LYME DISEASE IN ADULTS

GENERAL INFORMATION

WHAT IS LYME DISEASE?
• Lyme disease is an infectious disease caused by bacterial genospecies of Borrelia burgdorferi, which are transmitted to humans by black-legged ticks that are carriers.
• It is a notifiable disease (MADO) and is on the increase in Québec.
• It can affect several anatomical systems at the same time.

WHAT ARE THE DIFFERENT STAGES OF THE DISEASE?

Localized stage (sometimes called the early stage): Beginning of the infection before dissemination of the bacteria in the bloodstream.
• Main manifestation observed:
  → Not always present or noticed.
  → If present, usually appears 3 to 30 days after infection but can appear up to 3 months post-bite.

Isolated cutaneous manifestation (isolated erythema migrans)

Early disseminated stage
Bacterial dissemination via the bloodstream.
• Generally occurs when the local infection has not been detected or has not been treated effectively.
• Occurs a few days after isolated erythema migrans to a few weeks after infection (usually up to 6 months post-bite).
• Can include general systemic symptoms.
• Main manifestations observed:

Late disseminated stage
Complication of the early disseminated stage.
• Occurs a few weeks or even a few months after infection (usually up to a year post-bite).
• Main manifestation observed in North America:

Articular (Lyme arthritis)

RISK FACTORS

The risk of tick exposure:
• Depends on lifestyle, outdoor activities (recreation or work), places visited or place of residence, and being around pets that have been outdoors;
• Is present throughout the year but is negligible in the winter in Québec, except for people who travel to areas where the climate is favourable for ticks (Québec, other Canadian provinces, the United States, Europe).

If the bite is painless and the tick is small, the patient will often not have any recollection of having been bitten.
### CLINICAL PRESENTATION

- The diagnostic process should include:
  - A tick exposure risk assessment;
  - A thorough physical examination that includes a neurological examination and a search for erythema migrans and manifestations of the disseminated stage;
- Considering other possible clinical conditions (consult the [nonexhaustive list of differential diagnoses](#)).
- The clinical manifestations of Lyme disease are not mutually exclusive. The presentation, the severity of the manifestations, their duration and the speed of progression of the disease from one stage to the next vary from patient to patient.
- Refer to the [Lyme disease diagnostic support tool](#) to view the recommended algorithm and for information on when serological tests are indicated and how to interpret them.

### MAIN MANIFESTATIONS OF LYME DISEASE (other systems may be affected)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs and presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous manifestations</td>
<td>Little or no pain or itching.</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Neurological manifestations</td>
<td>Facial palsy (sometimes bilateral); Facial numbness; Deafness; Diplopia.</td>
</tr>
<tr>
<td></td>
<td>Lower motor neuron-type weakness affecting one or more nerve or root territories; Paresthesia or hypoesthesia affecting one or more nerve or root territories; Abolition of one or more deep tendon reflexes.</td>
</tr>
<tr>
<td></td>
<td>Headache; Nuchal pain or stiffness; Photophobia; Nausea; Vomiting.</td>
</tr>
<tr>
<td>Cardiac manifestations</td>
<td>Chest pain; Palpitations; Dyspnea; Syncope; Dizziness.</td>
</tr>
<tr>
<td>Articular manifestations</td>
<td>Joint swelling often worse than the pain and the other associated symptoms; In most cases, the knee is affected.</td>
</tr>
</tbody>
</table>

1. Examples of other manifestations: non-neurological ocular manifestations (uveitis, keratitis, conjunctivitis, episcleritis, retinitis and choroiditis).
2. General systemic symptoms may also be present: fever and chills, malaise, fatigue, muscle pain, joint pain, concentration and memory problems, headaches, isolated lymphadenopathy, flu-like syndrome (consistent with Lyme disease, particularly if it occurs during the summer), mononucleosis syndrome (consistent with Lyme disease, particularly if it occurs during the summer), asthenia, lethargy and anorexia.

