CEPProvidersEarly Lyme Disease Managementin Primary Care

This resource has been developed to support Canadian family physicians and primary care nurse practitioners to identify, diagnose and manage early Lyme disease. While the primary focus is early localized Lyme disease, certain signs and symptoms typically associated with early disseminated disease have been included as they may overlap into localized disease. Late disseminated Lyme disease and post-Lyme disease syndrome (PLDS) are not addressed in this resource. For more information on the phases of Lyme disease, please visit the <u>PHAC website for healthcare professionals.</u>¹

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SECTION A: About Lyme disease

- Lyme disease is the most common tick-borne infection in Canada.² The number of reported cases of Lyme disease increased nationally by over 1,000% between 2009 and 2017, from 144 cases to 2,025.²
- Lyme disease is caused by the bacteria *B. burgdorferi*, which is spread to humans through bites from infected blacklegged ticks (*Ixodes scapularis* nationally, and *Ixodes pacificus* in British Columbia).¹
- Lyme disease presents with varying symptoms, in phases that can overlap.¹ Early Lyme disease may be missed or misdiagnosed, which may allow the bacteria to disseminate through the bloodstream and cause serious illness that can last for months or years.¹ For the best outcome, it is vital to identify, diagnose and treat Lyme disease in the early phase.
- Serologic testing has poor sensitivity for early Lyme disease.^{3,4}



For more information about the phases of Lyme disease, please visit the PHAC website for healthcare professionals.¹

SECTION B: Clinical assessment

Step 1 : Perform a full-body skin exam to determine if the patient has erythema migrans (EM) rash.

EM is classically defined as a mainly flat, localized, expanding, uniformly red rash (with or without central clearing) appearing at the site of a tick bite.^{1,3,5,6} **In the majority of cases, EM rash will not present with a bullseye appearance.**^{1,6}

- While the majority of infected patients will develop an EM rash, a significant number of patients (at least 20%) will not.⁶
- The darker the patient's skin, the more difficult it may be to recognize EM rash.^{1,7}
- See the <u>PHAC website for healthcare professionals</u>¹ website for more photos of varied presentations of EM rash.

If the patient has a localized rash that has appeared within the last 48 hours but is still relatively small (<5cm in diameter), consider tracing the outline of the rash with a waterproof marker. Instruct the patient to return to the clinic if the rash expands past the outline. Continued expansion is suggestive of EM.



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	Exam reveals EM rash. ↓ Diagnose Lyme disease and treat immediately using	or	Exam reveals no rash, or a rash inconsistent with EM. ↓
	Section C, Antibiotic treatment (p. 5). Do not complete Steps 2 and 3.		Continue through Steps 2 and 3 to assess nonspecific symptoms and exposure risk.

Step 2 : Identify nonspecific signs and symptoms consistent with early localized Lyme disease.

Infected patients will develop a collection of nonspecific signs and symptoms within 3-30 days, ranging from mild to severe.^{1,3,6} Nonspecific signs and symptoms may be caused by many other illnesses, such as seasonal influenza. Before moving on to Step 3, rule out other potential causes of illness as per usual clinical practice. Unlike most self-limiting viral illnesses, early Lyme disease symptoms usually last for over 72 hours.⁸

Signs and symptoms consistent with early localized Lyme disease^{1,3,6,8}

- Subjective or objective fever
- · Generalized arthralgias and myalgias
- Fatigue
- Headache
- Swollen lymph nodes

Symptoms generally not associated with early localized Lyme disease⁸

- Nausea
- Sore throat
- Cough
- Runny nose
- GI symptoms

Continue to Step 3. Use the patient's symptoms, in combination with the patient's history taken in Step 3, to discern the level of suspicion of Lyme disease.

SECTION: Overview A <u>B</u> C D E F Resources References

Step 3 : Take a detailed patient history to determine if the patient could have been exposed to an infected tick.

To contract Lyme disease, a patient must have been fed on by an infected blacklegged tick. The patient must come into physical contact with the tick for it to attach and feed. Ticks do not fly or jump.⁹

Patients can come into contact with ticks:

- **Outdoors** in areas such as parks, meadows, wooded yards, campgrounds, golf courses and soccer fields.
- **Indoors** if a tick travelled inside on pets, clothing or outdoor gear (e.g. tents or boots).

