Tick-borne diseases
(excluding Lyme disease)

CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

PROTOCOL

Principal investigators

Kescha Kazmi, Hospital for Sick Children, Department of Pediatrics, University of Toronto, Toronto, Ontario, kescha.kazmi@sickkids.ca

Shaun K. Morris, Hospital for Sick Children, Department of Pediatrics, University of Toronto, Senior Scientist, Child Health Evaluative Sciences, SickKids Research Institute, Toronto, Ontario, shaun.morris@sickkids.ca

Co-investigators

Jason Brophy, Children's Hospital of Eastern Ontario, Department of Pediatrics, University of Ottawa, Ottawa, Ontario

Jared Bullard, The Children's Hospital of Winnipeg, Department of Pediatrics, University of Manitoba, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba

Heather Coatsworth, Mycobacteriology, Vector-borne and Prion Diseases Division, National Microbiology Branch, Public Health Agency of Canada

Jeannette Comeau, IWK Health Centre, Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia

Salima Gasmi, Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada, Groupe de Recherche en Épidémiologie des Zoonoses et Santé Publique (GREZOSP), Université de Montréal, Saint-Hyacinthe, Quebec

David M. Goldfarb, BC Children's and Women's Hospital & Health Centre, Department of Pathology and Laboratory Medicine, University of British Columbia, First Nations Health Authority, Vancouver, British Columbia

Sandra Isabel, CHU de Québec–Université Laval, Department of Pediatrics, Faculty of Medicine, Université Laval, Quebec, Quebec

Kirk Leifso, Department of Pediatrics, Kingston Health Sciences Centre, Queen's University, Kingston, Ontario

Muhammad Morshed, Zoonotic & Emerging Pathogen, BC Centre for Disease Control, Public Health Laboratory, Vancouver, British Columbia

Nicholas H. Ogden, Modelling Hub Division, Science Policy Integration Branch, Public Health Agency of Canada. Groupe de recherche en épidémiologie des

zoonoses et santé publique (GREZOSP), and Centre de Recherche en santé publique (CReSP), Université de Montréal, Montreal, Quebec

Jeffrey Pernica, Division of Infectious Diseases, Department of Pediatrics, McMaster University, Hamilton, Ontario

Christian Renaud, Division of Infectious Diseases, Department of Pediatrics, Centre Hospitalier Universitaire Sainte-Justine; Division of Microbiology, Department of Clinical Laboratory Medicine, OPTILAB Montreal—Centre Hospitalier Universitaire Sainte-Justine, Montréal, Quebec

Joan Robinson, Stollery Children's Hospital, Department of Pediatrics, University of Alberta, Edmonton, Alberta

Questions

- What is the minimum incidence of non-Lyme tick-borne diseases (TBDs) in children in Canada?
- What are the most common clinical features of non-Lyme TBDs that paediatric providers should be aware of?

Background

TBDs are increasingly becoming a significant public health concern in many parts of Canada. Lyme disease is emerging in eastern and central Canada due to geographic range expansion of the blacklegged tick, *Ixodes scapularis,* from the United States (US), driven by climate warming (1). Expansion of populations of other endemic tick vector species, in both geographic range and abundance, are also being seen, which may also be due to warmer temperatures, increased precipitation, land use changes, and extended periods of activity each year (2). These changes are placing more people at risk of acquiring TBDs (3–5). Children are at particular risk for TBDs as they often spend more time outdoors, tick attachment may go unnoticed, and early symptoms of TBDs may be mistaken for other childhood infections, delaying diagnosis and treatment (6). Children living in rural and remote areas of Canada, including Indigenous children, may be at increased risk of acquiring TBDs. Data from the US indicates that Indigenous populations experience higher rates of TBDs compared to other racial groups, emphasizing the need to monitor for similar trends in Canada (7,8).

In Canada, there are several tick species that can transmit illnesses to humans. Blacklegged ticks, *I. scapularis* and *Ixodes pacificus* are the primary vectors for Lyme disease (the most common TBD in Canada), anaplasmosis, and hard tick relapsing fever . *I. scapularis* can also transmit babesiosis and Powassan virus (4,9). Before 1998, the only known population of *I. scapularis* in Canada was in Long Point, Ontario (ON) (10,11). Since then, the geographic range of *I. scapularis* has expanded considerably into southern central and eastern Canada. *I. pacificus* is endemic to southern British Columbia (BC) (9). The Rocky Mountain wood tick (*Dermacentor andersoni*) is the primary vector for Rocky Mountain spotted fever and tick paralysis (4) and are found across BC, Alberta (AB), and western Saskatchewan (SK) (12). Soft tick relapsing fever, a disease caused by *Borrelia*

hermsii, is transmitted by the bite of a soft tick, *Ornithodoros hermsi* found in southern BC (4,13).

