Alberta Public Health Disease Management Guidelines

Rickettsial Infections

Alberta

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Health and Wellness Promotion Branch

Public Health and Compliance Branch

Alberta Health

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Case Definition

Confirmed Case

Clinical illness[A] with laboratory confirmation of infection:

- Seroconversion or significant (fourfold or greater) change in antibody titre to a *Rickettsia* spotted fever spp.[B] by immunofluorescence assay (IFA) in acute and convalescent phase serum specimens ideally taken at least 21 days apart

OR

- Detection of spotted fever *Rickettsia* spp. nucleic acid (e.g., PCR) in an appropriate clinical specimen (e.g., blood, tissue biopsy of eschar)[C]

OR

- Demonstration of spotted fever *Rickettsia* spp. in an appropriate clinical specimen (e.g., tissue biopsy of eschar) by immunostaining

OR

- Isolation of spotted fever *Rickettsia* spp. from an appropriate clinical specimen (e.g., blood, tissue biopsy of eschar)

Probable Case

Clinical illness[A] with likely exposure history[D] **and one of the following**:

- A single elevated (≥ 1:256) IFA serologic titre[E] to a spotted fever *Rickettsia* spp. and other possible causes[F] have been ruled out

OR

- Epidemiologically linked to a confirmed case

[A] Clinical illness is defined by fever and one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.[15]

[B] Refer to Appendix 1: Spotted Fever Group Rickettsia Clinical and Epidemiological Features for a list of spotted fever *Rickettsia spp.* known to be pathogenic in humans.

[C] Refer to the Public Health Laboratory (ProvLab) Guide to Services for current specimen collection and submission information.

[D] Likely exposures may include: history of a tick bite, recent travel or immigration (refer to Incidence section), recent flea/tick removal from pets, and activities that may result in contact with potential tick habitats including recreational pursuits (e.g., camping, hiking, hunting) and occupational activities (e.g., forestry work, farming, military exercises).[10]

[E] Refer to Diagnosis section for more information on laboratory interpretation.

[F] Other possible causes include, but are not limited to: false positive IgG IFA titres as a result of auto-immune disorders or other bacteria are rare but have been reported.[16,17]

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Table 1. Interpretation of *Rickettsia* Laboratory Results

PCR	Rickettsia IgG		Interpretation
	Acute	Convalescent	
Positive	**Any**	**Any**	**Confirmed case**
n/a	**1:64**	**1:256**	**Confirmed case** – fourfold or greater change in titre
n/a	**1:256**	**1:1024**	**Confirmed case** – fourfold or greater change in titre
n/a	**1:4096**	**1:1024**	**Confirmed case** – fourfold significant change in titre
n/a	**-**	**1:2048**	**Probable case**[G]
n/a	**-**	**1:512**	**Probable case**
n/a	**1:512**	**1:512**	**Not a case** (static titres) – For cases where an acute and convalescent specimen have been collected within an acceptable time period (at least 21 days or more) then either of the following may be occurring: • In the absence of recent exposure but the case was in an area known to have spotted fever group activity, this could be a sustained residual historic antibody response (e.g., untreated or late treatment). • In the absence of recent exposure, if the case has not ever been in an area known to be endemic for spotted fevers, then it is most likely to be a false positive due to some other unrelated cause.
n/a	**1:256**	**1:256**	
n/a	**<1:32**	**1:128**	**Not a case** – Likely no history of infection or may be past infection.
n/a	**<1:32**	**<1:32**	**Not a case** – Likely no history of infection or may be past infection.

[G] Timing of specimen collection can affect IgG titres. If collected later in the convalescent period a fourfold change in IgG titres may not occur. Discussion with the ProvLab microbiologist on-call is important when interpreting laboratory values and considering further testing.

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Reporting Requirements

Physicians, Health Practitioners and Others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases by mail, fax or electronic transfer within 48 hours (two business days).

Laboratories

All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the:

- Chief Medical Officer of Health (CMOH) (or designate), and
- MOH (or designate) of the zone.

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- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical/epidemiological information.

