

Tick-borne infectious diseases in Australia

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The incidence of tick-related medical problems in Australia is largely unknown. Appropriate diagnostic tests are not always available and, of all tick-related diseases, only Q fever is notifiable.¹ Anecdotally, however, many patients present to their doctor after a tick bite. This narrative review focuses on tick-borne infections but also touches briefly on other medical problems caused by tick bites.

Australian ticks

There are many different species of ticks in Australia. Only a few species are known to bite humans, and the microbes within these particular ticks — viruses, bacteria or protozoa — are potential causes of infection in humans who are bitten (Box).

However, the mere detection of a potential human pathogen in a tick does not mean that it can be transmitted to a person when bitten. To be transmitted to a person, the microbe must be present in the salivary glands of the tick while it is feeding.

Most studies of Australian ticks to date have investigated the whole microbiome of the tick and not their salivary glands specifically. Some pathogens may be present in the tick faeces, but transmission would require the patient to scratch the faeces into their skin — an unlikely scenario in most cases.

To be confident that a microbe in a tick is responsible for a particular illness in a patient bitten by that tick, it is essential to also detect the microbe in the sick patient, either directly by culture or detection of microbial nucleic acid or antigen, or indirectly by detecting newly produced antibodies to the microbe in the patient's blood. This requires the diagnostic laboratory to have assays that are both sensitive and specific for detecting the microbe in question. Few such assays are currently available in Australian diagnostic laboratories. Antibody assays are designed using antigens from a specific microbe and in many cases these microbes are not present in Australia. Such assays, even if reasonably sensitive and specific, must have acceptable positive and negative predictive values in Australia, so that patients and their doctors can have confidence in either a positive or negative result from any particular laboratory assay.

There have been two major studies of Australian ticks,^{2,3} which defined their variety and number. Australian ticks are divided into two large groups: soft-bodied and hard-bodied, comprising 14 and 56 species respectively.⁴ Five species of ticks have been introduced into Australia,⁴ but most are not important in biting humans. Of the endemic species, which are the majority, two are notorious for biting humans. On the east coast of Australia, the paralysis tick (*Ixodes holocyclus*) is the most notable; elsewhere in Australia, it is the ornate kangaroo tick (*Amblyomma triguttatum*). Both ticks are known to sometimes transmit human pathogens to people when they bite. The southern reptile tick (*Bothriocroton hydrosauri*) also bites humans and transmits infection (Box).³

There are four stages in the life history of ticks: egg, larva, nymph and adult (male and female). The larva, nymph and adult female (egg-producing) stages require a blood meal from a vertebrate animal to

Summary

- Tick bites in Australia can lead to a variety of illnesses in patients. These include infection, allergies, paralysis, autoimmune disease, post-infection fatigue and Australian multisystem disorder.
- Rickettsial (*Rickettsia* spp.) infections (Queensland tick typhus, Flinders Island spotted fever and Australian spotted fever) and Q fever (*Coxiella burnetii*) are the only systemic bacterial infections that are known to be transmitted by tick bites in Australia.
- Three species of local ticks transmit bacterial infection following a tick bite:
 - ▶ the paralysis tick (*Ixodes holocyclus*) is endemic on the east coast of Australia and causes Queensland tick typhus due to *R. australis* and Q fever due to *C. burnetii*;
 - ▶ the ornate kangaroo tick (*Amblyomma triguttatum*) occurs throughout much of northern, central and western Australia and causes Q fever; and
 - ▶ the southern reptile tick (*Bothriocroton hydrosauri*) is found mainly in south-eastern Australia and causes Flinders Island spotted fever due to *R. honei*.
- Much about Australian ticks and the medical outcomes following tick bites remains unknown. Further research is required to increase understanding of these areas.

metamorphose into the next life stage. The stages that most often cause problems to humans are nymphs and adult females.

Most people are bitten by ticks without any problem arising from this abnormal host–ectoparasite feeding interaction. Humans are incidental hosts and attached ticks are usually detected by the individual within a few hours, or a day at the most, and killed. Most are probably not even aware when they are bitten by a tick, as the tick injects a local anaesthetic into the skin. However, once it starts to feed, it becomes noticeable as it enlarges.

The range of problems that may occur after tick bites can be classified as follows: infection; allergy; paralysis; autoimmunity; post-infection fatigue; and Australian multisystem disorder.