While an established national surveillance program for Lyme disease has existed since 2009, (14) the incidence of other emerging TBDs in Canada is largely unknown, as many TBDs are not nationally notifiable. Anaplasmosis and babesiosis are reportable in some provinces. There were nearly 400 cases of anaplasmosis and 20 cases of babesiosis reported in Nova Scotia (NS) (15), Quebec (QC) (16), and ON (17) combined in 2023. NS in particular had an overall incidence of 29 per 100 000 population of anaplasmosis (15), possibly due to the emergence of *Anaplasma phagocytophilum* infections in naïve wildlife reservoir populations resulting in high infection prevalence in ticks (personal communication from those studying the anaplasmosis risk areas in southern QC). Anaplasmosis, babesiosis, and Powassan virus became nationally reportable illnesses in January 2024 (18–20). However, limited clinical and epidemiologic data are captured through the national human case surveillance system. It also utilizes passive surveillance, which relies on voluntary reporting, clinical recognition of disease, and appropriate laboratory testing. Lack of clinical recognition of emerging TBDs amongst healthcare providers is likely to contribute to under-reporting and therefore underestimation of disease burden. There is limited knowledge of clinical manifestations, epidemiology, and risk factors regarding TBDs in children, making it challenging to fully understand their incidence, geographic distribution, and clinical effects in this population. As climate change increases the risk of these diseases, enhancing prevention and surveillance efforts is crucial to control their spread in children.

Methods

Through the established methodology of the Canadian Paediatric Surveillance Program (CPSP), approximately 2700 paediatricians and paediatric subspecialists will receive a monthly electronic reporting form. Participants will be asked to voluntarily indicate if they have encountered a new case of a non-Lyme TBD acquired in Canada or abroad, meeting the case definition, within the prior 30 days. Physicians who report encountering a case will be directed to complete a detailed online clinical questionnaire that is based on the one used to explore paediatric Lyme disease cases in a previous CPSP study (21).

Case definition

Report any patient less than 18 years of age (up to their 18th birthday) with a **confirmed** *OR* **suspected** case of one of the following tick-borne diseases:

Anaplasmosis, babesiosis, Powassan virus, relapsing fever (hard tick relapsing fever or soft tick relapsing fever), Rocky Mountain spotted fever

- A **confirmed** case meets confirmatory laboratory criteria with or without meeting clinical criteria (see Appendix 1)
- A **suspected** case meets supportive laboratory criteria AND clinical criteria (see Appendix 1)

Tick paralysis

- A **confirmed** case meets confirmatory clinical criteria (see Appendix 1)

Exclusion criteria

- Cases with confirmation of an alternative diagnosis, including other TBDs not listed here, which fully explains all symptoms
- Cases diagnosed by methods and/or laboratories not recommended by the Public Health Agency of Canada or the U.S. Centers for Disease Control and Prevention

Objectives

The overall objective of this project is to improve the health of children at risk of, or affected by, TBDs in Canada.

1) Determine the minimum incidence of emerging non-Lyme TBDs in children seen by a paediatrician or paediatric subspecialist, by age, sex, region of tick exposure, and provincial/territorial residence, using national census data as the denominator
2) Identify emerging locations of TBD risk, sites of exposure of infected ticks, and environmental risk factors for TBDs
3) Define the clinical disease spectrum of non-Lyme TBDs among children in Canada
4) Describe treatment regimens (if any) and outcomes of various TBDs

Duration

May 2026 to April 2029

Expected number of cases

Over the three-year study period, a minimum of 30 cases of non-Lyme TBDs are expected. This number will likely increase over the course of the study due to i) increased awareness by the general public and healthcare providers following TBD education campaigns and ii) the proportion of the Canadian population exposed to infected ticks is predicted to increase because of the range expansion of tick populations in Canada.

