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Lyme disease in Canada

Developed by Katie Girgulis, Stephanie Zahradnik and Dr. Nicole Le Saux for PedsCases.com.

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Introduction:

Hi everyone – thanks for listening to this PedsCases Podcast. My name is Katie Girgulis, and I am a PGY3 Pediatric Resident at Dalhousie University and the IWK Health Centre. My name is Stephanie Zahradnik, currently a PGY4 Paediatric Infectious Diseases Resident at the University of Toronto and The Hospital for Sick Children. This podcast was created in collaboration with Dr. Nicole Le Saux, a Pediatric Infectious Disease physician at the Children’s Hospital of Eastern Ontario in Ottawa. Dr Le Saux is an author of the 2020 Canadian Paediatric Society practice point that will be reviewed in this podcast. Today, we are going to review an infection that has become increasingly common in many parts of Canada – Lyme disease.

We are going to start with a little “virtual poll”. Take a moment and think to yourself:

- (a) Have you seen ticks in your community?
- (b) Have you diagnosed a child with erythema migrans or another manifestation of Lyme disease (such as arthritis)?
- (c) Do you feel comfortable treating Lyme disease in children of different ages and clinical presentations?
- (d) Have you advised a family about what to do after a tick bite?

Depending on where you live and practice in Canada, you may be more or less familiar with Lyme disease. I know that I, for one, had limited exposure while I was training in Alberta. Now, living now in Nova Scotia, I have become much more familiar with Lyme disease! You likely share my sentiment if you work in parts of British Columbia, Manitoba, Ontario, Quebec, New Brunswick, or Nova Scotia – as these are all regions in Canada where there are plenty of black-legged ticks. Provincial Public Health authorities keep up to date data on where Lyme disease is more prevalent or “endemic.”

Before we dive into the details, let’s review the main learning objectives. By the end of this podcast, you should be able to:

1. State the cause of Lyme disease and how it is transmitted to humans

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2. Recognize the three phase of Lyme disease: early localized, early disseminated and late disseminated Lyme disease
3. Appropriately decide when serological testing for Lyme disease is required, and ensure that you are always sending to an approved Canadian laboratory
4. List treatment options for different manifestations of Lyme disease
5. Educate families about Lyme disease prevention

We will start with an overview of the disease. Lyme disease is a tick-borne infection. Specifically, it is caused by the spirochete bacteria *Borrelia burgdorferi*. It can be transmitted to humans through a bite from an infected black-legged tick; *Ixodes scapularis* in Eastern and Central Canada, and *Ixodes pacificus* in British Columbia. These ticks are primarily carried by mice (and other small rodents), small mammals, birds, and white-tailed deer. Ticks cannot jump or fly but are sneaky little fellas and will hang out in tall grasses or shrubs until something brushes by that they can attach on to. Of note, ticks can be tricky to spot. Un-engorged adult ticks are the size of a sesame seed, and nymphs are the size of a poppy seed! They often burrow in the skin at sites where their movement is impeded, such as the hairline, axilla, or at the elastic from clothing. Based on the life cycle of black-legged ticks, the highest risk for infection is late spring and summer.

Now, on to the clinical manifestations. Let's start with a case to help frame the discussion. You are working in a general pediatrics clinic in Nova Scotia. A 9-year-old girl presents with a red lesion on her back. Her mother noticed it two days ago, and it seems to be getting larger. The rash is not painful. You note an erythematous patch, 8cm in diameter. Her mother states that they were camping last week and brushed several ticks off the children's clothing, but she does not recall seeing a tick attached on her daughter's back. What should you do next?

1. Prescribe topical corticosteroids for possible dermatitis
2. Counsel the family to wait and watch the lesion. Arrange for follow-up in 1-2 weeks.
3. Provide a lab requisition for two-tier testing for Lyme disease
- 4. Prescribe a course of oral antibiotics for early Lyme disease**

The correct answer is (d), to diagnose Lyme disease and prescribe a course of oral antibiotics. We'll explain why.

Lyme disease can present early, with cutaneous disease (solitary erythema migrans (EM) lesions), or later, with isolated cutaneous lesions and/or extracutaneous disease.

Early localized Lyme disease typically presents an average of 7–10 days following the tick bite. A rash within the first 72 hours is most likely to be tick bite hypersensitivity, *not* Lyme disease. Most of you will probably remember the classic erythema migrans rash. This represents *early localized Lyme disease*. Classically, this is a flat, red, large (over 5 cm in diameter) patch. It sometimes has central clearing or blue-ish discoloration, and it is typically asymptomatic. It should not be hot or painful, which would suggest cellulitis, nor is it swollen and pruritic, which

can be seen with tick or insect bite hypersensitivity. Even with a single EM lesion, the child may experience symptoms such as low-grade fever, malaise, headache, myalgia or arthralgia; however, many go unnoticed.

