New and old hotspots for rickettsial spotted fever acquired in Tasmania, 2012–2017

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Abstract

Objective: To describe the epidemiology and clinical characteristics of Tasmania-acquired rickettsial disease notified to the Department of Health in Tasmania from 2012 to 2017 inclusive.

Methods: Data on *rickettsiosis* cases acquired and notified in Tasmania between 1 January 2012 and 31 December 2017 were analysed descriptively.

Results: Eighteen cases of rickettsial infection notified in Tasmania 2012–17 and likely acquired in the state met one of three case definitions: 12 confirmed (67%), four probable (22%), and two possible (11%). The mean number of cases per year was 3.0 (population rate 0.6 per 100,000 population/year); 60% of cases occurred in November and December. Cases were more commonly older males. Fever, lethargy, and rash were commonly reported symptoms. Thirteen cases were likely acquired on Flinders Island, three around Great Oyster Bay and two in the Midlands.

Conclusions: This study extends our knowledge of the epidemiology of rickettsial disease in Tasmania. This is the first account including confirmed cases acquired in the Midlands of Tasmania.

Implications for public health: Increased knowledge and awareness of epidemiology of rickettsial infection in Tasmania is essential for timely diagnosis and appropriate treatment. These findings bear wider relevance outside Tasmania because visitors may also be at risk.

Key words: Rickettsia, infectious diseases, epidemiology, surveillance, Flinders Island spotted fever

Rickettsial diseases are caused by the obligate intracellular bacteria in the order Rickettsiales that can be transmitted to humans via the bites of fleas, lice, ticks or mites.[1,2] Australia has several endemic rickettsial diseases: flea-borne murine typhus (*R. typhi*) and cat flea typhus (*R. felis*); mite-borne scrub typhus (*Orientia tsutsugamushi*); and the tick-borne spotted fever group (SFG), which includes Queensland tick typhus (*R. australis*), Flinders Island spotted fever (FISF; *R. honei*), and Australian spotted fever (*R. honei* subsp. *marmionii)*.[1,3,4] Epidemic typhus *(R. prowazekii)* occurred in Australia in the 18th and 19th centuries but is no longer endemic.[1,5]

Tasmania (population 524,700)[6] is an island state of Australia located 240 kilometres south of the mainland, consisting of the main island of Tasmania and several small, sparsely populated surrounding islands. FISF, the rickettsial infection typically associated with Tasmania, was first described in 1991 on Flinders Island, an island in Bass Strait off the north-east tip of Tasmania, by the island's sole general practitioner (GP), Robert Stewart, who had identified 26 cases of a spotted-fever-like illness over 17 years.[7] The causative agent has been identified as *R. honei*,[1,8] and the reptile associated tick *Bothriocroton hydrosauri* (Southern Reptile Tick, formerly *Aponomma hydrosauri*), which commonly feeds from native reptiles such as blue-tongued lizards and snakes, has been confirmed as its host (Figure 1).[9,10] Cases have not only been observed on Flinders Island, but also on Schouten Island, Tasmania, and in south-eastern South Australia, where *B. hydrosauri* are also endemic.[11] Additionally, two cases of locally acquired *R. honei* infection have been described in Western Australia,[12] while cases have also been described internationally.[13] Symptoms can include sudden onset fever and chills, myalgia, transient arthralgia and a maculopapular rash.[7] Treatment is usually with oral doxycycline;[2] however, azithromycin and rifampicin have also been used successfully.

Rickettsial infection is not nationally notifiable in Australia under the National Notifiable Disease Surveillance System (NNDSS), but surveillance currently occurs in three jurisdictions. Epidemic typhus caused by *R. prowazekii* is notifiable in New South Wales, while rickettsial infection is notifiable in Western Australia and Tasmania. In Tasmania, cases are notifiable under the *Public Health Act 1997*.[14] Positive rickettsial serology results (antibody titre ≥1:128 to a rickettsial group antigen) occurring in Tasmanian laboratories are forwarded to the Communicable Disease Prevention Unit (CDPU) and investigated. Standardised data collection on cases of *rickettsiosis* notified to CDPU was introduced at the beginning of 2012.

