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Update on Ontario's New Tick-Borne Diseases of Public Health Significance

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PHO Rounds May 21, 2024, 12:00 to 13:00 EDT

Land Acknowledgement

Toronto is situated on Treaty Land. Public Health respectfully acknowledges the traditional and ancestral territories of the First Nations, Inuit, and Métis Peoples, whose land we are hosted on today. We acknowledge that we are on lands of the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat, and are thankful for the enduring hospitality of the Peoples across Turtle Island that allow us to live and work today. We stand with all Indigenous People, past and present, in promoting the wise stewardship of these lands since time immemorial.

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The authors have no conflict of interests.

Learning Objectives

By the end of this session, participants will be able to:

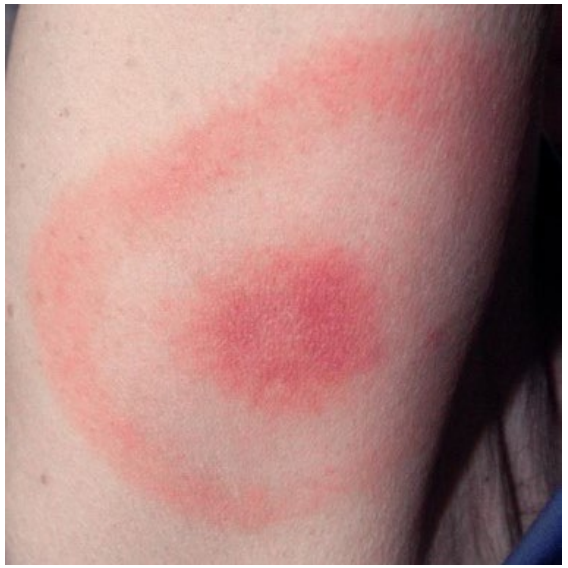
- Describe the epidemiology and clinical presentation of four tick-borne diseases of public health significance in Ontario
- Identify the testing recommendations and testing process for each tick-borne disease
- Interpret the laboratory investigations for each tick-borne disease and how they relate to a case investigation

Background: Tick-borne Diseases of Public Health Significance

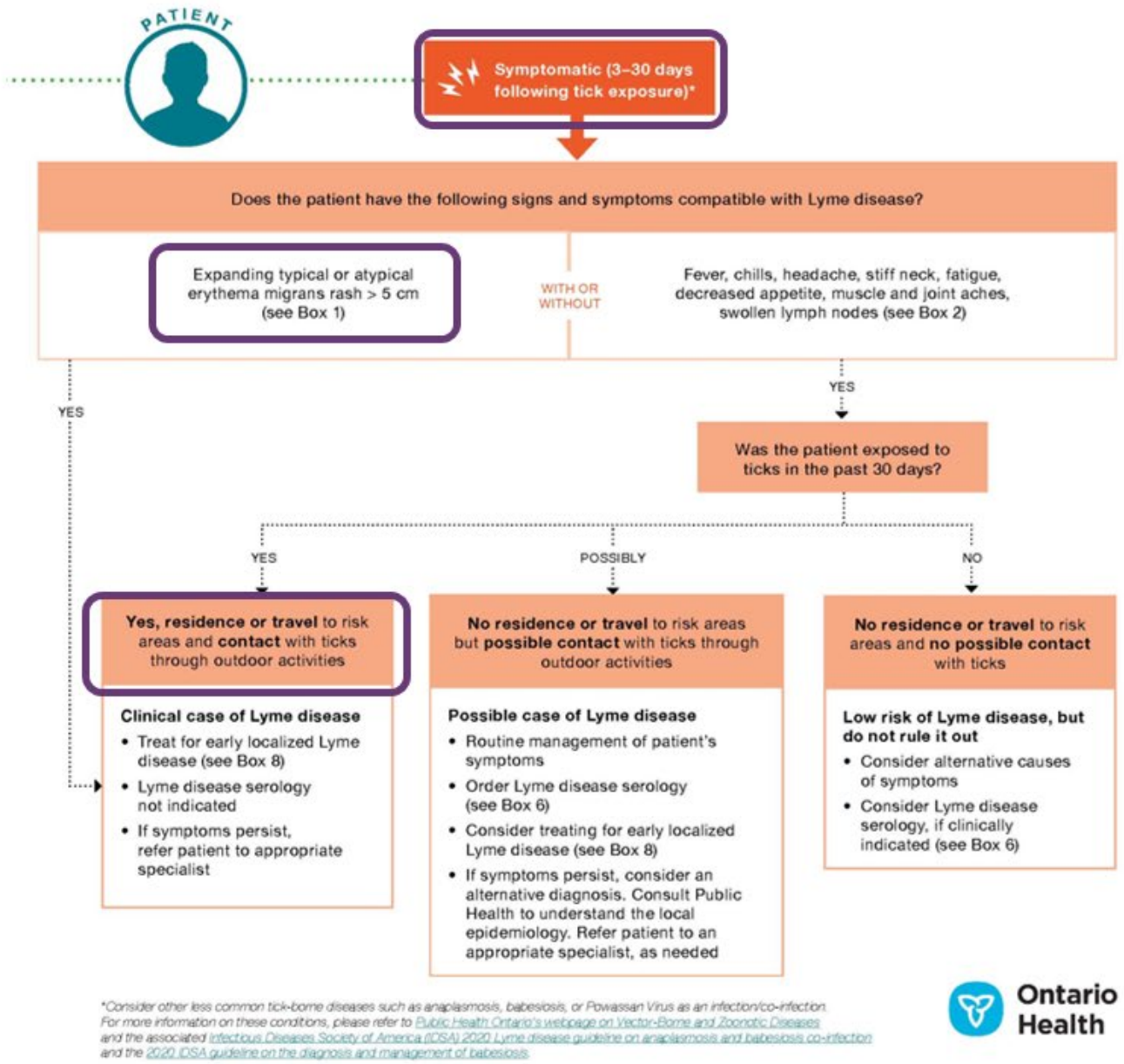
- Anaplasmosis, babesiosis and Powassan virus infection were designated as diseases of public health significance (DoPHS) on July 1, 2023
- Lyme disease has been a reportable DoPHS in Ontario since 1991
- All four tick-borne DoPHS are transmitted at varying degrees of intensity by blacklegged ticks (*Ixodes scapularis*) in Ontario
- It is anticipated that the prevalence of tick-borne diseases will increase in Ontario due to warming temperatures and land use changes

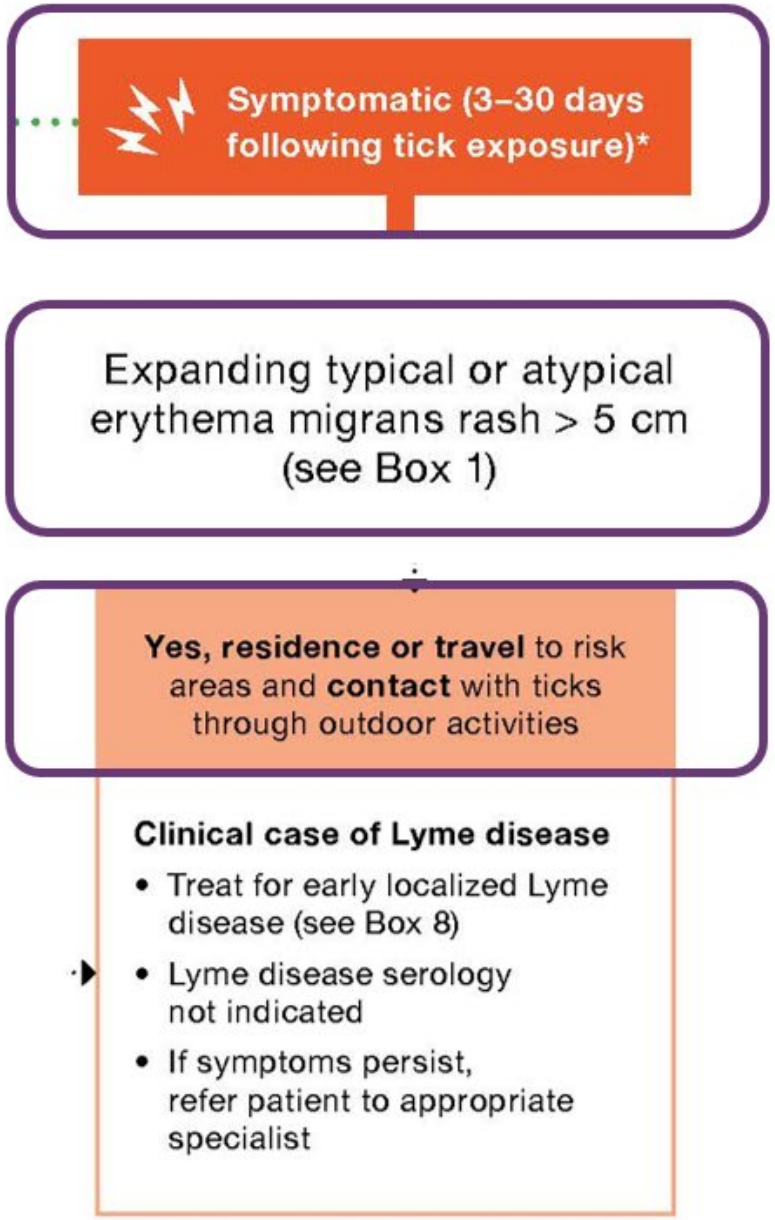
Case Introduction

- 68-year-old previously well retired nurse living in **Ottawa area** was **bitten by a tick** while gardening
- 36 hours after gardening, the tick was found and removed
- One week later, they developed a rash (see picture), fever, and myalgia
- Within two days of symptom onset, they visited their primary care provider
- Routine blood work was normal
- What would be the recommended clinical management?
  - A. Observation only
  - B. Skin biopsy for Lyme PCR
  - C. Serology testing for Lyme antibodies
  - D. Oral antibiotics (doxycycline, cefuroxime, or amoxicillin)
  - E. C and D



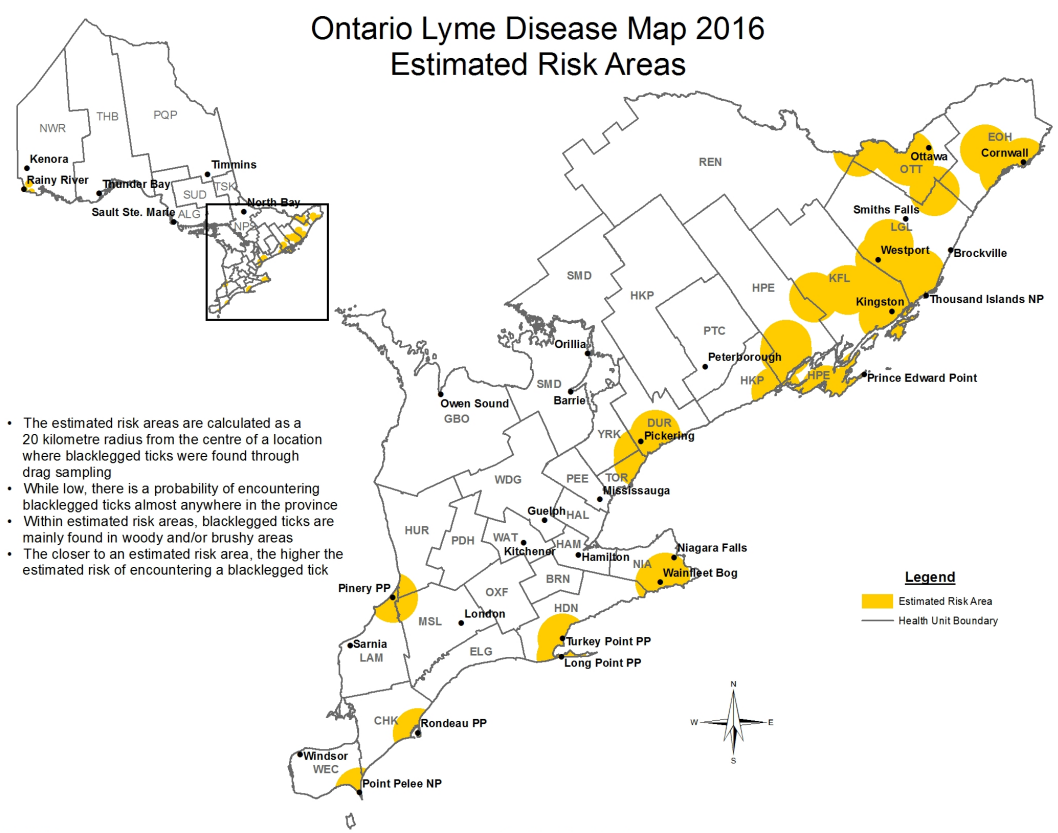
Source: Gathany J. CDC #9875. CDC/ James Gathany. Available from: https://phil.cdc.gov/Details.aspx?pid=9875



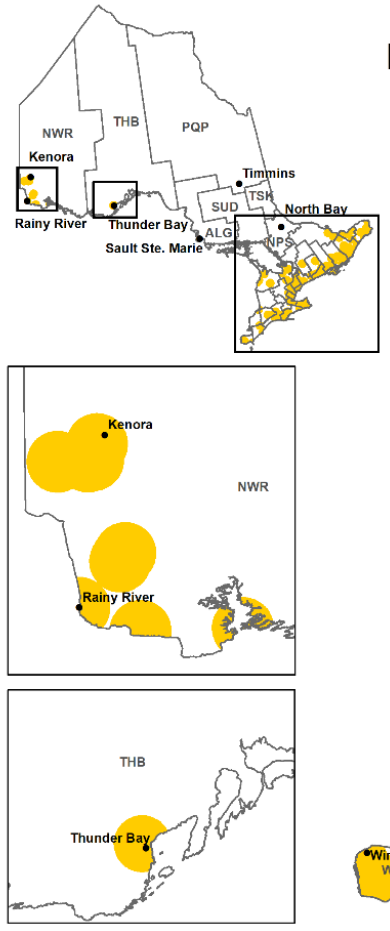


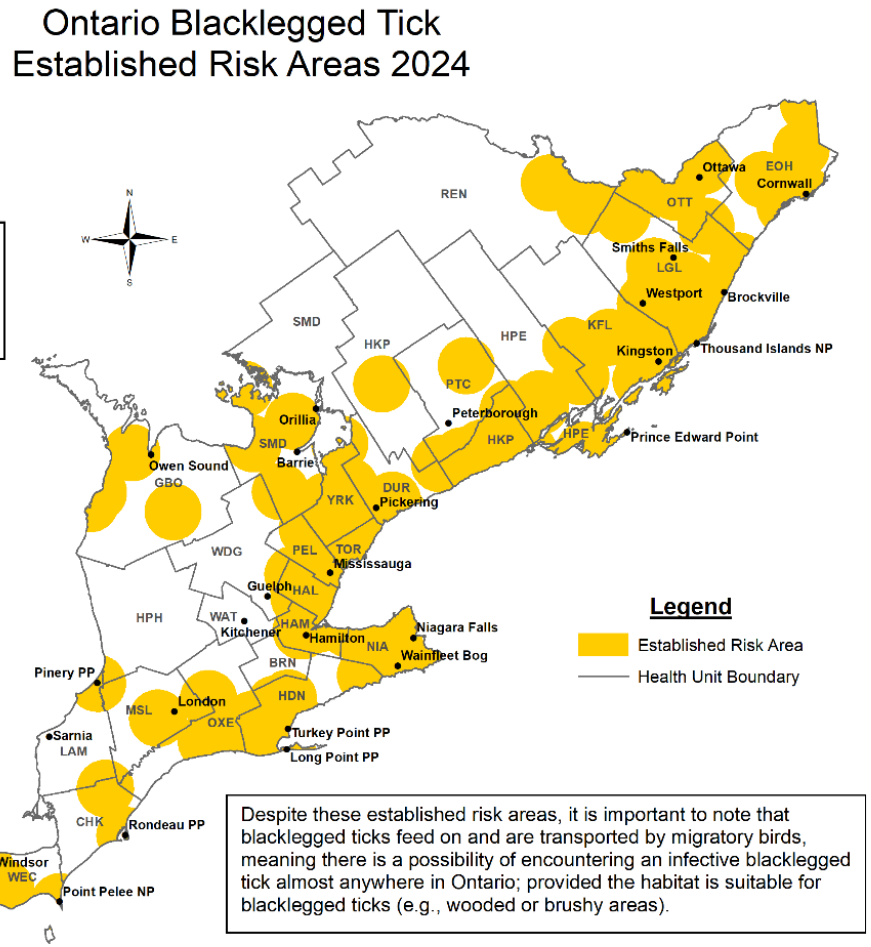
Source: Health Quality Ontario. Clinical guidance document: management of tick bites and investigation of early localized Lyme disease. Toronto, ON: King's Printer for Ontario; 2024. Available from: https://www.hqontario.ca/Portals/0/documents/evidence/qs-lyme-disease-clinical-guidance-2024-en.pdf