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Epidemiology

Etiology

Rickettsial infections are caused by *Rickettsia species (spp.),* bacterial organisms belonging to the *Rickettsiaceae* family[1] and are obligate intracellular parasites. First described by Howard Ricketts in 1906, currently 27 species have been documented, of which 17 are pathogenic for humans.[2] *Rickettsia peacockii and R. buchneri*, are tick symbionts and considered to be non-pathogenic, whereas *R. parkeri*, *R. slovaca* and *R. massilliae,* previously considered to be non-pathogenic, have since been shown to cause human infections.

There are three *Rickettsia* groups: spotted fevers group (SFG), typhus group (TG) and the scrub typhus group.[3] Scrub typhus (*Orientia tsutsugamushi*), previously categorized within the genus *Rickettsia*, is now classified in its own genus.[4] The typhus sub-group and scrub typhus are listed here for comparison purposes only. Refer to separate disease management guidelines for more details.

See Appendix 1: Spotted Fever Group Rickettsia Clinical and Epidemiological Features for a list of *Rickettsia spp.* known to be pathogenic in humans.

Clinical Presentation

The severity of rickettsial infections can vary depending on the health, age and immune status of the infected person, as well as the species of *Rickettsia.*[3,5] In most cases, symptoms usually begin with the sudden onset of fever, malaise, muscle pain, headache and chills.[6] Although a generalised macular papular rash is a hallmark of a rickettsial infection, there are exceptions, such as African tick bite fever (*R. africae)*, where an eschar is a more prominent finding and the rash may only appear in about half of these cases. Between 9–12% of confirmed Rocky Mountain spotted fever (RMSF) cases do not exhibit a rash and are often associated with mortality.[7]

Further complications of *R. rickettsii* infections, considered the most severe rickettsiosis, can affect central nervous system (CNS), cardiac and pulmonary systems and the gastrointestinal tract. There can also be renal involvement, disseminated intravascular coagulation and shock. The case fatality rate varies with each species but can reach as high as 80% for untreated cases of Rocky Mountain, Brazilian and Mediterranean SF, as well as scrub and epidemic typhus.[6] The prognosis is largely related to the timeliness of appropriate therapy initiation.[3] Long-term sequelae, mainly of RMSF cases, are neurologic or result from the amputation of limbs that have become gangrenous.[3] In contrast, infections of African tick bite fever have a mortality rate below 1%.

Diagnosis

Recent travel, clinical presentation and seasonality can be helpful guides in the differential diagnosis of rickettsial infections, as only 60% of patients may recall a recent tick bite.[8] The spectra of manifestations and symptoms are highly variable; hence, the differential can be broad and include some or all of the following, not listed in order of priority: typhoid fever, leptospirosis, infectious mononucleosis, bacterial sepsis, anaplasmosis, ehrlichiosis, meningococcemia, enteroviral infection, syphilis, disseminated gonococcal infection and dengue. Non-infectious etiologies can include drug reactions, thrombotic thrombocytopaenia purpura (TTP), and immune complex illness.

In general, antibody levels are detectable five to 10 days following fever; however, this can differ with some rickettsial species. For instance, African tick bite fever has a much later seroconversion (28 days for IgG and 25 days for IgM).[9] The reference standard for serological confirmation of a rickettsial infection is IFA testing using paired acute and convalescent sera.[10] A single elevated IFA antibody titre supports the diagnosis of a rickettsial infection but is not considered sufficient to confirm infection. Infections by any of the species within the spotted fever group will result in an elevated IFA antibody titre due to cross-reactivity.[11] In addition, early treatment can blunt the immune response.

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In some individuals, a previous infection can result in an elevated IgG titre, thus adding to the difficulty in interpreting laboratory results.[10] Furthermore, a small proportion of the general population may have IgG antibodies reactive to *R. rickettsia* antigens with no corresponding rickettsial infection.

