Canadian Guidelines on Sexually Transmitted Infections

Gonococcal Infections Chapter:
Revised: July 2013
GONOCOCCAL INFECTIONS

Table of Contents

Acknowledgements .......................................................................................................................... 5
Lead Authors .................................................................................................................................... 5
Expert Working Group ...................................................................................................................... 5
External Reviewers .......................................................................................................................... 6
Centre for Communicable Diseases and Infection Control contributors ................................. 6
GONOCOCCAL INFECTIONS ............................................................................................................. 7

Etiology ........................................................................................................................................... 7
Epidemiology ..................................................................................................................................... 7
  Antimicrobial resistance ................................................................................................................ 7
Individuals at Risk ............................................................................................................................ 8
  Special considerations ..................................................................................................................... 8
Prevention and Control .................................................................................................................... 8
Manifestations, Symptoms and Major Sequelae ............................................................................. 8
  Table 1. Manifestations .................................................................................................................. 9
  Column 1: neonates and infants ..................................................................................................... 9
  Table 2. Symptoms ........................................................................................................................ 9
  Table 3. Major sequelae ................................................................................................................ 10

Laboratory Testing/Diagnosis and Specimen Collection/Transport ............................................. 10
  Nucleic acid amplification tests (NAATs) .................................................................................... 10
  Culture ......................................................................................................................................... 10
  Specimen collection .................................................................................................................. 11
  Specimen transport ................................................................................................................ 11
  Table 4. Recommended routine specimen sites and tests .......................................................... 12

Management .................................................................................................................................... 14
  Consideration for other STIs ....................................................................................................... 14
  Considerations in children ......................................................................................................... 15
  Table 5. Recommended patient management: test results available ..................................... 15
Acknowledgements

**Lead Authors**

Barbara Romanowski, MD, FRCPC  
Joan Robinson, MD, FRCPC  
Tom Wong, MD, MPH, FRCPC

**Expert Working Group**

Joshua Bergman, RN, BScN, MPH, Clinical Instructor, Alberta Health Services, Edmonton STI Clinic;  
Max Chernesky, PhD, Professor Emeritus, McMaster University, St Joseph’s Healthcare, Hamilton;  
William A. Fisher, PhD, Distinguished Professor, Departments of Psychology and Obstetrics and Gynaecology, University of Western Ontario;  
Annie-Claude Labbé, MD, FRCPC, Associate Professor, Department of Microbiology Infectious Diseases and Immunology, Faculty of Medicine, Université de Montréal; Department of Infectious Diseases and Medical Microbiology, Hôpital Maisonneuve-Rosemont;  
Tim T.Y. Lau, PharmD, FCSHP, Pharmacotherapeutic Specialist, Infectious Diseases & Antimicrobial Stewardship, Pharmaceutical Sciences, Vancouver General Hospital; Clinical Associate Professor, Faculty of Pharmaceutical Sciences, University of British Columbia;  
Ed Lee, MDCM, Medical Director, Hassle Free Clinic, Toronto;  
Richard Lester, MD, FRCPC, Medical Head, Division of STI/HIV Control, BC Centre for Disease Control. Clinical Assistant Professor in the Division of Infectious Diseases, Department of Medicine, University of British Columbia;  
Irene Martin, BSc, Head, Streptococcus and STI Unit, Bacteriology and Enterics Division, National Microbiology Laboratory, Public Health Agency of Canada;  
Gina Ogilvie, MD, DrPH, Medical Director, Clinical Prevention Services, BCCDC; Associate Professor, Family Practice, Obstetrics & Gynecology, School of Population & Public Health, University of British Columbia;  
Sam Ratnam, PhD, Surveillance and Reference Services Advisor, National Microbiology Laboratory, Public Health Agency of Canada;  
Ron Read, MD, PhD, FRCPC, Associate Professor, Medicine, Microbiology and Infectious Diseases, University of Calgary; Consultant in Infectious Diseases, Provincial Medical Director, STI (South), STI Program, Alberta Health Services;  
Joan Robinson, MD, FRCPC, Pediatric Infectious Diseases Physician, University of Alberta and Stollery Children’s Hospital;  
Barbara Romanowski, MD, FRCPC, Clinical Professor of Medicine, Division of Infectious Diseases, Faculty of Medicine and Dentistry, University of Alberta;  
Ameeta Singh, BMBS, MSc, FRCPC, Clinical Professor, Division of Infectious Diseases, Department of Medicine, University of Alberta; Medical Director, Alberta Health Services-STI Clinic, Provincial Medical Director, STI (North), Alberta Health Services;
Marc Steben, MD, CCFP, FCFP, Medical advisor, Sexually Transmitted Infections Unit, Institut national de santé publique du Québec; Medical director, Clinique A;

Mark H. Yudin, MD, MSc, FRCSC, Associate Professor, University of Toronto, Department of Obstetrics, Gynecology, and Reproductive Infectious Diseases, St. Michael’s Hospital;

Tom Wong, MD, MPH, FRCPC, Director, Professional Guidelines and Public Health Practice, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada;

External Reviewers

Health professionals with specialized expertise volunteered their time as external reviewers for this guideline chapter. The Agency and the Expert working group would like to thank those individuals for their valuable time and input.

Centre for Communicable Diseases and Infection Control contributors

Writing/editorial support:
Catherine Dickson, MD, MSc
Margaret Gale-Rowe, MD, MPH, DABPM
Cathy Latham-Carmanico, RN, BScN,
Christine Weir, RN, MSc, CIC

Project management and support:
Manon Fiset
Simon Foley, BA (hons)

Research support:
Dana Paquette, PhD
Lisa Marie Pritchard, BSc, MSc

This document is intended to provide information to public health and clinical professionals and does not supersede any provincial/territorial legislative, regulatory, policy and practice requirements or professional guidelines that govern the practice of health professionals in their respective jurisdictions, whose recommendations may differ due to local epidemiology or context.
GONOCOCCAL INFECTIONS

**Etiology**
- Caused by Neisseria gonorrhoeae.

**Epidemiology**
- Since 1997, there has been a gradual but steady increase in reported cases of gonococcal infection. Most affected are males 20 to 24 years of age and females 15 to 19 years of age. Infection rates are increasing more rapidly among females than among males.\(^{(1)}\)
- A network of people with high-transmission activities may play a key role in current prevalence levels and in sustaining infections within a community.