Blacklegged Tick (*Ixodes scapularis*) Risk Areas in Ontario



- The estimated risk areas are calculated as a 20 kilometre radius from the centre of a location where blacklegged ticks were found through drag sampling
- While low, there is a probability of encountering blacklegged ticks almost anywhere in the province
- Within estimated risk areas, blacklegged ticks are mainly found in woody and/or brushy areas
- The closer to an estimated risk area, the higher the estimated risk of encountering a blacklegged tick

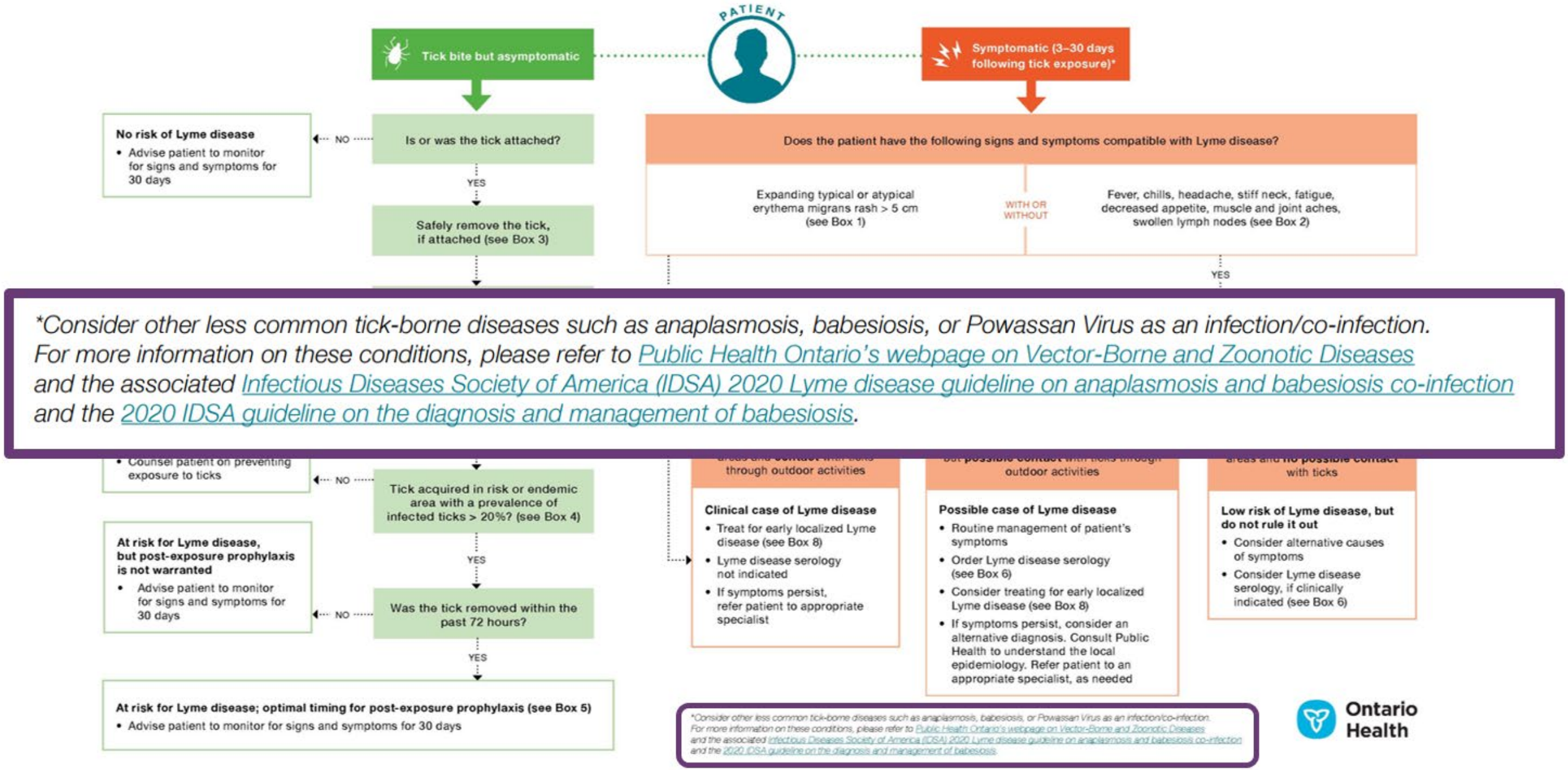




Despite these established risk areas, it is important to note that blacklegged ticks feed on and are transported by migratory birds, meaning there is a possibility of encountering an infective blacklegged tick almost anywhere in Ontario; provided the habitat is suitable for blacklegged ticks (e.g., wooded or brushy areas).

Sources: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario Lyme disease estimated risk areas map [Internet]. Toronto, ON: Queen's Printer for Ontario; 2016 [cited 2024 May 14]. Available from: https://www.publichealthontario.ca/-/media/Documents/L/2017/lyme-disease-risk-area-map-2016.pdf?rev=70ab6a2872764a21a76c2d70b0a59734&sc_lang=en

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario blacklegged tick established risk areas 2024 [Internet]. Toronto, ON: King's Printer for Ontario; 2024 [cited 2024 May 14]. Available from: https://www.publichealthontario.ca/-/media/Documents/O/24/ontario-blacklegged-tick-established-risk-areas-2024.pdf?rev=d7dafd390245466483d51e910f02c882&sc_lang=en



Source: Health Quality Ontario. Clinical guidance document: management of tick bites and investigation of early localized Lyme disease. Toronto, ON: King's Printer for Ontario; 2024. Available from: https://www.hqontario.ca/Portals/0/documents/evidence/qs-lyme-disease-clinical-guidance-2024-en.pdf

Epidemiology of Tick-Borne Diseases of Public Health Significance in Ontario

Characteristics of Confirmed and Probable Anaplasmosis and Babesiosis Cases in Ontario (January 1–December 31, 2023)

Case Characteristic	Anaplasmosis, n (%)	Babesiosis, n (%)
Confirmed cases	17 (42.5)	8 (53.3)
Probable Cases	23 (57.5)	7 (46.7)
Total Number of Confirmed and Probable Cases	**40**	**15**
Female	10 (25.0)	10 (66.7)
Male	30 (75.0)	5 (33.3)
<18 years of age	0 (0.0)	0 (0.0)
20—29 years of age	0 (0.0)	2 (13.3)
30–39 years of age	1 (2.5)	2 (13.3)
40–49 years of age	3 (7.5)	2 (13.3)
50–59 years of age	7 (17.5)	1 (6.7)
60–69 years of age	13 (32.5)	4 (26.7)
70–79 years of age	13 (32.5)	3 (20.0)
80+ years of age	3 (7.5)	1 (6.7)
Number of hospitalizations	17 (42.5)	6 (40.0)
Number of deaths	0	0

Data source: iPHIS data

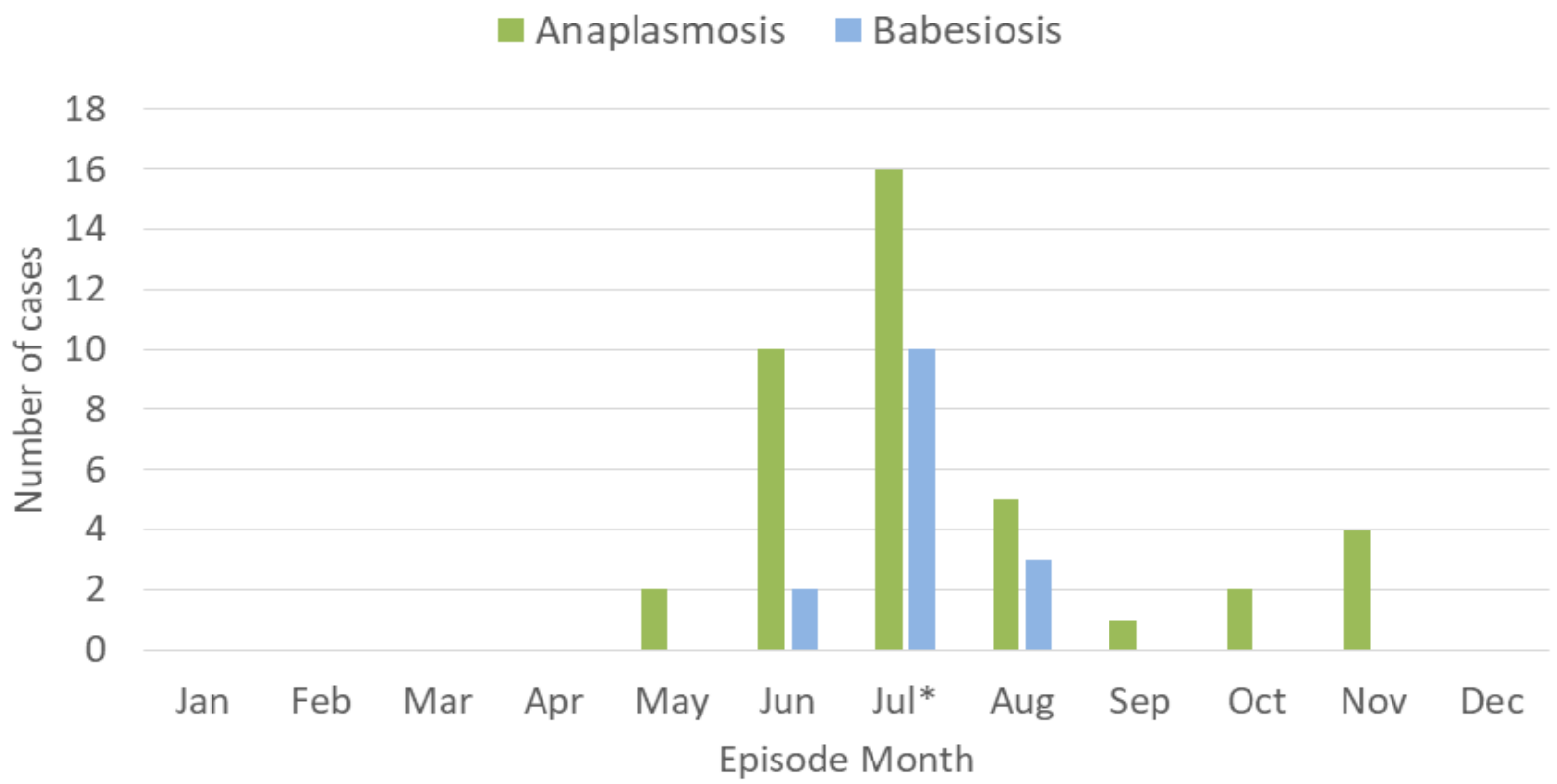
Powassan virus infection

- 0 confirmed + probable cases reported in 2023

Lyme disease

- 1795 confirmed + probable cases reported in 2023

Seasonal Trends of Confirmed and Probable Anaplasmosis and Babesiosis Cases in Ontario (January 1–December 31, 2023)

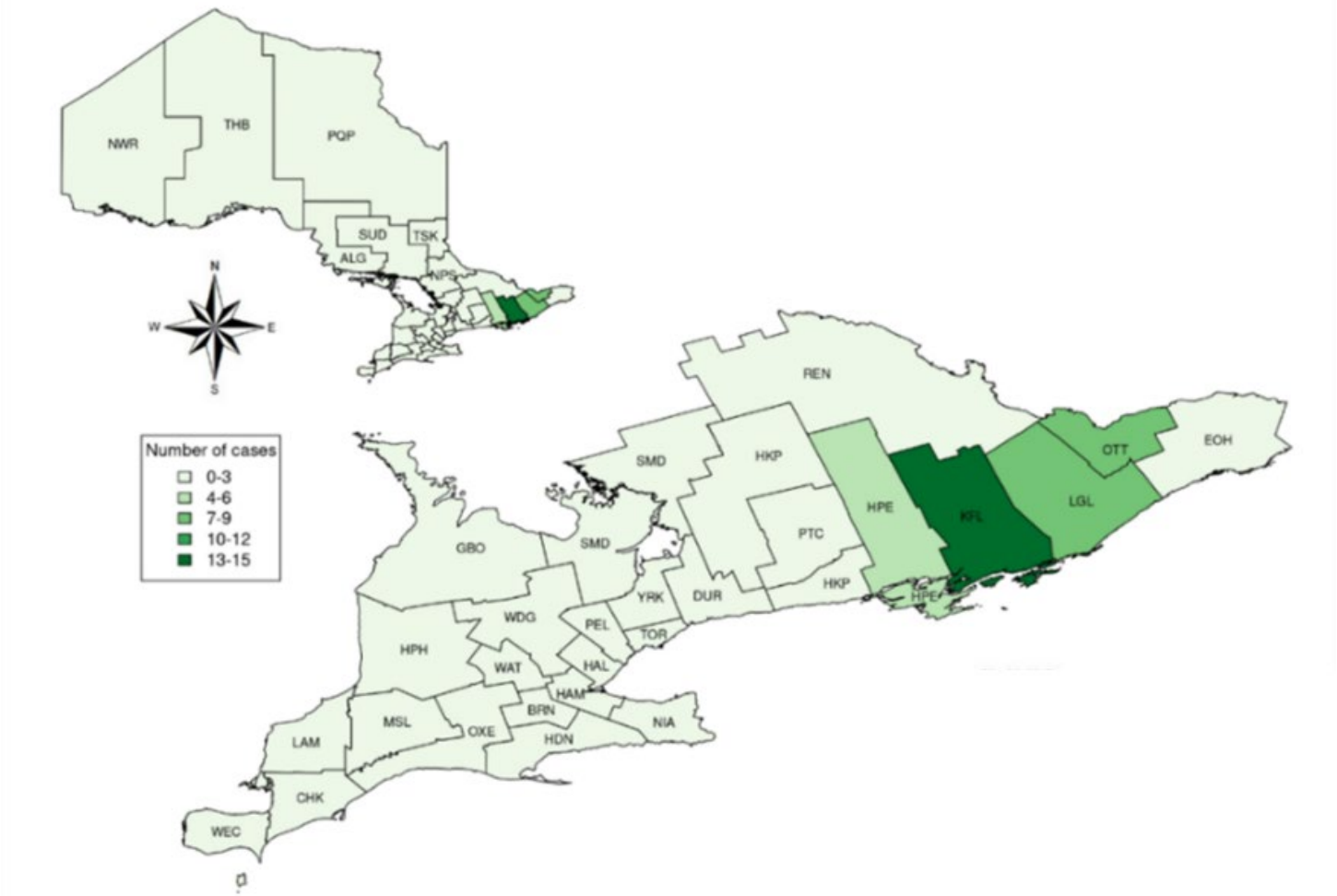


Data source: iPHIS data

Note: Cases are shown by episode month (first available of onset, specimen collection, or reported month)

*Anaplasmosis and babesiosis were designated as diseases of public health significance on July 1, 2023. However, for some cases, onset of illness occurred prior to July 1, 2023

Number of Confirmed and Probable Anaplasmosis Cases by Reported Location of Exposure in Ontario (January 1-December 31, 2023)