The existing literature on rickettsial infection in Tasmania describes cases of FISF on Flinders Island, one case on Schouten Island[11] and a case of *rickettsiosis*, assumed to be

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R. honei, acquired on the Freycinet Peninsula or Maria Island.[15] However, the geographical distribution and other epidemiological characteristics of rickettsial disease in Tasmania outside of Flinders Island are not well understood. A cluster of four rickettsial infection cases was identified on Flinders Island in December 2017, prompting the authors to review the surveillance data. The aim of this study was to review all *rickettsiosis* notifications in Tasmania over the six years from 2012 to 2017 inclusive and report the clinical and epidemiological characteristics of these cases.

Methods

Study population

Confirmed, probable, and possible rickettsiosis cases notified to CDPU between 1 January 2012, when the standardised case report form was introduced, and 31 December 2017, were included. Cases where travel history was unknown or that were likely acquired outside of Tasmania, based on overseas or interstate travel during the exposure period, were excluded. Confirmed cases required laboratory definitive evidence, including detection (culture or nucleic acid test) of *Rickettsia* species in a clinical specimen, or seroconversion or a fourfold or greater rise in serum antibody titre to rickettsial group antigen between acute and convalescent phase sera specimens. Probable cases required clinical evidence and a single elevated antibody titre of equal to or greater than 1:256 to a rickettsial group antigen. Possible cases required clinical evidence and a single antibody titre of 1:128 to a rickettsial group antigen. Clinical evidence was defined as a clinically compatible illness (fever and at least one of headache, myalgia, rash, or eschar).

Data collection

Rickettsial infections were notified to CDPU by Tasmanian laboratories and followed up within five days of notification. Further details about the illness, contact details, and permission to contact the patient were obtained from the testing clinician. A questionnaire was administered via telephone to the patient by a public health nurse or doctor, collecting information on demographics, clinical details of the illness, history of rickettsial infection and travel history (overseas, interstate, and intrastate). If only one serology test had been performed, a repeat serology two weeks later was recommended to confirm the diagnosis. Case details including demographic, hospitalisation and basic laboratory data were entered into the Tasmanian Notifiable Disease Database (TNDD).

For this retrospective descriptive analysis of notified cases, data were extracted from the TNDD into Excel (Microsoft, Version 16, 2016). Original case reports were reviewed, and additional data not recorded in the TNDD, including clinical details, tick bite exposure, previous rickettsial disease, travel history, and detailed laboratory data, were added to the dataset.

Laboratory investigations

All cases had immunoglobulin G (IgG)-specific antibody titres against *Rickettsia* antigen performed by indirect immunofluorescence assay (IFA). Testing varied depending on which pathology provider was used. The majority were tested for spotted fever group (SFG), typhus group (TG) and scrub typhus group (STG). SFG antigen included *R. australis* (Queensland Tick Typhus), *R. honei* (FISF), and *R. africae* (African Tick Bite Fever); TG antigen included *R. typhi* (murine typhus); and STG included *Orientia tsutsugamushi*. Seven cases had one or both samples tested at the Australian Rickettsial Reference Laboratory in Geelong, and had titres against specific antigens, rather than groups. These included *R. australis* (Queensland Tick Typhus), *R. honei* (FISF), *R conorii* (Mediterranean Spotted Fever), *R. africae* (African Tick Bite Fever) *R. rickettsii* (Rocky Mountain Spotted Fever) and *R. felis* (cat flea typhus/Flea-borne Spotted Fever) in the SFG; *R. typhi* (murine typhus) and *R. prowazekii* (Epidemic typhus) in the TG; and *Orientia tsutsugamushi and O. chuto* in the STG. IgG titres ≥1:128 were considered positive.