The recollection of a tick bite is not a requirement to diagnose Lyme disease. Many people will not recall or be aware of tick bites because ticks are small and their bites are painless.^{1,3,9} If your patient remembers a tick bite, incorporate information from <u>Section F. Tick bite</u> management (p.8) into the assessment.



In the last 30 days, has the patient or the patient's pet been in woody or grassy areas such as parks, meadows, wooded yards, campgrounds, golf courses, soccer fields, etc.?

Unlikely to have been exposed to blacklegged ticks. Ticks must come into physical contact in order to attach and feed. Consider an alternative diagnosis.



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Plea tha an a list. info During outdoor activity, did the patient or the patient's pet come into contact with grass, underbrush, trees or leaf litter?

Use this table to assess whether the patient visited an area with elevated risk. Click on a province abbreviation to see detailed risk information for that province. While cases of Lyme disease have been reported in every province, the overall risk of Lyme disease varies considerably from province to province and within individual provinces.² It is possible for patients to contract Lyme disease in low and

moderate risk areas as ticks are spreading due to climate change.²

<1 case / 100,000 Lowest risk	1-19 cases / 100,000 20-49 cases / Moderate risk Higher ri (highest in Ca	isk Very high risk	
Province / territory	Overall provincial risk (based on incidence rate) ²	Moderate or higher risk areas within province?	
<u>BC</u> ¹⁰	Lowest risk	yes	
<u>AB</u> ¹¹	Lowest risk	no	
<u>SK</u> ¹²	Lowest risk	no	
<u>MB</u> ¹³	Moderate risk	yes	
<u>ON</u> ¹⁴	Moderate risk	yes - including very high risk areas	
<u>QC</u> ¹⁵	Moderate risk	yes	
<u>NB</u> ¹⁶	Moderate risk	yes	
<u>NL</u> ¹⁷	Lowest risk	no	
<u>NS</u> ¹⁸	Higher risk	yes - including very high risk areas	
<u>PEI</u> ¹⁹	Moderate risk	yes	
NT/YT/NU ²	There have been no reported cases of Lyme disease in the territories since the Public Health Agency of Canada began tracking cases in 2009.		

		yes V
Canada		Where did this outdoor activity take place?
		outside Canada
	Risk (based on incidence rate)	Jurisdiction
nited_ ates ²⁰	Moderate risk	Illinois, Indiana, Iowa, Maryland, Michigan, Massachusetts, New York, North Dakota, Ohio, Virginia, Washington D.C.
	Higher risk	Connecticut, Delaware, Minnesota, New Jersey, West Virginia, Wisconsin
	Very high risk	Maine, New Hampshire, Pennsylvania, Rhode Island, Vermont
ase note this is not exhaustive For more primation	Moderate risk	Belarus, Belgium, Bulgaria, Croatia, Finland, Hungary, Norway, Poland, the Russian Federation, Serbia, Slovakia
risk areas Europe, see e <u>Resources</u> ge.	Higher risk	the Czech Republic, Estonia, Lithuania
	Very high risk	Slovenia

Steps 2 and 3 reveal symptoms inconsistent with early Lyme disease **and/or** low probability of exposure to infected ticks.

Continue to Step 4 to consider options based on clinical suspicion.

Steps 2 and 3 reveal symptoms suggestive of early Lyme disease

and high probability of exposure to infected ticks.

Unlikely to be Lyme disease. Consider an alternative diagnosis.

or

Step 4 : Choose a management option based on clinical suspicion and patient preference.

Clinical diagnosis of early Lyme disease in patients without EM rash can be difficult.⁸

If symptoms and exposure history raise clinical suspicion of early Lyme disease, there are two options for management. While neither option has been validated, both are reasonable.⁸ Use the table below to make an informed decision in collaboration with your patient.²²

Extra care should be taken to promptly diagnose and treat early Lyme disease in pregnant women.^{8,9,23}

However, evidence for adverse effects on the fetus is weak and has been limited to retrospective case reports.^{9,23,24} Reassure pregnant patients that:

- No negative effects on the fetus have been found when mothers receive appropriate antibiotic treatment.^{9,24}
- Current evidence does not support the transmission of B. burgdorferi through breastfeeding.^{9,24}

Management options for patients without EM rash⁸

Option A: Treat empirically. Based on a high degree of clinical suspicion, treat empirically during acute infection.