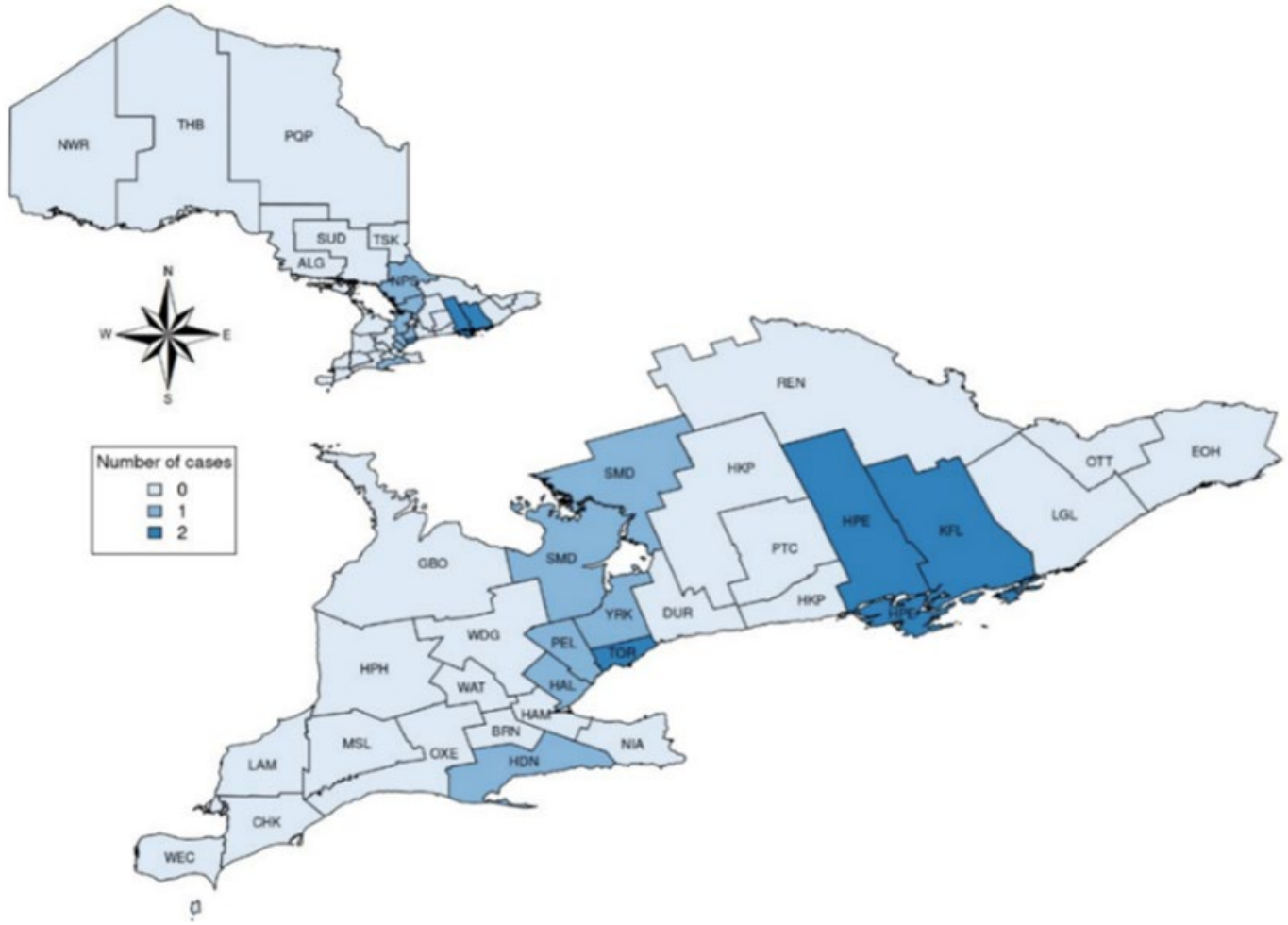


Code	Public health unit
ALG	Algoma District
BRN	Brant County
CHK	Chatham-Kent
DUR	Durham Regional
EOH	Eastern Ontario
GBO	Grey Bruce
HAL	Halton Regional
HAM	City of Hamilton
HDN	Haldimand-Norfolk
HKP	Haliburton-Kawartha-Pine Ridge District
HPE	Hastings and Prince Edward Counties
HPH	Huron Perth Public Health
HUR	Huron County
KFL	Kingston-Frontenac and Lennox & Addington
LAM	Lambton
LGL	Leeds-Grenville and Lanark District
MSL	Middlesex-London
NIA	Niagara Regional
NPS	North Bay Parry Sound District
NWR	Northwestern
OTT	City of Ottawa
OXE	Oxford Elgin-St. Thomas
PDH	Perth District
PEL	Peel Regional
PQP	Porcupine
PTC	Peterborough County-City
REN	Renfrew County and District
SMD	Simcoe Muskoka District
SUD	Sudbury and District
THB	Thunder Bay District
TOR	City of Toronto
TSK	Timiskaming
WAT	Waterloo
WDG	Wellington-Dufferin-Guelph
WEC	Windsor-Essex County
YRK	York Regional

Data source: iPHIS data

Note: Cases can report multiple exposure locations (e.g. multiple different public health units in Ontario). As result there may be more exposure locations reported than the total number of cases.

Number of Confirmed and Probable Babesiosis Cases by Reported Location of Exposure in Ontario (January 1-December 31, 2023)



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MSL	Middlesex-London
NIA	Niagara Regional
NPS	North Bay Parry Sound District
NWR	Northwestern
OTT	City of Ottawa
OXE	Oxford Elgin-St. Thomas
PDH	Perth District
PEL	Peel Regional
PQP	Porcupine
PTC	Peterborough County-City
REN	Renfrew County and District
SMD	Simcoe Muskoka District
SUD	Sudbury and District
THB	Thunder Bay District
TOR	City of Toronto
TSK	Timiskaming
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WEC	Windsor-Essex County
YRK	York Regional

Data source: iPHIS data

Note: Cases can report multiple exposure locations (e.g. multiple different public health units in Ontario). As result there may be more exposure locations reported than the total number of cases.

Clinical Presentation of Tick-Borne Diseases of Public Health Significance

Infection Background – Lyme Disease

- **Etiologic agent:** helical bacterium *Borrelia burgdorferi sensu lato*
  - Main species in North America: ***B. burgdorferi sensu stricto***
  - Rare cases of *B. mayonii* reported in Minnesota, Wisconsin, and North Dakota
  - In Europe: mainly *B. afzelii, B. garinii,* and *B. burgdorferi s.s.*
- **Transmission:** Infected tick must be attached ≥ 24-36 hours to transmit
- **Incubation period:** symptoms of early localized Lyme disease can occur 3 to 30 days after a tick bite (usually 7-14 days)

Image source: CDC #6631. CDC. Available from: https://phil.cdc.gov/Details.aspx?pid=6631

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Lyme disease. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-lyme-disease-en-2023.pdf
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Clinical Presentation – Lyme Disease

- **Early localized disease (3 to 30 days following bite):**
  - Fever, generalized arthralgia and myalgia, headache, lymphadenopathy
  - Erythema migrans rash - Expanding rash >5 cm, occurs in 70-80% of infected patients
- **Early disseminated disease (weeks to months following bite):**
  - Fatigue, general weakness, multiple erythema migrans lesions
  - Peripheral/central nervous system involvement, cardiac symptoms
- **Late disseminated Lyme disease (weeks to months following bite):**
  - Musculoskeletal – arthritis, Baker's cyst
  - Neurological – meningitis, subacute mild encephalopathy, polyneuropathy

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Lyme disease. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-lyme-disease-en-2023.pdf
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Infection Background – Anaplasmosis

- **Etiologic Agent:** intracellular bacterium *Anaplasma phagocytophilum*
  - Infects granulocytes* such as neutrophils
  - Other species mainly infect ruminants and canids (e.g., *A. marginale, A. central*)
- **Transmission:** Infected tick must be attached ≥ 12-24 hours to transmit
  - Rare case reports of transfusion-transmitted infections
- **Incubation period:** Symptoms typically appear 1-2 weeks (range 5-21 days) after infected tick bite

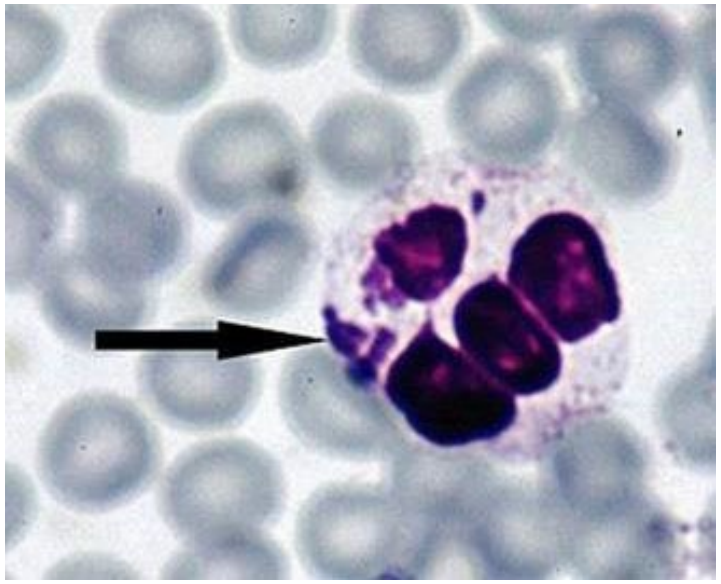

Image source: Walker AR. Anaplasma phagocytophilum. WikiMedia Commons; 2012. Available from: https://commons.wikimedia.org/wiki/File:Anaplasma-phagocytophilum-sheep.jpg

*previously called "human granulocytic ehrlichiosis"

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Anaplasmosis. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-anaplasmosis-en-2023.pdf
Minnesota. Department of Health. About Anaplasmosis [Internet]. St. Paul, MN: Minnesota. Department of Health; [2024] [cited 2024 May 15]. Available from: https://www.health.state.mn.us/diseases/anaplasmosis/basics.html

Clinical Presentation – Anaplasmosis

- **Acute febrile illness (duration usually ≤ 2 weeks)**
  - Symptoms can include fever, fatigue, chills, severe headache, myalgia, abdominal pain, nausea, vomiting, diarrhea, and/or loss of appetite
- Severe or more prolonged illness if delayed treatment, advanced age, or impaired immune system
  - Can include respiratory failure, bleeding problems, organ failure, and/or death
- Symptoms rarely reported include respiratory symptoms, central nervous symptoms, and rash (< 10%)

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Anaplasmosis. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-anaplasmosis-en-2023.pdf
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Infection Background – Babesiosis

- **Etiologic Agent:** intracellular eukaryotic parasite *Babesia*
  - Infects erythrocytes (i.e. red blood cells)
  - Main species in North America: ***B. microti***
- **Transmission:** Infected tick must be attached ≥ 36-48 hours to transmit
  - Multiple transfusion-transmitted infections in US (blood screening in US since 2020)
- **Incubation period:** Symptoms typically appear 1-4 weeks after infected tick bite and up to 24 weeks after blood transfusion

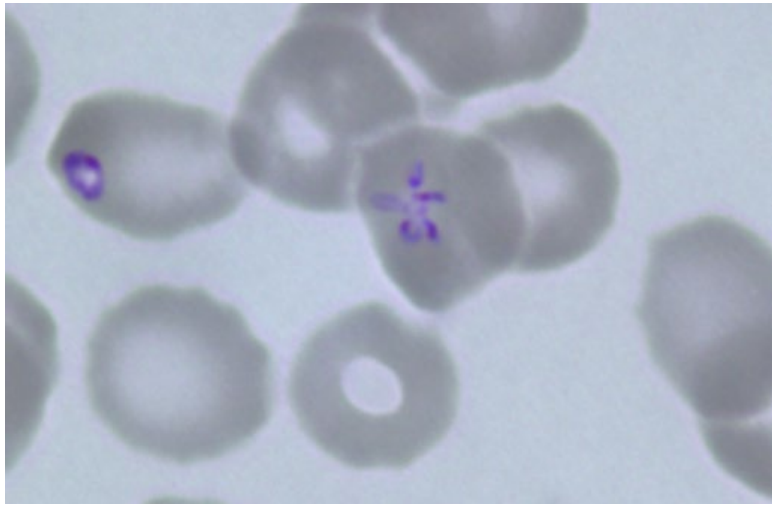

Image source: PHO's laboratory.

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Babesiosis. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-babesiosis-en-2023.pdf
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Clinical Presentation – Babesiosis

- Many (20-50%) infections remain asymptomatic
- **Acute/subacute febrile illness** (duration usually ≤ 2-4 weeks)
  - Symptoms can include fever, chills, sweats, body aches, loss of appetite, or fatigue
  - Hemolytic anemia, jaundice and dark urine (haemoglobinuria)
- Residual submicroscopic parasitemia may persist for months
- Severe, more prolonged, or relapsing illness if delayed treatment, advanced age, impaired immunity, or impaired splenic function
  - Can include respiratory failure, bleeding problems, organ failure, and/or death

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Babesiosis. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-babesiosis-en-2023.pdf
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Infection Background – Powassan Virus

- **Etiologic Agent:** Powassan virus (part of the *Flavivirus* genus)
  - Lineage 1 ("prototype") transmitted by *I. cookei* and *I. marxi*
  - Lineage 2 ("deer tick virus") transmitted by *I. scapularis*
- **Transmission:** Transmission via bite of infected tick can may occur in as little as 15 minutes
  - Rare case reports of transfusion-transmitted infections
- **Incubation period:** Symptoms typically appear 1 week to 1 month after infected tick bite

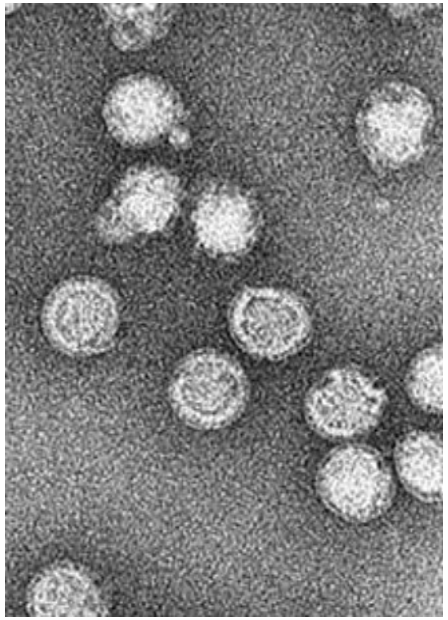

Image source: Stiasny K, Kössl C, Lepault J, Rey FA, Heinz FX. Characterization of a structural intermediate of Flavivirus membrane fusion. PLOS Pathogens. 2007;3(2):e20. Available from: https://doi.org/10.1371/journal.ppat.0030020. Figure 4, Electron micrographs of TBE virus at pH 8.0, 10.0, and 5.4.