Data analysis

Descriptive data analysis was performed exploring patterns over time, age and sex distribution, geographic distribution, and clinical and laboratory features of confirmed, probable, and possible cases. Population rates were calculated using the Australian Bureau of Statistics mid-year Tasmanian population estimate for each year.[3] Data were analysed in Stata/IC (StataCorp LLC, Texas USA, Version 15.0). Likely place of acquisition was assessed based on residential location and report of overseas, interstate, and intrastate travel in the 10 days prior to onset of illness. Likely place of acquisition was mapped using ArcMap (ESRI, Version 10.6, 2018).

Ethics

Data were collected under the provisions of the *Public Health Act* of Tasmania (1997), and the data analysis and report with the approval of the Australian National University Ethics Committee (Protocol 2017/909).

Results

There were 47 *rickettsiosis* cases in the TNDD notified between 1 January 2012 and 31 December 2017. Of these, 19 did not meet a case definition and five were repeat notifications. Three cases likely acquired outside of Tasmania were excluded: one acquired in South Africa, one acquired in Western Australia, and one acquired in the Northern Territory or Queensland. Additionally, two cases where travel history was unknown were excluded. Eighteen cases were included in the analysis.

Figure 1: Blotched blue-tongue lizard (*Tiliqua nigrolutea*) with Southern Reptile Ticks (*Bothriocroton hydrosauri*), Flinders Island, Tasmania.

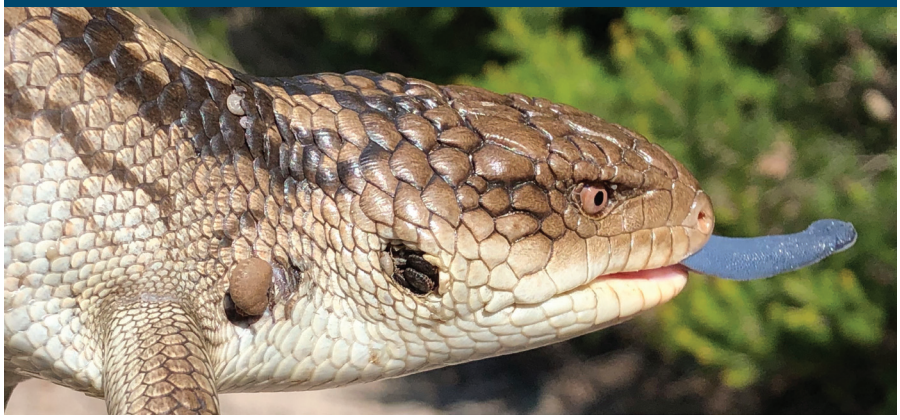


Photo courtesy of Robert Stewart.

Laboratory investigations

Fourteen cases (78%) had two blood samples taken for IFA and four (22%) had one. The median time between onset of illness and the first serology sample was four days (range 0–42 days) and the median time between first and second serology samples was 14.5 days (range 4–43 days).

Twelve (67%) cases demonstrated seroconversion or a fourfold or greater rise in antibody titre to either SFG or multiple *Rickettsia* species and were classified as confirmed cases. An additional four cases (22%) had single high titres and were classified as probable cases (cases 2, 3, 10 and 11). Two cases (11%) had low titres (1:128) and were classified as possible cases (cases 4 & 18; Table 1).

In the six cases who had IFA against individual species rather than groups, there was evidence of significant cross-reactivity, with all cases having positive titres of the same dilution against several species, including *R. honei* (Table 1).

Incidence and patterns over time

A mean of 3.0 cases per year were notified between 2012 and 2017 (range 2 to 4; Figure 2). The mean annual rate of notification was 0.6 per 100,000 population/year (range 0.4 to 0.8 per 100,000 population/year).

The date of onset rather than date of notification is shown in Figure 2 (one case notified in January 2012 had onset in December 2011). There was a distinct seasonal pattern, with 11 of the 17 cases with onset during the years 2012 to 2017 (where a full calendar year was included) occurring in the last quarter of the year (mostly in November and December), four with onset in the first quarter and only two in either the second or third quarter.

An increase in notifications was noted in the late 2017, with five cases with onset in the last quarter of 2017 (Figure 2). Three confirmed and one probable case were part of an identified cluster on Flinders Island, with dates of onset between 4 and 27 November 2017.

