AUGUST 2020 UPDATE

PHARMACOLOGICAL TREATMENT

STBBI – SYNDROMIC APPROACH

CERVICITIS AND URETHRITIS EPIDIDYMITIS/ EPIDIDYMO-ORCHITIS PELVIC INFLAMMATORY DISEASE (PID) PROCTITIS

GENERAL CONSIDERATIONS

- „This guide is a decision support tool for use when a clinical evaluation has led to the identification of a syndrome, and it deals exclusively with the management of clinical syndromes potentially associated with STBBIs prior to obtaining laboratory test results (syndromic approach).
- „The appropriate microbiological tests should be performed for all exposed sites. A culture to screen for Neisseria gonorrhoeae is still a test of choice if signs or symptoms are present, in addition to obtaining a specimen to check for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* with a nucleic acid amplification test (NAAT) (further details appendix).

MANAGEMENT

INTERVENTION WITH THE INFECTED PATIENT

The intervention should include:

- A clinical assessment including a physical examination, identifying STBBI risk factors and checking for STBBIs based on the risk factors and clinical manifestations;
- A recommendation to abstain from sexual contact for up to 7 days after a single-dose treatment **OR** until the completion of a multi-dose treatment **AND** until the symptoms have resolved[2]:
  - In case of doubt regarding abstinence, a recommendation to use barrier methods for all types of sexual contact (genital, oral-genital, anal or oral-anal);
- Support for the infected patient in the process aimed at notifying and treating his/her sexual partners. The regional public health department (DSP) can provide support in this regard.

INTERVENTION WITH SEXUAL PARTNERS

Partners should be contacted if they have had sexual contact with the infected patient:

- Within the 60 days preceding the onset of symptoms or specimen collection; **OR**
- While the patient had symptoms; **OR**
- Before the completion of a multi-dose treatment or less than 7 days after a single-dose treatment.

In certain situations, checking for partners over a longer period of time may be warranted.

The intervention should include:

- A clinical assessment, including identifying STBBI risk factors;
- Screening for the infection to which the patient may have been exposed and for other STBBIs, based on the risk factors identified. Consult the tool *ITSS à rechercher selon les facteurs de risque décelés*;
- If there are no signs or symptoms, an epidemiological treatment without waiting for the screening test results: decision algorithm;
- If there are signs or symptoms: a syndromic approach;
- Support for the person in the process aimed at notifying and treating his/her sexual partners, if the microbiological test results are positive.

For further information, consult the following tools: *Personne exposée à une ITSS : que faire?* and *Soutenir la personne atteinte d'une ITSS pour qu'elle avise ses partenaires : quatre étapes.*

NOTIFIABLE DISEASES (MADO)

The clinician is required to report laboratory-confirmed cases of C. trachomatis, N. gonorrhoeae and LGV infection to the regional DSP (further details in appendix).

MEDICATION FREE OF CHARGE

For persons registered with the Québec health insurance plan (RAMQ) and who have a valid health insurance card, claim slip or temporary proof of eligibility for medication: enter on the prescription the code **K** (for the infected patient) or **L** (for partners). The cost of 1% lidocaine without epinephrine is covered by the free program in the context of treating STIs or an associated syndrome when "diluent for ceftriaxone" is noted on the prescription.

1. For cases of suspected sexual abuse, refer to the Guide d'intervention médicosociale pour répondre aux besoins des victimes d'agression sexuelle.
2. If the individual does not comply with the abstinence instructions, consult an experienced colleague to determine the appropriate management.

CERVICITIS AND URETHRITIS

CLINICAL MANIFESTATIONS[1]

CERVICITIS:

- Abnormal vaginal discharge
- Intermenstrual or post-coital vaginal bleeding
- Purulent or mucopurulent endocervical exudate
- Do not mistake erythema associated with an ectropion with that associated with cervicitis

URETHRITIS :

- Dysuria
- Urethral discomfort
- Urethral discharge
- Pollakiuria, hematuria, vesical tenesmus and urinary
- frequency are rarely associated with urethritis. A more in-depth assessment is required if any of these symptoms is observed.