Pros

 Enables early treatment, potentially relieving a patient's suffering sooner and halting disease progression before it reaches the disseminated stage

Cons

- May expose a patient to unnecessary antibiotics if initial diagnosis of Lyme proves incorrect. The harms of this can include:
 - An increased risk of antibiotic-associated adverse events/complications
 - Risk of developing resistance to antibiotics
 - Delayed identification of true cause of symptoms

Option B: Wait and watch. Monitor patient for symptom persistence or worsening, or development of new symptoms. Consider ordering serologic testing, and treat if serology is positive.

Pros

Resistance is a global health problem and preserving the efficacy of our current antibiotics is essential

Cons

- May prolong patient's suffering due to potentially significant delays in reporting test results
- Increased risk of Lyme-associated morbidity (neurologic, cardiac and rheumatologic)

If selecting option A, see <u>Section C. Antibiotic treatment (p. 5).</u>

If selecting option B:

- Treat symptoms as per usual clinical practice
- Consider ordering serologic testing. See <u>Section D.</u> <u>Serologic testing (p. 6)</u>
 - Instruct the patient to return to the clinic if:
 - Symptoms persist or worsen after ~1 week Suspected EM rash continues to expand
 - Provide a copy of the <u>patient tool</u> to help inform the patient about symptoms and prevention of Lyme disease

or

SECTION C: Antibiotic treatment

Prescribe antibiotics according to Table 1. Doxycycline is the recommended first-line antibiotic for Lyme disease.^{1,3,5,25} It is the most effective at preventing severe complications if started in the early phase.³

The recommended treatment duration for early Lyme disease is 21 days.³ While some providers may be tempted to prescribe shorter courses, due to the acute nature of the infection as well as recommendations from other sources,^{1,5,25} this practice should be avoided. There is some evidence suggesting that shorter courses may result in lower cure rates while not significantly reducing the number of adverse events.³

Both laboratory and clinically-diagnosed cases of Lyme disease are nationally notifiable.²⁶ See <u>PHAC's National Case</u> <u>Definition for Lyme disease</u> to determine if a patient's case is reportable.

Table 1. Antibiotic treatment of early localized Lyme disease ^{1,3,25-28}						
Age	Line	Drug	Dosage	Frequency	Maximum	Duration
Adults	1st	Doxycycline	100 mg orally	Twice/day	N/A	21 days
	2nd	Cefuroxime axetil	500 mg orally	Twice/day	N/A	21 days
		Amoxicillin	500 mg orally	Three times/day	N/A	21 days
Children	1st	Doxycycline	4 mg/kg orally	Daily, 2 divided doses	100 mg per dose	21 days
(< 18 years)	2nd	Amoxicillin	50 mg/kg orally	Daily, 3 divided doses	500 mg per dose	21 days
		Cefuroxime axetil	30 mg/kg orally	Daily, 2 divided doses	500 mg per dose	21 days

Special populations:

- **Pregnant women**: Doxycycline is contraindicated during pregnancy, and should not be used for the treatment of early Lyme disease in pregnant women. Pregnant women should be treated using appropriate antibiotics for their stage of pregnancy.^{1,3,25}
- **Children:** A growing consensus accepts the safety of doxycycline use with children <8 years old, for 21 days or less.²⁷ Historically doxycycline has been contraindicated in children <8 years old due to its potential to cause teeth staining.

For all patients, refer to post-treatment follow-up recommendations in Section E (p. 7).

SECTION: Overview A B C <u>D</u> E F Resources References

SECTION D: Serologic testing

Providers should only consider serologic testing to assist with diagnosis if: 1) they understand the appropriate use of the testing algorithm; and, 2) they are uncertain about clinically diagnosing a patient who is only exhibiting nonspecific symptoms.^{1,3} Antibiotic treatment for early Lyme disease may inhibit seroconversion and impact the validity of serologic tests.^{3,8}

Cautions^{1,3,8} **Testing and Diagnosis: Choosing to Test: Interpreting Test Results:** DO NOT test asymptomatic patients DO NOT rely on test results alone to make DO NOT use as a test of cure DO NOT test patients who have EM a diagnosis DO NOT use 2-tiered test to rash. They can be diagnosed and DO NOT rule out early Lyme disease in measure treatment response treated without serologic testing. patients with negative results DO NOT use either tier as a stand-alone test

Standard two-tiered testing (STTT) algorithm^{1,3,29,30}

Modified two-tiered testing (MTTT) algorithm³¹

This information is for general guidance. Laboratory testing procedures may vary by province/territory.