In the early stages, the infection may be detected in blood by PCR and in skin biopsies using immunostains or PCR. However, PCR detection in blood is not considered as sensitive because of the possibility of low numbers of *Rickettsiae* that can circulate in the blood in the absence of disease.[10] The direct IFA test on skin lesions identifies organisms and allows the diagnosis to be made when the rash appears (three to five days). The rash may be difficult to detect in individuals with darker skin, contributing to delay in diagnosis and an increase in fatality. Culture is generally not done due to the risk of transmission to laboratory personnel. The analysis of ticks should not be performed as part of the diagnosis as it is a time consuming process.

Interpretation of serology can be challenging, depending on when the specimens were collected during the course of the individual's illness. Each case will be reviewed on an individual basis by Alberta Health, ProvLab and Alberta Health Services public health staff to determine the final classification of the case for surveillance purposes.

Treatment

- Serological evidence of infection occurs no earlier than the second week of illness in any of the rickettsial diseases; therefore, treatment should be initiated on clinical and epidemiological evidence.[5,6,10]
- Tetracycline, in particular doxycycline, is the treatment of choice.[3,6]

Reservoir

With the exception of *R. akari* (mite) and *R. felis* and *R. typhi* (flea), the majority of *Rickettsiae* are maintained in nature in a cycle of ticks and their respective hosts. Hence the spatial distribution of the infected ticks, mites and fleas defines the geographic areas of risk for humans.

Transmission

Infection is typically transmitted by the bite of an infected tick, mite or flea. In humans, the tick must be attached and feed for at least two to 20 hours before the rickettsiae become reactivated and infectious.[10] An infected crushed tick or the feces of an infected tick entering a break in the skin or on mucous membranes are considered other sources of infection.[6]

Transfusion-associated transmission has been reported but is rare.[12]

Infections have been reported in laboratory settings due to accidental inoculation, contamination of mucous membranes or exposure to aerosols.[13]

Incubation Period

The incubation period for the spotted fever *Rickettsia* species range from two to 21 days, possibly depending on the size of the inoculum.[3]

Period of Communicability

Rickettsial infections are not transmitted from person to person.[5,6,10] The tick itself remains infective for life (about 18 months).

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Host Susceptibility

Susceptibility is universal. Factors that increase the risk of more severe rickettsial infections include:

- either young or advanced age,
- alcoholism,
- glucose-6-phosphate dehydrogenase (G6PD) deficiency, or
- immunodeficiency.[6]

The duration that antibodies persist after recovery from the infection varies and depends on the *Rickettsia* species and on host factors.[10]

Incidence

Rickettsial infections have been notifiable in Alberta since 1985.[14] Rickettsial infections are not nationally notifiable, making the incidence difficult to obtain.

Rickettsial infections occur worldwide and are often named after the location in which they are first identified. RMSF can be acquired in Alberta, while other Rickettsial infections are found elsewhere (see Appendix 1 for more information). Each year in Alberta, zero to three cases are reported, the majority of which are acquired via travel to Africa (*likely R. africae*).

Refer to the Interactive Health Data Application (IHDA) for more information.

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Public Health Management

Key Investigation

- Confirm that the client meets the case definition.
- Obtain a history of illness including the date of onset, and signs and symptoms.
- Determine the possible source of infection for all confirmed and probable cases, taking into consideration the incubation period, reservoir and mode of transmission. Assessment may include determining, obtaining or identifying:
  - recent travel history (including camping) to or emigration from an area with known tick activity (refer to Appendix 1),
  - occupation (e.g., animal handler, wildlife ranger, parks officer, works outside, etc.),
  - recent outdoor recreational activities,
  - recent tick bite, and
  - recent contact with household pets.
- Identify individuals who may have been exposed to the same source (e.g., individuals living in the same household, co-travellers).

Management of a Case

- Consultation with an infectious diseases physician is advised.
- Check carefully for ticks and remove them if they are present.

Management of Contacts

Rickettsial infections are not transmitted from person to person. However, it is prudent to identify symptomatic co-travellers or others that may have been exposed to the same source, and direct them to their health care practitioner for diagnosis and treatment as necessary.

Preventive Measures

Educate the public on the following.