ETIOLOGY

- *C. trachomatis* and *N. gonorrhoeae*.
- If the test results are negative and the symptoms persist, consider the possibility that other pathogens, such as *Mycoplasma genitalium* or *Trichomonas vaginalis*, are present and consult an experienced colleague.
- Signs and symptoms suggestive of cervicitis can be due to other causes as well, including contraceptive methods. If there are no STBBI risk factors and no signs of pelvic inflammatory disease, the clinician can wait for the laboratory tests results before treating, provided that a reliable way of contacting the individual and that a method for issuing a prescription, if applicable, are agreed upon.

TREATMENT

1ST CHOICE:
Ceftriaxone[2] 250 mg IM in a single dose
AND
Doxycycline[3] 100 mg PO BID x 7 days

2ND CHOICE :
Ceftriaxone[2] 250 mg IM in a single dose **OR** cefixime 800 mg PO in a single dose
ET
Azithromycin[4] 2 g PO in a single dose

HISTORY OF ALLERGIC REACTION

TO A PENICILLIN ANTIBIOTIC[5]	TO A CEPHALOSPORIN
Click here to consult the antibiotic therapy decision support algorithm.	See the treatment option below.

Gentamicin[6] 240 mg IM (in two 3-ml injections)
AND
Azithromycin[4] 2 g PO in a single dose

FOLLOW-UP

CERVICITIS:

- Investigate further or consult an experienced colleague
- if the symptoms persist beyond 48 to 72 hours or reappear after the completion of treatment.
- Tests of *cure are recommended*, depending on the pathogens identified.

URETHRITIS:

- It can take up to 7 days for the symptoms to disappear.
- Investigate further or consult an experienced colleague if the symptoms persist or reappear.
- Tests of cure are recommended, depending on the pathogens identified.

1. Syndromes do not always present all of the clinical manifestations listed.
2. To reduce the discomfort associated with injection, the preferred diluent for ceftriaxone is 1% lidocaine without epinephrine.
3. Doxycycline is contraindicated in pregnant women. If required, it is compatible with breastfeeding if the duration of treatment is less than 3 weeks.
4. If the patient vomits within an hour after taking azithromycin, administer a prophylactic antiemetic and then another dose of azithromycin.
5. Penicillin G or V, ampicillin, amoxicillin, cloxacillin or piperacillin.
6. Not approved by Health Canada for this indication.

EPIDIDYMITIS/EPIDIDYMO-ORCHITIS

CLINICAL MANIFESTATIONS[1]

- Progressive and typically unilateral testicular pain[2]
- Tenderness of the epididymis or the testicle upon palpation
- Palpable swelling of the epididymis
- Urethral discharge
- Hydrocele
- Erythema or edema of the scrotum on the affected side
- Fever

Consultation with an experienced colleague and hospitalization should be considered when severe pain or fever suggests another diagnosis (testicular torsion, testicular infarction, abscess or necrotizing fasciitis). High fever is unusual and indicates a complicated infection. A more in-depth assessment is recommended.

ETIOLOGY AND TREATMENT

C. trachomatis or *N. gonorrhoeae* in a male with STBBI risk factors	Bâtonnets Gram négatif acquis par exemple lors de manipulations urologiques ou de relations sexuelles anales insertives non protégées	Une combinaison des deux étiologies précédentes
With STBBI risk factors AND with no risk of infection by Gram-negative rods	**With no STBBI risk factors AND with a risk of infection by Gram-negative rods[5]**	**With STBBI risk factors AND with a risk of infection by Gram-negative rods[5]**
Ceftriaxone[3,4] 250 mg IM in a single dose **AND** Doxycycline[3] 100 mg PO BID x 14 days	Initiate treatment with ciprofloxacin[3,6] 500 mg PO BID for 10 to 14 days **AND** reassess upon receiving the results of the antibiogram executed on the strain isolated from the urine culture	Ceftriaxone[3,4] 250 mg IM in a single dose **AND** Levofloxacin[3,6] 500 mg PO daily x 10 days

HISTORY OF ALLERGIC REACTION

TO A PENICILLIN ANTIBIOTIC[7]	TO A CEPHALOSPORIN
Clic here to consult the antibiotic therapy decision support algorithm.	See the treatment option below.
Consult an experienced colleague.	