**Legend:**
- Photos available as a diagnostic aid.
**TREATMENT PRINCIPLES**

- In a patient who presents with a cutaneous manifestation with no other manifestations suggestive of the disseminated stage:
  - If there is some hesitation between a diagnosis of infectious cellulitis and one of erythema migrans of Lyme disease, opt for a treatment that would cover both diseases (e.g., cefuroxime axetil).
- As soon as a diagnosis of erythema migrans is made, antibiotic therapy can be initiated immediately (serological tests are not indicated in this case).
- After diagnosing a manifestation attributable to Lyme disease (e.g., isolated erythema migrans), the clinician should always check for signs and symptoms of involvement in other anatomical systems in order to choose the appropriate antibiotic therapy.
- In situations where neurological, cutaneous (multiple erythema migrans), cardiac or articular manifestations might be attributed to Lyme disease, based on the clinical presentation, and while waiting for the laboratory test results, antibiotic therapy could be initiated after a discussion with one or more medical specialists or an experienced colleague.
- Doxycycline and beta-lactams are the preferred treatments for the main manifestations of Lyme disease. In the event that these drugs cannot be prescribed (e.g., an absolute contraindication, a history of very severe allergic reaction to penicillins), macrolides can be used to treat isolated erythema migrans. However, for the other clinical manifestations, the choice of antibiotic should be discussed with a medical specialist.

**ANTIBIOTIC THERAPY**

**IMPORTANT INFORMATION ON THE USE OF DOXYCYCLINE DURING PREGNANCY AND BREASTFEEDING**

- In pregnant women: doxycycline is contraindicated for treating any of the clinical manifestations of Lyme disease.
- In breastfeeding women: doxycycline might be considered:
  - First-line treatment for cutaneous, neurological or cardiac manifestations after an informed discussion with the patient:
    - Tetracyclines are found in low concentrations in breast milk, and the available data indicate that there is no detectable trace of tetracycline in the serum of exposed infants;
    - According to several reference works on drugs during pregnancy, the short-time use of tetracyclines is acceptable.
  - Another treatment option for articular manifestations in patients with a history of very severe allergic reaction to a penicillin antibiotic.

**CUTANEOUS MANIFESTATIONS WITH OR WITHOUT GENERAL SYSTEMIC SYMPTOMS**

<table>
<thead>
<tr>
<th></th>
<th>1ST LINE</th>
<th>OTHER OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>** Antibiotic and dosage</td>
<td>Duration</td>
<td>Antibiotic and dosage</td>
</tr>
<tr>
<td><strong>Isolated erythema migrans with no general systemic symptoms</strong></td>
<td>Doxycycline PO 100 mg BID</td>
<td>10 days (10-14 days)</td>
</tr>
<tr>
<td><strong>Isolated erythema migrans with general systemic symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Multiple erythema migrans ± general systemic symptoms</strong></td>
<td></td>
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</tr>
</tbody>
</table>

Reasons for consulting, or referring the patient to, one or more medical specialists:
- Neurological, cardiac or articular manifestations occur during treatment.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the cutaneous manifestations with or without general systemic symptoms to Lyme disease needs to be re-examined.

1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.
### Neurological Manifestations (Neuroborreliosis)

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>1st Line</th>
<th>Other Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral nervous system involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(e.g., cranial mononeuritis or multiple mononeuritis, plexopathy or radiculopathy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline PO</td>
<td>100 mg BID</td>
<td>Amoxicillin PO</td>
</tr>
<tr>
<td></td>
<td>14 days (14-21 days)</td>
<td>500 mg TID or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefuroxime axetil PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 mg BID</td>
</tr>
<tr>
<td><strong>Central nervous system involvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(including optic neuritis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>or Meningitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone IV</td>
<td>2 000 mg QD</td>
<td>Cefotaxime IV</td>
</tr>
<tr>
<td></td>
<td>14 days (10-28 days)</td>
<td>2 000 mg TID or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penicillin G IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18 - 24 million units divided every 4 hours</td>
</tr>
</tbody>
</table>

**Reasons for consulting, or referring the patient to, one or more medical specialists:**

- Suspicion of neuroborreliosis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- The occurrence of articular manifestations during treatment. In such case, consideration might be given to prolonging the treatment to 28 days.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the neurological manifestations to neuroborreliosis needs to be re-examined.

### Cardiac Manifestations (Lyme Carditis)

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>1st Line</th>
<th>Other Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1st degree AV block</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with PR interval &lt; 300 ms2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline PO</td>
<td>100 mg BID</td>
<td>Amoxicillin PO</td>
</tr>
<tr>
<td></td>
<td>14 days (14-21 days)</td>
<td>500 mg TID or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefuroxime axetil PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 mg BID</td>
</tr>
<tr>
<td><strong>1st degree AV block</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with PR interval &gt; 300 ms3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-degree AV block (2nd- or 3rd-degree)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone IV</td>
<td>2 000 mg QD</td>
<td>Cefotaxime IV</td>
</tr>
<tr>
<td></td>
<td>14 days (2nd- or 3rd-degree)</td>
<td>2 000 mg TID or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penicillin G IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18 - 24 million units divided every 4 hours</td>
</tr>
</tbody>
</table>

**Reasons for consulting, or referring the patient to, one or more medical specialists:**

- Suspicion of Lyme carditis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- Examining the possibility of switching to the PO route.
- The occurrence of neurological or articular manifestations during treatment. In such case, consideration might be given to changing the antibiotic or the duration of treatment.
- Symptoms persist post-treatment.
- The antibiotic therapy fails, or the attribution of the cardiac manifestations to Lyme carditis needs to be re-examined.