**Antimicrobial resistance**
- A national enhanced surveillance protocol has been developed to integrate epidemiologic and treatment failure data into existing laboratory-based monitoring of antimicrobial resistant *N. gonorrhoeae*. This surveillance is important to rapidly identify changes in antimicrobial susceptibility and assess risk factors associated with the development of resistance. This information enables early identification and prevention of the spread of drug-resistant gonorrhea and assists in identifying appropriate treatment regimens.\(^{(2,3)}\)
- **Local public health should be promptly notified of cefixime, ceftriaxone or azithromycin treatment failures.** Prompt notification will allow provincial and territorial STI prevention and control programs to quickly identify emerging patterns of antimicrobial resistance within their jurisdictions. This will enable provinces and territories to collaborate with the Public Health Agency of Canada to issue timely electronic alerts through the Canadian Network for Public Health Intelligence (CNPHI).
- The growing shift towards the use of nucleic acid amplification testing (NAAT) rather than culture has resulted in fewer samples being submitted for susceptibility testing, making it difficult to get an accurate picture of drug resistance. The number of Canadian isolates found to be resistant to penicillin and/or tetracyclines is high.\(^{(4)}\) These antimicrobial agents should not be used for the treatment of gonorrhea.
- Quinolone resistance has been steadily increasing in Canada.\(^{(4)}\) In certain regions of the country, quinolone resistance is significantly higher than the national rate. **Quinolones are not recommended for the treatment of *N. gonorrhoeae* in Canada** unless resistance rates are known to be under 5%.\(^{(5-7)}\) (Clinicians should refer to the Treatment section of this chapter for recommendations on the use of quinolones in Canada).
- Shifts in minimal inhibitory concentrations (MICs) for third-generation oral and injectable cephalosporins have been increasing in Canada and globally, particularly among men who have sex with men (MSM).\(^{(4,5,8-27)}\)
- The reported rates of antimicrobial resistance in Canada are calculated from samples that have been submitted by individual provinces and territories to the National Microbiology Laboratory (NML). Isolates are submitted to NML when the provincial laboratories identify resistance to at least one antibiotic or if the provincial laboratories do not perform antimicrobial susceptibility testing. The total number of isolates cultured in all provinces is used as the denominator to calculate resistance proportion. 4
- Please refer to your local and provincial and territorial public health officials for specific information about antimicrobial resistance patterns in your region.

**Individuals at Risk**
- Individuals who have had sexual contact with a person with a confirmed or suspected gonococcal infection.
- Individuals who have had unprotected sex with a resident of an area with high gonorrhea burden and/or high risk of antimicrobial resistance.
- Individuals with a history of previous gonococcal infection; a Canadian passive surveillance study reported re-infection to be at least 2 percent per year.\(^{(28)}\)
- Individuals with a history of other STIs, including HIV.
- Sex workers and their sexual partners.
- Sexually active youth under 25 years of age.
- Street-involved youth and other homeless populations.
- Men who have unprotected sex with men.
- Individuals who have had sex with multiple partners.

**Special considerations**
- HIV transmission and acquisition is enhanced in people with gonococcal infections.\(^{(29,30)}\)

**Prevention and Control**
- Case finding and partner notification are critical in controlling infection.
- At the time of diagnosis, reviewing and providing education on prevention practices should include discussion of:
  - The risk of re-infection,
  - The need for the index case and his/her contact(s) to abstain from unprotected sex until at least 3 days after completion of treatment and the case/contact(s) are asymptomatic (in other words, signs and symptoms have resolved),
  - Strategies for effective prevention practices (Clinicians should refer to the *Primary Care and Sexually Transmitted Infections* chapter), and finally
  - Discussions should also include the prevention of reproductive sequelae.
- Individuals with concerns about STIs and/or pregnancy prevention should be provided with information to encourage consistent safe sexual practices.

**Manifestations, Symptoms and Major Sequelae**
- Usual incubation period is 2 to 7 days.
• Infection is often asymptomatic in females and symptomatic in males. In both males and females, rectal and pharyngeal infections are more likely to be asymptomatic.\(^{(31)}\)

*Table 1. Manifestations*\(^{(31-38)}\)
This table lists the manifestations of gonococcal infections in neonates, infants, children, and female and male youth and adults.

**Column 1: Neonates and infants**
• The manifestations in neonates and infants include ophthalmia neonatorum, conjunctivitis, sepsis, and disseminated gonococcal infection (for example, arthritis, dermatitis, endocarditis, meningitis).

**Column 2: Children**
• The manifestations in children include urethritis, vaginitis, conjunctivitis, pharyngeal infection, proctitis, and disseminated gonococcal infection (for example, arthritis, dermatitis, endocarditis, meningitis).

**Column 3: Female youth and adults**
• The manifestations in female youth and adults include cervicitis, pelvic inflammatory disease, urethritis, perihepatitis, and Bartholinitis.

**Column 4: Male youth and adults**
• The manifestations in male youth and adults include urethritis and epididymitis.

**Column 5: Both female and male youth and adults**
• The manifestations in both female and male youth and adults include conjunctivitis, proctitis, pharyngeal infection, and disseminated gonococcal infection (for example, arthritis, dermatitis, endocarditis, meningitis).

*Table 2. Symptoms*\(^{(39-41)}\)
This table lists the symptoms of gonococcal infections in females and males.

**Column 1: Symptoms in females**
• The symptoms in females include vaginal discharge, dysuria, abnormal vaginal bleeding, lower abdominal pain, deep dyspareunia, and rectal pain and discharge with proctitis; for proctitis, clinicians should refer to the *Sexually Transmitted Intestinal and Enteric Infections* chapter.

**Column 2: Symptoms in males**
• The symptoms in males include urethral discharge, dysuria, urethral itch, testicular pain and/or swelling or symptoms of epididymitis, rectal pain and discharge with proctitis; for proctitis, clinicians should refer to the *Sexually Transmitted Intestinal and Enteric Infections* chapter.
**Table 3. Major sequelae** \(^{31,36,38}\)

This table lists the major sequelae of gonococcal infections in females and males.

**Column 1: Major sequelae in females**

- The major sequelae in females include pelvic inflammatory disease, infertility, ectopic pregnancy, chronic pelvic pain, reactive arthritis (oculo-urethro-synovial syndrome), and disseminated gonococcal infection (for example, arthritis, dermatitis, endocarditis, meningitis).

**Column 2: Major sequelae in males**

- The major sequelae in males include epididymo-orchitis, reactive arthritis (oculo-urethro-synovial syndrome), infertility (rare), and disseminated gonococcal infection (for example, arthritis, dermatitis, endocarditis, meningitis).

**Laboratory Testing/Diagnosis and Specimen Collection/Transport**

**Nucleic acid amplification tests (NAATs)**

- Due to the higher sensitivity and specificity of the most recently approved commercial NAATs, they can increase the number of cases diagnosed.\(^{42,43}\) However, culture is strongly recommended because it allows for testing of antimicrobial susceptibility.\(^{44}\)
- NAATs may be the only available testing method in some jurisdictions.
- Where a NAAT is used, sentinel surveillance mechanisms using culture are important to ensure continued monitoring for antimicrobial resistance.\(^{13}\)
- NAAT may be done at the time of presentation **without individuals having to wait 48 hours post-exposure**; this is based on expert opinion, which assumes that NAAT is able to detect small amounts of DNA or RNA.
- Validated NAATs can be used to detect rectal and oropharyngeal infections. Although no products are currently licensed in Canada; individual laboratories may offer NAATs after in-house laboratory validation, including confirmation of positives with culture or a second NAAT.\(^{42}\)
- If a NAAT is used as a test of cure (clinicians should refer to indications for test of cure in the Follow-up section of this chapter), specimen collection should be **delayed for 2 to 3 weeks after completion of treatment**.\(^{45,46}\)

**Culture**

- As well as providing clinicians with important case management information, cultures are critical for improved public health monitoring of antimicrobial resistance patterns and trends.\(^{13,47-51}\)
- Depending on the clinical situation, consideration should be given for collection of samples using both culture and NAAT, especially in symptomatic patients.
- Cultures obtained less than 48 hours after exposure may give false negative results.
- All suspected treatment failures should be investigated using culture, allowing for antimicrobial susceptibility testing.
Culture is strongly recommended in the following situations:
- To determine antimicrobial sensitivities prior to treatment, when possible,
- As a test of cure for suspected treatment failure or in situations where there is an increased probability of treatment failure (clinicians should refer to the Follow-up section of this chapter),
- For symptomatic MSM,
- To evaluate pelvic inflammatory disease (PID), and
- If the infection was acquired in countries or areas with high rates of antimicrobial resistance.
- In the case of sexual abuse/sexual assault (rectal, pharyngeal, vaginal), clinicians are advised that when a NAAT is used to screen victims of sexual abuse or sexual assault for medico-legal purposes, two different primer pairs should be used in the laboratory (42,52) (clinicians should refer to the Laboratory Diagnosis of Sexually Transmitted Infections chapter).