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Powassan virus infection. Effective July 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Jul; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-powassan-en-2023.pdf
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Clinical Presentation – Powassan Virus

- **Acute prodromal phase** (duration usually 1-3 days)
  - Asymptomatic or mild to severe symptoms may occur such as fever, headache, nausea, vomiting, asthenia, or myalgia
  - May be a transient period of remission after the acute prodromal phase, followed by worsening neurological deterioration
- **Neuroinvasive disease** (duration usually weeks)
  - May cause meningitis and/or encephalitis with focal neurologic findings such as confusion, loss of coordination, difficulty speaking, paralysis, seizures, or coma
  - In people with severe disease, case fatality rate is 5-10% and of those that survive, ~50% may have long-term problems such as recurring headaches, loss of muscle mass and strength, and memory problems

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Powassan virus infection. Effective July 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Jul; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-powassan-en-2023.pdf
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Summary Table of Tick-Borne DoPHS Clinical Presentation

Criteria	Lyme disease	Anaplasmosis	Babesiosis	Powassan virus
Tick Bite Risk	**≥ 24-36 hours**	≥ 12 to 24 hours	**≥ 36-48 hours**	≤ 15 minutes
Incubation	3 to 30 days	5 to 21 days	1 to 4 weeks (tick bite) or 1 to 24 weeks (transfusion)	1 to 5 weeks
Skin Lesions	**Erythema migrans** (70%)	Maculopapular (≤ 10%)	Petechiae (rare, if severe)	Morbiliform (rare)
Other Differential Symptoms	Arthralgia, headache, **lymphadenopathy, subacute or late manifestations**	Arthralgia, headache, occasionally multi-organ failure	High fever, dark urine, severe if low immunity or low splenic function	**Encephalitis** after short prodrome (1-3 days) and 50% have sequelae
Routine blood work	Usually normal in early localized cases	**Leukopenia** (> 45%), **thrombocytopenia** (>70%), **high transaminases** (>50%)	**Hemolytic anemia** (> 90%) **thrombocytopenia** (> 60%), **high transaminases** (> 70%)	Usually normal (< 15% thrombocytopenia)

Sources: Sanchez E, Vannier E, Wormser GP, Hu LT. Diagnosis, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis and Babesiosis. JAMA. 2016;315(16):1767-1777. Available from: https://doi.org/10.1001/jama.2016.2884
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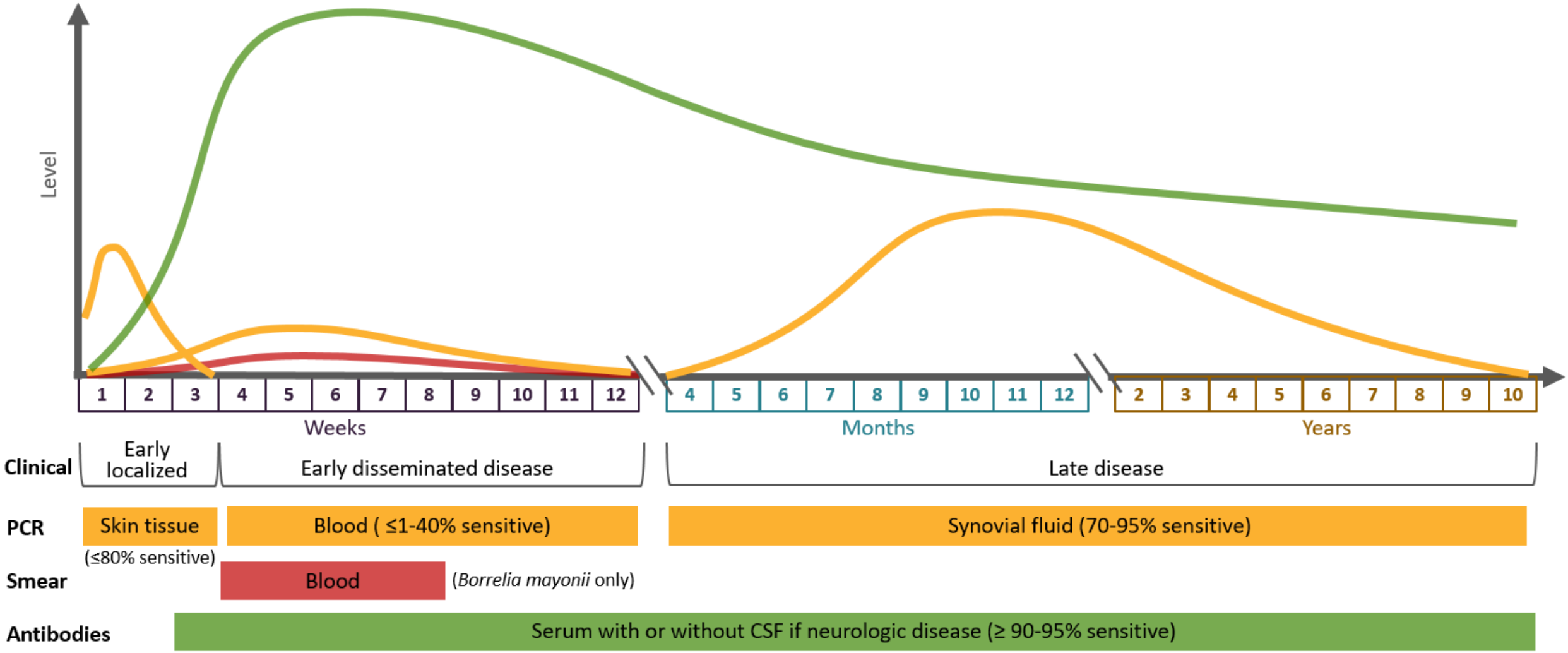
Testing for Tick-Borne Diseases of Public Health Significance

Lyme Disease – Dynamics of Infection From Symptom Onset

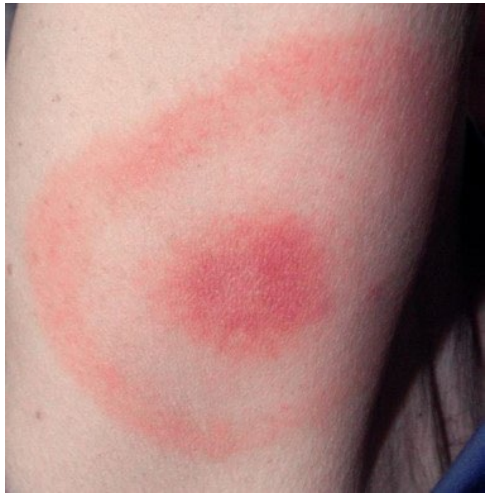


Source: Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JWR, et al. Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: https://doi.org/10.1038/nrdp.2016.90

Lyme Disease – Dynamics of Infection From Symptom Onset

Testing During Early Localized Disease

- **Clinical diagnosis** usually sufficient
- **Biopsy PCR** unnecessarily invasive
- **Serum antibodies** not yet reliably positive (acute phase)



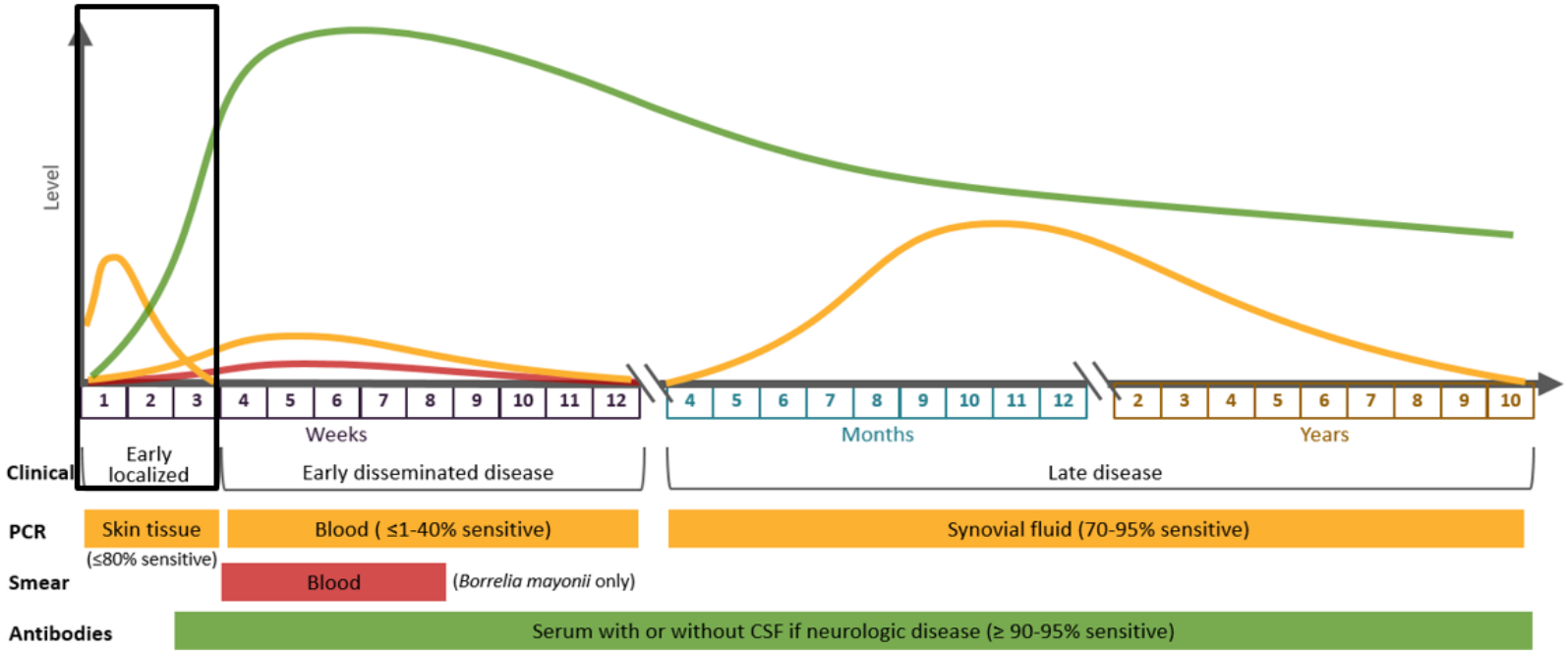


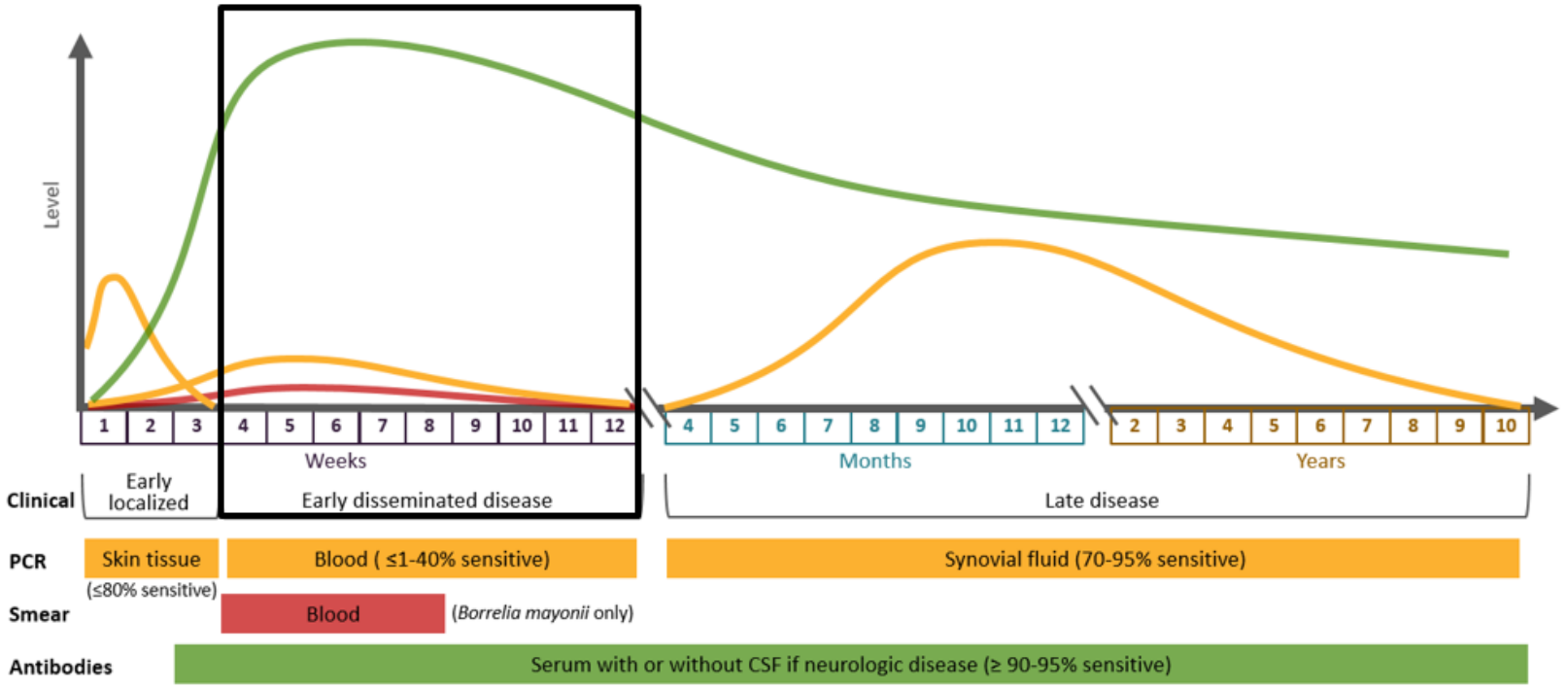
Image source: Gathany J. CDC #9875. CDC/ James Gathany. Available from: https://phil.cdc.gov/Details.aspx?pid=9875

Source: Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JWR, et al. Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: https://doi.org/10.1038/nrdp.2016.90

Lyme Disease – Dynamics of Infection From Symptom Onset

Testing During Early Disseminated Disease

- **Serum antibodies** usually positive (convalescent phase)
  - Note: sensitivity may be reduced if patient received treatment
- If neuroborreliosis suspected: **CSF-to-serum antibody** level may be helpful
- **Blood PCR** not sensitive
- **Blood smear microscopy** only useful if B. mayonii suspected

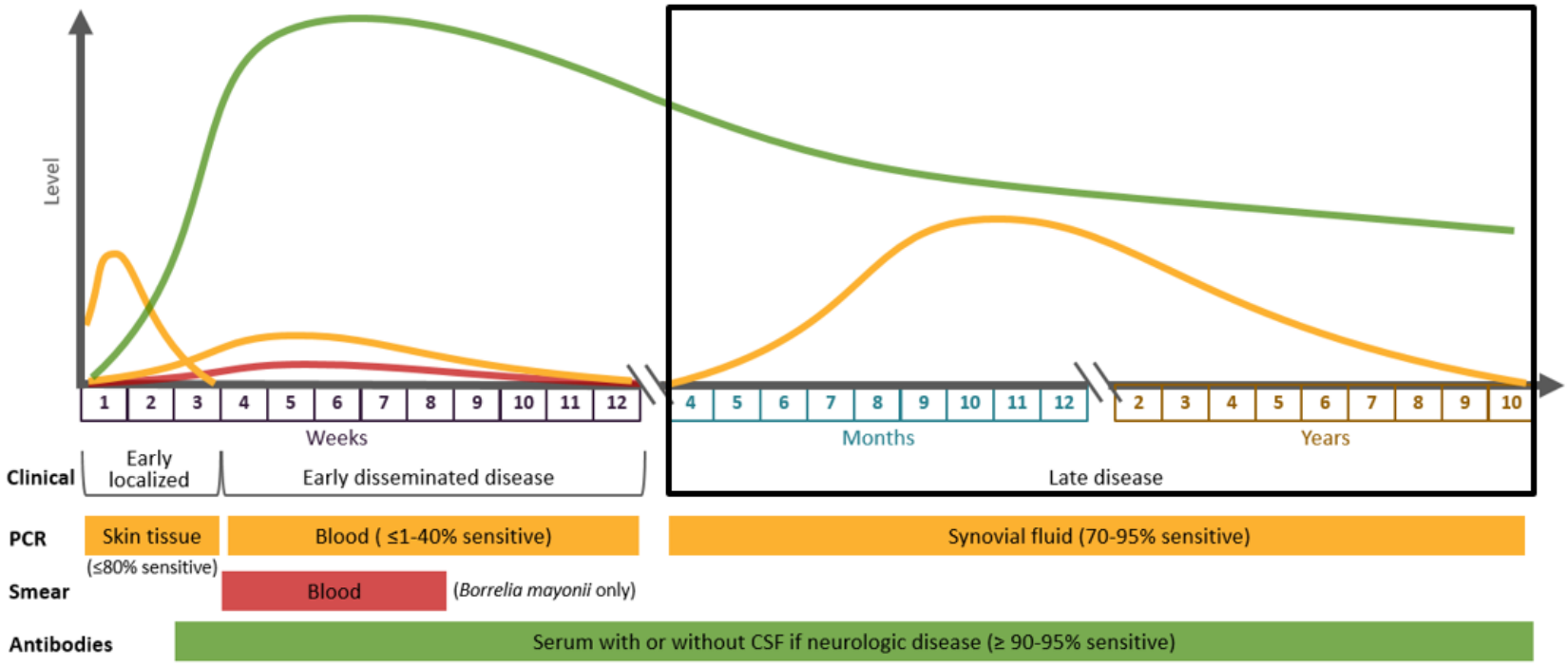


Source: Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JWR, et al. Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: https://doi.org/10.1038/nrdp.2016.90