So, if you see this large, red, asymptomatic patch spreading over several days, think early Lyme disease or Stage 1. You may ask, should I do any testing to confirm the diagnosis? And the answer is NO. At this stage, it is a clinical diagnosis and serological testing has poor sensitivity. In other words, most people with a single EM lesion are seronegative at the time of initial presentation. With a typical lesion on a child living in an endemic region, you have enough evidence to diagnose erythema migrans and prescribe treatment. There are several options for the treatment of early Lyme disease. Treatment should consist of either doxycycline for 10 days, or amoxicillin or cefuroxime for 14 days. Azithromycin is second line because of lower efficacy of 80%. Note that doxycycline, if used for less than 21 days, is no longer contraindicated in children. There are excellent tables in the CPS practice point that you can save for your reference – Table 2 outlines antibiotics and dosing, and Table 3 reviews antibiotic route and duration for the different manifestations of Lyme disease.

An EM lesion if left untreated often self-resolves, typically over 3-4 weeks. In that scenario, hematogenous dissemination of the spirochete can occur weeks to months following initial infection and result in end-organ involvement. This is known as *early disseminated Lyme disease* or Stage 2. Most cases of early disseminated Lyme disease are associated with non-specific manifestations such as fatigue, general weakness, arthralgias and/or myalgias. Fever is much more common in the disseminated stage than in the localized stage. Serum antibodies for *Borrelia* are almost always positive in this phase.

The most common manifestations of this early disseminated phase are multiple EM lesions, with or without nervous system and uncommonly, cardiac manifestations. Multiple EM lesions can be anywhere on the body and typically are smaller than the primary lesion. These can be evanescent and fairly subtle.

Neurologic manifestations of early disseminated LD (also known as Lyme borreliosis) usually develop several weeks after the initial infection. The most common manifestation is a cranial neuritis, most commonly a unilateral seventh nerve palsy but other cranial nerves can be involved. It is important to note that in contrast to Lyme disease cranial nerve palsies, the treatment for idiopathic facial nerve palsy (aka Bell's palsy) includes corticosteroids. Therefore, a careful history should be taken to support the diagnosis of Lyme disease at the time of presentation of a facial nerve palsy. Other neurologic presentations include meningitis, or other radiculoneuritis (rarely encephalopathy). Lyme meningitis can present with symptoms of headache and low-grade fever, with or without neck stiffness. CSF studies show moderate pleocytosis similar to viral meningitis, with a lymphocytic predominance and no evidence of bacterial infection.

Our next case is a 12-year-old female. She presents to a Pediatric Emergency Department with a one-week history of worsening headache and new neck pain/stiffness. On review of systems, you learn that 1 month prior she had a localized skin lesion, myalgias, headache, and malaise. This illness self-resolved. Today, her temperature is 38.3 C, her vitals are otherwise normal for age, and she does not appear toxic. Exam is remarkable for mild meningismus and photosensitivity. There is no papilledema or focal neurologic findings. A lumbar puncture is performed. You send for routine CSF chemistries, gram stain and bacterial cultures. The results come back showing clear colourless fluid, WBC of 120, with a lymphocytic predominance of 80%, normal protein and glucose, and a negative gram stain. What other investigations would you recommend?

The correct answer is serological testing for antibodies to *Borrelia burgdorferi*. In the clinical setting of a recent (1-2 month) history of probably untreated localized EM and a clinical presentation suggestive of culture negative subacute meningitis, early disseminated Lyme disease presenting as meningitis is a distinct possibility. Serum antibody testing is the best method to support the clinical diagnosis and PCR testing of the CSF is not recommended.

The most accurate method of testing for Lyme disease is 2-tiered serology. A very important point to remember is that all testing should be performed at an approved Canadian laboratory. Unfortunately, there are many private labs outside Canada that are not approved by Health Canada, and therefore test accuracy is not validated. The ELISA test alone is sensitive but not specific, as antibodies against other spirochetes, viral infections, and even some autoimmune disease can lead to false positive results. If the ELISA is positive, a Western blot test is automatically done to look at individual proteins and patterns of reactivity that are more specific. A positive IgM alone in the disseminated phase is usually a false positive. Of note, antibodies to *Borrelia* species can persist for YEARS. Therefore, it is not useful to repeat serology to look for “treatment response”. In the uncommon circumstance that the tick bite occurred outside of North America, you should contact the lab to request supplemental testing to detect other species of *Borrelia*, such as those found in Europe.

Next, let’s discuss cardiac manifestations (Lyme carditis) as this is also a manifestation of early disseminated Lyme disease usually occurring within several days to about a month after the initial infection. Carditis, however, is an uncommon manifestation of Lyme disease occurring in less than 4% of patients with Lyme disease. Patients may complain of chest pain, dyspnea, palpitations, shortness of breath, light-headedness or syncope. The most common evidence of carditis is atrioventricular nodal block (usually a prolonged PR interval) as seen in an electrocardiogram. If patients do not have the above symptoms, an electrocardiogram is not recommended. If a conduction abnormality is detected, a cardiologist should be consulted. Since carditis is a manifestation of early disseminated disease, serology is usually positive.