Specimen collection
- Due to high rates of concomitant infection, specimens should be taken for the diagnosis of both gonococcal and chlamydial infections (53) (clinicians should refer to the Laboratory Diagnosis of Sexually Transmitted Infections chapter).
- For information on routine specimen sites, tests and clinical considerations, clinicians should refer to Table 4. For further information on specimen collection, clinicians should refer to the Laboratory Diagnosis of Sexually Transmitted Infections chapter.

Specimen transport
- Successful culture of specimens requires proper collection and transportation of appropriate specimens or immediate inoculation of medium. (54,55) Consult with your laboratory for specific instructions on enhancing pathogen survival.
- NAAT is appropriate when transport and storage conditions are not conducive to maintaining the viability of N. gonorrhoeae. (54)
- For further information on specimen collection and transport, clinicians should refer to the Laboratory Diagnosis of Sexually Transmitted Infections chapter.
**Table 4. Recommended routine specimen sites and tests**

This table is intended to guide clinicians in making decisions for appropriate specimen collection and choice of tests from various anatomical sites in postpubertal males and females.

Clinicians should refer to the *Sexual Abuse in Peripubertal and Prepubertal Children* and the *Laboratory Diagnosis of Sexually Transmitted Infections* chapters for guidance on specimen collection in prepubertal males and females.

**First row of the table**

The specimen site is urethral.

The test type is a Gram stain to detect Gram-negative intracellular diplococci under the microscope.

Doing a urethral swab for Gram stain is only appropriate for postpubertal males with symptoms.

A positive gram stain result is generally diagnostic of gonorrhea.

**Second row of the table**

The specimen site is urethral.

The test type is either culture or NAAT for laboratory detection of *N. gonorrhoeae*.

Urethral testing is considered optimal for all postpubertal males.

For females with a urethral syndrome, for example dysuria or pyuria, the urethra is also considered an optimal test site. For those without urethral symptoms either a cervical swab or urine test is recommended.

**Third row of the table**

The specimen site is endocervical in postpubertal females.

The test type is a Gram stain to detect Gram-negative intracellular diplococci under the microscope.

Doing an endocervical swab for Gram stain has lower sensitivity than in male urethral specimens and therefore, is not routinely recommended.
Fourth row of the table

The specimen site is endocervical or vaginal in postpubertal females.

The test type is either culture or NAAT for laboratory detection of *N. gonorrhoeae*; both are considered optimal testing methods.

Clinicians should consider the following four points related to the use of endocervical or vaginal swabs:

1. Vaginal swabs for NAAT are as accurate as cervical swabs.

AND

2. Self-obtained vaginal swabs can also be used when a pelvic examination is not warranted or refused by the individual, or when the setting is inappropriate (for example, non-conventional settings). A physical examination is preferable, and more invasive specimens may be needed for diagnostic purposes in some situations.

AND

3. If the cervix has been surgically removed, urine NAAT, or vaginal swabs for culture or NAAT should be collected.

AND

4. Urethral specimens can also be collected if a woman is menstruating at the time of the exam.

Fifth row of the table

The specimen type is a first catch urine of 10 to 20 milliliters that can be sampled any time of the day in males or females where a urethral swab or pelvic examination is not practical.

The test type is a NAAT.

Clinicians are advised that in females, first catch urine may have reduced performance when compared to NAAT for cervical swabs.

Sixth row of the table

The specimen type is an oropharyngeal swab for all females with a history of performing oral sex OR for males with a history of performing oral sex who are high risk of exposure – for example, MSM, multiple sexual partners, or sex with a partner who is at high risk of infection.

The test type is culture or validated NAAT for laboratory detection of *N. gonorrhoeae*.

Clinicians are advised that for pharyngeal specimens, culture is preferred but that a validated NAAT may be used if culture is not available.

Seventh and final row of the table

The specimen type is a rectal swab.
The test type is culture or validated NAAT for laboratory detection of \textit{N. gonorrhoeae}.

This specimen test site is recommended for females with anogenital symptoms, as colonization can occur without anal penetration.\textsuperscript{(57)}

\textbf{AND}

For females and MSM with a history of receptive anal intercourse, whether or not condoms were used.

For all specimen collection and test types, clinicians should refer to the NAAT tests and culture sections that precede this table for specific guidance on the use of these testing methods.

\textbf{Management}

- Appropriate samples (as listed above) should be obtained prior to treatment.
- Management choices should be based on the site of infection and on laboratory test results (\textit{Table 5}) unless presumptive treatment is to be provided for syndromic management (such as, mucopurulent cervicitis [MPC], non-gonococcal urethritis [NGU], PID or epididymitis) (\textit{Table 6}) or if the patient is being treated as a contact. When making treatment decisions, relevant history, physical examination and epidemiologic factors should be considered.
- All confirmed cases need to be treated and suspected cases should be considered for treatment.
- For treatment of PID, clinicians should refer to the \textit{Pelvic Inflammatory Disease} chapter.
- For treatment of epididymitis/epididymo-orchitis, clinicians should refer to the \textit{Epididymitis} chapter.

\textbf{Consideration for other STIs}

- Obtain a specimen to test for chlamydial infection (clinicians should refer to the \textit{Chlamydial Infections} chapter).
- Obtain a blood sample for serologic testing for syphilis.
- HIV counselling and testing are recommended.
- Immunization is recommended for:
  - hepatitis B for all individuals being evaluated or treated for an STI, if not already immune, and
  - hepatitis A for high-risk individuals (for example, MSM, injection drug users) if not already immune. (For a complete list of individuals at increased risk of hepatitis A, clinicians should refer to the \textit{Canadian Immunization Guide, Part 4, Active Vaccines}, available at the link that follows: \url{http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-hepa-eng.php}).
- Discuss human papillomavirus (HPV) vaccine with male and female patients as per the recommendations outlined in the \textit{National Advisory Committee on Immunization (NACI)}

**Considerations in children (clinicians should refer to the Sexual Abuse in Peripubertal and Prepubertal Children chapter).**

- Sexual abuse should be considered when genital, rectal or pharyngeal gonorrhea is diagnosed in any child after the neonatal period.\(^{37,58}\)
  - Consultation with an experienced colleague should be sought.
- Every province and territory has legislation that requires the reporting of suspected or confirmed sexual abuse of children.
- Siblings and other children who may be at risk should also be evaluated.\(^{37}\)
- All individuals named as contacts in suspected sexual abuse cases should be located and clinically evaluated; prophylactic treatment may or may not be offered and the decision to treat should be based on history, clinical findings and test results.
- Local public health authorities should be notified; they may be able to provide guidance on evaluating suspected source cases.