FOLLOW-UP

- The diagnosis and treatment should be reassessed if there is no clinical improvement within 48 to 72 hours after the start of treatment.
- Examine the patient again approximately 1 month after the completion of treatment to check that there are no persistent testicular abnormalities.
- Tests of cure are recommended, depending on the pathogens identified.

1. Syndromes do not always present all of the clinical manifestations listed.
2. Testicular torsion should be considered if there is acute pain (more common in males under 20 years of age). It constitutes a surgical emergency.
3. Not approved by Health Canada for this indication.
4. To reduce the discomfort associated with injection, the preferred diluent for ceftriaxone is 1% lidocaine without epinephrine.
5. Specimens to check for C. trachomatis and N. gonorrhoeae (NAAT and culture) must be obtained and a urine culture done before treatment is initiated.
6. A warning has been issued about the use of quinolones in patients under 18 years of age. Consult an experienced colleague.
7. Penicillin G or V, ampicillin, amoxicillin, cloxacillin or piperacillin.

PELVIC INFLAMMAORY DISEASE (PID)

CLINICAL MANIFESTATIONS[1]

The following manifestations, associated or not with cervicitis, are indicative of a pelvic inflammatory disease diagnosis:

- Deep dyspareunia;
- Fever;
- Lower abdominal tenderness, adnexal tenderness (unilateral or bilateral) or cervical motion tenderness.

The non-detection of *C. trachomatis* or *N. gonorrhoeae* in specimens taken during the clinical assessment does not rule out a diagnosis of pelvic inflammatory disease.

ETIOLOGY

Treatment regimens should cover a broad spectrum of pathogens, including STBBI pathogens, in addition to accounting for the polymicrobial nature of pelvic inflammatory diseases.

TREATMENT PRINCIPLES

- This guide presents only orally and intramuscularly administered treatments.
- Rule out the possibility of pregnancy.
- Intrauterine device (IUD): Immediate removal is not required. An assessment is recommended 48 to 72 hours after the start of antibiotic therapy. However, the antibiotic therapy must be started prior to the removal, if applicable, of the IUD.
- If antibiotic therapy is initiated on an inpatient basis, outpatient therapy should continue until the completion of 14 days of therapy.

Critères d'hospitalisation ou d'orientation vers un collègue expérimenté :

- Suspected surgical emergency (e.g., appendicitis or ectopic pregnancy)
- Severe impairment of overall condition, nausea, vomiting or high fever
- Suspected tubo-ovarian abscess
- Pregnancy
- Moderate or severe immunosuppression
- Anticipated problem with compliance with outpatient antibiotic therapy
- Intolerance to outpatient antibiotic therapy
- No clinical response after 3 days of antibiotic therapy

TREATMENT

Ceftriaxone[2, 3] 250 mg IM in a single dose

AND

Doxycycline[2, 4] 100 mg PO BID x 14 days

AND

Metronidazole[2, 5] 500 mg PO BID x 14 days

HISTORY OF ALLERGIC REACTION

TO A PENICILLIN ANTIBIOTIC[6]	TO A CEPHALOSPORIN
Cliquer ici pour consulter l'algorithme pour aider dans le choix de l'antibiothérapie.	See the treatment option below.

Consult an experienced colleague.

FOLLOW-UP

- Patients should be closely monitored and be re-examined 3 days after treatment initiation to check for clinical improvement.
- Tests of cure are recommended, depending on the pathogens identified.

1. Syndromes do not always present all of the clinical manifestations listed.
2. Not approved by Health Canada for this indication.
3. To reduce the discomfort associated with injection, the preferred diluent for ceftriaxone is 1% lidocaine without epinephrine.
4. Doxycycline is contraindicated in pregnant women. If required, it is compatible with breastfeeding if the duration of treatment is less than 3 weeks.
5. In the event of incapacitating nausea or vomiting, recommend that metronidazole be discontinued in favour of doxycycline.
6. Penicillin G or V, ampicillin, amoxicillin, cloxacillin or piperacillin.

