Editor's key points

- Two-tier serologic testing is the mainstay for differentiating Lyme arthritis (LA) from other arthritides.
- Presentation of LA is more common in children than adults and most often involves the knee. Physicians should have a high index of suspicion for LA in a child (or adult) who presents with a first episode or recurring arthritis.
- The absence of a known tick bite or erythema migrans rash does not exclude the possibility of Lyme disease. In fact, most LA patients will not recall having had either.
- Cases with erythema migrans associated with Lyme disease–endemic regions, or laboratory-confirmed cases with a compatible clinical history, should be treated with antibiotics in accordance with expert guideline recommendations.

Child with 3-year history of joint pain and swelling

Kieran Michael Moore MD CCFP(EM) FCFP FRCPC Nicholas Papadomanolakis-Pakis MSc MPA Julia Lew Linna Li MD MPH CCFP Kirk Leifso MD MSc FRCPC FAAP

Lyme disease (LD) is the most reported vector-borne disease in North America, caused by the spirochete *Borrelia burgdorferi*. In central and eastern Canada, *B burgdorferi* is transmitted by *Ixodes scapularis* (the blacklegged tick), and by *Ixodes pacificus* (the western blacklegged tick) in western Canada. The reported incidence of human LD cases in Canada has increased substantially since 2009.[1] The increasing prevalence of *B burgdorferi*–infected ticks in Canada has important implications for family physicians, particularly those who practise in LD-endemic areas. We present a case of Lyme arthritis (LA) in a child in southeastern Ontario with a 3-year history of recurrent joint pain and swelling.

Case

In December 2015, an 8-year-old boy presented to a pediatric clinic with a 2-week history of painful left knee swelling and difficulty walking. There was no history of injury or trauma. The family reported that he had a mild upper respiratory tract infection 6 weeks previously. The patient was otherwise healthy, without a relevant medical or surgical history such as a history of inflammatory bowel disease. He had a risk of tick exposure, as his family reported frequent camping trips in a Lyme-endemic region. Neither the patient nor his parents recalled him having a tick bite or rash consistent with erythema migrans (EM). He lived in southeastern Ontario and had not traveled outside the region in the previous year. His family history was relevant for juvenile idiopathic arthritis (JIA) and rheumatoid arthritis.

On examination, the child was afebrile, appeared well, and had no difficulties walking. Findings of neurologic and ocular examinations were normal. Examination of the left knee revealed a large effusion with tenderness to palpation but without warmth or erythema. There was full active range of motion, with mild pain at the extremes of flexion and extension. The remainder of the physical examination findings were normal and he had no EM rash. The boy underwent bilateral knee ultrasound scans for suspected reactive arthritis (ReA), which revealed large left and small right effusions with associated regional inflammatory synovitis. Bloodwork results showed mildly elevated inflammatory markers: an erythrocyte sedimentation rate of 45 mm/h and a C-reactive protein level of 21.4 mg/L (**Table 1**). Test results for antinuclear antibodies were negative. He was diagnosed with presumed viral ReA and was treated with nonsteroidal anti-inflammatory drugs, resulting in gradual pain relief. However, the boy continued to experience recurring joint swelling every few weeks.

In December 2017, the boy returned to his family physician with a history of recurring painful knee swelling in flares lasting 5 to 14 days before resolving. Occasionally his elbow, ankles, and shoulder joints were involved. There was never small joint involvement. On repeat examination he was afebrile and able to walk. The family reported history of a recurring eczematous rash on his abdomen and buttocks. Both knees were tender to palpation and there was mild pain on passive flexion and extension. The remaining physical examination findings were normal.

The boy was referred to a pediatrician for possible JIA or psoriatic arthritis. He was seen in February 2018, 26 months after initial symptom onset.