**Table 5. Recommended patient management: test results available**

**Positive Gram stain results:**

- If Gram-negative intracellular diplococci are observed, treatment for both gonococcal and chlamydial infection should be provided.\(^{32,53,54,59}\)
- The presence of extracellular Gram-negative diplococci is an equivocal finding and confirmation by culture/NAAT should be performed. If the individual is at high risk of infection and follow-up is not assured, treatment should be provided for gonococcal infection while waiting for laboratory test results.\(^{59,60}\)
- The presence of polymorphonuclear leukocytes without diplococci does not indicate or exclude gonococcal infection but suggests non-gonococcal urethritis. (clinicians should refer to the Urethritis chapter).\(^{59,60}\)

**Positive culture or NAAT results:**

- Is diagnostic of gonorrhea; treatment for both gonococcal and chlamydial infection should be provided.\(^{32,42,53}\)

**Table 6. Recommended patient management: test results pending**

**In the case where urethral/cervical mucopurulent discharge is observed and test results are pending:**

- Treatment should be provided for both gonococcal and chlamydial infection if partner is infected with gonorrhea or if follow-up is not assured.\(^{32,53,59}\)
Treatment

Medication-specific considerations and contraindications

- Patients should optimally be treated with combination gonorrhea infection therapy in response to increasing antimicrobial resistance.\(^{(61)}\)
- This combination therapy also includes effective treatment for chlamydia due to high rates of concomitant infection.\(^{(7,32,53,59)}\)
- Combination therapy using medications with two different mechanisms of action is thought to improve treatment efficacy as well as to potentially delay the emergence of cephalosporin-resistant gonorrhea.
- Based on pharmacokinetic considerations, an effective treatment for gonorrhea should maintain serum levels at least 4 times the minimum inhibitory concentration (MIC) for a minimum of 20 hours to effectively treat infection caused by an organism with reduced sensitivity to an antimicrobial agent.\(^{(15)}\)
- Directly observed therapy with single-dose regimens is desirable.\(^{(32,62)}\)
- Clinicians should base their treatment choices and tailor recommendations on local epidemiologic data where available.

Cephalosporins

- Cefixime and ceftriaxone should not be given to patients who are allergic to cephalosporins.
- Cross-sensitivity between penicillin and second- or third-generation cephalosporins such as ceftriaxone, cefixime, cefoxitin and cefotaxime is low. However, patients with a history of immediate hypersensitivity reaction to penicillin (for example, anaphylaxis, urticarial rash, bronchospasm) may be at increased risk of similar reactions with all cephalosporins. If cephalosporins are administered to patients hypersensitive to penicillin, a protocol (for example, epinephrine, airway management, etc.) to respond to serious reactions should be in place.
The recommended diluent for ceftriaxone is 1 percent lidocaine without epinephrine to a final concentration of 250 to 350 milligrams per milliliter\textsuperscript{63} to reduce discomfort.

The Expert Working Group for the Canadian Guidelines on Sexually Transmitted Infections reviewed the scientific literature to address safety, efficacy, reported treatment failures and rising MICs. Their review resulted in the following recommendations:

- There is scientific evidence that cefixime 800 milligrams is safe and effective in treating gonococcal infections.\textsuperscript{9,64-68} Pharmacodynamic studies have shown that 800 milligrams of cefixime compared to 400 milligrams, increases the period when the free drug concentration exceeds the MIC. Therefore, a dosage of 800 milligrams may be more effective than the previously recommended 400 milligrams at reducing the risk of gonococcal treatment failure in settings of reduced cephalosporin susceptibility.\textsuperscript{9,15,27}
- No data exists on the efficacy of cefixime 800 milligrams in pregnancy. However, based on safety and efficacy data for the use of cefixime 400 milligrams, a single dose of cefixime 800 milligrams may be considered for use in pregnant women.
- The penetration of cefixime into the oropharynx is not ideal and cases of treatment failure with cefixime have been reported.
- There are limited data on the effectiveness of oral cefixime 800 milligrams in treating a pharyngeal infection.
- There are more efficacy data on the use of ceftriaxone than of cefixime for treating uncomplicated infection\textsuperscript{67} and in situations where higher tissue penetration is necessary to achieve cure (such as pharyngeal infection\textsuperscript{69-71} and complicated cases such as PID\textsuperscript{72,73} and epididymitis/epididymo-orchitis\textsuperscript{74}). Ceftriaxone 250 milligrams intramuscularly is now recommended for pharyngeal infection, PID and epididymitis/epididymo-orchitis.
- Ceftriaxone is recommended as the preferred treatment for gonococcal infections in MSM (clinicians should refer to Table 8 in this chapter) due to recent cases of cefixime treatment failures reported primarily among MSM.

**Quinolones**

- Due to the rapid increase in quinolone-resistant N. gonorrhoeae, quinolones such as ciprofloxacin, levofloxacin and ofloxacin are no longer recommended for treating gonococcal infections in Canada.\textsuperscript{5,6,22,27}
- Quinolones should ONLY be given as an alternative treatment IF:
  - Antimicrobial susceptibility testing is available and quinolone susceptibility is demonstrated;  
  OR IF
  - Local quinolone resistance is under 5% AND a test of cure can be performed.
- Quinolones should be avoided in prepubertal children.
Azithromycin

- Azithromycin should not be used as monotherapy unless cephalosporins are contraindicated (for example, history of anaphylactic reaction to penicillin or allergy to cephalosporin), as resistance has been reported.\(^{(75-78)}\)
- The recommended dose of azithromycin 2 grams for gonococcal infections is associated with a significant incidence of gastrointestinal adverse effects.
  - Taking azithromycin with food may minimize these effects.
  - Prophylactic antiemetics may be used, unless contraindicated.
  - If vomiting occurs within 1 hour post-administration, a repeat dose should be given.
- Azithromycin can cause potentially life-threatening arrhythmias, especially in individuals taking a multi-day course of the medication \(^{(79)}\), and who:
  - have prolonged QT interval,
  - have clinically significant bradycardia,
  - have arrhythmias,
  - have heart failure,
  - are taking antiarrhythmic agents and other medications known to prolong the QT interval,
  - have low serum potassium or magnesium,
  - are elderly.

Table 7. Recommended treatment of uncomplicated anogenital and pharyngeal infection in adults and youth greater than or equal to 9 years of age. \(^{(7,15,65-67,71,80-88)}\)

This is a table for the recommended treatment of uncomplicated anogenital and pharyngeal infection in adults and youth greater than or equal to 9 years of age.

It does not include men who have sex with men (MSM), clinicians should refer to table 8 for this population.

The first section of the table contains the preferred and alternate treatment recommendations for anogenital infections, and the second section of the table contains the preferred and alternate treatment recommendations for pharyngeal infections.

The preferred treatment recommendations are based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes this table.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.
Lists the preferred treatment options for uncomplicated anogenital infection in adults and youth greater than or equal to 9 years of age – it includes urethral, endocervical, vaginal and rectal infections.

The preferred combination therapy for uncomplicated anogenital infection in adults and youth greater than or equal to 9 years of age is either ceftriaxone 250 milligrams intramuscularly in a single dose

OR

cefixime 800 milligrams orally, in a single dose. These are A-1 recommendations; either ceftriaxone or cefixime should be given with azithromycin 1 gram orally, in a single dose; this is a B-2 recommendation.