Viral infections

Although there are several viral infections associated with ticks in other parts of the world (eg, tick-borne encephalitis virus in Europe), there are no definite tick-borne viral infections of humans yet discovered in Australia. The seabird soft tick (*Ornithodoros capensis*) has been shown to contain several viruses including the Saumarez Reef virus.⁵ When this tick bites humans, a dermatological condition develops in some patients, but it is not yet clear whether this is due to a virus or an allergen in the tick saliva. A phlebovirus present in an Australian bird tick (*I. eudyptidis*) is pathogenic for the shy albatross^{6,7} and is closely related to the human pathogenic viruses that cause severe fever with thrombocytopenia syndrome and Heartland virus disease. This suggests that human pathogenic viruses may be present in Australian ticks, although there is currently no evidence of *I. eudyptidis* biting humans.

Australian tick species known to bite humans, and associated pathogens and diseases

Tick species	Common name	Known human pathogen	Disease	Possible human pathogen
<i>Ixodes holocyclus</i>	Paralysis tick (scrub tick in Queensland)	<i>Rickettsia australis</i>	Queensland tick typhus	<i>Candidatus</i> Neoehrlichia spp.
		<i>Coxiella burnetii</i>	Q fever	<i>Bartonella henselae</i> ; <i>Ehrlichia</i> spp.
<i>Ixodes tasmani</i>	Common marsupial tick	<i>R. australis</i>	Queensland tick typhus	<i>Candidatus</i> <i>R. tasmanensis</i>
		<i>R. honei</i> subsp. <i>marmionii</i>	Australian spotted fever	<i>Bartonella</i> spp.
<i>Ixodes cornuatus</i>	Southern paralysis tick	<i>R. australis</i>	Queensland tick typhus	
<i>Amblyomma triguttatum</i>	Ornate kangaroo tick	<i>C. burnetii</i>	Q fever	<i>R. gravesii</i> ; <i>Anaplasma</i> sp.; <i>Ehrlichia</i> sp.
<i>Bothriocroton hydrosauri</i>	Southern reptile tick	<i>R. honei</i>	Flinders Island spotted fever	
<i>Haemaphysalis novaeguinae</i>	No common name	<i>R. honei</i> subsp. <i>marmionii</i>	Australian spotted fever	
<i>Haemaphysalis longicornis</i>	Bush tick (introduced, not native to Australia)			<i>Babesia</i> sp.
<i>Ornithodoros capensis</i>	Seabird soft tick			Virus

Bacterial infections

Many different bacteria have been detected in Australian tick species,⁸⁻¹³ mostly using molecular techniques. Some are known human pathogens or are closely related phylogenetically to known human pathogens; others are unique bacteria that are part of the tick microbiome.

Apart from the occasional local bacterial infection at the tick bite site (eschar), there are only two definite, known systemic infections following tick bites in Australia — rickettsial infection and Q fever — although there are other possible microbial pathogens and possibly as yet unknown infections (Box).

The two genera of bacteria currently confirmed as Australian tick-transmitted human pathogens are rickettsial species and *Coxiella burnetii*.

Rickettsial species

In Australia, rickettsial species cause Queensland tick typhus, Flinders Island spotted fever and Australian spotted fever. However, tick-transmitted rickettsiae in various parts of the world have recently been reviewed,¹⁴ and the findings emphasise the possibility that Australian clinicians may encounter patients who have returned to Australia after travelling and who present with a tick-borne infection contracted in another country.

The first case of Australian tick typhus was reported in 1946 from north Queensland¹⁵ and later that same year a series of cases, including the isolation of the causative agent, *Rickettsia australis*, from patients was described.¹⁶ The organism has since been isolated from a patient in south-east Queensland¹⁷ and from *I. holocyclus* and *I. tasmani* ticks.¹⁸ Queensland tick typhus was the first tick-transmitted infection recognised in Australia. It is seen regularly on the east coast of Australia from the Torres Strait Islands to the south-eastern corner of Victoria. The northern suburbs of Sydney are a particularly common location for transmission of this infection.^{19,20} Although often a mild condition involving fever, rash and eschar and readily treated with a short course of doxycycline, the infection may be severe^{21,22} or fatal,²³ and may have unusual features.²⁴ In north-eastern New South Wales, 15.4% of paralysis ticks contained *R. australis*.¹³ Hence, being bitten by this tick, in this location, appears to offer a 1 in 6 risk of being infected with the rickettsia.