Lyme Disease – Dynamics of Infection From Symptom Onset

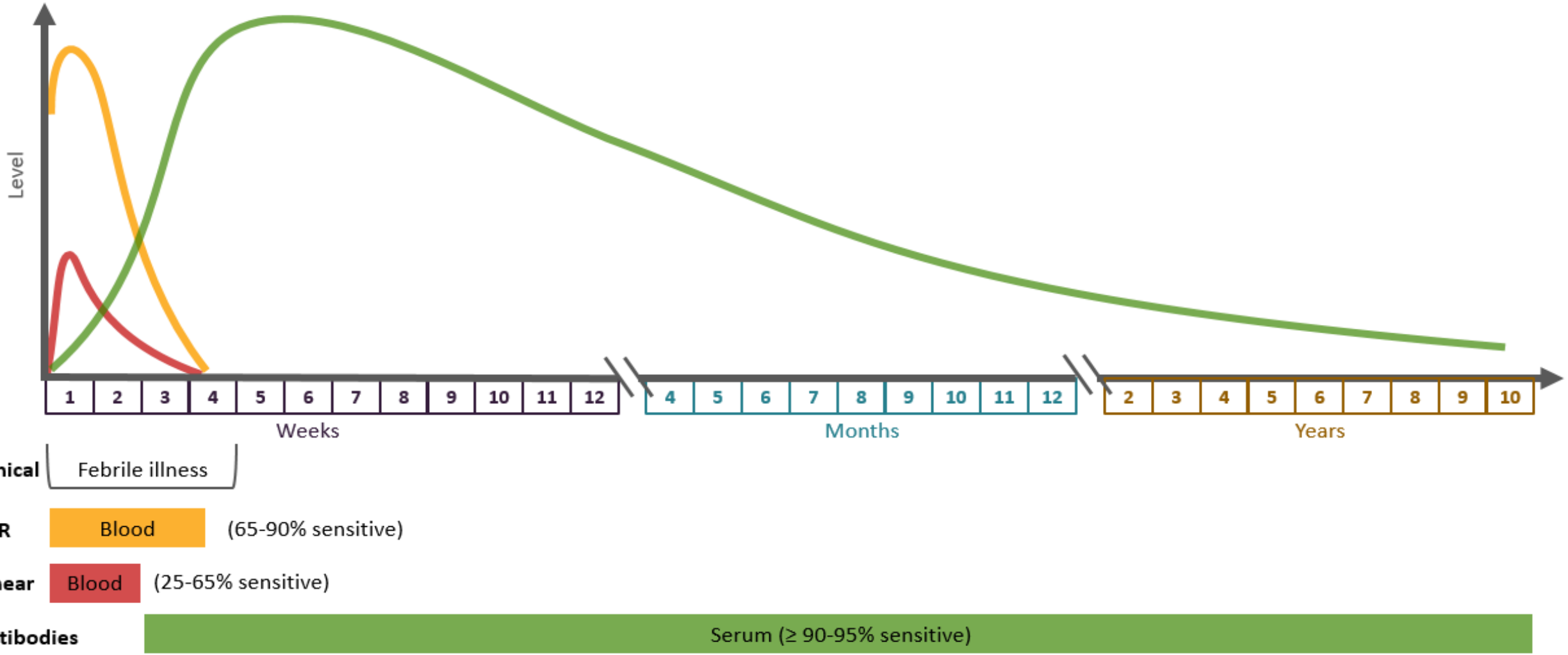
Testing During Late Disease

- **Serum antibodies** usually remain positive
- If suspect Lyme arthritis: **synovial fluid PCR** may be positive



Source: Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JWR, et al. Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: https://doi.org/10.1038/nrdp.2016.90

Anaplasmosis – Dynamics of Infection From Symptom Onset

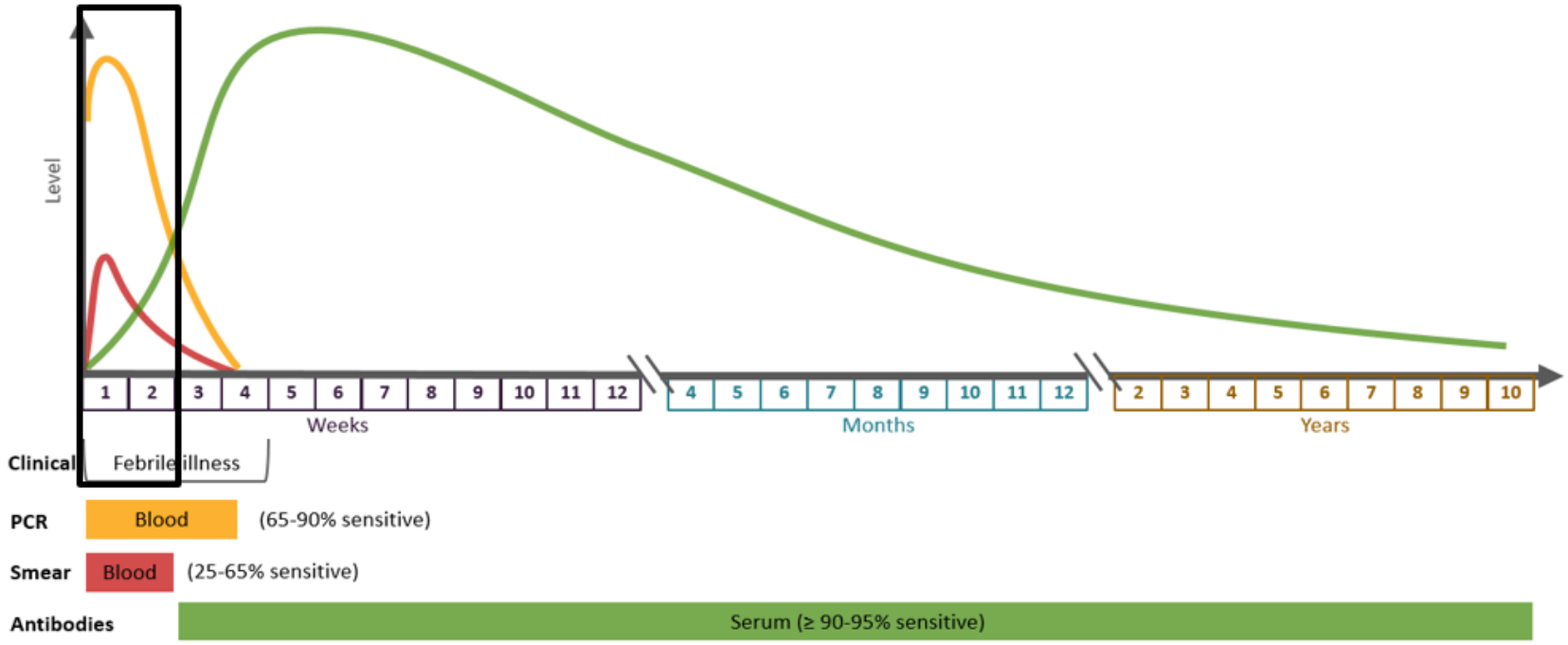


Source: Schotthoefer AM, Meece JK, Bertz PD, Ivacic LC, Zhang K, Weiler T, et al. Comparison of a real-time PCR method with serology and blood smear analysis for diagnosis of human Anaplasmosis: importance of infection time course for optimal test utilization. J Clin Microbiol. 2013;51(7):2147-53. Available from: https://doi.org/10.1128/JCM.00347-13

Anaplasmosis – Dynamics of Infection From Symptom Onset

Testing During Acute Febrile Illness (≤ 2 Weeks From Onset)

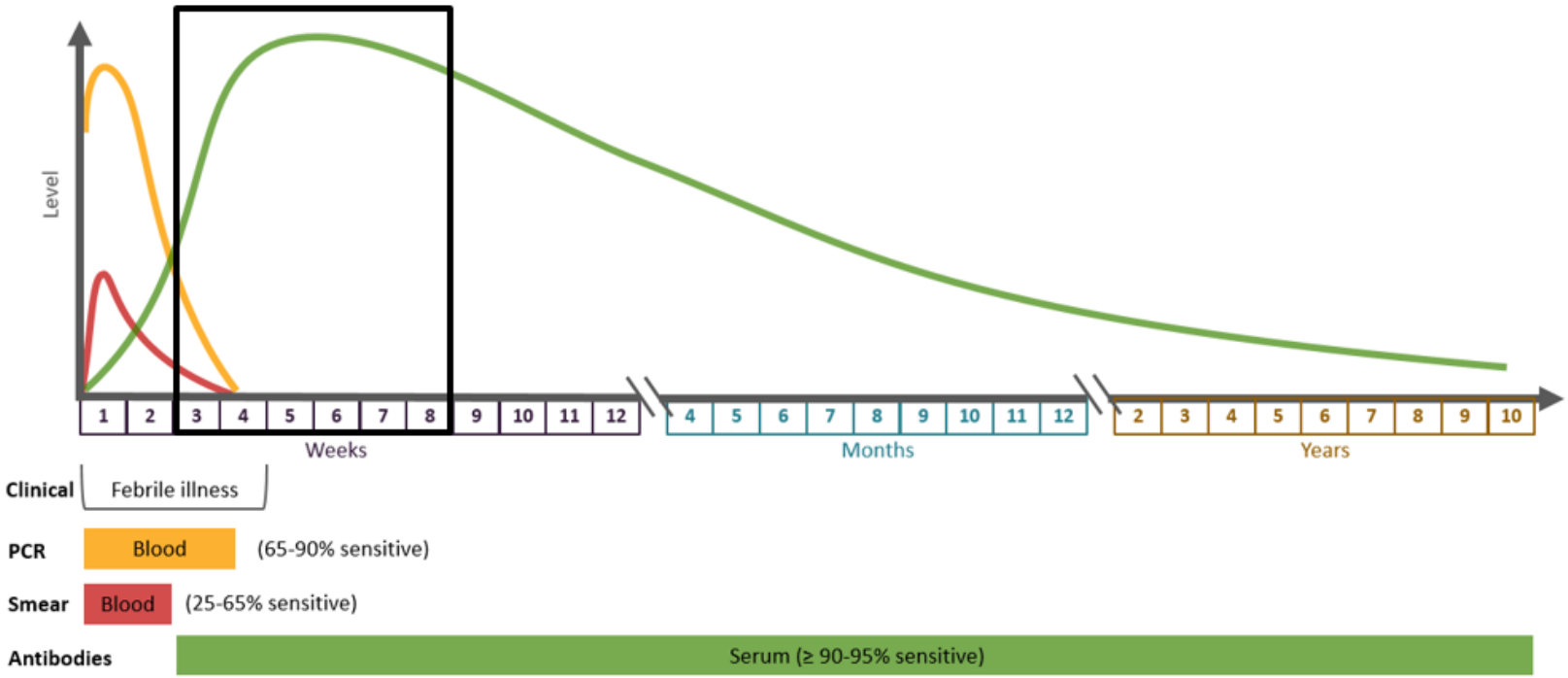
- **Blood PCR** usually positive
- **Blood smear microscopy** not usually sensitive
- **Serum antibodies** not yet reliably positive (acute phase)
    - Note: Can collect acute serum *if* also planning to collect a paired convalescent phase serum



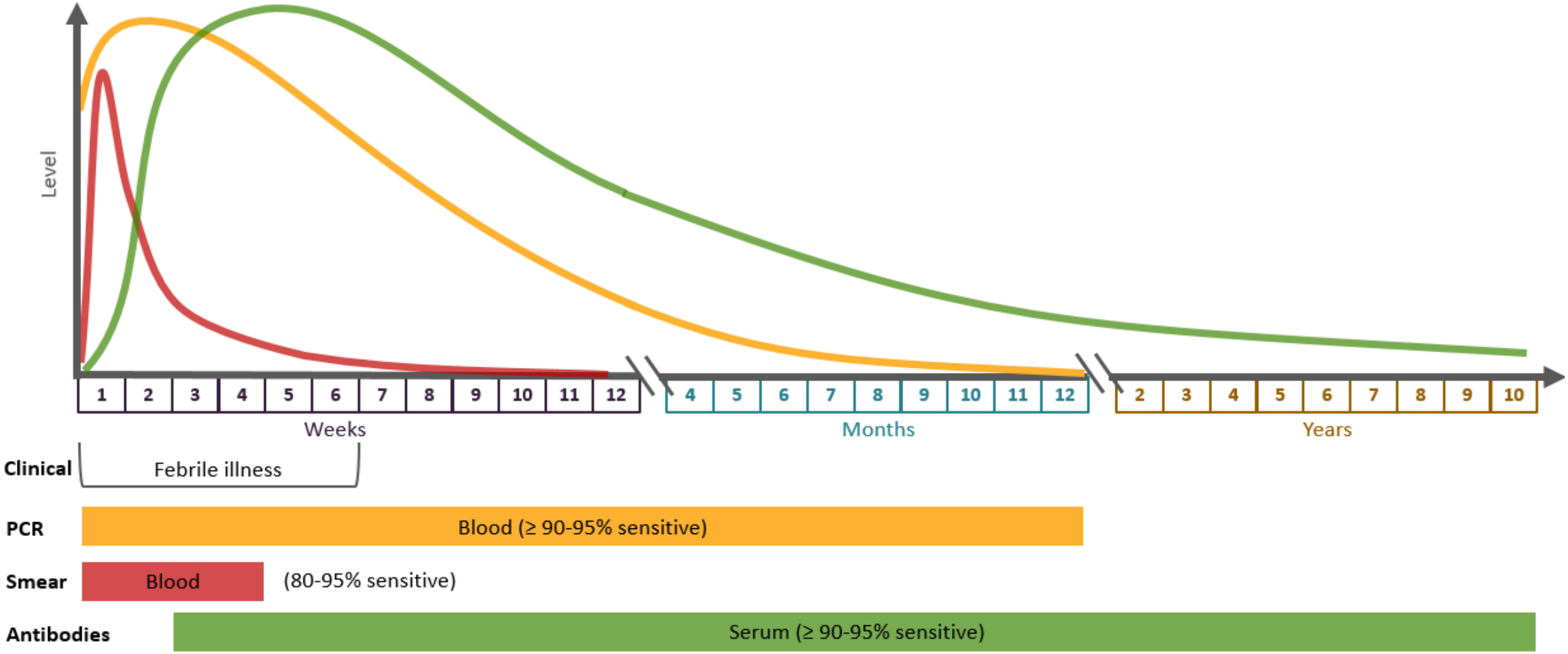
Anaplasmosis – Dynamics of Infection From Symptom Onset

Testing During Subacute Illness (≥ 2 Weeks From Onset)

- **Serum antibodies** usually positive (convalescent phase)
  - 4-fold increase in titres from acute phase to convalescent phase is confirmatory
  - Residual antibody levels may persist for months to years
  - Note: sensitivity may be reduced if patient received treatment, and potential cross-reactivity with *Ehrlichia*



Babesiosis – Dynamics of Infection From Symptom Onset

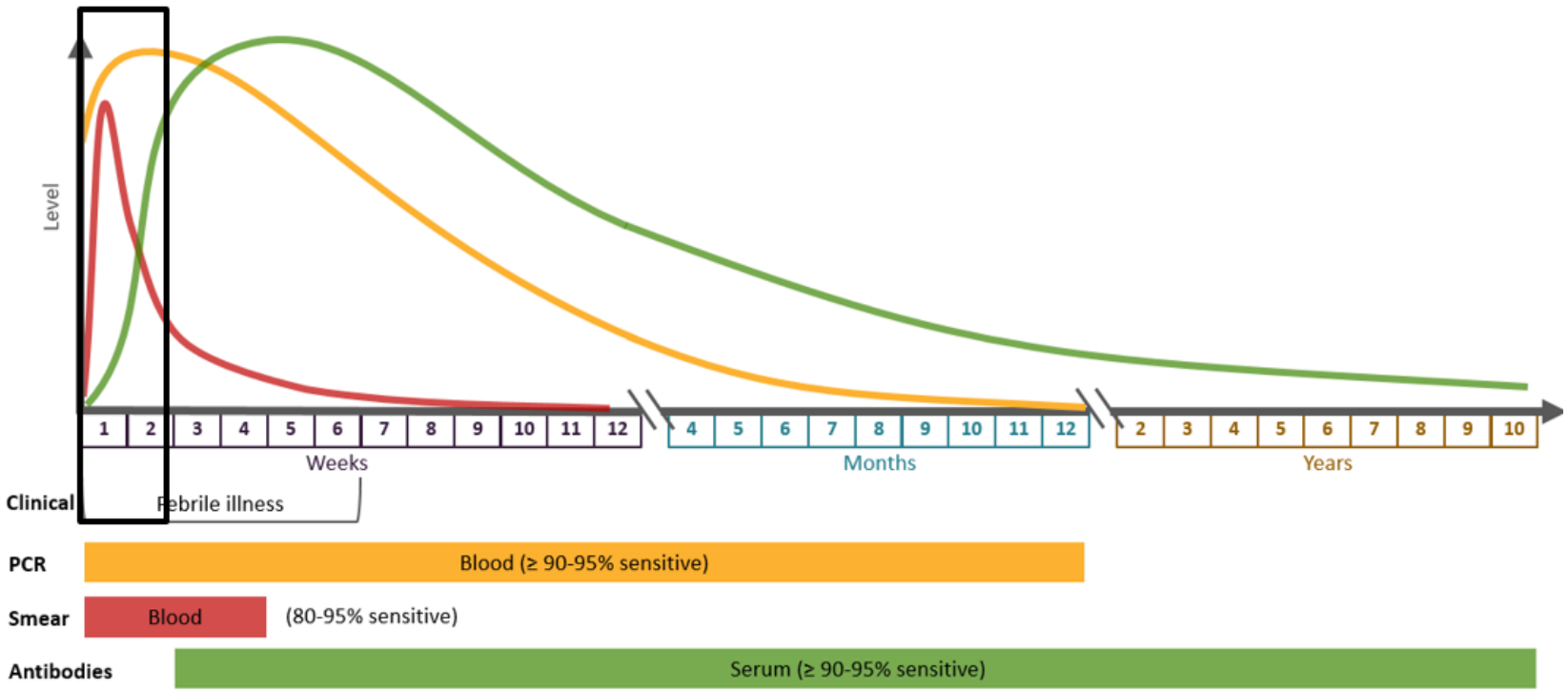


Source: Krause PJ , Spielman A, Telford 3rd SR, Sikand VK, McKay K, Christianson D, et al. Persistent parasitemia after acute babesiosis. N Engl J Med. 1998;339(3);160-5. Available from: https://doi.org/10.1056/NEJM199807163390304