Clinicians are advised that, combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

AND furthermore that, doxycycline is contraindicated in pregnant and breastfeeding women.

Regarding the recommendation for the 800 milligram dose of cefixime, clinicians are advised that there is scientific evidence that cefixime 800 milligrams is safe and effective in treating gonococcal infections. Pharmacodynamic studies have shown that 800 milligrams of cefixime compared to 400 milligrams, increases the period when the free drug concentration exceeds the MIC. Therefore, a dosage of 800 milligrams may be more effective than the previously recommended 400 milligrams at reducing the risk of gonococcal treatment failure in settings of reduced cephalosporin susceptibility.
First section, second row of table 7

Lists alternate treatment options for uncomplicated anogenital infection in adults and youth greater than or equal to 9 years of age - it includes urethral, endocervical, vaginal and rectal infections.

One alternate treatment option for uncomplicated anogenital infection in adults and youth greater than or equal to 9 years of age is combination therapy with spectinomycin 2 grams intramuscularly, in a single dose; this is an A-1 recommendation. The spectinomycin should be given with azithromycin 1 gram orally, in a single dose; this is a B-2 recommendation.

Clinicians are advised that spectinomycin is only available through Health Canada’s Special Access program.

Clinicians are also advised that, combination therapy of spectinomycin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

AND furthermore that, doxycycline is contraindicated in pregnant and breastfeeding women.

The second alternate treatment option for uncomplicated anogenital infection in adults and youth greater than or equal to 9 years of age is azithromycin 2 grams orally, in a single dose; this is an A-1 recommendation.

Clinicians are advised that, for anogenital infection, azithromycin 2 grams orally, in a single dose should only be considered as an alternate treatment option if there is a history of severe allergy to cephalosporins. It is important to recognize the 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.

Second section, first row of table 7

Lists the preferred treatment option for uncomplicated pharyngeal infection in adults and youth greater than or equal to 9 years of age.

The preferred combination therapy for uncomplicated pharyngeal infection in adults and youth greater than or equal to 9 years of age is ceftriaxone 250 milligrams intramuscularly in a single dose; this is an A-1 recommendation. The ceftriaxone should be given with azithromycin 1 gram orally, in a single dose; this is a B-3 recommendation.
Clinicians are advised that, combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

AND furthermore that, doxycycline is contraindicated in pregnant and breastfeeding women.

Second section, second row of table 7

Lists alternate treatment options for uncomplicated pharyngeal infections in adults and youth greater than or equal to 9 years of age.

One alternate treatment option for uncomplicated pharyngeal infection in adults and youth greater than or equal to 9 years of age is combination therapy with cefixime 800 milligrams orally, in a single dose; this is a B-3 recommendation. The cefixime should be given with azithromycin 1 gram orally, in a single dose; this is a B-3 recommendation.

Regarding the recommendation for the 800 milligram dose of cefixime, clinicians are advised that there is scientific evidence that cefixime 800 milligrams is safe and effective in treating gonococcal infections.\textsuperscript{(9,64-68)} Pharmacodynamic studies have shown that 800 milligrams of cefixime compared to 400 milligrams, increases the period when the free drug concentration exceeds the MIC. Therefore, a dosage of 800 milligrams may be more effective than the previously recommended 400 milligrams at reducing the risk of gonococcal treatment failure in settings of reduced cephalosporin susceptibility.\textsuperscript{(9,15,27)}

Clinicians are also advised that combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

AND furthermore that, doxycycline is contraindicated in pregnant and breastfeeding women.

The second alternate treatment option for uncomplicated pharyngeal infection in adults and youth greater than or equal to 9 years of age is azithromycin 2 grams, orally, in a single dose; this is an A-1 recommendation.

Clinicians are advised that, for pharyngeal infection, azithromycin 2 grams orally, in a single dose, should only be considered as an alternate treatment option if there is a history of severe allergy to cephalosporins. It is important to recognize the 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.
Table 8. Recommended treatment of uncomplicated anogenital and pharyngeal infections in men who have sex with men (MSM) (15,65-67,71,80-84)

This is a table for the recommended treatment of uncomplicated anogenital and pharyngeal infections in men who have sex with men.

The first section of the table contains the preferred and alternate treatment recommendations for anogenital infections, and the second section of the table contains the preferred and alternate treatment recommendations for pharyngeal infections.

The preferred treatment recommendations are based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes table 7.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

**First section, first row of table 8**
Lists the preferred treatment options for uncomplicated anogenital infection for MSM and includes urethral and rectal infections.

The preferred combination therapy for uncomplicated anogenital infections in MSM is ceftriaxone 250 milligrams intramuscularly in a single dose; this is an A-1 recommendation. The ceftriaxone should be given with azithromycin 1 gram orally, in a single dose; this is a B-2 recommendation.

Clinicians are advised that, combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

**First section, second row of table 8**
Lists three alternate treatment options for uncomplicated anogenital infection for MSM and includes urethral and rectal infections.

One alternate treatment option for uncomplicated anogenital infection in MSM is combination therapy with cefixime 800 milligrams orally, in a single dose; this is an A-1 recommendation. The cefixime should be given with azithromycin 1 gram orally, in a single dose; this is a B-2 recommendation.

Regarding the recommendation for the 800 milligram dose of cefixime, clinicians are advised that there is scientific evidence that cefixime 800 milligrams is safe and effective in treating
Pharmacodynamic studies have shown that 800 milligrams of cefixime compared to 400 milligrams, increases the period when the free drug concentration exceeds the MIC. Therefore, a dosage of 800 milligrams may be more effective than the previously recommended 400 milligrams at reducing the risk of gonococcal treatment failure in settings of reduced cephalosporin susceptibility.

Clinicians are also advised that combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

A second alternate treatment option for uncomplicated anogenital infection in MSM is combination therapy with spectinomycin 2 grams intramuscularly in a single dose; this is an A-1 recommendation. The spectinomycin should be given with azithromycin 1 gram orally, in a single dose; this is a B-2 recommendation.

Clinicians are advised that spectinomycin is only available through Health Canada’s Special Access program.

Clinicians are also advised that combination therapy of spectinomycin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

The third alternate treatment option for uncomplicated anogenital infection in MSM is azithromycin 2 grams orally, in a single dose; this is an A-1 recommendation.

Clinicians are advised that, for anogenital infection in MSM, azithromycin 2 grams orally, in a single dose, should only be considered as an alternate treatment option if there is a history of severe allergy to cephalosporins. It is important to recognize the 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.
**Second section, first row of table 8**

Lists one preferred combination treatment option for uncomplicated pharyngeal infection in MSM.

The preferred treatment for uncomplicated pharyngeal infection in MSM is ceftriaxone 250 milligrams intramuscularly in a single dose; this is an A-1 recommendation. The ceftriaxone should be given with azithromycin 1 gram orally, in a single dose; this is a B-3 recommendation.

Clinicians are advised that, combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

**Second section, second row of table 8**

Lists alternate treatment options for uncomplicated pharyngeal infection in MSM.

The alternate treatment for uncomplicated pharyngeal infection in MSM is combination therapy with cefixime 800 milligrams orally, in a single dose; this is a B-3 recommendation. The cefixime should be given with azithromycin 1 gram orally, in a single dose; this is a B-3 recommendation.