Table 1. Laboratory values: *Bolded values indicate clinically important results or results outside the reference range.*

VARIABLE	PEDIATRIC REFERENCE RANGE*	RESULT IN 2015	RESULT IN 2018
Complete blood count			
• Leukocytes, × 10^9/L	4.5-13.5	11.8	8.3
• Erythrocytes, × 10^{12}/L	4.00-5.20	4.61	4.43
• Hemoglobin, g/L	115-155	129	131
• Hematocrit, L/L	0.340-0.400	0.371	0.360
• MCHC, g/L	300-360	348	**364**
• Platelet count, × 10^9/L	150-400	**513**	389
• Red blood cell distribution width, %	10.5-13	12.1	11.5
Differential count, × 10^9/L			
• Neutrophils	1.50-8.60	6.79	3.84
• Lymphocytes	1.50-7.00	3.36	2.96
• Monocytes	0.20-0.80	**1.44**	**0.86**
• Eosinophils	0.00-0.70	0.18	0.62
• Basophils	0.00-0.10	0.05	0.03
ESR, mm/h	3-13	**45**	5
CRP, mg/L	0-1	**21.4**	0.2
Rheumatoid factor, kIU/L	0-22	NA	< 15
HLA-B27	NA	NA	Negative
Antinuclear antibody	NA	Negative	NA
Lyme serology			
• IgM and IgG ELISA	NA	NA	**Reactive**
• IgM Western blot	NA	NA	Negative
• IgG Western blot	NA	NA	**Reactive**

CRP—C-reactive protein, ELISA—enzyme-linked immunosorbent assay, ESR—erythrocyte sedimentation rate, Ig—immunoglobulin, MCHC—mean corpuscular hemoglobin concentration, NA—not applicable.
*Reference ranges used at Kingston Health Sciences Centre for pediatric patients.

His mother reported that he had become more fatigued over the past year and that his joint symptoms worsened with activity. Findings of a complete physical examination were unremarkable.

A workup was initiated by the consultant pediatrician. Bilateral knee x-ray scans showed no abnormalities. Results of a complete blood count with differential count were normal. Lyme serology tests were done and the results were reactive for immunoglobulin (Ig) M and IgG on enzyme-linked immunosorbent assay, with reactive IgG Western blot results (**Table 1**). The boy was diagnosed with LA and prescribed amoxicillin for 21 days. He was referred to the pediatric rheumatology department for further evaluation.

In April 2018, the patient was seen in the pediatric rheumatology department and was still experiencing episodic oligoarthritis of the large joints, with limitations to function and ongoing fatigue. Given his ongoing symptoms, doxycycline was prescribed for 28 days. At follow-up in July 2018, all symptoms had resolved and examination findings were normal.

Differential diagnosis

One of the challenges in diagnosing pediatric LA is differentiating it from other causes of infectious or inflammatory arthritis, namely septic arthritis, acute ReA, and nonsystemic-onset JIA. The main clinical features of each are listed in **Table 2**.[2-6]

Discussion

There are 3 main clinical stages of LD.[7] The early localized stage develops within 30 days of infection and is characterized by EM, a generally asymptomatic expanding erythematous patch, with or without central clearing, measuring greater than 5 cm. Erythema migrans might be accompanied by nonspecific flulike symptoms. If early LD goes unrecognized and untreated, or there are no specific clinical symptoms, patients might progress to early disseminated disease 1 to 3 months after infection. This stage can include multiple EM, severe headaches, neck stiffness, fatigue, neurologic symptoms (cranial neuropathy, radiculopathy, lymphocytic meningitis), or carditis (heart block). Should infection go untreated for longer than 3 months, symptoms of late disseminated LD might occur and last for months or years, with arthritis being the most common late disseminated manifestation in children.

Lyme arthritis most commonly presents as monoarticular arthritis, often affecting large joints, particularly the knees; oligoarticular and polyarticular involvement can also be observed.[3] Affected joints are typically markedly swollen and mildly tender, with minimal effect on walking. Recurrence of LA is frequent in the same joint, but other joints might become affected. Lyme arthritis should be considered in all cases of pediatric arthritis where the patient has had possible tick exposure. Serologic testing is the mainstay for differentiating LA from other arthritides.[3] However, even with reactive Lyme serology results, other causes of arthritis are possible.