Demographic characteristics

Twelve cases (67%) were male and six (33%) were female. The median age was 60 years (range 35–77 years). Indigenous status was unknown for seven cases but, among the remaining 11, none reported being Aboriginal and/or Torres Strait Islander.

Thirteen of the cases provided their occupation, with five retired (28%), and four working on farms (31%). Other reported occupations included a bulldozer driver, a welder, a retailer and a teacher.

Clinical characteristics

All but one case (95%) reported fever. Other commonly reported symptoms were lethargy (89%), rash (83%), myalgia and/or arthralgia (72%), and headache (72%), see Table 2. Unsolicited reported symptoms included chills and/or sweats (n=3), itchiness (n=1), shortness of breath (n=1), anorexia (n=1), nausea (n=1), sore throat (n=1), dry mouth (n=1) and photophobia (n=1).

A description was given for seven of the 15 persons with a rash and included 'widespread' or 'full body' (n=3), 'full body sparing face and hands' (n=1), 'purpuric rash lower legs' (n=1), and 'mainly on trunk with patches on legs' (n=1). One confirmed case reported being red and swollen at the location of a suspected tick bite. A description was given for four of the 13 cases with myalgia and/or arthralgia and included 'aches whole body', 'ankle pain and swelling', 'all joints', and 'arthralgia of knees, shoulders, and fingers'.

Six cases (33%) reported a tick bite, while three (17%) reported a bite of unknown origin. Hospitalisation status was known for eight cases, with five reporting hospitalisation and three reporting no hospitalisation. No cases died of their disease.

Place of acquisition

Thirteen cases were likely acquired on Flinders Island (11 residents and 2 visitors),

Table 2: Clinical presentation of cases (n=18).

Symptom	Number of cases reporting symptom	
	n	%
Fever	17	95
Lethargy	16	89
Rash	15	83
Myalgia/arthralgia	13	72
Headache	13	72
Other	7	39

Table 1: Summary of serology results and cases classification, by case.

Case number	Year & quarter (Q) of onset	Number of blood samples	IgG titre against Rickettsia antigen by IFA	Case classification
1	Q4, 2011	2	Four-fold increase to SFG (1:512 and 1:8192)	Confirmed
2	Q1, 2012	1	Single positive titre to SFG (1:4096) and TG (1:128)	Probable
3	Q1, 2012	1	Single positive titre to SFG (1:1024)	Probable
4	Q3, 2013	1	Single positive titres to multiple species: *R. australis, R. honei, R. conorii, R. africae, R. rickettsii* (1:128 to all)	Possible
5	Q4, 2013	2	Seroconversion to multiple species: *R. australis, R. honei, R. conorii, R. africae, R. rickettsii* (1:256 to all)	Confirmed
6	Q4, 2013	2	Four-fold increase to SFG (1:512 and 1:8192)	Confirmed
7	Q1, 2014	2	Seroconversion to SFG (negative and 1:2048)	Confirmed
8	Q1, 2014	2	Seroconversion to SFG (negative and 1:2048) Positive titres to STG (1:256 and 1:128)	Confirmed
9	Q2, 2014	2	Seroconversion to multiple species: *R. australis* (≥1:1024), *R. honei* (≥1:1024), *R. conorii* (1:256), *R. africae* (1:256), *R. rickettsii* (1:256), *R. felis* (1:128), *R. prowazekii* (1:256), *R. typhi* (1:128)	Confirmed
10	Q4, 2014	2	Positive titre to SFG on two samples with no seroconversion (1:2048 and 1:2048)	Probable
11	Q4, 2015	2	Positive titre to SFG on two samples with no seroconversion (1:16384 and 1:32768) Positive titre to TG with no seroconversion (1: 256 and 1:256)	Probable
12	Q4, 2015	2	Seroconversion to SFG (negative and 1:1024)	Confirmed
13	Q4, 2016	2	Seroconversion to multiple species: *R. australis* (≥1:1024), *R. honei* (≥1:1024), *R. conorii* (≥1:1024), *R. africae* (≥1:1024), *R. rickettsii* (≥1:1024), *R. felis* (≥1:1024)	Confirmed
14	Q4, 2016	2	Seroconversion to SFG (negative to 1:4096) Positive titres to STG (1:256 and 1:128)	Confirmed
15	Q4, 2017	2	Seroconversion to SFG (negative to 1:8192)	Confirmed
16	Q4, 2017	2	Seroconversion to SFG (negative to 1:1024)	Confirmed
17	Q4, 2017	2	Seroconversion to multiple species: *R. australis* (≥1:1024), *R. honei* (≥1:1024), *R. conorii* (≥1:1024), *R. africae* (≥1:1024), *R. rickettsii* (≥1:1024), *R. felis* (1:256), *R. prowazekii* (≥1:1024), *R. typhi* (≥1:1024)	Confirmed
18	Q4, 2017	1	Single positive titres to multiple species: *R. australis, R. honei, R. rickettsii, R. felis, R. prowazekii, R. typhi* (1:128 to all)	Possible