Regarding the recommendation for the 800 milligram dose of cefixime, clinicians are advised that there is scientific evidence that cefixime 800 milligrams is safe and effective in treating gonococcal infections. Pharmacodynamic studies have shown that 800 milligrams of cefixime compared to 400 milligrams, increases the period when the free drug concentration exceeds the MIC. Therefore, a dosage of 800 milligrams may be more effective than the previously recommended 400 milligrams at reducing the risk of gonococcal treatment failure in settings of reduced cephalosporin susceptibility.

Clinicians are also advised that combination therapy of a cephalosporin with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

Clinicians are advised that for uncomplicated pharyngeal infection in MSM, in case of severe allergy to cephalosporins, azithromycin 2 grams orally may be considered as an alternate treatment option; this is an A-1 recommendation.
### Table 9. Recommended treatment of uncomplicated anogenital and pharyngeal infection in children less than 9 years of age\(^{(31,39,89)}\)

This is a table for the recommended treatment of uncomplicated anogenital and pharyngeal infections in children under 9 years of age.

There is an important note in this table related to neonates, birth to one month of age, with uncomplicated anogenital and pharyngeal infections. It reads, in neonates the recommended dosage for ceftriaxone is 25 to 50 milligrams per kilogram; to a maximum dose of 125 milligrams, given intramuscularly in a single dose.

Clinicians are advised that in neonates, routine combination therapy with a macrolide is not recommended due to the association with pyloric stenosis. Testing should be done for chlamydia and if results are positive, treatment should be provided as per table 4 in the Chlamydial Infections chapter.

The first section of the table contains the preferred and alternate treatment recommendations for anogenital infections, and the second section of the table contains the preferred and alternate treatment recommendations for pharyngeal infections.

The preferred treatment recommendations are based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes table 7 in this chapter.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

#### First section, first row of table 9

Lists the preferred treatment options for uncomplicated anogenital infection for children less than 9 years of age, except for neonates, and includes urethral, vaginal and rectal infections.

There are two preferred combination therapy options listed.

One preferred treatment option for uncomplicated anogenital infection in children less than nine years of age, except for neonates, is ceftriaxone 50 milligrams per kilogram intramuscularly, in a single dose, to a maximum dose of 250 milligrams. This is an A-2 recommendation. The ceftriaxone should be given with azithromycin 20 milligrams per kilogram, orally, in a single dose; to a maximum dose of 1 gram; this is a B-2 recommendation.
The second preferred treatment option for uncomplicated anogenital infection in children less than nine years of age, except for neonates, is cefixime 8 milligrams per kilogram given orally, twice a day for two doses; to a maximum dose of 400 milligrams per dose; this is a B-3 recommendation. The cefixime should be given with azithromycin 20 milligrams per kilogram, orally, in a single dose; to a maximum dose of 1 gram; this is a B-2 recommendation.

Regarding the treatment option of oral cefixime in children less than nine years of age, except for neonates, clinicians are advised that whenever possible, oral therapies are recommended for children. Recommendations for the use of cefixime are based on data showing efficacy in the treatment of infections caused by organisms similar to *N. gonorrhoeae*. Because there is limited experience with the use of cefixime in children with gonococcal infections, antimicrobial susceptibility should be ascertained and a follow-up culture ensured. If follow-up cannot be ensured, ceftriaxone should be used in place of cefixime.

First section, second row of table 9

Lists the alternate treatment option for uncomplicated anogenital infection for children less than 9 years of age, except for neonates, and includes urethral, vaginal and rectal infections.

The alternate treatment for uncomplicated anogenital infection in children less than nine years of age, except for neonates, is combination therapy with spectinomycin 40 milligrams per kilogram, intramuscularly in a single dose; to a maximum dose of 2 grams; this is an A-2 recommendation. The spectinomycin should be given with azithromycin 20 milligrams per kilogram, given orally, in a single dose; to a maximum dose of 1 gram; this is a B-2 recommendation.

Clinicians are advised that spectinomycin is only available through Health Canada’s Special Access program.

Second section, first row of table 9

Lists one preferred combination treatment option for uncomplicated pharyngeal infection in children less than 9 years of age, except for neonates.

The preferred treatment for uncomplicated pharyngeal infection in children less than 9 years of age, except for neonates, is ceftriaxone 50 milligrams per kilogram intramuscularly, in a single dose; to a maximum dose of 250 milligrams; this is an A-2 recommendation. The ceftriaxone should be given with azithromycin 20 milligrams per kilogram, given orally, in a single dose; to a maximum dose of 1 gram; this is a B-3 recommendation.
Lists one alternate combination treatment option for uncomplicated pharyngeal infection in children less than 9 years of age, except for neonates.

The alternate treatment for uncomplicated pharyngeal infection in children less than 9 years of age, except for neonates, is cefixime 8 milligrams per kilogram given orally, twice a day for two doses; to a maximum of 400 milligrams per dose; this is an A-2 recommendation. The cefixime should be given with azithromycin 20 milligrams per kilogram, given orally, in a single dose; to a maximum dose of 1 gram; this is a B-3 recommendation.

Regarding the treatment option of oral cefixime in children less than nine years of age, except for neonates, clinicians are advised that whenever possible, oral therapies are recommended for children. Recommendations for the use of cefixime are based on data showing efficacy in the treatment of infections caused by organisms similar to N. gonorrhoeae. Because there is limited experience with the use of cefixime in children with gonococcal infections, antimicrobial susceptibility should be ascertained and a follow-up culture ensured. If follow-up cannot be ensured, ceftriaxone should be used in place of cefixime.

Table 10. Recommended treatment of gonococcal ophthalmia and disseminated infections in adults and youth greater than and equal to 9 years of age

This is a table for the recommended treatment of gonococcal ophthalmia and disseminated infections, including disseminated gonococcal arthritis, meningitis and endocarditis in adults and youth greater than and equal to 9 years of age.

The preferred combination treatment regimens are based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes Table 7 in this chapter.

The table lists preferred initial combination therapies and usual duration of therapy. Clinicians are advised that consultation with an experienced colleague should be sought and that all cases should be discussed with an infectious diseases expert.

For all treatment options listed, clinicians are advised that, combination therapy of ceftriaxone with azithromycin 1 gram orally, in a single dose, is preferred over the alternate combination therapy of doxycycline 100 milligrams orally, twice a day for 7 days, due to significant rates of tetracycline-resistant gonorrhea and concerns regarding compliance with a 7-day treatment regimen.

AND furthermore that doxycycline is contraindicated in pregnant and breast feeding women.
There is an important note in the table advising clinicians that hospitalization is indicated for meningitis and may also be indicated for other disseminated infections.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

**Preferred treatment for disseminated gonococcal arthritis in adults and youth greater than and equal to 9 years of age**

The preferred treatment for disseminated gonococcal arthritis in adults and youth greater than and equal to nine years of age is ceftriaxone 2 grams, given intravenously or intramuscularly, daily for 7 days; this is an A-2 recommendation. Azithromycin 1 gram should be given orally in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

**Preferred treatment for disseminated gonococcal meningitis in adults and youth greater than and equal to 9 years of age**

The preferred treatment for gonococcal meningitis in adults and youth greater than and equal to nine years of age is ceftriaxone 2 grams, given intravenously or intramuscularly, daily for 10 to 14 days; this is an A-2 recommendation. Azithromycin 1 gram should be given orally in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

- Clinicians are advised that intramuscular administration of ceftriaxone for disseminated gonococcal meningitis should only be considered if an intravenous line is not available.