Babesiosis – Dynamics of Infection From Symptom Onset

Testing During Acute Febrile Illness (≤ 2 Weeks From Onset)

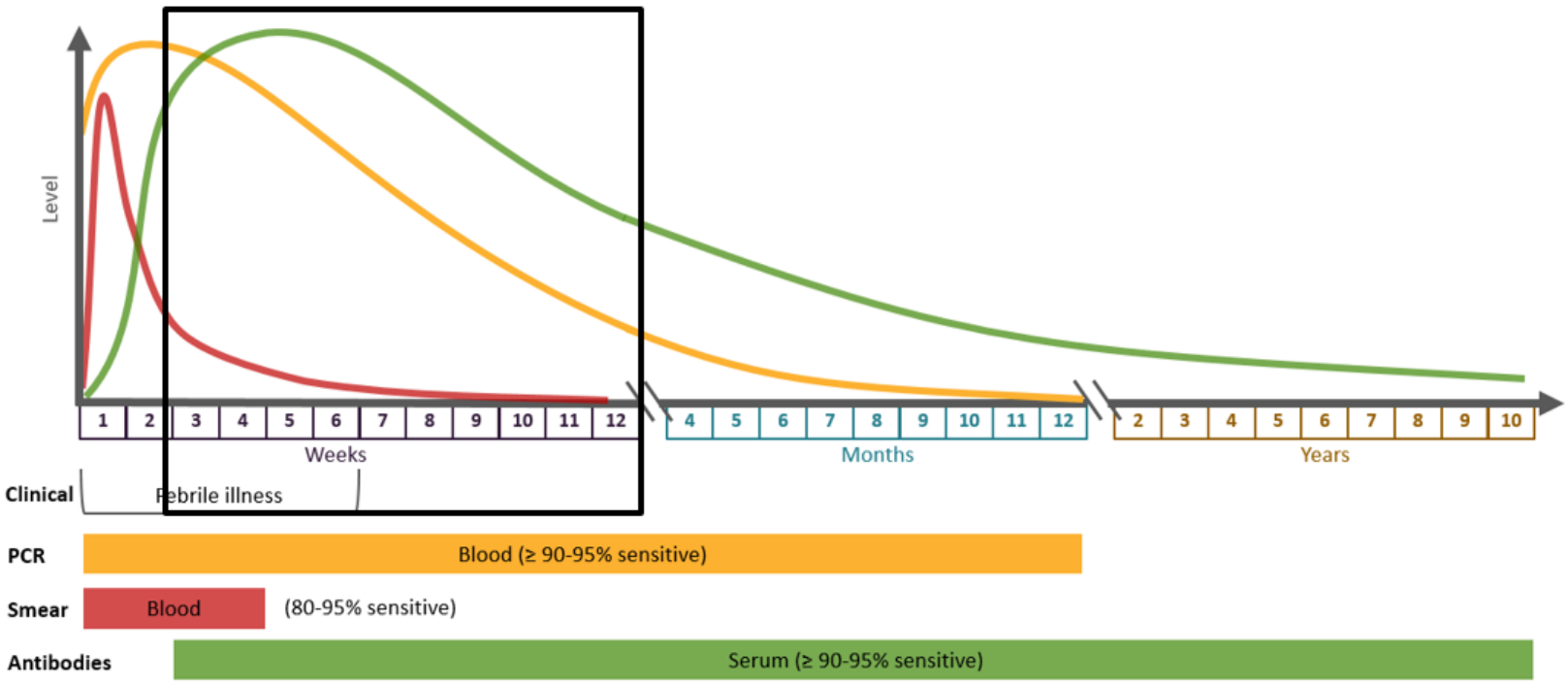
- **Blood smear microscopy** usually positive
  - Repeat smears may be needed if very early symptoms
- **Blood PCR** usually positive
  - Currently costly and long turnaround time
- Serum antibodies not yet reliably positive (acute phase)



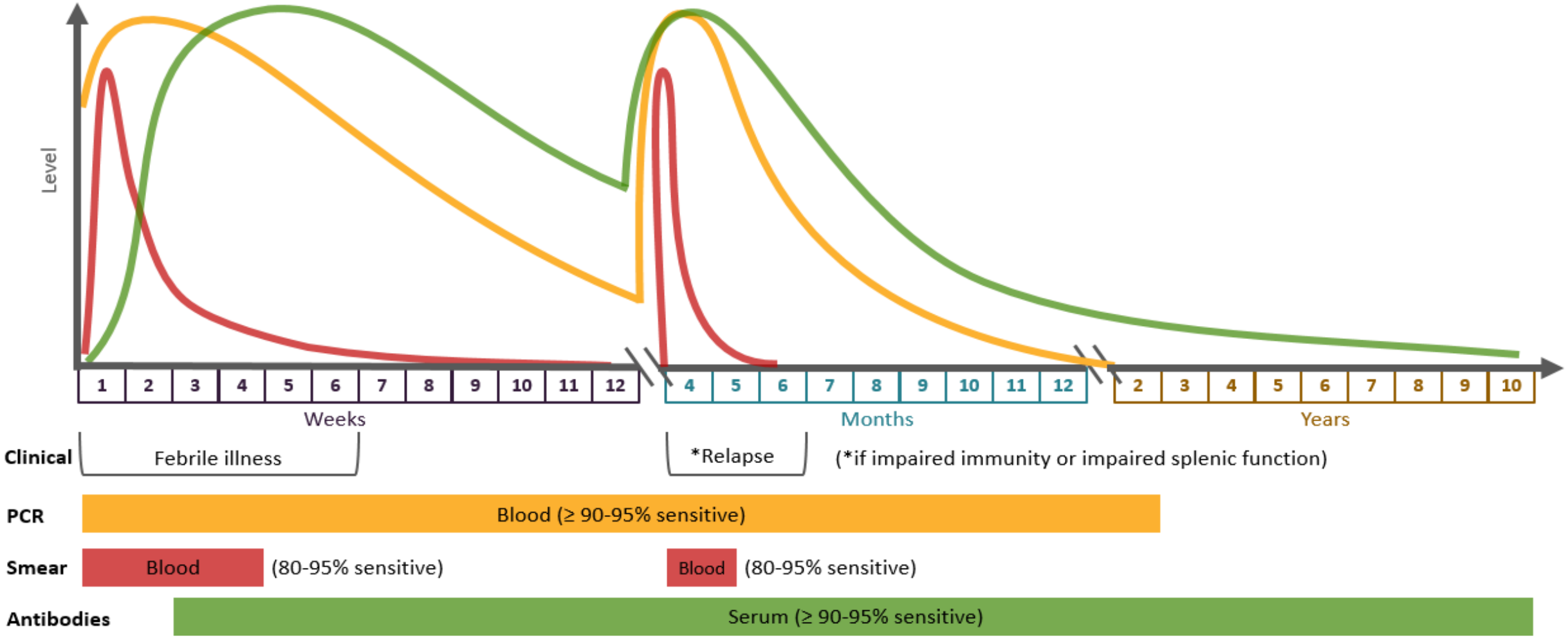
Babesiosis – Dynamics of Infection From Symptom Onset

Testing During Subacute Illness (≥ 2 Weeks From Onset)

- **Blood smear microscopy** sensitivity variable
- **Blood PCR** usually positive
  - May intermittently persist for months
- **Serum antibodies** usually positive
  - Limited advantage over PCR in most cases, rarely useful

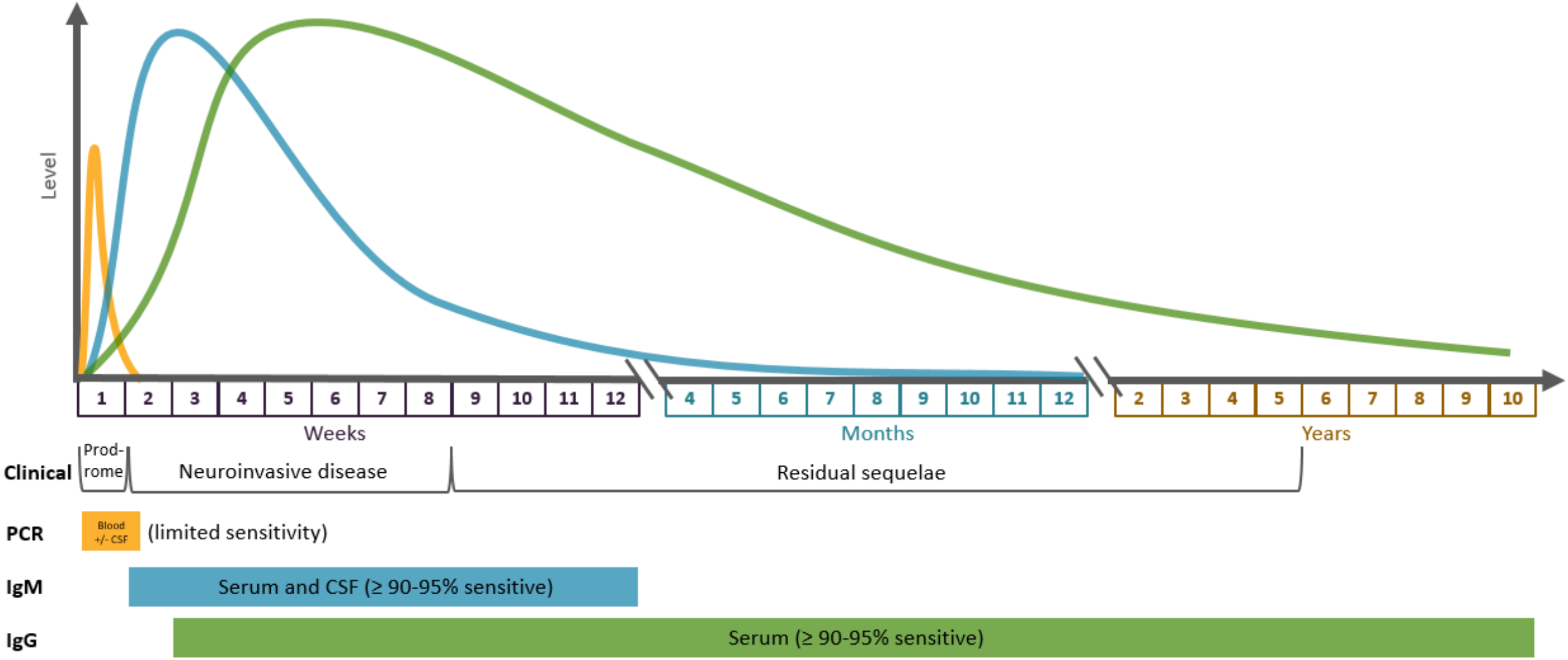


Babesiosis – Dynamics of Infection From Symptom Onset (*including relapse)



Source: Krause PJ , Spielman A, Telford 3rd SR, Sikand VK, McKay K, Christianson D, et al. Persistent parasitemia after acute babesiosis. N Engl J Med. 1998;339(3);160-5. Available from: https://doi.org/10.1056/NEJM199807163390304

Powassan Virus Disease – Dynamics of Infection From Symptom Onset

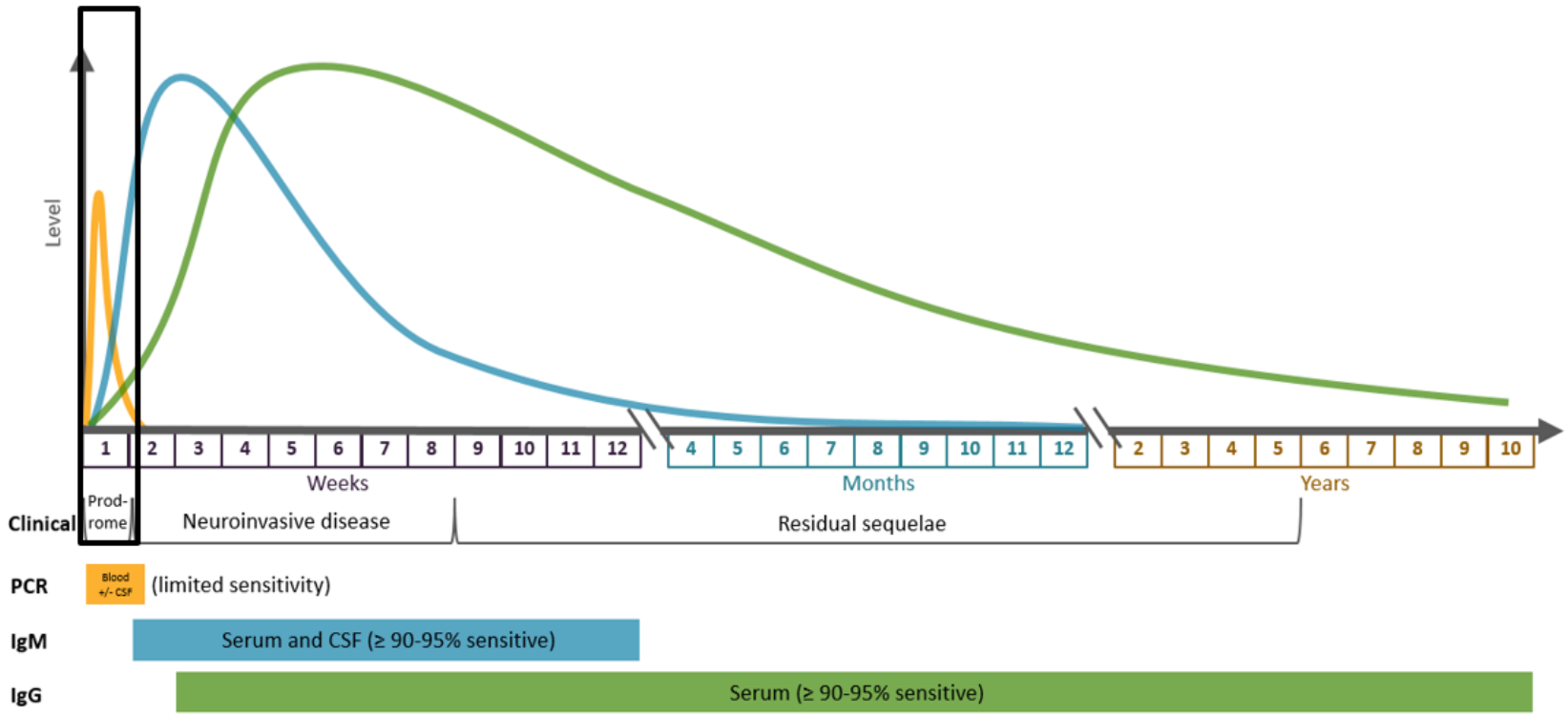


Source: Kemenesi G, Banyai K. Tick-Borne Flaviviruses, with a Focus on Powassan Virus. Clin Microbiol Reb. 2018;32(1); e00106-17. Available from: https://doi.org/10.1128/CMR.00106-17.