The following are the estimated number of cases per TBD:

- **Anaplasmosis:** In 2023, anaplasmosis was reportable in ON, QC, and NS. There were 0 cases in children in ON and QC and 2 cases in the 5–14 year age range in NS (15–17). The US has an average incidence of anaplasmosis for the 0–19 age group of 2 per million population (31). Approximately 6.2 million people under the age of 19 live in provinces that are endemic for *Ixodes* sp. ticks (32). Based on these data, we anticipate roughly 0–5 cases per year.
- **Babesiosis:** In Canada, there were no cases of babesiosis reported in children in ON, QC, and NS in 2023 (15–17). Less than 50 cases of babesiosis were reported in the 0–19 age group in the US in 2020, therefore we anticipate 0–1 cases per year of babesiosis (33).
- **Powassan virus:** In Canada, there were no cases of Powassan virus reported in children in ON, QC, and NS in 2023 (15–17). In the US, 49 cases total in all

age groups were reported in 2023 (34). Therefore, we anticipate 0–1 cases per year.

- **Relapsing fever:** Relapsing fever is not a nationally notifiable disease in Canada or the US. The incidence of relapsing fever in North America is unknown. We anticipate 0–1 cases per year.
- **Rocky Mountain spotted fever:** This TBD is very rare in Canada and predominantly seen in BC. The BC Centre for Disease Control (BCCDC) sees 0–3 cases per year (35). We anticipate 0–1 cases per year.
- **Tick paralysis:** This TBD is very rare in Canada and predominantly seen in BC. BCCDC sees 0–2 cases per year. We anticipate 0–1 cases per year (36).

Study limitations

As with any voluntary surveillance system, the CPSP relies on participants to report cases to generate data. Resulting rate estimations must therefore be considered minimum incidence rates. The CPSP mechanism does not include family physicians and any cases diagnosed and managed by family doctors will not be captured. Furthermore, it is likely that not all data points will be available for every patient and therefore exploration of several predisposing factors may be limited depending on data completeness and reporting rates. Given the small number of estimated cases per TBD, there is a chance that data will have to be suppressed where case counts are fewer than five. Additionally, older adolescents may not receive care from a paediatrician and therefore would not be included in the case capture.

Ethical approval

- Health Canada and Public Health Agency of Canada Research Ethics Board
- The Hospital for Sick Children Research Ethics Board

Analysis

Descriptive data will be analyzed to quantitatively summarize demographic variables. If case counts meet the threshold of five or more cases, rates of events and risk factors will be calculated using proxy population denominators from census data. Outputs will include estimates of annual incidence among children in different provinces and territories and geographic regions (for comparison with national surveillance data and estimation of under-reporting for diseases that are nationally notifiable), maps of geographic locations of infection, proportions of severe and non-severe illness, treatment regimens used (if any) and outcomes of these, and the proportions of infections acquired in different environments (urban vs. rural).

Knowledge translation

Study results will be disseminated through peer-reviewed publications, presentations at national and international scientific meetings, and CPSP channels (e.g., newsletters, annual reports). Key findings will be adapted into plain-language summaries and infographics and shared through public health partners to promote public awareness.

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Appendix 1

Anaplasmosis

Confirmatory laboratory tests include:

- Four-fold or greater increase in *Anaplasma phagocytophilum* IgG-specific antibody titres by indirect immunofluorescence assay (IFA) between acute and convalescent sera taken 2-4 weeks apart; **OR**
- Detection of *A. phagocytophilum* nucleic acid by molecular methods from an appropriate clinical specimen (e.g., whole blood, buffy coat, cerebrospinal fluid [CSF], or bone marrow/tissue biopsy); **OR**
- Detection of *A. phagocytophilum* antigen by immunohistochemistry (IHC) in a biopsy/autopsy sample; **OR**
- Isolation of *A. phagocytophilum* in cell culture from an appropriate clinical specimen followed by molecular confirmation

Supportive laboratory tests include:

- Elevated *A. phagocytophilum* IgG antibody titres by IFA where the endpoint titre is four-fold greater than the screening dilution of the assay; **OR**
- Identification of typical morulae (microcolonies of *A. phagocytophilum*) in the cytoplasm of granulocytes by microscopic examination from a peripheral blood smear

Clinical criteria include:

- Fever AND at least one of the following: headache, malaise/asthenia, arthralgia/myalgia, mild anemia, thrombocytopenia, leukopenia, elevated hepatic transaminase concentrations, or elevated numbers of immature neutrophils

Babesiosis

Confirmatory laboratory tests include:

- Detection of *Babesia* species *(*e.g., *Babesia microti, B. duncani*, *B. divergens, B. venatorum)* nucleic acid by molecular methods from a whole blood specimen; **OR**
- Identification of *Babesia* sp. organisms by microscopic examination from an appropriate specimen (e.g., Giemsa-stained blood smear)

Supportive laboratory tests include:

- *B. microti* total or IgG antibody titres ≥ 1:64 by IFA; **OR**
- *B. divergens* total or IgG antibody titres ≥ 1:256 by IFA; **OR**
- *B. duncani* total or IgG antibody titres ≥ 1:512 by IFA

Clinical criteria include:

- Fever AND at least one of the following: fatigue, chills, sweats, headache, anorexia, dark urine, jaundice, myalgia, arthralgia, hepatosplenomegaly, hemolytic anemia, or thrombocytopenia

Powassan virus (POWV)

Confirmatory laboratory tests include:

- Serological detection of POWV IgM by enzyme-linked immunosorbent assay (ELISA) and observation of an increase in POWV neutralizing antibody titres by plaque reduction neutralization testing (PRNT) between acute and convalescent serum; **OR**
- Four-fold increase in total antibody titre by hemagglutination inhibition (HI) assay between acute and convalescent serum and detection of neutralizing antibodies by PRNTs ≥20; **OR**
- Seroconversion (negative to positive) of POWV IgM by ELISA or total antibody titre by HI assay between acute and convalescent sera and detection of neutralizing antibodies by PRNT ≥20; **OR**
- POWV IgM in CSF by ELISA and a neutralizing antibody titre by PRNT ≥20; **OR**
- Isolation of POWV in cell culture from an appropriate clinical specimen (e.g., tissue, blood, CSF, or other body fluid); **OR**
- Detection of POWV antigen by IHC from an appropriate clinical specimen; **OR**
- Detection of POWV nucleic acid by molecular methods from an appropriate specimen

Supportive laboratory tests include:

- Serological detection of POWV IgM by ELISA or HI titre ≥20 AND detection of neutralizing antibody titres by PRNT ≥20 on a single serum sample;
- Serological detection of POWV IgM by ELISA without a significant increase in neutralizing antibody titre by PRNTs between acute and convalescent serum samples

Clinical criteria include:

- At least one of the symptoms of the initial febrile phase (include fever, sore throat, drowsiness, headache, and disorientation) or neuroinvasive disease (fever, vomiting, respiratory distress, loss of coordination, speech difficulties, paralysis, or seizures)

Relapsing fever (hard tick relapsing fever [HTRF] or soft tick relapsing fever [STRF])

Confirmatory laboratory tests include:

- Detection of relapsing fever *Borrelia* sp. (e.g., *B. miyamotoi*, *B. hermsii*) nucleic acid in an appropriate clinical specimen by molecular method;
- Four-fold increase in *B. hermsii* total antibody titre by IFA between acute and convalescent serum (for STRF only)

Supportive laboratory tests include:

- Direct observance of spirochetes suggestive of *Borrelia* sp. on peripheral blood smear, bone marrow, or cerebrospinal fluid;
- Elevated *B. hermsii* antibody titres by IFA (for STRF only)

Clinical criteria include:

- Acute onset of fever or chills AND one or more of the following symptoms or signs: headache, sweats/chills, myalgia, arthralgia, malaise/fatigue, rash, abdominal cramps, nausea, vomiting, diarrhea, dizziness, confusion/altered mental status, photophobia, leukopenia, thrombocytopenia, or elevated aminotransferase levels

Rocky Mountain spotted fever

Confirmatory laboratory tests include:

- Detection of *Rickettsia rickettsii* nucleic acid in an appropriate clinical specimen by molecular methods; **OR**
- Four-fold increase in IgG-specific antibody titre reactive with *R. rickettsii* antigen by IFA between paired serum specimens (one taken in the first two weeks after illness onset and a second taken two to ten weeks after acute specimen collection); **OR**
- *R. rickettsii* antigen in a biopsy or autopsy specimen by IHC

Supportive laboratory tests include:

- Elevated IgG antibody reactive with *R. rickettsii* antigen by IFA within 60 days of illness onset

Clinical criteria include:

- Fever AND one or more of the following: rash, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation

Tick paralysis

Confirmatory clinical criteria include:

- Acute, ascending flaccid paralysis with rapid resolution of symptoms following tick removal