with nine being confirmed, two probable, and two possible. Three cases were likely acquired around Great Oyster Bay: one in Swansea (probable), one in Dolphin Sands (probable), and one in Coles Bay (confirmed). Two further cases were likely acquired in the Midlands: one in Ross (confirmed) and one in Tunnack (confirmed), see Figure 3. Two of the cases acquired around Great Oyster Bay had onset of illness in the first quarter of 2012 and the cases in the Midlands had onset of illness in the first and second quarter of 2014.

Discussion

Between 2012 and 2017 inclusive, a total of 18 confirmed, probable and possible rickettsial infection cases were notified in Tasmania that were likely acquired in the state, at a rate of 0.6 per 100,000 population/year. This number may significantly underestimate the true incidence of cases occurring in the community, due to the limitations inherent with passive surveillance data. Some cases may not have sought medical advice due to mild illness or other factors; clinical presentation is similar to many other illnesses, particularly viral infections; and – perhaps most importantly – to diagnose rickettsial infection, the clinician must first consider it in their differential diagnosis and order the appropriate laboratory tests. Making the diagnostic connection may be further hindered by the patient not reporting a tick bite. In this sample, only 50% reported a bite of any kind, and only 30% a tick bite.

Tasmania is a popular tourist destination, with 1.26 million visitors in the year ending December 2017,[16] and an estimated 1,500 adults holidaying on Flinders Island per year.[17]{Tourism Tasmania, 2009 #172} A high proportion of visitors undertake outdoor activities that may put them at risk of tick bites.[18] Although it is likely that some visitors to Tasmania will develop rickettsial disease, they may seek medical advice after leaving the island. Treating clinicians outside of Tasmania may not be aware of the risk and not perform the appropriate tests. Additionally, as rickettsial infection is not nationally notifiable, many infections acquired by visitors are unlikely to be captured in the surveillance systems of other jurisdictions.

Despite being often described as a mild illness,[2] FISF can be severe. Recently, the death of a middle-aged woman due to acute infection of *R. honei* has been described in Queensland,[19] and another severe case was reported in New South Wales that required intensive care (Dr Stephen R. Graves, personal communication). In our surveillance data, half of cases with hospitalisation status reported were hospitalised. This proportion may overestimate true hospitalisation rates, due to the likelihood that this sample is biased towards severe disease. Although much is still unknown about the causes of severe disease and complications, treatment with doxycycline may reduce the risk.[2] Furthermore, prompt treatment is likely to reduce burden of disease as duration of illness without treatment is approximately 19 days but can be as long as six weeks.[7]

This work sheds new light on the geographical distribution of rickettsial infection in Tasmania. Previously cases of FISF in Tasmania have been described only on Flinders Island,[7] and Schouten Island off the Freycinet Peninsula on the east coast of Tasmania,[11] with one case of rickettsial infection, assumed to be *R. honei,* acquired on the Freycinet Peninsula or Maria Island,[15]

Figure 2: Epidemic curve of notified rickettsial infection cases, Tasmania, 2012-2017.