**Preferred treatment for disseminated gonococcal endocarditis in adults and youth greater than and equal to 9 years of age**

The preferred treatment for disseminated gonococcal endocarditis in adults and youth greater than and equal to nine years of age is ceftriaxone 2 grams, given intravenously or intramuscularly, daily for 28 days; this is an A-2 recommendation. Azithromycin 1 gram, should be given orally in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

- Clinicians are advised that intramuscular administration of ceftriaxone for disseminated gonococcal endocarditis should only be considered if an intravenous line is not available.

**Preferred treatment for gonococcal ophthalmia in adults and youth greater than and equal to 9 years of age**

The preferred treatment for gonococcal ophthalmia in adults and youth greater than and equal to nine years of age is ceftriaxone 2 grams, given intravenously or intramuscularly, in a single dose; this is an A-2 recommendation. The ceftriaxone should be given with azithromycin 1 gram, orally in a single dose; this is a B-3 recommendation.
Table 11. Recommended treatment of gonococcal ophthalmia and disseminated infections in children greater than 1 month to less than 9 years of age\(^{(31,39)}\)

This is a table for the recommended treatment of gonococcal ophthalmia and disseminated infections, including disseminated gonococcal arthritis, meningitis and endocarditis in children greater than 1 month to less than 9 years of age.

For treatment recommendations for neonates (birth to one month old), clinicians should refer to the *Recommended treatment of neonates* section in this chapter.

There is an important note in the table advising clinicians that hospitalization is indicated for disseminated infections in children greater than 1 month and less than nine years of age and that consultation with an expert in infectious diseases should be initiated as soon as possible.

The table lists preferred initial combination therapies and usual duration of therapy for children greater than one month and less than nine years of age.

Clinicians are advised that consultation with an experienced colleague should be sought and that all cases should be discussed with an infectious diseases expert.

The preferred combination treatment regimens are based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes *Table 7* in this chapter.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

**Preferred treatment for disseminated gonococcal arthritis in children greater than 1 month to less than 9 years of age:**

The preferred treatment for gonococcal arthritis in children greater than 1 month to less than 9 years of age is ceftriaxone 50 milligrams per kilogram, given intravenously or intramuscularly, daily for 7 days, to a maximum dose of 1 gram per day; this is an A-3 recommendation. Azithromycin 20 milligrams per kilogram, to a maximum dose of 1 gram, should be given orally in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

- Clinicians are advised that intramuscular administration of ceftriaxone for disseminated gonococcal arthritis should only be considered if an intravenous line is not available.
**Preferred treatment for disseminated gonococcal meningitis in children greater than 1 month to less than 9 years of age:**

The preferred treatment for disseminated gonococcal meningitis in children greater than 1 month to less than 9 years of age is ceftriaxone 50 milligrams per kilogram, intravenously or intramuscularly every 12 hours for 10 to 14 days, to a maximum dose of 1 gram per dose and 2 grams per day; this is an A-3 recommendation. Azithromycin 20 milligrams per kilogram, to a maximum dose of 1 gram, should be given orally, in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

- Clinicians are advised that intramuscular administration of ceftriaxone for disseminated gonococcal meningitis should only be considered if an intravenous line is not available.

**Preferred treatment for disseminated gonococcal endocarditis in children greater than 1 month to less than 9 years of age:**

The preferred treatment for disseminated gonococcal endocarditis in children greater than 1 month to less than 9 years of age is ceftriaxone 50 milligrams per kilogram, intravenously or intramuscularly, every 12 hours for 28 days, to a maximum dose of 1 gram per dose and 2 grams per day; this is an A-3 recommendation. Azithromycin 20 milligrams per kilogram, to a maximum dose of 1 gram, should be given orally, in a single dose with the first dose of ceftriaxone; this is a B-3 recommendation.

- Clinicians are advised that intramuscular administration of ceftriaxone for disseminated gonococcal endocarditis should only be considered if an intravenous line is not available.

**Preferred treatment for gonococcal ophthalmia beyond the neonatal period in children greater than 1 month to less than 9 years of age:**

The preferred treatment for gonococcal ophthalmia beyond the neonatal period in children greater than 1 month to less than 9 years of age is ceftriaxone 50 milligrams per kilogram, intravenously or intramuscularly, in a single dose, to a maximum dose of 2 grams; this is an A-3 recommendation. The ceftriaxone should be given with azithromycin 20 milligrams per kilogram, to a maximum dose of 1 gram, given orally, in a single dose; this is a B-3 recommendation.

**Recommended treatment of neonates**

- It is important that neonates born to infected untreated mothers be tested and that treatment be initiated without waiting for test results.
- Culture conjunctivae prior to administering antibiotics. If the infant is unwell in any way, also culture blood and cerebrospinal fluid to rule out disseminated infection.

**Table 12. Neonates born to women with untreated gonorrhea**

This is a table that provides one preferred treatment option for neonates born to women with untreated gonorrhea.
The preferred treatment is based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians are referred to the related section that precedes Table 7 in this chapter.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

The preferred treatment for neonates born to women with untreated gonorrhea is ceftriaxone 25 to 50 milligrams per kilogram, intramuscularly, in a single dose, to a maximum dose of 125 milligrams; this is an A-3 recommendation.

There are two important notes to clinicians. They are as follows:

- Prophylactic treatment for possible chlamydial co-infection is not recommended unless follow-up cannot be assured.
- Testing should be done for chlamydia and if results are positive, treatment should be provided as per Table 4 in the Chlamydial Infections chapter.

Table 13. Ophthalmia neonatorum

This is a table that provides one preferred treatment option for neonates with ophthalmia neonatorum.

Clinicians are advised that hospitalization and consultation with an expert in infectious diseases should be initiated as soon as possible.

There are 3 important notes within the table that advise clinicians on the initial management of ophthalmia neonatorum. They are as follows:

- Routine gonococcal combination therapy with a macrolide is not recommended due to the association with pyloric stenosis.
- Irrigate eyes immediately with sterile normal saline and at least hourly as long as necessary to eliminate discharge.
- Appropriate infection prevention and control precautions are necessary for all cases.

The preferred treatment is based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes Table 7 in this chapter.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with
The preferred treatment for neonates with opthalmia neonatorum is ceftriaxone 25 to 50 milligrams per kilogram, intramuscularly in a single dose, to a maximum dose of 125 milligrams; this is an A-2 recommendation.

Clinicians are advised that prophylactic treatment for possible chlamydial co-infection is not recommended unless follow-up cannot be assured. Testing should be done for chlamydia and if results are positive, treatment should be provided as per table 4 in the Chlamydial Infections chapter.

**Table 14. Neonates with disseminated gonococcal arthritis, meningitis or endocarditis**

This is a table that provides one preferred treatment option for neonates with disseminated gonococcal arthritis, meningitis or endocarditis. The table lists preferred therapy and recommended duration of therapy.

There is an important note in the table advising clinicians that hospitalization is indicated for disseminated infections and that consultation with an expert in infectious diseases should be initiated as soon as possible.

Clinicians are advised that routine gonococcal combination therapy with a macrolide is not recommended due to the association with pyloric stenosis.

