clinicians to local public health authorities in all provinces and territories.

Where applicable, cervicitis should be reported as per jurisdictional regulations.

7.2 Partner notification

Case finding and partner notification are critical to the prevention and control of STIs.

Evaluate and treat partners depending on the suspected etiology.

Regardless of clinical findings, if an STI is suspected or confirmed, notify, evaluate, and treat all sexual partners from 60 days prior to symptom onset or date of specimen collection.

If an STI is not suspected and treatment of the index case is deferred, partner notification should be deferred until the index case results are available.

8 Acknowledgements

The Public Health Agency of Canada would like to thank the following individuals for their contribution to the development of this guideline.

Cervicitis Sub-Working Group
Dr. Ron Read
Dr. Annie-Claude Labbé
Dr. Ameeta Singh

External reviewers
Dr. Josephine Lusk
Senior Staff Specialist and Clinic Director, Short Street Centre, St George Hospital

Dr. Paul Nyirjesy
Professor of Obstetrics and Gynecology/Drexel University College of Medicine

9 References

(1) Brunham RC, Paavonen J, Stevens CE, Kiviat N, Kuo C, Critchlow CW, et al. Mucopurulent cervicitis—the ignored counterpart in women of urethritis in men. N Engl J Med 1984; 311(1):1-6.

(2) Lusk MJ, Garden FL, Rawlinson WD, Naing ZW, Cumming RG, Konecny P. Cervicitis aetiology and case definition: a study in Australian women attending sexually transmitted infection clinics. Sex Transm Infect 2016 May; 92(3):175-181.

(3) Schwebke JR, Weiss HL. Interrelationships of bacterial vaginosis and cervical inflammation. Sex Transm Dis 2002; 29(1):59-64.

(4) Marrazzo JM. Mucopurulent cervicitis: no longer ignored, but still misunderstood. Infect Dis Clin North Am 2005 Jun; 19:333-349.

(5) Taylor S, Lensing S, Schwebke J, Lillis R, Mena L, Nelson A, et al. Prevalence and treatment outcome of cervicitis of unknown etiology. Sex Transm Infect 2013; 40(5):379.

(6) Marrazzo J, Martin D. Management of women with cervicitis. Clin Infect Dis 2007; 3(44):102.

(7) Repke J, Berlin L, Spence M, Horn J, Niebyl J, Kanchanaraksa S, et al. Reproducibility of the diagnosis of cervicitis in pregnancy. 1988; 5(3):242.

(8) Marrazzo JM, Handsfield HH, Whittington WLH. Predicting chlamydial and gonococcal cervical infection: implications for management of cervicitis. Obstet Gynecol 2002; 100(3):579-584.

(9) Taylor SN. Cervicitis of unknown etiology. Curr Infect Dis Rep 2014;16(7).

(10) Lis R, Rowhani-Rahbar A, Manhart L. Mycoplasma genitalium infection and female reproductive tract disease: a meta-analysis. Clin Infect Dis 2015; 61(3):418.

(11) Manhart LE, Critchlow CW, Holmes KK, Dutro SM, Eschenbach DA, S tevens CE, et al. Mucopurulent cervicitis and *Mycoplasma genitalium*. J Infect Dis 2003; 187(4):650-657.

(12) Corey L, Wald A. Genital herpes. In: Holmes K, Sparling P, Stamm W, Piot P, Wasserheit J, Corey L, et al, editors. Sexually Transmitted Diseases. 4th ed.: New York : McGraw-Hill, Medical; 2008. p. 399-437.

(13) Schwebke J, Schulien M, Zajackowski M. Pilot study to evaluate the appropriate management of patients with coexistent bacterial vaginosis and cervicitis. Infect Dis Obstet Gynecol 1995; 3(3):199.

(14) Elias J, Frosch M, Vogel U. Neisseria. In: Jorgensen J, Pfaller M, Carroll K, Funke G, Landry M, Richter S, et al, editors. Manual of clinical microbiology, Volume 1. 11th ed.: Washington, DC : ASM Press, 2015; 2015. p. 635-651.

(15) Steben M. Clinical manifestations and diagnosis of HPV-related disease. JOGC 2007; 29(8):S11.

(16) Cunningham F, Leveno K, Bloom S, Spong C, Dashe J, Hoffman B, et al. Maternal Physiology. In: Cunningham F, Leveno K, Bloom S, Spong C, Dashe J, Hoffman B, et al, editors. Williams Obstetrics. 24 th ed.: McGraw-Hill Education / Medical; 2014.

http://accessmedicine.mhmedical.com/content.aspx?bookid=1057&sectionid=59789139. Accessed May 29, 2017.

(17) Critchlow C, Wölner-Hanssen P, Eschenbach D, Kiviat N, Koutsky L, Stevens C, et al. Determinants of cervical ectopia and of cervicitis: age, oral contraception, specific cervical infection, smoking, and douching. Am J Obstet Gynecol 1995; 173(2):534.

(18) Duarte K, MacNamara M. Cervicitis, Ectropion, and True Erosion. In: Domino F, editor. The 5 Minute Clinical Consult Standard 2015, The, 23rd Edition. 23 rd ed.: Lippincott Williams & Wilkins; 2014. p. 220.

(19) Castle P, Hillier S, Rabe L, Hildesheim A, Herrero R, Bratti M, et al. An association of cervical inflammation with high grade cervical neoplasia in women infected with oncogenic human papillomavirus (HPV). Cancer Epidemiol Biomarkers Prev 2001; 10:1021.

(20) Lusk M, Garden F, Cumming R, Rawlinson W, Naing Z, Konecny P. Cervicitis: a prospective observational study of empiric azithromycin treatment in women with cervicitis and non-specific cervicitis. Int J STD AIDS 2017; 28(2):120.

(21) Cu-Uvin S, Hogan JW, Caliendo AM, Harwell J, Mayer KH, Carpenter CC, et al. Association between bacterial vaginosis and expression of human immunodeficiency virus type 1 RNA in the female genital tract. Clin Infect Dis 2001 Sep 15; 33(6):894-896.

(22) Seck K, Samb N, Tempesta S, et al. Prevelance and Risk Factors of Cervicovaginal HIV-1 and HIV-2 infected women in Dakar, Senegal. Sexually Transmitted Infections 2001; 77:190-193.

(23) Mcclelland RS, Wang CC, Mandaliya K, Overbaugh J, Reiner MT, Panteleeff DD, et al. Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. AIDS 2001 Jan 5;15(1):105-110.

(24) Wright TJ, Subbarao S, Ellerbrock T, Lennox J, Evans-Strickfaden T, Smith D, et al. Human immunodeficiency virus 1 expression in the female genital tract in association with cervical inflammation and ulceration. Am J Obstet Gynecol 2001; 184(3):279.

(25) Gaydos C, Maldeis NE, Hardick A, Hardick J, Quinn TC. *Mycoplasma genitalium* as a contributor to the multiple etiologies of cervicitis in women attending sexually transmitted disease clinics. Sex Transm Dis 2009; 36(10):598-606.

(26) Anagrius C, Lore B, Jensen J. Treatment of Mycoplasma genitalium. Observations from a Swedish STD clinic. PLoS ONE [Electronic Resource] 2013; 8(4):e61481.

(27) Taylor-Robinson D. Diagnosis and antimicrobial treatment of Mycoplasma genitalium infection: sobering thoughts. Expert Rev Anti Infect Ther 2014 Jun; 12(6):715.

(28) Horner PJ, Martin DH. Mycoplasma genitalium Infection in Men. J Infect Dis 2017 Jul 15; 216 (suppl 2): S396.