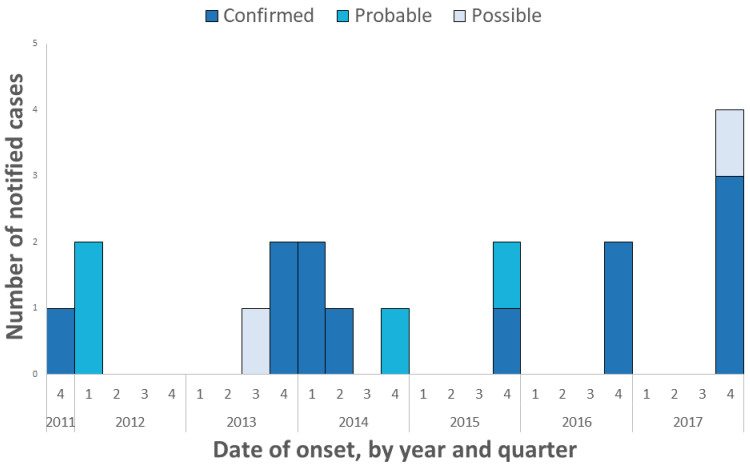
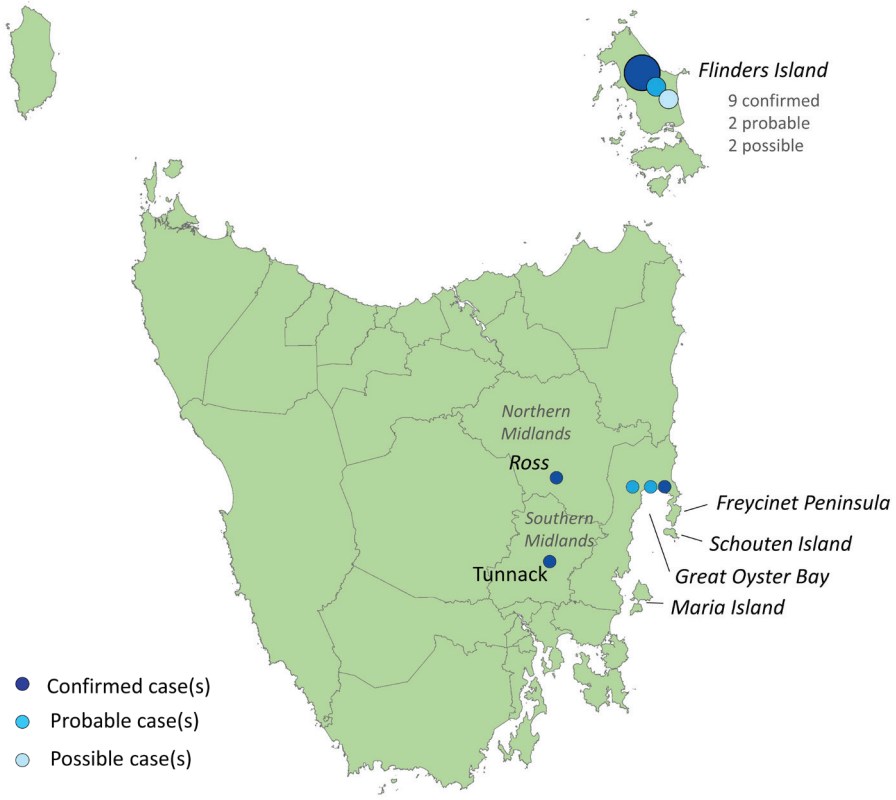


Figure 3: Likely place of acquisition of rickettsial infection cases, Tasmania, 2012-2017.



an island further down the east coast (Figure 3). As the invertebrate host *Bothriocroton hydrosauri* is distributed throughout Tasmania,[20] it has been postulated that FISF is likely to be distributed more widely, but this is the first published evidence of cases likely acquired outside of these locations. Of note, this is the first description of cases likely acquired in other locations around Great Oyster Bay and of confirmed cases in the Midlands. A significant limitation of the data, however, is that there may be testing bias, with clinicians in areas with known previous cases more likely to consider rickettsiosis and test for it. Our impression is that there is high awareness of rickettsial infection among medical practitioners and the community on Flinders Island, but less awareness elsewhere in Tasmania.