Powassan Virus Disease – Dynamics of Infection From Symptom Onset

Testing During Prodromal Phase (≤ 1 Weeks From Onset)

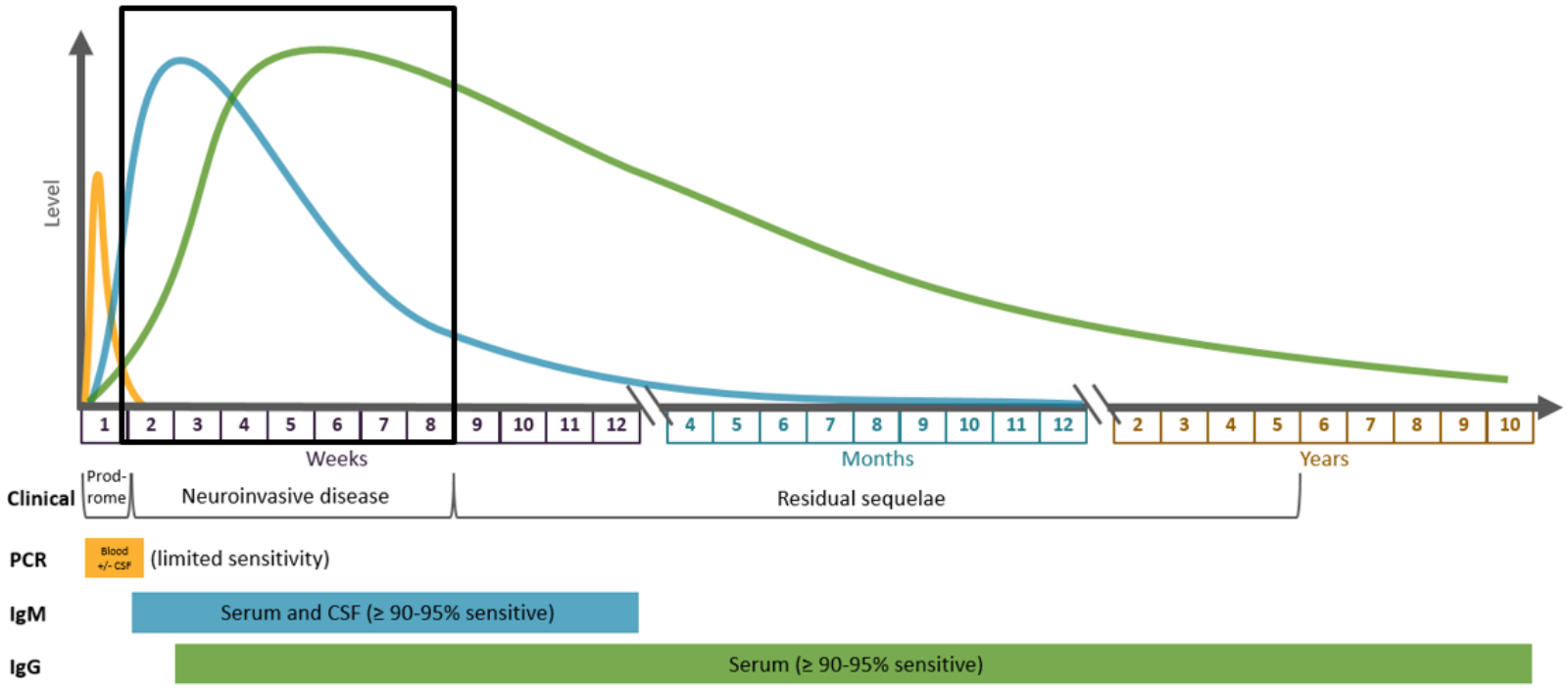
- **Blood (+/- CSF) PCR** may be positive but limited evidence
    - Mainly useful if impaired immunity
- **Serum and CSF IgM and IgG antibodies** not yet reliably positive (acute phase)
    - Note: Can collect acute serum *if* also planning to collect a paired convalescent phase serum



Powassan Virus Disease – Dynamics of Infection From Symptom Onset

Testing During Neuroinvasive Disease (≥ 1 Week From Onset)

- **Blood and CSF PCR** usually negative
- **Serum and CSF IgM antibodies** usually peak between 2nd and 4th week from onset
  - **CSF IgM** usually confirmatory (not routinely available)
  - Serum IgM may persist for ≥ 12 months
- **Serum IgG antibodies** usually peak between 4th and 6th week from onset
  - 4-fold increase in titres from acute phase to convalescent phase is confirmatory



Summary Table of Tick-Borne DoPHS Diagnostic Tests

Consideration	Lyme disease	Anaplasmosis	Babesiosis	Powassan virus
Tick Bite Risk	**≥ 24-36 hours**	≥ 12 to 24 hours	**≥ 36-48 hours**	≤ 15 minutes
Incubation	3 to 30 days	5 to 21 days	1 to 4 weeks (tick bite) or 1 to 24 weeks (transfusion)	1 to 5 weeks
Skin Lesions	**Erythema migrans** (70%)	Maculopapular (≤ 10%)	Petechiae (rare, if severe)	Morbiliform (rare)
Other Differential Symptoms	Arthralgia, headache, **lymphadenopathy, subacute or late manifestations**	Arthralgia, headache, occasionally multi-organ failure	High fever, dark urine, severe if low immunity or low splenic function	**Encephalitis** after short prodrome (1-3 days) and 50% have sequelae
Routine Core Lab Tests	Usually normal in early localized cases	**Leukopenia** (> 45%), **thrombocytopenia** (>70%), **high transaminases** (>50%)	**Hemolytic anemia** (> 90%) **thrombocytopenia** (> 60%), **high transaminases** (> 70%)	Usually normal (< 15% thrombocytopenia)
Main Diagnostic Tests	**Early localized:** Clinical **Other stages:** Serology (paired)	**Acute illness:** PCR **Subacute illness** Serology (paired)	**Acute, prolonged, or relapsing illness:** Smears +/- PCR	**Prodrome:** PCR? **Encephalitic stage:** Serology (paired)
Main Treatment Options	Doxycycline, amoxicillin, cefuroxime, or ceftriaxone	Doxycycline	Atovaquone plus azithro-mycin, or clindamycin plus quinine	None (supportive)

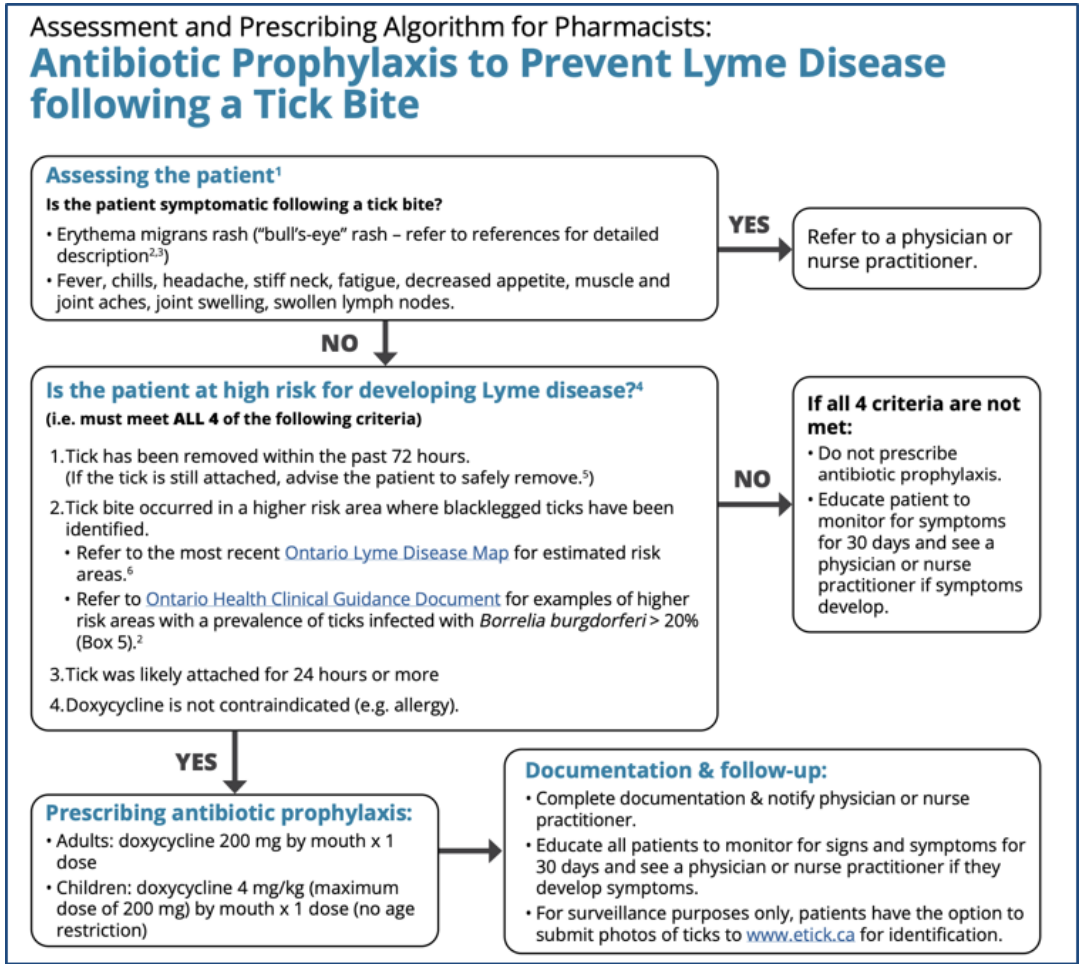
Source: Rodino KG, Theel ES, Pritt BS. Tick-Borne Diseases in the United States. Clin Chem. 2020;66(4):537-548. Available from: https://doi.org/10.1093/clinchem/hvaa040

Testing Following Seasonal *Ixodes* Tick Exposure in Risk Areas

No symptoms

↓

No testing
(consider Lyme disease post-exposure management as appropriate)



Assessment and Prescribing Algorithm for Pharmacists:

Antibiotic Prophylaxis to Prevent Lyme Disease following a Tick Bite

Assessing the patient[1]

Is the patient symptomatic following a tick bite?

- Erythema migrans rash ("bull's-eye" rash – refer to references for detailed description[2,3])
- Fever, chills, headache, stiff neck, fatigue, decreased appetite, muscle and joint aches, joint swelling, swollen lymph nodes.

YES → Refer to a physician or nurse practitioner.

NO ↓

Is the patient at high risk for developing Lyme disease?[4]

(i.e. must meet ALL 4 of the following criteria)

1. Tick has been removed within the past 72 hours.
   (If the tick is still attached, advise the patient to safely remove.[5])
2. Tick bite occurred in a higher risk area where blacklegged ticks have been identified.
   - Refer to the most recent Ontario Lyme Disease Map for estimated risk areas.[6]
   - Refer to Ontario Health Clinical Guidance Document for examples of higher risk areas with a prevalence of ticks infected with *Borrelia burgdorferi* > 20% (Box 5).[2]
3. Tick was likely attached for 24 hours or more
4. Doxycycline is not contraindicated (e.g. allergy).

NO → **If all 4 criteria are not met:**

- Do not prescribe antibiotic prophylaxis.
- Educate patient to monitor for symptoms for 30 days and see a physician or nurse practitioner if symptoms develop.

YES ↓

Prescribing antibiotic prophylaxis:

- Adults: doxycycline 200 mg by mouth x 1 dose
- Children: doxycycline 4 mg/kg (maximum dose of 200 mg) by mouth x 1 dose (no age restriction)

→ **Documentation & follow-up:**

- Complete documentation & notify physician or nurse practitioner.
- Educate all patients to monitor for signs and symptoms for 30 days and see a physician or nurse practitioner if they develop symptoms.
- For surveillance purposes only, patients have the option to submit photos of ticks to www.etick.ca for identification.

Source: Public Health Ontario. Assessment and Prescribing Algorithm for Pharmacists: Antibiotic Prophylaxis to Prevent Lyme Disease following a Tick Bite. Toronto, ON: King's Printer for Ontario; 2024. Available from: https://www.publichealthontario.ca/-/media/Documents/L/2023/lyme-disease-assessment-prescribing-algorithm-antibiotic-prophylaxis.pdf

Testing Following Seasonal *Ixodes* Tick Exposure in Risk Areas

Typical isolated erythema migrans (EM) lesion

↓

No testing
(clinical diagnosis
generally sufficient)

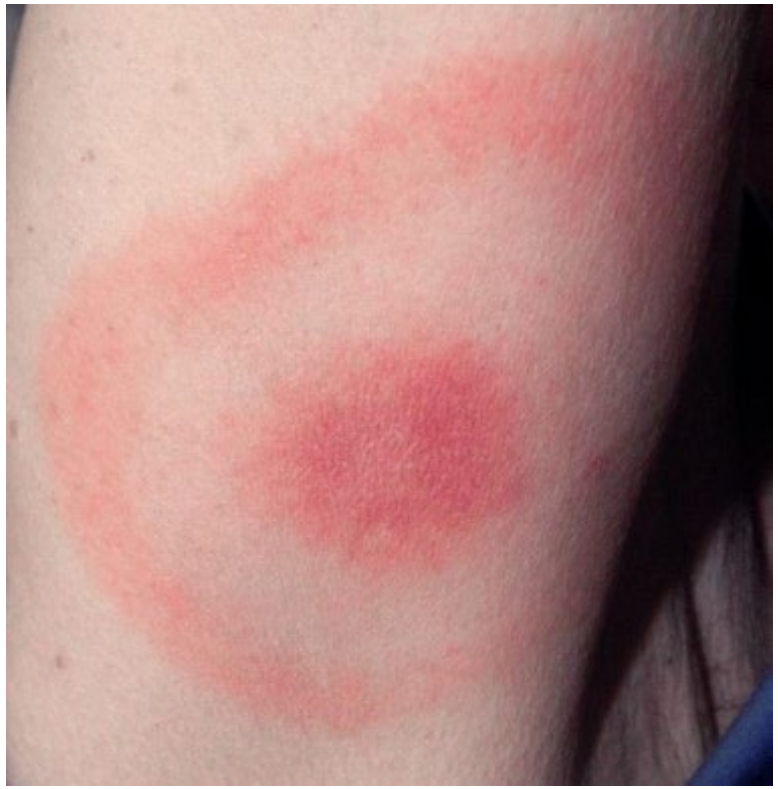
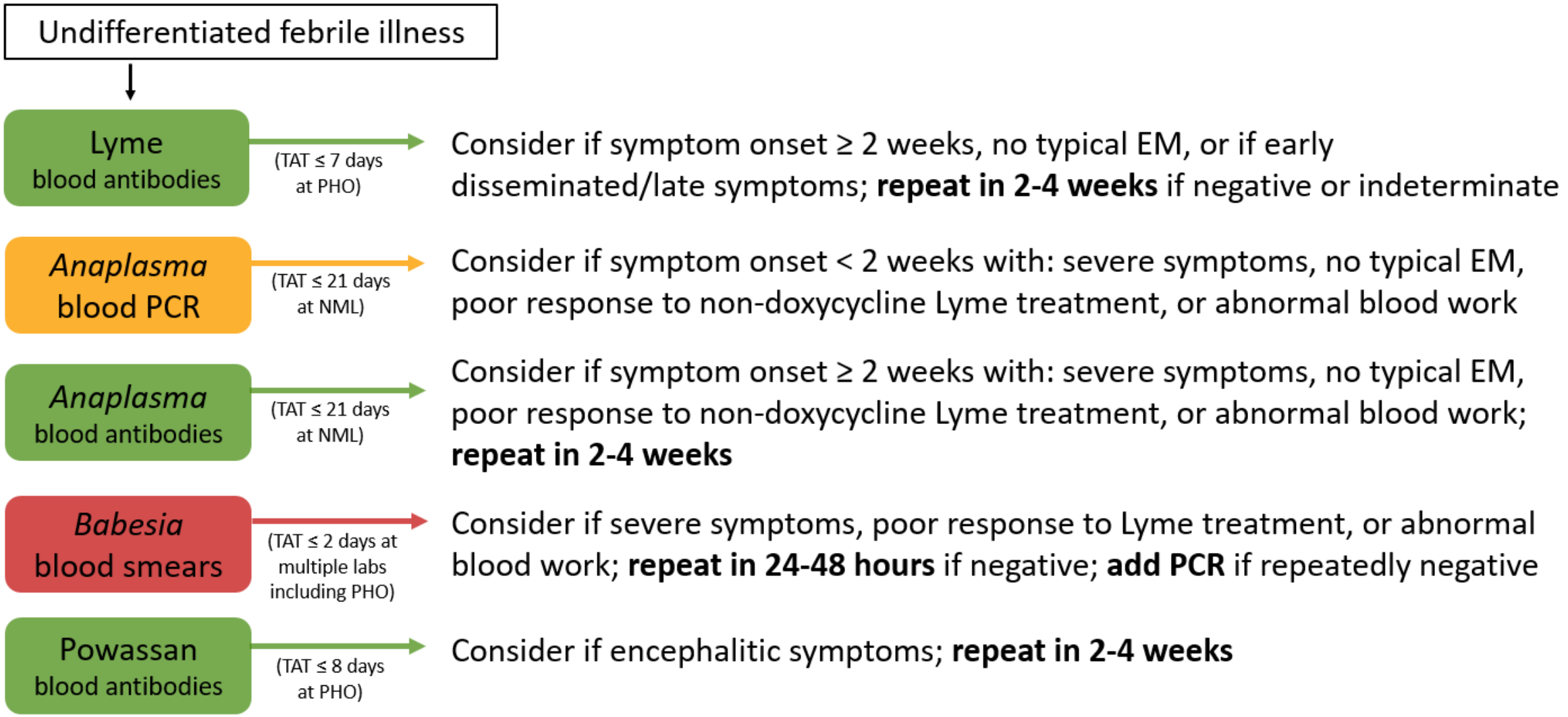