RECTITE

CLINICAL MANIFESTATIONS[1]

- Mucopurulent rectal discharge
- Anorectal pain
- Bloody stool
- Tenesmus
- Constipation

ETIOLOGY

- *N. gonorrhoeae*, *C. trachomatis* (LGV and non-LGV genotypes), *Treponema pallidum* (syphilis) and the herpes simplex virus
- Inflammatory bowel disease
- Tissue damage caused by the insertion of foreign bodies

If diarrhea and abdominal cramping occur, consider an infection by enteropathogens, such as *Shigella* spp. or *Campylobacter* spp., which can be transmitted by oral-anal contact.

TREATMENT PRINCIPLES

In addition to screening for N. gonorrhoeae by culture and NAAT and for C. trachomatis by rectal NAAT, it is strongly recommended to serologically test all patients with proctitis for syphilis and the human immunodeficiency virus (HIV).

TREATMENT IF STBBI ETIOLOGY

1ST CHOICE:	2ND CHOICE:
Ceftriaxone[2] 250 mg IM in a single dose **AND** Doxycycline[3, 4] 100 mg PO BID x 7 days	Cefixime 800 mg PO in a single dose **AND** Azithromycin[3, 5] 2 g PO in a single dose **AND** Doxycycline[3, 4] 100 mg PO BID x 7 days

HISTORY OF ALLERGIC REACTION

TO A PENICILLIN ANTIBIOTIC[6]	TO A CEPHALOSPORIN
Clic here to consult the antibiotic therapy decision support algorithm.	See the treatment option below.

Gentamicin[3] 240 mg IM (in two 3-ml injections)
AND
Azithromycin[3, 5] 2 g PO in a single dose

FOLLOW-UP

- A clinical follow-up is required until the symptoms resolve.
- If the patient tests positive for C. trachomatis with an LGV genotype, initiate or continue treatment with doxycycline3, 4 100 mg PO BID for a total of 21 consecutive days. For further details, consult the MSSS's clinical tool on LGV.
- Tests of cure are recommended, depending on the pathogens identified.

1. Syndromes do not always present all of the clinical manifestations listed.
2. To reduce the discomfort associated with injection, the preferred diluent for ceftriaxone is 1% lidocaine without epinephrine.
3. Not approved by Health Canada for this indication.
4. Doxycycline is contraindicated in pregnant women. If required, it is compatible with breastfeeding if the duration of treatment is less than 3 weeks.
5. If the patient vomits within an hour after taking azithromycin, administer a prophylactic antiemetic and then another dose of azithromycin.
6. Penicillin G or V, ampicillin, amoxicillin, cloxacillin or piperacillin.

ANTIBIOTIC RESISTANCE

N. gonorrhoeae resistance to the different antibiotics is increasing rapidly, and the recommended treatments may eventually be modified according to strains' changing susceptibility to these drugs. Close vigilance by practitioners is required. Here is a summary of N. gonorrhoeae antibiotic resistance in Québec. For further details, consult the LSPQ's website.

- Resistance to quinolones and tetracyclines is well established.
- Resistance to azithromycin is rapidly on the increase.
- Resistance to third-generation cephalosporins is emerging.

REINFECTION

To check that there is no reinfection, recommend to all persons infected with *C. trachomatis* or *N. gonorrhoeae* that they have a screening test 3 to 6 months after the treatment of the initial infection. Screening following a documented infection is in addition to the previously performed test of cure, if indicated.

TESTS OF CURE

- When laboratory test (culture or NAAT) results show the presence of C. trachomatis or N. gonorrhoeae, determine whether a test of cure is indicated.