Finally, the joints. Lyme arthritis (as opposed to arthralgia) is a manifestation of late of Lyme disease (Stage 3), and occurs greater than 3 months after the initial infection. Knees are the most common location, and children classically present with unilateral swelling in a single joint, caused by joint effusion. Typically, the effusion is more impressive than any other signs of inflammation such as pain, erythema or warmth. This may also be intermittent with some resolution after a few weeks. Again, the diagnosis is especially suspected when one has a history of past EM that was untreated, isolated knee involvement and lack of fever. Patients will have positive Lyme serology. Testing the synovial fluid for antibodies or PCR is not recommended, as these tests are less sensitive. Synovial fluid should be sent for cell count and culture and clinical response to treatment should be assured.

Alright – you should now be familiar with how to recognize and diagnose late Lyme disease. Next up – treatment. Whip out those handy tables from the CPS practice point, as they also include guidance for late or extracutaneous disease. Oral doxycycline x14 days is recommended for cranial nerve palsy, and meningitis. IV ceftriaxone is used to treat Lyme meningitis initially as one should exclude bacterial meningitis. Once stable, doxycycline can be used. Any of amoxicillin, doxycycline, or cefuroxime can be used for arthritis, but the treatment duration for Lyme arthritis is 28 days. Phew, that’s a lot to remember. So, I recommended you refer to the practice point next time you are initiating treatment for late Lyme disease. A good clinical pearl is to remember the possibility of a Jarisch-Herxheimer reaction. This is when a child develops symptoms such as fever, headache, and myalgias within the first 24 hours of antibiotic treatment as the bacteria die. This “reaction” is transient and NSAIDs can be used for symptom management.

Now we will move on to our third and final case of the podcast. A mother phones your general pediatrics clinic after noticing a tick attached on her 3-year-old son’s leg. They were playing outside in the park this morning, and she found the tick this evening when she was getting him ready for a bath. She asks for your advice. What do you recommend?

1. Monitor the area for the next week. She should phone back if he develops a red circular rash on his leg.
2. **Follow Health Canada’s instructions on how to remove an attached tick. Since it has been attached less than 24 hours, no prophylaxis is required.**
3. Treatment with amoxicillin PO x14 days
4. Post-exposure prophylaxis with a single dose of PO doxycycline

The correct answer is (b). The overall risk of Lyme disease after a tick bite is low (around 3% in endemic areas), but the risk increases with longer duration of tick attachment. Prophylaxis with a single dose of doxycycline can be offered within 72 hours of a tick bite if the tick has been attached for more than 36 hours. If the tick was identified and removed within 24-36 hours, the risk of Lyme disease is low, and no antibiotics are required. Since you are well-informed about Lyme disease, you could explain this rationale to the mother. If the tick had been attached for

36-72 hours, you could prescribe this 3yo boy a dose of doxycycline, which is approved for use in any age as of 2021 for <21 day treatment courses.

Health Canada & Public Health have some excellent information on their website about tick removal. You can find the link here www.canada.ca/en/public-health/services/diseases/lyme-disease/health-professionals-lyme-disease.html. You should also advise her about general preventative strategies including wearing long sleeves and pants when outside in areas known to have ticks, tucking pants into socks, applying DEET insect repellent to clothing and any exposed skin, performing a full body “tick check” after spending time outdoors, and showering within a few hours of returning home in order to rinse off any ticks that have not yet attached.

That’s it for today. Before we leave, let’s finish with some key take-home points from the podcast:

1. Lyme disease is an infection caused by the spirochete *Borrelia burgdorferi*, which is transmitted to humans via the bite of a black-legged tick.
2. Three clinical Stages of Lyme disease are recognized: Early infection (Stage 1) is characterized by a localized erythema migrans lesion presenting 3 to 21 days after infection. Early infection (Stage 2) is characterized as a disseminated infection 3-6 weeks or months after infection with either one of the following features: multiple erythema migrans lesions, nerve palsies, headaches, or carditis, usually accompanied by malaise and or mild fever. Stage 3 is a late manifestation, usually with monoarthritis, and occurs more than 3 months after infection.
3. Lyme disease at all stages is a clinical diagnosis. Serology is only reliably positive in the early disseminated or late phases. Approved serologic testing is available at provincial /territorial Canadian laboratories. An IgM response alone is likely to be a false positive.
4. Multiple oral antibiotics are effective for treating Lyme disease – including doxycycline, amoxicillin, and cefuroxime. Doxycycline is now approved for short term use in children of all ages. Refer to the CPS practice point for guidance on dosing and duration of treatment depending on the clinical manifestation.
5. A single dose of doxycycline for post-exposure prophylaxis is indicated if a tick bite occurred in an endemic area and the tick has been attached 36 to 72 hours.

Thanks for listening to PedsCases podcasts. We hope you learned a thing or two about Lyme disease!

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