In Canada, laboratory testing for Lyme disease traditionally involves a sequential, two-tiered testing algorithm. The first tier is an enzyme immunoassay, followed by the second tier (western blot) in the event that the first tier is positive or equivocal.

The first tier is ordered from your provincial lab. For all provinces, except Ontario and British Columbia, positive/equivocal samples are automatically sent to the National Microbiology Laboratory (NML) for confirmatory testing using the second tier. For Ontario and British Columbia, second-tier testing is only sent to the NML if European exposure is suspected. Otherwise, second-tier tests are conducted in-province.^{29,30}

Required information for lab requisitions may vary by province/region. **Providers should indicate if the potential exposure to a tick occurred in Europe, as different tests are required to detect European species of Borrelia.** The duration of symptoms should also be indicated, as testing for IgM antibodies should be avoided in patients who have been ill for \geq 1 month (in these patients, IgG antibodies must be positive in order to diagnose Lyme disease).



Consider consulting with or referring to an appropriate specialist³⁸

In 2019, the U.S. FDA approved a modified two-tiered test (MTTT) as an alternative to the standard two-tiered test (STTT) based on evidence that showed MTTT performance to be equivalent or better than the STTT.³¹ In the MTTT, the second tier is an additional EIA/ELISA (instead of a western blot) which can be performed concurrently with the first-tier EIA/ELISA.

- Access: All Canadian labs will use the STTT but may not use the new MTTT (at time of this resource's publication).^{1,8}
- **Turnaround time:** EIA test results are returned more quickly than western blots. Faster results (~1 week) may support more timely treatment decisions.^{8,31}

SECTION E: Monitoring and follow-up

The majority of patients who receive an appropriate antibiotic for an appropriate duration are cured once therapy is finished, and show a resolution of all signs and symptoms.^{1,3,5} However, some patients may have symptoms that persist after therapy.^{1,3,5} Immediately following the completion of antibiotic treatment, assess the patient for evidence of disease persistence or progression.⁸ Include the patient in your decision-making as you consider the next steps.²²

It is possible for patients to become infected with more than one tick-borne pathogen.⁵ In Canada, the most common tick-borne infections other than Lyme disease are anaplasmosis (caused by *Anaplasma phagocytophilum*), babesiosis (caused by species of Babesia) and Powassan virus disease.³² **Potential co-infection should be suspected in patients who present with symptoms that are more severe than commonly observed in cases of early Lyme disease alone, especially those with:**⁵

- High-grade fever for >48 hours, despite receiving appropriate antibiotic treatment for Lyme disease
- Unexplained leukopenia, thrombocytopenia or anemia
- No improvement (or worsening) of nonspecific symptoms despite resolution of EM rash

Ð Satisfied with symptom resolution Not satisfied with symptom resolution \downarrow Have the patient monitor any Adults: Treat symptoms as per regular clinical practice, and consider the remaining symptoms for continuing following as appropriate:3,8 Second round of treatment with an alternative antibiotic.^{3,5} See Section resolution. Encourage the patient to return C. Antibiotic Treatment (p. 5). to the clinic if remaining symptoms Alternative diagnosis. persist. Schedule subsequent Referral to infectious disease specialist. assessments as requested by Possibility of co-infection. See below for further information. the patient.22

Children: If symptoms persist after a complete course of antibiotics, treat symptoms as per regular clinical practice, and refer the patient to an infectious disease specialist.³⁸

If you are suspicious of co-infection:

Consider a referral to an infectious disease specialist.⁸

Share the patient tool and highlight

methods of prevention to avoid

future infection.