	C. TRACHOMATIS INFECTION	*N. GONORRHOEAE* INFECTION
INDICATIONS	A test of cure **is not recommended** in cases of *C. trachomatis* infection, except in the following situations: ▸ Persistence or appearance of signs or symptoms ▸ Pregnancy ▸ An anticipated treatment compliance problem ▸ A treatment regimen other than one of those recommended is being used ▸ Rectal *C. trachomatis* infection treated with azithromycin ▸ *C. trachomatis infection of genotype* $L_{1\text{-}3}$ (LGV)	A test of cure is **recommended in all cases** of gonococcal infection, especially in the following situations: ▸ Persistence or appearance of signs or symptoms ▸ Pregnancy ▸ An anticipated treatment compliance problem ▸ A treatment regimen other than one of those recommended is being used ▸ A pharyngeal infection (even if treated with ceftriaxone) ▸ The use of a treatment regimen combining gentamicin and azithromycin, given a history of allergic reaction ▸ Known resistance or reduced susceptibility1 to one of the antibiotics used ▸ Partner of a person in whom resistance or reduced susceptibility1 to one of the antibiotics used has been demonstrated
SPECIMENS AND TESTS	NAAT performed as soon as possible, starting from 3 weeks after the completion of treatment	**In the case of a pharyngeal infection[2]:** NAAT[3] and culture performed as soon as possible, from 2 weeks after the completion of treatment, **OR** culture[4] done as soon as possible, from 3 days and up to 2 weeks after the completion of treatment. **In the case of a non-pharyngeal infection[2]:** NAAT performed as soon as possible, from 2 weeks after the completion of treatment[5]. If the patient presents with symptoms at the follow-up visit, obtain a culture specimen as well. A culture performed as soon as possible, from 3 days and up to 2 weeks after the completion of treatment, can also be considered.

1. Cut-off for reduced susceptibility to cefixime set at a minimum inhibitory concentration (MIC) ≥ 0.125 mg/L.
2. If a follow-up appointment is scheduled for 2 weeks after the completion of treatment, the patient should be advised to return earlier if symptoms persist or appear. In such case, culture specimens should be obtained.
3. A NAAT performed on a throat specimen may be associated with false-positive results. For positive follow-up pharyngeal NAATs, consult Appendix 4 of the INSPQ's explanatory guide for further details on management.
4. An additional NAAT specimen may be taken from 2 weeks onwards at the clinician's discretion.
5. If the follow-up NAAT result is positive, it is advisable to obtain a culture specimen, provided this does not delay treatment.

STBBI-RELATED PREVENTIVE INTERVENTIONS

When a person consults a medical practitioner, for instance, about an STBBI, contraception or a routine clinical examination, the practitioner should:

- Inquire about STBBI risk factors and screen accordingly, as many people are asymptomatic and do not know that they are infected;
- Inform the person about safer sexual practices and encourage consistent use;
- Vaccinate against hepatitis A and B and the human papillomavirus as indicated in the *Protocole d'immunisation du Québec*.

Preexposure prophylaxis (PrEP) may be considered in certain populations at risk for contracting HIV. If necessary, consult the following tool from the MSSS *Guide PPrE pour les professionnels de la santé du Québec.*

A variety of STBBI-related preventive intervention tools are available on the MSSS's website, such as:

- *Guide québécois de dépistage des ITSS*
- *ITSS à rechercher selon les facteurs de risque décelés*
- *Prélèvements et analyses recommandés chez une personne asymptomatique - Infections à* Chlamydia trachomatis *ou à* Neisseria gonorrhoeae *- Lymphogranulomatose vénérienne*
- *Prélèvements et analyses recommandés chez une personne asymptomatique - Syphilis, hépatites B et C, VIH*
- *Personne exposée à une ITSS : que faire?*
- *Soutenir la personne atteinte d'une ITSS pour qu'elle avise ses partenaires : quatre étapes*
- *Estimation du risque associé aux activités sexuelles*
- *Vaccination et ITSS*
- *Ressources – Intervention préventive relative aux ITSS*
- *Site Internet, dépliants et brochures à l'intention des patients* (e. g., *Entre caresses et baisers, une ITSS s'est faufilée… Il faut en parler)*

REFERENCES

To consult the references, see the report in support of the OUG.