When there is high clinical suspicion of LA supported by a history of EM or possible tick exposure, 2-tier serology testing for *B burgdorferi* might be ordered.[8] Dependent on pretest probability, a reactive enzyme-linked immunosorbent assay result followed by a reactive immunoblot test result establishes the diagnosis of LD. Initiation of antibiotic treatment can be considered while waiting for results if there is high clinical suspicion of LD.[8] The recommended treatment for LA in children 8 years of age and older is 28 days of doxycycline or β-lactams.[9] The long-term prognosis of appropriately treated LA in children is excellent.[10] In pediatric patients who continue to experience mild residual joint swelling after the initial course of treatment, the oral antibiotic regimen might be repeated.[9]

Table 2. Pediatric clinical presentations for LA, septic arthritis, ReA, and JIA

PRESENTATION OR VARIABLE	LA	SEPTIC ARTHRITIS	ReA	NONSYSTEMIC JIA
Effusion	Common (warmth)	Common (warmth and erythema)	Common (warmth)	Common (warmth and erythema)
No. of joints involved	Monoarticular (63%) ≥2 Active joints (27%)	Monoarticular (80% to 90%)	Oligoarticular Monoarticular	Oligoarticular (50% to 60%) Polyarticular (15% to 25%)
Most commonly involved joints	Knee (>90%) Ankle (25%) Knee and ankle (56%)	Knee (>50% in adults) Hip (15% in adults)	Hip Knee Ankle	Knee Wrist Ankle
Refusal or inability to weight bear	Uncommon	Common	Common	Uncommon
Pain with passive range of motion	Mild	Severe	Moderate to severe	Mild to moderate
Fever (>38.5°C)	Uncommon	Common	Uncommon	Uncommon
Rash	Might have remote history; rash not concurrent with arthritis (erythema migrans)	Common (localized redness of affected joint)	Common (erythema nodosum, keratoderma blennorrhagicum)	Uncommon

JIA—juvenile idiopathic arthritis, LA—Lyme arthritis, ReA—reactive arthritis.
Data from Hannu,[2] Arvikar and Steere,[3] Shirtliff and Mader,[4] Shapiro et al,[5] and Gerber et al.[6]

A small percentage of patients might experience persistent arthritis for months or years despite appropriate treatment for LA, and their symptoms can be successfully managed with nonsteroidal anti-inflammatory drugs.[3]

Unfortunately, the diagnosis of LD might have been delayed in this case. Although the child was initially prescribed an appropriate course of antibiotics to treat early LD, it does not follow the guideline recommendation of 28 days for LA.[9] Physicians should be aware of their local LD epidemiology, take a history of travel and possible tick exposure, and understand the various clinical presentations of this emerging infection. Lyme arthritis should be considered in patients with possible tick exposure who present with inflammatory oligoarthritis that might be fluctuating and migratory. In Ontario, approximately 42% of patients with LD report arthritic symptoms[11]; children are more likely than adults are to develop arthritis as their first LD manifestation.[12,13] In 30% of LD cases, patients do not recall a history of a tick bite[14] and EM might not be present; in fact, up to 79% of children with LA do not recall a rash.[13]

Clinical and laboratory-confirmed cases of LD are reportable to local public health agencies.[15] There are several resources available to help physicians identify, diagnose, and manage LD and educate patients on the risk and prevention of LD (**Box 1**).

Conclusion

Our case highlights the importance of differentiating LA from other possible causes of similar presentations. Physicians should have a high index of suspicion for LA in a child (or adult) who presents with a first episode or recurring arthritis in a Lyme-endemic region.

Box 1. Recent online resources for LD assessment, management, education, and prevention

Public Health Agency of Canada information on LD for health professionals:
https://www.canada.ca/en/public-health/services/diseases/lyme-disease/health-professionals-lyme-disease.html

Health Quality Ontario clinical guidance document:
http://www.hqontario.ca/Portals/0/documents/evidence/qs-clinical-guidance-lyme-disease-en.pdf

Government of Canada LD prevention tool kit:
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/lyme-disease-prevention-toolkit.html

US Centers for Disease Control and Prevention treatment guideline for early and late LD:
https://www.cdc.gov/lyme/treatment/index.html

Canadian Paediatric Society practice point for LD:
https://www.cps.ca/en/documents/position/lyme-disease-children

LD—Lyme disease.