Image source: Gathany J. CDC #9875. CDC/ James Gathany. Available from: https://phil.cdc.gov/Details.aspx?pid=9875

Testing Following Seasonal Ixodes Tick Exposure in Risk Areas

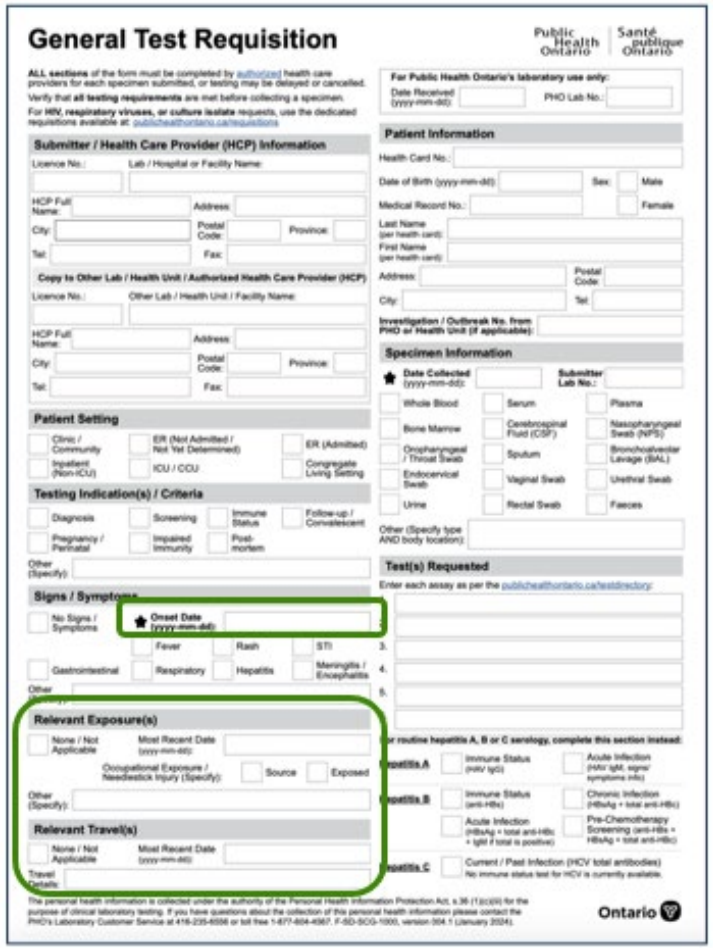


Supplemental Testing Options in Ontario for Tick-Borne DoPHS

PHO approval required

Lyme skin tissue PCR	(TAT ≤ 21 days at NML)	Invasive and rarely needed for patient diagnosis and management, only consider if diagnostic challenges with early atypical lesion(s)
Lyme synovial fluid PCR	(TAT ≤ 21 days at NML)	Mainly relevant if suspecting late Lyme arthritis with diagnostic uncertainty following serological results
Lyme CSF antibodies	(TAT ≤ 21 days at NML)	Mainly relevant if suspecting early disseminated neuroborreliosis and CSF collection planned; requires parallel collection of serum
Babesia blood antibodies	(TAT ≤ 21 days at NML)	Mainly relevant if negative PCR following treatment or confirmed blood transfusion/organ transplant exposure event
Powassan blood or CSF PCR	(TAT variable at NML)	Mainly relevant if early prodromal phase with impaired immunity (suggesting potentially lower serology sensitivity)

Test Requisition Requirements



General Test Requisition

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ALL sections of the form must be completed by authorized health care providers for each specimen submitted, or testing may be delayed or cancelled.
Verify that **all testing requirements** are met before collecting a specimen.
For **HIV, respiratory viruses, or culture isolate** requests, use the dedicated requisitions available at: publichealthontario.ca/requisitions

For Public Health Ontario's laboratory use only:
Date Received (yyyy-mm-dd):
PHO Lab No.:

Submitter / Health Care Provider (HCP) Information
Licence No.:
Lab / Hospital or Facility Name:
HCP Full Name:
Address:
City:
Postal Code:
Province:
Tel:
Fax:

Copy to Other Lab / Health Unit / Authorized Health Care Provider (HCP)
Licence No.:
Other Lab / Health Unit / Facility Name:
HCP Full Name:
Address:
City:
Postal Code:
Province:
Tel:
Fax:

Patient Setting
Clinic / Community
ER (Not Admitted / Not Yet Determined)
ER (Admitted)
Inpatient (Non-ICU)
ICU / CCU
Congregate Living Setting

Testing Indication(s) / Criteria
Diagnosis
Screening
Immune Status
Follow-up / Convalescent
Pregnancy / Perinatal
Impaired Immunity
Post-mortem
Other (Specify):

Signs / Symptoms
No Signs / Symptoms
Onset Date (yyyy-mm-dd):
Fever
Rash
STI
Gastrointestinal
Respiratory
Hepatitis
Meningitis / Encephalitis
Other

Relevant Exposure(s)
None / Not Applicable
Most Recent Date (yyyy-mm-dd):
Occupational Exposure / Needlestick Injury (Specify):
Source
Exposed
Other (Specify):

Relevant Travel(s)
None / Not Applicable
Most Recent Date (yyyy-mm-dd):
Travel Details:

Patient Information
Health Card No.:
Date of Birth (yyyy-mm-dd):
Sex:
Male
Female
Medical Record No.:
Last Name (per health card):
First Name (per health card):
Address:
Postal Code:
City:
Tel:
Investigation / Outbreak No. from PHO or Health Unit (if applicable):

Specimen Information
Date Collected (yyyy-mm-dd):
Submitter Lab No.:
Whole Blood
Serum
Plasma
Bone Marrow
Cerebrospinal Fluid (CSF)
Nasopharyngeal Swab (NPS)
Oropharyngeal / Throat Swab
Sputum
Bronchoalveolar Lavage (BAL)
Endocervical Swab
Vaginal Swab
Urethral Swab
Urine
Rectal Swab
Faeces
Other (Specify type AND body location):

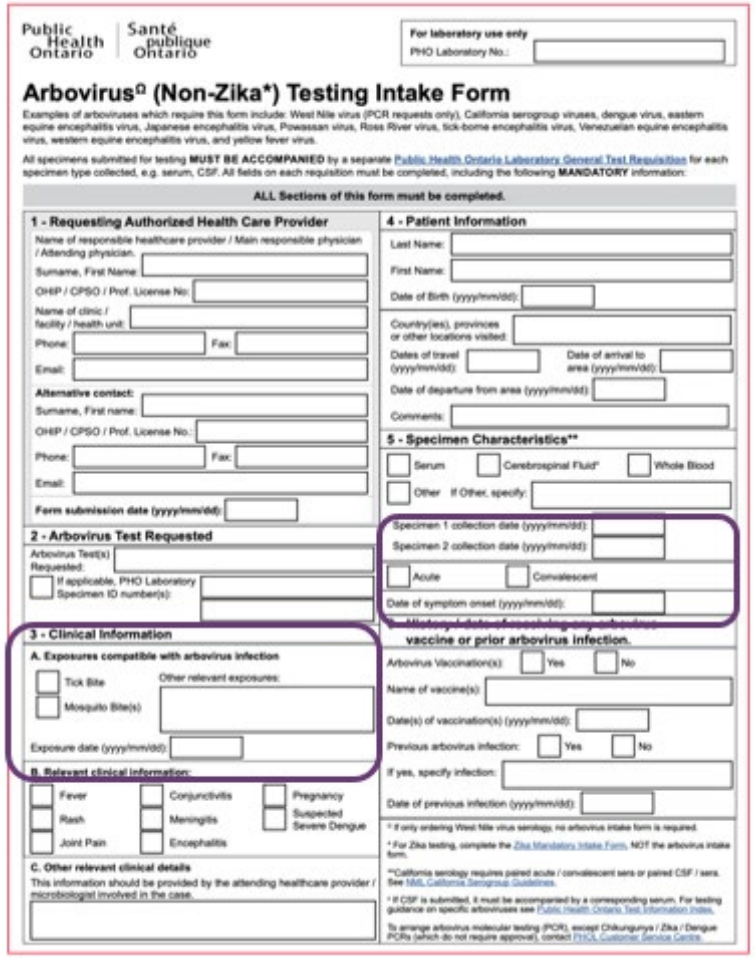
Test(s) Requested
Enter each assay as per the publichealthontario.ca/testdirectory:
1.
2.
3.
4.
5.

For routine hepatitis A, B or C serology, complete this section instead:
Hepatitis A: Immune Status (HAV IgG); Acute Infection (HAV IgM, signs/symptoms info)
Hepatitis B: Immune Status (anti-HBs); Chronic Infection (HBsAg + total anti-HBc)
Acute Infection (HBsAg + total anti-HBc + IgM if total is positive); Pre-Chemotherapy Screening (anti-HBs + HBsAg + total anti-HBc)
Hepatitis C: Current / Past Infection (HCV total antibodies)
No immune status test for HCV is currently available.

The personal health information is collected under the authority of the Personal Health Information Protection Act, s.36 (1)(c)(ii) for the purpose of clinical laboratory testing. If you have questions about the collection of this personal health information please contact the PHO's Laboratory Customer Service at 416-235-6556 or toll free 1-877-604-4567. F-SD-SCG-1000, version-304.1 (January 2024).

Ontario

Always provide **exposure/travel** history and **symptom onset** date



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For laboratory use only
PHO Laboratory No.:

Arbovirus[Ω] (Non-Zika*) Testing Intake Form

Examples of arboviruses which require this form include: West Nile virus (PCR requests only), California serogroup viruses, dengue virus, eastern equine encephalitis virus, Japanese encephalitis virus, Powassan virus, Ross River virus, tick-borne encephalitis virus, Venezuelan equine encephalitis virus, western equine encephalitis virus, and yellow fever virus.

All specimens submitted for testing **MUST BE ACCOMPANIED** by a separate Public Health Ontario Laboratory General Test Requisition for each specimen type collected, e.g. serum, CSF. All fields on each requisition must be completed, including the following **MANDATORY** information:

ALL Sections of this form must be completed.

1 - Requesting Authorized Health Care Provider
Name of responsible healthcare provider / Main responsible physician / Attending physician:
Surname, First Name:
OHIP / CPSO / Prof. License No:
Name of clinic / facility / health unit:
Phone:
Fax:
Email:
Alternative contact:
Surname, First name:
OHIP / CPSO / Prof. License No:
Phone:
Fax:
Email:
Form submission date (yyyy/mm/dd):

2 - Arbovirus Test Requested
Arbovirus Test(s) Requested:
If applicable, PHO Laboratory Specimen ID number(s):

3 - Clinical Information
A. Exposures compatible with arbovirus infection
Tick Bite
Mosquito Bite(s)
Other relevant exposures:
Exposure date (yyyy/mm/dd):
B. Relevant clinical information:
Fever
Rash
Joint Pain
Conjunctivitis
Meningitis
Encephalitis
Pregnancy
Suspected Severe Dengue
C. Other relevant clinical details
This information should be provided by the attending healthcare provider / microbiologist involved in the case.

4 - Patient Information
Last Name:
First Name:
Date of Birth (yyyy/mm/dd):
Country(ies), provinces or other locations visited:
Dates of travel (yyyy/mm/dd):
Date of arrival to area (yyyy/mm/dd):
Date of departure from area (yyyy/mm/dd):
Comments:

5 - Specimen Characteristics**
Serum
Cerebrospinal Fluid*
Whole Blood
Other
If Other, specify:
Specimen 1 collection date (yyyy/mm/dd):
Specimen 2 collection date (yyyy/mm/dd):
Acute
Convalescent
Date of symptom onset (yyyy/mm/dd):
vaccine or prior arbovirus infection.
Arbovirus Vaccination(s):
Yes
No
Name of vaccine(s):
Date(s) of vaccination(s) (yyyy/mm/dd):
Previous arbovirus infection:
Yes
No
If yes, specify infection:
Date of previous infection (yyyy/mm/dd):

[Ω] If only ordering West Nile virus serology, no arbovirus intake form is required.
* For Zika testing, complete the Zika Mandatory Intake Form, NOT the arbovirus intake form.
** California serology requires paired acute / convalescent sera or paired CSF / sera. See NML California Serogroup Guidelines.
* If CSF is submitted, it must be accompanied by a corresponding serum. For testing guidance on specific arboviruses see Public Health Ontario Test Information Index.
To arrange arbovirus molecular testing (PCR), except Chikungunya / Zika / Dengue PCRs (which do not require approval), contact PHOL Customer Service Centre.

If **Powassan virus** testing (serology or PCR) requested, **also** complete the arbovirus intake form

Implications for practice

- In 2023, the number of reported cases of Lyme disease in Ontario were much higher than cases of anaplasmosis, babesiosis, or Powassan virus
- Clinical signs and symptoms along with blood work can be helpful to guide the diagnosis, but testing may be needed to distinguish between anaplasmosis, babesiosis, Powassan virus and Lyme disease
- For individuals being investigated for Lyme disease, consider anaplasmosis, babesiosis and Powassan Virus as an alternate diagnosis or a co-infection
- Optimal diagnostic test may depend on timing relative to symptom onset

Sources: Ontario. Ministry of Health; Ministry of Long-Term Care. Infectious disease protocol, 2023. Appendix 1: Case definitions and disease-specific information. Disease: Lyme disease. Effective April 2023 [Internet]. Toronto, ON: King's Printer for Ontario; 2023 [modified 2023 Apr; cited 2024 May 15]. Available from: https://files.ontario.ca/moh-ophs-lyme-disease-en-2023.pdf
Public Health Agency of Canada. Lyme disease: for health professionals [Internet]. Ottawa, ON: Government of Canada; 2023 [cited 2024 May 7]. Available from: https://www.canada.ca/en/public-health/services/diseases/lyme-disease/health-professionals-lyme-disease.html

Case Introduction – Continued

- The patient is diagnosed with early localized Lyme disease and started on a 14-day course of amoxicillin
- They return to their health care provider within 5 days of starting treatment (i.e., 7 days from symptom onset) with worsening febrile symptoms including headache, stiff neck, fatigue, and confusion
- The physician is concerned about possible co-infection with other tick-borne diseases of public health significance. Among other tests requested, which of the following tests may be considered?

A. Blood antibodies (paired) for Lyme
B. Blood PCR for *Anaplasma*
C. Blood smears for *Babesia*
D. Blood antibodies (paired) for Powassan virus
E. All of the above

Questions?

For More Information About This Presentation, Contact:

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