Institut national d'excellence en santé et en services sociaux
Québec

STBBI - SYNDROMIC APPROACH

ASSESS THE SEVERITY OF THE INITIAL REACTION

SEVERITY OF PREVIOUS ALLERGIC REACTION TO PENICILLIN ANTIBIOTICS

Vague history

Unconvincing history reported by patient or family

Non-severe reaction

Immediate reaction[1]

Isolated cutaneous involvement

(urticaria and/or angioedema)

or

Delayed reaction[2,3]

Isolated cutaneous involvement

(Rash and/or urticaria and/or angioedema)

- Reaction in childhood[3]
- Reaction in adulthood
  - Distant past (≥ 10 years)
  - Recent

Severe reaction

Immediate reaction

Anaphylaxis[4]

or

Delayed reaction

Severe skin reaction

desquamation, pustules, vesicles, purpura with fever or joint pain, but **no** DRESS, SJS/TEN, or AGEP)

Serum sickness[3]

or

Penicillin allergy

CONFIRMED[5]

(severe or non-severe reaction only)

Very severe reaction

Immediate reaction

Anaphylactic shock

(with or without intubation)

or

Delayed reaction

Hemolytic anemia
Kidney damage
Liver damage

DRESS, SJS/TEN, AGEP

DECISION-MAKING FOR CHOOSING A BETA-LACAM AND THE CONDITIONS OF ADMINISTRATION

THE FOLLOWING CAN BE PRESCRIBED SAFELY

DISSIMILAR cephalosporins

Cefixime **OR** Ceftriaxone

according to treatment recommendations

PRESCRIBE THE FOLLOWING WITH CAUTION

DISSIMILAR cephalosporins

Cefixime **OR** Ceftriaxone

according to treatment recommendations

The 1st dose should **always** be administered under medical supervision.

If history of :

- **Immediate reactions,** a drug provocation test should be performed;
- **Delayed reactions,** the patient or his/her family should be informed of the possible risk of recurrence in the days following initiation of the antibiotic.

!

IF A BETA-LACTAM[6] CANNOT BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED...

according to the treatment recommendation in case of a history of allergic reaction

AVOID PRESCRIBING

A beta-lactam[6]

Choose another class of antibiotics.

and

PRESCRIBE THE FOLLOWING

according to the treatment recommendation in case of a history of allergic reaction

1. Immediate reaction (type I or IgE-mediated): generally occurs within 1 hour following the **first dose** of an antibiotic.
2. Delayed reaction (type II, III or IV): can occur at any time, starting 1 hour following the administration of an antibiotic.
3. The delayed skin reactions and serum sickness-like reactions that appear in children receiving antibiotic therapy are generally non-allergic and can be of viral origin.
4. Anaphylaxis without shock or intubation: requires increased vigilance.
5. With no recommendations concerning other beta-lactams.
6. Penicillins, cephalosporins and carbapenems.

AGEP : acute generalized exanthematous pustulosis;
DRESS : drug reaction with eosinophilia and systemic symptoms;
SJS : Stevens–Johnson syndrome;
TEN : toxic epidermal necrolysis.

For further information, see the interactive tool and the decision-making tool.

Further information on pharyngeal NAATs positive for *N. gonorrhoeae*

- „ For pharyngeal N. gonorrhoeae infections detected by NAAT, the specimen is sent to the LSPQ for confirmation. See the INSPQ's explanatory guide for the recommendations concerning management in light of a positive preliminary NAAT result for N. gonorrhoeae on a pharyngeal specimen. These recommendations are grouped together in the INSPQ guide in the form of a management algorithm:
  - Appendix 3: "Algorithme clinique pour la prise en charge des infections à *N. gonorrhoeae* ; prélèvement initial".

Further information on notifiable diseases (MADO)

- When the specimen is sent to the LSPQ to confirm the *N. gonorrhoeae*-positive NAAT result, the microbiology laboratory immediately reports the case to the DSP, based on the preliminary result.
- The LSPQ will send the final confirmatory test result to the DSP. The initial notifier does not have to submit a second form, regardless of the result of the confirmatory test.