The seasonal pattern is consistent with previous literature and is not unexpected, as summer is when reptiles are most active and humans are likely to spend more time outdoors, increasing the risk of tick bites. During the cluster of cases on Flinders Island in November 2017, there were anecdotal reports of residents seeing snakes and lizards with 'big ticks' on them, demonstrating the close proximity of humans and Southern Reptile Ticks. Similarly, the preponderance of cases among older males has been previously described,[7,11] and is perhaps explained by a higher chance of them working or engaging in leisure activities outdoors.

The clinical picture among these cases is consistent with previous reports of FISF and particularly with Stewart's findings in his case series from Flinders Island in 1991.[7] Fever, headache, myalgia and/or arthralgia, and rash were prominent features. As in our study, Stewart also reported a varying distribution of the rash and both blanching and purpuric lesions. Similarly, rickettsial infections occurring in Queensland have shown a wide variety of dermatological manifestations, including maculopapular, macular, vesicular, and purpuric rashes.[21] In our cases, there were no specific reports of cough or eschar, although one person described redness and swelling at the site of a suspected tick bite. This contrasts with Stewart's case series, in which 46% had a cough and 46% had a skin lesion other than the rash. However, we did not specifically solicit these symptoms and signs, and our clinical data are limited by the collection of surveillance data via questionnaire over the telephone with the patient, rather than direct clinical history and examination. Lethargy was reported in 90% of cases, although duration could not be ascertained. Chronic fatigue has been previously associated with rickettsial infection.[22,23]

We assume that the 18 infections described in this paper represent FISF due to *R. honei* infection, based on known epidemiology of rickettsioses in Australia. However, given the significant cross-reactivity seen with rickettsial serology infection it is possible that another rickettsial species could be responsible for some of these cases. *Ixodes tasmani*, another tick common in Tasmania, has been associated with spotted fever elsewhere in Australia.[1,24] Izzard et al.[24] found that 55% of *I. tasmani* ticks collected from Tasmanian Devils in 2005/06 were polymerase chain reaction (PCR) positive for a *Rickettsia* species, subsequently named *Candidatus* Rickettsia tasmanensis. This tick is known to bite humans, but further research is needed to understand whether this new rickettsial species is a potential human pathogen.[3]

The only preventative measure against rickettsial infection is to minimise exposure to ticks and thus reduce the risk of tick bites. Current advice is to wear long sleeves and long pants, use tick repellent on skin and clothes and sleep on a raised camp bed when camping. In an attempt to raise awareness, CDPU has developed a factsheet on FISF and has liaised with Environmental Heath Officers and Parks and Wildlife Service Tasmania to distribute information to both residents and visitors.[25]

Based on this review, CDPU has changed the surveillance case definition for rickettsial infection in Tasmania to include those cases with a single high titre and clinical evidence as probable cases. The aim of this change is to have a more sensitive case definition that improves Tasmanian rickettsial infection surveillance.

Conclusion

This review of *rickettsiosis* notifications in Tasmania between 2012 and 2017 extends knowledge of the epidemiology of rickettsial infection and FISF within Tasmania over recent years. In particular, it shows that rickettsial infection can be acquired in locations around Great Oyster Bay and the Midlands area. It is possible that the distribution is wider still, given that the Southern Reptile Tick is distributed throughout Tasmania. These findings have wider relevance outside Tasmania as its many visitors, many of whom undertake outdoor activities, may also be at risk. Increased awareness of potential infection by clinicians is essential to accurately diagnose and appropriately treat rickettsial infections, thus reducing the burden of the disease. Although these data add to our understanding of the epidemiology of rickettsial infection in Tasmania, our knowledge in this complex area remains incomplete and further work is needed, particularly with regard to other potential human rickettsial pathogens.

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