- Doxycycline is effective at treating anaplasmosis. The treatment regime for Lyme disease should also resolve anaplasmosis.^{5,33}
- Doxycycline alone is not effective for treating babesiosis or Powassan virus disease.⁵

Visit the U.S. Centers for Disease Control and Prevention websites for more information on <u>babesiosis³⁴</u> and <u>anaplasmosis³³</u>, or the Public Health Agency of Canada website for more information on <u>Powassan virus disease.³⁵</u>

SECTION F: Tick bite management

To transmit Lyme disease, a blacklegged tick infected with *B. burgdorferi* **must attach to a person and feed for an extended period of time (most evidence suggests a minimum of 24 hours).**^{1,5,9} The likelihood of disease transmission increases with attachment time.⁹ If a tick has been feeding, it will become engorged, but this level of engorgement is often difficult to determine in practice.

The images to the right may help to identify blacklegged ticks and determine if a recently-discovered tick was attached long enough to transmit disease. It may be very difficult for patients and healthcare professionals to identify tick species and estimate attachment time, especially if a tick has been damaged during removal.⁸







_ Unfed blacklegged ticks (deer ticks)³⁶

 Unfed American dog ticks (wood ticks)³⁶

Levels of engorgement in adult blacklegged ticks as a result of feeding on $blood^{36}$



- Use Section B. Clinical assessment (p. 2) to check for signs and symptoms of early Lyme disease. Note that signs and symptoms of early Lyme disease may take up to 30 days to appear after infection.
- Provide a copy of the <u>patient tool</u>, which will provide more information on course, treatment and prevention of Lyme disease.
- Advise the patient to monitor for symptom development over the next few weeks.
- If the tick was removed within the last 72 hours, and all other criteria are met, consider offering post-exposure prophylaxis.⁵See below for more information.

Remove tick:37,38

- Do not use sharp forceps. Use blunt, medium tipped, angled forceps to grasp the head of the tick as close to the skin as possible.
- Do not use a twisting or jerking motion to remove the tick. Use perpendicular traction, taking care not to twist or crush the tick. If the



mouthparts break off and remain in the skin, remove them with forceps.

- Clean the area with an antiseptic solution.
- Record the date in the patient's record.
- Instruct the patient to monitor for signs and symptoms for the next 30 days.
- Provide a copy of the <u>patient tool</u>, which will provide more information on course, treatment and prevention of Lyme disease.
- Dispose of the tick. Do not submit ticks for testing to seek confirmation of Lyme disease. See the <u>PHAC website</u>³⁸ for information on submitting ticks for **surveillance purposes only**.
- If the patient meets all of the criteria, consider post-exposure prophylaxis (below).⁵

Post-exposure prophylaxis⁵

Post-exposure prophylaxis is not generally recommended. Providers may consider prophylactic treatment in **asymptomatic patients** if all the following criteria are met:

- Attached tick can be positively identified as a blacklegged tick (see images above)
- Tick was engorged and estimated to have been attached for >24 hours
- Prophylaxis can be started within 72 hours of tick removal
- Tick was acquired in an area where the infectivity rate of the tick population with *B. burgdorferi* is ≥20%. [Note: Infectivity rate is not uniformly collected in Canada. However, recent reports have shown that areas of Ontario, Manitoba and Nova Scotia have infection rates ≥20%.^{39,40,41} Many provinces and U.S. states instead estimate incidence rate by confirmed and probable cases.]
- Doxycycline is not contraindicated

If all of the above criteria are met:

- A single prophylactic dose of doxycycline may be given to adults (200mg) and children (for children under 45kg, 4 mg/kg to a maximum dose of 200 mg). Recent research suggests a single dose of doxycycline is safe for pregnant women.^{42,43}
- If doxycycline is contraindicated, do not offer an alternative antibiotic. Antibiotics other than doxycycline have not been proven effective.^{1,5}
- As post-exposure prophylaxis is not 100% effective, patients should be monitored for the development of signs and symptoms for 30 days.^{5,44}