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1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.
2. PO therapy should be accompanied by serial ECGs for monitoring purposes.
3. Cardiac monitoring should be done in cases where treatment is administered intravenously.
**ARTICULAR MANIFESTATIONS (LYME ARTHRITIS)**

<table>
<thead>
<tr>
<th></th>
<th>1ST LINE</th>
<th>OTHER OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic and dosage</strong></td>
<td><strong>Duration</strong></td>
<td><strong>Antibiotic and dosage</strong></td>
</tr>
<tr>
<td>Lyme arthritis</td>
<td>Doxycycline PO 100 mg BID</td>
<td>28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence of Lyme arthritis</td>
<td>Doxycycline PO 100 mg BID</td>
<td>28 days</td>
</tr>
</tbody>
</table>

**Reasons for consulting, or referring the patient to, one or more medical specialists:**

- Suspicion of Lyme arthritis (clinical evaluation and decision to be made regarding 1st-line antibiotic therapy).
- The antibiotic therapy fails, or the attribution of the arthritis to Lyme disease needs to be re-examined.
- Symptoms persist post-treatment despite two courses of antibiotic (the decision not to prescribe a new antibiotic should be made on a case-by-case basis).

**Additional information:**

- The use of corticosteroids should be avoided when treating Lyme arthritis with antibiotics.
- Consideration may be given to using nonsteroidal antiinflammatories (NSAIDs) for the PRN treatment of pain, in addition to antibiotics.
- An intra-articular corticosteroid injection or the use of a disease-modifying antirheumatic drug might be considered after appropriate antibiotic therapy. If need be, the opinion of a medical specialist or an experienced colleague should be sought.

1. The time intervals proposed for the durations of treatment are based on the selected primary studies, clinical practice recommendations and guidelines.

**HISTORY OF ALLERGIC REACTION TO PENICILLINS**

<table>
<thead>
<tr>
<th>CONFIRMED ALLERGY TO PENICILLINS</th>
<th>CROSS-ALLERGIES TO DISSIMILAR CEPhALOSPORINS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Of 100 people who report a history of allergy to a penicillin, a diagnosis of allergy will be confirmed in:</td>
<td>Of 100 people with a confirmed allergy to penicillins, a cross-reaction with a “dissimilar” cephalosporin may be observed in:</td>
</tr>
<tr>
<td>Fewer than 10 of them (adults)</td>
<td>1 or 2 of them</td>
</tr>
<tr>
<td>Cefotaxime 1.08 (0.27; 4.22)</td>
<td>Absolute risk (95% confidence interval)</td>
</tr>
<tr>
<td>Ceftriaxone 0.43 (0.07; 2.62)</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime axetil 0.79 (0.18; 3.33)</td>
<td></td>
</tr>
</tbody>
</table>

Carefully assess the patient’s allergy status during the visit before considering an antibiotic other than a “dissimilar” cephalosporin.

Cliquez here to view the algorithm specific to Lyme disease.
INFORMATION TO BE GIVEN TO THE PATIENT

ASK THE PATIENT:

- To watch for Lyme disease symptoms during the observation period, as well as during and after treatment (refer to the follow-up sheet);
- To take a photo including a measuring device, if applicable, of the redness if doubt persists as to it being attributed to Lyme disease.
- To contact a health professional, if necessary.

INFORM THE PATIENT:

- That they can take an antipyretic/analgesic (e.g., acetaminophen or ibuprofen) in addition to their antibiotic therapy to relieve the pain and general systemic symptoms.
- That a Jarisch-Herxheimer reaction could occur after antibiotic therapy is initiated. This systemic inflammatory reaction can occur when treating an infection caused by spirochete bacteria, such as those in the *Borrelia burgdorferi* group.
  - However, it should not result in the antibiotic being discontinued. If in doubt, a health professional must be contacted.