- Ticks in Alberta can transmit diseases such as RMSP; however, the risk of acquiring this disease is low.
- When travelling to any area known to have ticks:[5]
  - walk on cleared trails whenever possible, and avoid walking in tall grassy or wooded areas;
  - wear light-coloured clothing and cover up as much skin as possible (e.g., hat, long-sleeved shirt, long pants with the legs tucked into socks or boots);
  - use a bug spray that contains the chemical DEET (N, N-diethyl-meta-toluamide), Icaridin, or IR3535 to repel ticks and reapply as frequently as directed – Permethrin is superior protection against ticks on clothing only (not on skin);
  - check for ticks after leaving a grassy or wooded area where ticks may live – the most common locations of tick attachment are head, neck, behind ears, sock line, belt line, axillae and groin;
  - check pets for ticks after they have been outside – these ticks can fall off pets and attach themselves to people; and
  - place outdoor clothing in dryer on high heat for one hour to kill unattached ticks.
- For information on how to remove a tick safely, how to submit a tick or about tick surveillance in Alberta refer to the Alberta Tick Surveillance Program webpage.

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Appendix 1: Spotted Fever Group Rickettsia Clinical and Epidemiological Features

References 3,5,10,13,15 *apply to this Appendix.*

Rickettsial Infection	Species	North America	Central America	South America	Europe	North Africa	Sub-Saharan Africa	Asia, Middle East, Russia	Australia, N.Z., Papua NG, Oceania	Worldwide	Rash (% of Cases)	Rash Type	Eschar	Enlarged Lymph Nodes
Rocky Mountain spotted fever (SF)* (Brazilian SF)	*R. rickettsii*	✓	✓	✓							90%	45% Purpuric	No	No
African tick bite fever*	*R. africae*		✓				✓		✓		30%	Vesicular	100% multiple	Yes
Aneruptive fever	*R. helvetica*	✓			✓			✓			No	—	No	No
Astrakhan SF	*R. conorii caspia*				✓		✓				100%	Macular	23%	No
Cat flea rickettsiosis/Flea-borne SF	*R. felis*										Yes	Macular	Yes	Unknown
Far Eastern SF	*R. heilongjiangensis*							✓			Yes	Macular	Yes	Yes
Flinders Island SF, Thai tick typhus	*R. honei*							✓	✓		85%	8% purpuric	28%	Yes
Indian tick typhus	*R. conorii indica*				✓			✓						
Israeli SF	*R. conorii israelensis*				✓	✓		✓			100%	Macular	Rare	No
Japanese SF	*R. japonica*							✓			100%	Macular	90%	No
Lymphangitis associated rickettsiosis	*R. sibirica mongolotimonae*				✓		✓				Yes	Macular	Yes (could be multiple)	No
Maculatum infection, Tidewater SF, America boutonneuse fever	*R. parkeri*	✓	✓	✓							No	No	Yes	Yes
Mediterranean SF or Boutonneuse fever	*R. conorii conorri*				✓	✓	✓	✓			97%	10% purpuric	72%	Rare
Mediterranean SF-like disease	*R. massiliae*		✓		✓									
Mediterranean SF-like disease	*R. monacensis*													
North Asian tick typhus Siberian tick typhus	*R. sibirica* subsp. *sibirica*							✓			100%	Macular	77%	Yes
Queensland tick typhus	*R. australis*								✓		100%	Vesicular	65%	Yes
Rickettsialpox	*R. akari*									✓	100%	Vesicular	100%	Yes
Rickettsiosis	*R. aeschlimannii*					✓	✓				Yes	—	Yes	No
Tick-borne lymphadenopathy (TIBOLA), Dermacentor-borne necrosis and lymphadenopathy (DEBONEL)	*R. slovaca,*				✓			✓			No	Macular	Yes	Yes
	R. raoultii							✓						

**Most commonly reported to Alberta Health*

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Appendix 2: Revision History

Revision Date	Document Section	Description of Revision
November 2021	General	• Updated Template • Diagnosis and Treatment section moved to Epidemiology • Updated web links

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