Risk area resources: Canada, U.S. and Europe

National	Government of Canada surveillance website: https://www.canada.ca/en/public-health/services/diseases/lyme-disease/surveil
	 Most recent data/report (2017): https://www.canada.ca/en/public-health/services/reports-publications/canada-communi- cable-disease-report-ccdr/monthly-issue/2017-43/ccdr-volume-43-10-october-5-2017/surveillance-surveillance-lyme-dis- ease-canada-2009-2015.html
BC	 Surveillance website: http://www.bccdc.ca/health-info/diseases-conditions/lyme-disease-borrelia-burgdorferi-infection#Epi- demiology Interactive map: http://www.bccdc.ca/health-professionals/data-reports/reportable-diseases-data-dashboard
AB	 Surveillance website: <u>https://www.alberta.ca/lyme-disease-tick-surveillance.aspx</u> Most recent data/report: (2018): <u>https://open.alberta.ca/dataset/f0b7698f-03d4-4d32-858f-141ec7c3c108/resource/1cb2646b-bcdb-4299-84d6-7c1737518daa/download/tick-surveillance-2018-summary-report.pdf</u> Interactive map: <u>https://public.tableau.com/profile/ellehojpublic#!/vizhome/Ticks_AB/AlbertaTicks</u>
SK	 Surveillance website: <u>https://www.saskatchewan.ca/residents/health/diseases-and-conditions/lyme-disease#risk-in-saskatchewan</u> Most recent data/report: (2019) <u>https://publications.saskatchewan.ca/api/v1/products/100547/formats/111004/download</u>
MB	 Surveillance website: <u>https://www.gov.mb.ca/health/publichealth/cdc/tickborne/surveillance.html</u> Most recent data/report: (2017) <u>https://www.gov.mb.ca/health/publichealth/cdc/tickborne/docs/tbd_report2017.pdf</u>
ON	 Surveillance website: <u>https://www.publichealthontario.ca/en/diseases-and-conditions/infectious-diseases/vector-borne-zoo-notic-diseases/lyme-disease</u> Most recent data/report: (2018) <u>https://www.publichealthontario.ca/data-and-analysis/infectious-disease/reportable-disease-trends-annually#/34</u>
QC	 Surveillance website: <u>https://www.msss.gouv.qc.ca/professionnels/zoonoses/maladie-lyme/surveillance-de-la-maladie/</u> Most recent data/report: (French – 2017): <u>https://www.inspq.qc.ca/en/node/14523</u> (English – 2016): <u>https://www.inspq.qc.ca/en/publications/2417</u>
NB	 Surveillance: <u>https://www2.gnb.ca/content/gnb/en/departments/ocmoh/cdc/content/vectorborne_andzoonotic/Tick-Borne_Diseases/ticks.html</u> Most recent data/report: (2017) <u>https://www2.gnb.ca/content/gnb/en/departments/ocmoh/cdc/content/vectorborne_andzoonotic/Tick-Borne_Diseases/brief.html#1</u>
NL	 Surveillance: <u>https://www.faa.gov.nl.ca/agrifoods/animals/health/ticks/location_ixodes.html</u> Most recent data/report: (2015): <u>https://www.faa.gov.nl.ca/agrifoods/animals/health/pdf/ds_08_006.pdf</u>
NS	 Surveillance: <u>https://novascotia.ca/dhw/populationhealth/</u> Most recent data/report (2017): <u>https://novascotia.ca/dhw/populationhealth/documents/Annual-Notifiable-Disease-Surveil-lance-Report-2017.pdf</u>
PEI	PEI Public Health: https://www.princeedwardisland.ca/en/information/health-and-wellness/lyme-disease-in-pei
NT	NT Public Health: <u>https://www.hss.gov.nt.ca/en/services/tick-borne-diseases</u>
NU	• NU Public Health: <u>https://www.gov.nu.ca/sites/default/files/nu_communicable_diseases_manualcomplete_2018_0.pdf</u>
YT	YT Department of Health and Social Services: http://www.hss.gov.yk.ca/pdf/comm_diseases.pdf

International

U.S.	 Center for Disease Control (CDC) Lyme disease maps: <u>https://www.cdc.gov/lyme/datasurveillance/maps-recent.html</u> Lyme disease incidence rates by state: <u>https://www.cdc.gov/lyme/stats/tables.html</u>
Europe	 European Centre for Disease Prevention and Control - Borreliosis: <u>https://www.ecdc.europa.eu/en/borreliosis</u> WHO Lyme fact sheet: <u>http://www.euro.who.int/en/media-centre/sections/fact-sheets/2014/03/fact-sheets-world-health-day-2014-vector-borne-diseases/fact-sheet-lyme-borreliosis-in-europe</u>

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SECTION: Overview A B C D E F Resources References

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