The preferred treatment is based on general consensus of the Expert Working Group. For information on antimicrobial resistance and medication-specific considerations and contraindications, clinicians should refer to the related section that precedes Table 7 in this chapter.

All treatment recommendations have quality and levels of evidence. Clinicians should refer to Section 1 of the guidelines or refer to the appended excerpt which was sent with this chapter for interpretation of the grading system.

The preferred treatment for neonates with disseminated gonococcal arthritis, meningitis or endocarditis is cefotaxime 50 milligrams per kilogram, intravenously or intramuscularly, every 6 hours for 10 to 14 days; this is an A-3 recommendation.

- Clinicians are advised that intramuscular administration of cefotaxime for disseminated gonococcal infections should only be considered if an intravenous line is not available.

Clinicians are also advised that prophylactic treatment for possible chlamydial co-infection is not recommended unless follow-up cannot be assured. Testing should be done for
chlamydia and if results are positive, treatment should be provided as per table 4 in the Chlamydial Infections chapter.

**Reporting and Partner Notification**

- Case finding and partner notification are critical strategies for maintaining control of gonococcal infections in Canada.
- Local public health authorities may assist with partner notification and with appropriate referral for clinical evaluation, testing, treatment and health education.
- Gonococcal infections are reportable in all provinces and territories; positive test results should be reported to local public health authorities.
- All partners who have had sexual contact with the index case within 60 days prior to symptom onset or date of specimen collection (if the index case is asymptomatic) should be notified, tested and empirically treated regardless of clinical findings and without waiting for test results.\(^{(32,62)}\)
- The length of time for the trace-back period should be extended in the following three circumstances:
  1. To include additional time between the date of testing and date of treatment,
  2. If the index case states that there were no partners during the recommended trace-back period, the most recent partner should be notified, and
  3. If all partners traced (according to recommended trace-back period) test negative, the last partner prior to the trace-back period should be notified.
- When a neonate is confirmed to have gonorrhea, the mother and her most recent sexual partner plus any other partners within 60 days of delivery should be located, clinically evaluated and empirically treated regardless of clinical findings and without waiting for test results.

**Follow-up**

- Repeat screening for individuals with a gonococcal infection is recommended 6 months post-treatment.\(^{(28)}\)
- Follow-up cultures for test of cure from all positive sites should be done 3–7 days after the completion of therapy, particularly in the following situations:
  - All pharyngeal infections,\(^{(69)}\)
  - Persistent symptoms or signs post-therapy,\(^{(32,62)}\)
  - Case treated with a regimen other than ceftriaxone, where ceftriaxone is first line,
  - Quinolones were given for treatment in the absence of susceptibility testing,
  - Case is linked to another case with documented antimicrobial resistance to the treatment given,
  - Antimicrobial resistance to the administered therapy is documented,\(^{(32,62)}\)
  - Case is linked to a treatment failure case that was treated with the same antibiotic,\(^{(32)}\)
Treatment failure for gonorrhea has occurred previously in the individual,
- Compliance is uncertain,
- There is re-exposure to an untreated partner,
- Infection occurs during pregnancy,\(^{(86)}\)
- Disseminated gonococcal infection is diagnosed,
- Case is a child,
- Follow-up testing should also be considered for PID if \(N.\) gonorrhoeae was initially isolated, and
- Women undergoing therapeutic abortion (TA) who have a positive test result for gonococcal infection, as they are at increased risk of developing pelvic inflammatory disease.

- If NAAT is the only choice for test of cure, tests should not be done for 2 to 3 weeks after treatment \(^{(45,46)}\) to avoid false-positive results due to the presence of non-viable organisms.

**Treatment Failure**\(^{(5)}\)

**Definition**

Treatment failure is defined as absence of reported sexual contact during the post-treatment period **AND one of the following three conditions:**

1. The presence of intracellular Gram-negative diplococci on microscopy in specimens taken at least 72 hours after completion of treatment,
   OR
2. Positive \(N.\) gonorrhoeae on culture of specimens taken at least 72 hours after completion of treatment,
   OR
3. Positive NAAT of specimens taken at least 2 to 3 weeks after completion of treatment.

**Recommended management of primary cephalosporin treatment failures**

For cephalosporin combination therapy treatment failures (such as cefixime 800 milligrams orally or ceftriaxone 250 milligrams intramuscularly plus azithromycsin 1 g orally), **local public health authorities should be promptly notified.** This will allow for the provincial and territorial STI programs to work with the Public Health Agency of Canada to post alerts related to treatment failures in Canada.

It is strongly recommended that treatment be guided by antimicrobial susceptibility test results to determine the appropriate antimicrobial agent in consultation with an expert in infectious diseases and local public health authorities.
A test of cure by culture is strongly recommended and should be collected 3 to 7 days after completion of treatment.
References


(6) Tapsall J, WHO Collaborating Center for STD and HIV. Antimicrobial resistance in Neisseria gonorrhoeae. 2001; Available at the link that follows: http://www.who.int/emc, 2013.


(16) de Vries HJ, van der Helm JJ, Schim van der Loeff MF, van Dam AP. Multidrug-resistant Neisseria gonorrhoeae with reduced cefotaxime susceptibility is increasingly common in men who have sex with men, Amsterdam, the Netherlands. Euro Surveill 2009 Sep 17;14(37):19330.


time for test-of-cure when diagnosing gonorrhoea with a nucleic acid amplification test. Acta
Derm Venereol 2012 May;92(3):316-319.

(47) Dillon JA. Sustainable Antimicrobial Surveillance Programs Essential for Controlling

(48) Kirkcaldy RD, Ballard RC, Dowell D. Gonococcal resistance: are cephalosporins next?

(49) Macdonald NE, Stanbrook MB, Flegel K, Hebert PC, Rosenfield D. Gonorrhea: what

(50) Tapsall JW, Ndowa F, Lewis DA, Unemo M. Meeting the public health challenge of
multidrug- and extensively drug-resistant Neisseria gonorrhoeae. Expert Rev Anti Infect Ther
2009 Sep;7(7):821-834.

(51) Unemo M, Shipitsyna E, Domeika M, Eastern European Sexual and Reproductive
Health (EE SRH) Network Antimicrobial Resistance Group. Recommended antimicrobial
treatment of uncomplicated gonorrhoea in 2009 in 11 East European countries:
implementation of a Neisseria gonorrhoeae antimicrobial susceptibility programme in this
region is crucial. Sex Transm Infect 2010 Nov;86(6):442-444.

(52) Black CM, Dreibe EM, Howard LA, Fajman NN. Multicenter study of nucleic acid
amplification tests for detection of Chlamydia trachomatis and Neisseria gonorrhoeae in

trachomatis among patients infected with and treated for Neisseria gonorrhoeae in sexually

(54) Ng LK, Martin IE. The laboratory diagnosis of Neisseria gonorrhoeae. Med Microbiol

39.

(56) Davies PO, Low N, Ison CA. The role of effective diagnosis for the control of

(57) McCormack WM, Stumacher RJ, Johnson K, Donner A. Clinical spectrum of gonococcal


(69) Ota KV, Fisman DN, Tamari IE, Smieja M, Ng LK, Jones KE, et al. Incidence and treatment outcomes of pharyngeal Neisseria gonorrhoeae and Chlamydia trachomatis