ADVISE THE PATIENT:

- That, as a general rule, they should recover completely after the antibiotic therapy, especially if they are treated early and for erythema migrans.
- That for certain manifestations of the disseminated stages (e.g., facial palsy and arthritis), symptoms may persist for weeks or even months after appropriate antibiotic therapy, hence a possible significant impact on their quality of life.
- To consult a health professional if the symptoms do not improve or if they recur after the end of treatment.

MONITORING

- The clinical condition of a patient diagnosed with Lyme disease who experiences persistent symptoms after antibiotic therapy should be reevaluated jointly with one or more medical specialists, depending on the symptoms, if severity and duration of the symptoms since the end of treatment seem unusual and cannot be explained by other likely clinical conditions.

\[\text{Serological tests are not indicated for monitoring the effectiveness of antibiotic therapy.}\]

MAIN REFERENCES


LYME DISEASE IN ADULTS

ASSESS THE SEVERITY OF THE INITIAL REACTION AND ASSESS THE RISKS INVOLVED

Vague history

Unconvincing history reported by patient or family

Non-severe reaction

Immediate reaction

Isolated cutaneous involvement
(urticaria and/or angioedema)

Delayed reaction

Isolated cutaneous involvement
(MPR and/or urticaria and/or angioedema)

Severe reaction

Immediate reaction

Anaphylaxis

Delayed reaction

Severe skin reaction
(desquamation, pustules, vesicles, purpura with fever or joint pain, but no DRESS, SJS/TEN, AGEP)

Allergy to penicillins CONFIRMED
(non-severe and severe reaction only)

Very severe reaction

Immediate reaction

Anaphylactic shock
(with or without intubation)

Delayed reaction

Hemolytic anemia
Renal involvement
Hepatic involvement
DRESS, SJS/TEN, AGEP

SEVERITY OF PREVIOUS ALLERGIC REACTION TO PENICillin ANTIBiotics

Reaction in childhood

Long time ago (≥10 years)

Reaction in adulthood

Recent

THE FOLLOWING CAN BE PRESCRIBED SAFELY:

DISSIMILAR cephalosporins
Cefuroxime axetil OR Ceftriaxone IV
OR Cefotaxime IV

* IV administration if the PO option is not tolerated.

PRESCRIBE THE FOLLOWING WITH CAUTION:

DISSIMILAR cephalosporins
Cefuroxime axetil OR Ceftriaxone IV
OR Cefotaxime IV ONLY

* IV administration if the PO option is not tolerated.

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.

Avoid prescribing:

Amoxicillin
Penicillin G

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.

Avoid prescribing:

Amoxicillin
Penicillin

IF NEITHER DOXYCYCLINE NOR A BETA-LACTAM CAN BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED:

Azithromycin
Clarithromycin

To treat isolated EM

To treat isolated EM

AVOID PRESCRIBING:

Beta-lactam

Choose another class of antibiotics.
If strong indication of a beta-lactam, obtain a consultation with specialized services.

IF NEITHER DOXYCYCLINE NOR A BETA-LACTAM CAN BE ADMINISTERED, THE FOLLOWING CAN BE PRESCRIBED:

Azithromycin
Clarithromycin

To treat isolated EM

1. Immediate reaction (type I or IgE-mediated): usually occurs within one hour after taking the first dose of a drug.
2. Delayed reaction (type II, III or IV): may occur at any time from 1 hour after administration of a drug.
3. Delayed skin reactions and serum sickness-like reactions that occur in children on antibiotic therapy are generally nonallergic and may be of viral origin.
4. Anaphylaxis without shock or intubation requires an extra level of vigilance.
5. With no recommendations concerning other beta-lactams.
6. Penicillins, cephalosporins and carbapenems.
7. Unless the patient has a heart defect due to possible QT interval prolongation.

For further information on the clinical manifestations, consult the interactive tool.

AGEP: acute generalized exanthematous pustulosis;
DRESS: drug reaction with eosinophilia and systemic symptoms;
EM: erythema migrans;
MP R: maculopapular rash;
SJS: Stevens–Johnson syndrome;
TEN: toxic epidermal necrolysis.
LYME DISEASE IN ADULTS

Alternatives if neither doxycycline nor a beta-lactam can be administered to treat isolated erythema migrans

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin¹</td>
<td>500 mg QD PO</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg BID PO</td>
<td>14-21 days</td>
</tr>
</tbody>
</table>

¹ Unless the patient has a heart defect due to possible QT interval prolongation.