A different rickettsial infection (Flinders Island spotted fever) has been observed in patients from Flinders Island, Tasmania.^{25,26} *R. honei* was isolated from febrile patients²⁷ and shown to be genetically different from *R. australis*. The tick vector was the southern reptile tick, which is known to bite humans, and on Flinders Island, 63% of these ticks were found to contain *R. honei*.²⁸ Flinders Island spotted fever is now known to also occur in South Australia,^{29,30} Western Australia³¹ and other parts of the world.¹⁴

A related bacterium, *Rickettsia honei* subsp. *marmionii*, causes a similar infection, Australian spotted fever, and has been detected in the ticks *I. tasmani* (unpublished data) and *Haemaphysalis novaeguinae* in Queensland,³² and has been associated with several cases of human disease in eastern Australia.³³

Two further species of rickettsia identified in Australian ticks may be considered potential human pathogens, although their presence in febrile patients is yet to be confirmed. *Rickettsia gravesii* has been detected in ornate kangaroo ticks in WA³⁴ and Queensland (unpublished data). In a WA study, rogainers (outdoor recreationists) had a significantly higher seroprevalence to spotted fever group rickettsiae than controls with minimal bush exposure,³⁵ suggesting exposure to a possible tick-transmitted rickettsia. A Tasmanian study found that 55% of *I. tasmani* ticks collected from Tasmanian devils contained rickettsial DNA. Further molecular characterisation of the DNA demonstrated sufficient divergence from previously described species to designate this new organism *Candidatus* *Rickettsia tasmanensis*.³⁶ Because *I. tasmani* is known to bite humans, this rickettsia must be considered as a potential human pathogen.

Coxiella burnetii

This bacterium causes Q fever and usually infects humans by inhalation of infectious aerosols from carrier vertebrate animals such as goats, sheep, cattle and domestic pets. However, it is present in both paralysis ticks¹³ and ornate kangaroo ticks,^{37,38} and although, anecdotally, there are other cases of Q fever being transmitted by ticks, there is only one published case where the patient developed pericarditis, a rare presentation of Q fever, after being bitten by an ornate kangaroo tick.³⁹

In north-eastern NSW, 5.6% of paralysis ticks contained the *com1* gene of *C. burnetii*.¹³ This bacterium has been isolated from the

bandicoot tick (*Haemaphysalis humerosa*) from both sides of Australia,^{40,41} although it is unlikely that this tick species bites humans.

Other possible bacterial pathogens causing rickettsial illness

Candidatus Neoehrlichia mikurensis has been shown to be a human pathogen in other countries,¹⁴ causing febrile illness and post-infection fatigue especially in immunocompromised patients. Recent Australian studies demonstrated the presence of *Candidatus* Neoehrlichia spp. in paralysis ticks,^{11,12} but their presence in Australian patients is yet to be shown.

Anaplasma and *Ehrlichia* species have been detected by molecular means in paralysis and ornate kangaroo ticks,¹¹ and these bacteria from the ornate kangaroo tick in the southwest of WA have been named *Anaplasma bovis* strain *Yanchep* and *Candidatus* Ehrlichia occidentalis, respectively (personal communication, Alex Gofton, PhD student, Vector and Waterborne Pathogens Research Group, Murdoch University, January 2017). Certain species of these bacterial genera are known to be human pathogens (eg, *E. chaffeensis*, *A. phagocytophilum*). There is thus a possibility that these Australian bacteria may also be human pathogens.

Although a *Borrelia* species has been detected in the Australian echidna tick (*Bothriocroton concolor*),⁴² this bacterium belongs to a unique clade unrelated to the *Borrelia* species responsible for causing Lyme disease. This tick is not known to bite humans, so the bacterium is unlikely to be a human pathogen. A *Borrelia* species detected in native rats was not virulent for a human after experimental challenge.⁴³ Lyme disease bacteria are probably not present in Australian ticks.^{10,44,45}

Francisella spp. are tick-transmitted bacteria that cause classic tularaemia. The tropical reptile tick from northern Australia (*Amblyomma fimbriatum*), which is not known to bite humans, has been shown to contain DNA from this bacterium.⁴⁶ A case of a localised *Francisella* infection following a bite from a ring-tail possum has been reported,⁴⁷ but it is not yet clear whether tularaemia is a tick-transmitted infection in Australia.

Protozoal infections

Babesia spp. are recognised human and animal pathogens transmitted by tick bites, especially in the northern hemisphere. In Australia, cattle are often infected with *B. bigemina* and/or *B. bovis* (cattle tick fever) via the bite of the Australian cattle tick (*Rhipicephalus australis*); and dogs with *B. vogeli* and/or *B. gibsoni* via the brown dog tick (*R. sanguineus*) and possibly the bush tick (*Haemaphysalis longicornis*).^{48,49} Only the bush tick is thought to bite humans.