Dr Moore is Medical Officer of Health at Kingston, Frontenac, and Lennox & Addington (KFL&A) Public Health, Program Director of Public Health and Preventive Medicine at Queen's University in Kingston, Ont, and Professor in the Department of Emergency and Family Medicine at Queen's University. **Mr Papadomanolakis-Pakis** is a research assistant at KFL&A Public Health. **Ms Lew** is a medical student at Queen's University and a research assistant at KFL&A Public Health. **Dr Li** is a fifth-year public health resident in the Department of Public Health and Preventive Medicine at Queen's University. **Dr Leifso** is a pediatrician at Kingston Health Sciences Centre and Assistant Professor in the Department of Pediatrics at Queen's University.

Competing interests
None declared

Correspondence
Dr Kieran Michael Moore; e-mail **kieran.moore@kflaph.ca**

References

1. Government of Canada. *Surveillance of Lyme disease.* Ottawa, ON: Government of Canada; 2018. Available from: **https://www.canada.ca/en/public-health/services/diseases/lyme-disease/surveillance-lyme-disease.html**. Accessed 2018 Jun 3.
2. Hannu T. Reactive arthritis. *Best Pract Res Clin Rheumatol* 2011;25(3):347-57.
3. Arvikar SL, Steere AC. Diagnosis and treatment of Lyme arthritis. *Infect Dis Clin North Am* 2015;29(2):269-80.
4. Shirtliff ME, Mader JT. Acute septic arthritis. *Clin Microbiol Rev* 2002;15(4):527-44.
5. Shapiro E, Kaplan S, Torchia M. *Lyme disease: clinical manifestations in children*. Waltham, MA: UpToDate; 2018.
6. Gerber MA, Zemel LS, Shapiro ED. Lyme arthritis in children: clinical epidemiology and long-term outcomes. *Pediatrics* 1998;102(4 Pt 1):905-8.
7. Government of Canada. *For health professionals: Lyme disease*. Ottawa, ON: Government of Canada; 2018. Available from: **https://www.canada.ca/en/public-health/services/diseases/lyme-disease/health-professionals-lyme-disease.html**. Accessed 2019 Oct 10.
8. National Institute for Health and Care Excellence. *Lyme disease: diagnosis and management. Evidence review for the management of Lyme arthritis.* London, Engl: National Guideline Centre; 2018. Available from: **https://www.nice.org.uk/guidance/ng95/evidence/g-management-of-lyme-arthritis-pdf-4792271013**. Accessed 2020 Aug 28.
9. Lyme disease. In: Committee on Infectious Diseases, American Academy of Pediatrics. *Red book: 2018-2021 report of the Committee on Infectious Diseases.* 31st edn. Itasca, IL: American Academy of Pediatrics; 2018. p. 515-22.
10. Szer IS, Taylor E, Steere AC. The long-term course of Lyme arthritis in children. *N Engl J Med* 1991;325(3):159-63.
11. Johnson KO, Nelder MP, Russell C, Li Y, Badiani T, Sander B, et al. Clinical manifestations of reported Lyme disease cases in Ontario, Canada: 2005-2014. *PLoS One* 2018;13(6):e0198509.
12. Daikh BE, Emerson FE, Smith RP, Lucas FL, McCarthy CA. Lyme arthritis: a comparison of presentation, synovial fluid analysis, and treatment course in children and adults. *Arthritis Care Res* (Hoboken) 2013;65(12):1986-90.
13. Glaude PD, Huber AM, Mailman T, Ramsey S, Lang B, Stringer E. Clinical characteristics, treatment and outcome of children with Lyme arthritis in Nova Scotia. *Paediatr Child Health* 2015;20(7):377-80.
14. Hu L, Steere A, Mitty J. *Patient education: Lyme disease symptoms and diagnosis (beyond the basics).* Waltham, MA: UpToDate; 2018.
15. Public Health Agency of Canada. *Case definition: list of nationally notifiable diseases.* Ottawa, ON: Government of Canada; 2018. Available from: **http://diseases.canada.ca/notifiable/diseases-list**. Accessed 2019 Oct 1.

This article has been peer reviewed.
Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2020;66:820-3