A single case of human babesiosis caused by *B. microti* has been described in an Australian man who lived in close proximity to dogs but who did not recall being bitten by a tick and had not travelled outside of Australia for nearly 40 years.⁴⁹ This was thought to have been a locally acquired infection, but there have been no subsequent cases of human babesiosis diagnosed in Australia.

Allergy following tick bites

A local allergic reaction to ticks is not uncommon and may take the form of urticaria or induration (due to tick saliva), scrub itch (due to infestations of nymphs) or rash.⁵⁰⁻⁵²

Occasionally, the allergic reaction can be systemic, including wheezing, anaphylaxis and even death.⁵³ Severe allergy has recently been described following prior sensitisation of a patient due to the ingestion of red meat.⁵⁴

Paralysis following tick bites

I. holocyclus is known as the Australian paralysis tick because it injects a mixture of neurotoxins into its host when it bites. The role of these toxins for the tick is uncertain, but they often have a profound impact on the host animal. The toxins, known as holocyclotoxins, are small, cyclic polypeptides similar to botulinum toxin. They can affect native animals, family pets and occasionally humans, especially if they are small,^{55,56} and may cause ataxia followed by an ascending, symmetrical, flaccid paralysis similar to Guillain-Barré syndrome. Cranial nerves may be involved, leading to facial paralysis or ophthalmoplegia. The paralysis can extend even after the tick has been removed. There have been human deaths due to tick toxin, but not for many decades.⁵⁵

Autoimmunity following tick bites

There is one report of Graves' disease developing in a patient bitten by an unknown species of Australian tick in WA.⁵⁷ The patient also had mild rickettsial infection following the bite. It was hypothesised that molecular homology between the thyroid-secreting hormone receptor of the patient and the rickettsial ATPase enzyme resulted in the synthesis of an antibody that cross-reacted with the host thyroid receptor, leading to increased synthesis of thyroid hormones.

Post-infection fatigue

This phenomenon is well known to be a consequence of several infections (eg, Ross River virus infection, Q fever, Epstein-Barr virus infection), although the antecedent infection may not be clearly identified by the patient. It is not yet widely recognised as a problem following rickettsial infection, although it has been suggested by a study involving two large cohorts of fatigued and non-fatigued patients,⁵⁸ and a case report.⁵⁹ In addition, there was a report of endemic typhus in SA,⁶⁰ where patients often had a prolonged fatigue-like condition.

Australian multisystem disorder

This term has been proposed to describe patients with a range of symptoms of currently unknown aetiology, although they have been linked to tick bites in Australia.⁴⁵ The main symptoms are fatigue, joint and muscle pain, and neurocognitive impairment, but vary from patient to patient. This is the group of patients who may have described themselves as having chronic Lyme (or Lyme-like) disease.⁴⁴

Because so little is known about the medical effects of tick bites in Australia, it is important for medical practitioners to keep an open mind when dealing with patients who speak of problems associated with tick bites. While the patient may well have other underlying medical issues brought to light by the tick bite, a considered investigation of the whole clinical story is indicated.

If the tick bite is recent (eg, within 4 weeks) and the patient is symptomatic, an EDTA blood sample should be sent to a diagnostic laboratory for microbial polymerase chain reaction testing and culture, accompanied by a serum sample for antibody testing. This acute serum should be stored by the laboratory and tested in parallel with a later serum from the patient, looking for seroconversion or a significant rise in antibody titre, if the patient continues to be unwell

and has not responded to treatment. The second (convalescent) serum is an important sample, as it may well contain antibodies to the causative microbe that were absent in the first (acute) serum.

However, when the tick bite has occurred some time ago (more than 8 weeks), serology is difficult to interpret, because antibody titres are stable and may reflect either recent or long-past infection.

In relation to Lyme disease, given the likely absence of the relevant bacteria in Australian ticks,^{10,44,45} there is little value in laboratory testing for the disease if the patient has not been to an endemic region of the world.

Conclusion

Much remains to be learned about the medical consequences of tick bites in Australia. While rickettsial infections are currently the most commonly known, it is likely that ongoing research will reveal new

tick-borne viral, bacterial and protozoal infections, including the possibility of zoonotic transmission from wild and domestic mammals and birds which have been bitten by ticks.

This highlights the importance of the One Health concept (<https://www.cdc.gov/onehealth>), which recognises the importance of the interaction between human health, animal health and the environment, and will enable the identification of new and emerging diseases.

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