



Australian Government

Department of Health  
and Aged Care

# **Guidance Note for medical practitioners and hospitals**

Introduction to ticks, Australian ticks and tick-  
borne diseases and illnesses

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## List of abbreviations

Abbreviations	Descriptions
ASF	Australian spotted fever
ATBF	African tick bite fever
CDC	Centers for Disease Control and Prevention
DNA	Deoxyribonucleic acid
DSCATT	Debilitating Symptom Complexes Attributed to Ticks
ED	Emergency departments
ELISA	Enzyme-linked immunosorbent assay
FGF	Fibroblast growth factor
FISF	Flinders Island spotted fever
HGF	Hepatocyte growth factor
HME	Human monocytic ehrlichiosis
MMA	Mammalian meat allergy
PDGF	Platelet-derived growth factor
QTT	Queensland tick typhus
STARI	Southern tick-associated rash illness
TBE	Tick-borne encephalitis
TGF	Transforming growth factor
US	United States

# About this Guidance Note

## Purpose and objective

This Guidance Note is part of a series of Guidance Notes on ticks, tick-borne diseases, tick-induced allergies and Debilitating Symptom Complexes Attributed to Ticks (DSCATT).

In response to the 2016 Senate Community Affairs References Committee's Final Report *Inquiry into the growing evidence of an emerging tick-borne disease that causes a Lyme-like illness for many Australian patients*, the Australian Government commissioned the development of educational and awareness materials related to DSCATT, as well as a clinical pathway and multidisciplinary care model to support clinicians' decision-making on differential diagnosis and referral pathways for patients presenting with DSCATT. The purpose of the Guidance Notes is to provide evidence-based guidance for clinicians in community and hospital settings, as well as providing a reference source on DSCATT topics.

## Topics covered in this Guidance Note

This Guidance Note introduces the major concepts, issues and diseases and illnesses related to ticks, globally and in Australia. It includes a brief introduction to ticks and tick-borne diseases globally to provide international context, highlighting the increasing spread and public health threat from tick-borne diseases. It does provide information on some important concepts about ticks, such as how they bite and the effect of tick saliva on the host. Some of this information is on overseas ticks and some of it pertains to Australian ticks.

This Guidance Note primarily focuses on Australian ticks, describes the ecology of Australian ticks and identifies the diseases they are known to cause (Queensland tick typhus (QTT), Flinders Island spotted fever (FISF), Australian spotted fever (ASF), and Q fever). This Guidance Note does not provide detailed information about these four diseases, as these are covered in the *Australian endemic tick-borne diseases* Guidance Note. This Guidance Note does not provide detailed information about tick-induced allergies or tick paralysis. Further detail about tick-induced allergies and tick paralysis is provided in the *Tick-induced allergies: tick anaphylaxis and mammalian meat allergy, and tick-associated toxicosis and paralysis* Guidance Note. This Guidance Note does not cover in detail overseas acquired tick-borne diseases such as Lyme disease. Further detail about Lyme disease and the tick vectors that transmit Lyme disease is provided in the *Overseas-acquired tick-borne diseases: Lyme disease* Guidance Note.

Acknowledging the current evidence and questions about what pathogens are in Australian ticks, particularly with respect to DSCATT experienced by some Australians, this Guidance Note covers the findings of Australian research on ticks and also on tick-borne diseases that are not known to be acquired by humans in Australia currently. These subjects were outside of the scope of the DSCATT Clinical Pathway, as the pathway focusses on known Australian tick-borne diseases.

This Guidance Note is based on information freely available to the public, from published peer-reviewed literature, and Australian and international guidance and guidelines, with a focus on literature published in the past 10 years. In this Guidance Note, where published peer-reviewed papers were not freely available to the public but are of high importance as they relate to the Australian situation, this literature was included. Studies and publications cited by the authors of articles included in this Guidance Note are provided as in text citations. This approach allows for articles published outside of the past 10 years and articles

that are not freely available to the public to be acknowledged and provides easy access for readers who may wish to explore an article further.

In this Guidance Note and in the series of Guidance Notes on ticks, tick-borne diseases, tick-induced allergies and DSCATT, there is some repetition of content between the Guidance Notes and within the Guidance Notes, where appropriate. This approach enables each Guidance Note to be read as a standalone document, rather than requiring the reader to read from start to finish. The repetition between sections within a Guidance Note allows the reader to read each section as a standalone section, rather than being referred to other sections within the Guidance Note. The Contents page of each Guidance Note is hyperlinked to sections within the Guidance Note to enable the reader to easily access information. Additionally, readers are also referred to other Guidance Notes in this series where additional information can be found.

A short video on [how to remove a tick](#) by killing the tick *in situ* with ether-containing sprays is available here:

**Important!** Watch this video about how to safely remove a tick<sup>1</sup>  
<https://www.allergy.org.au/patients/insect-allergy-bites-and-stings>

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<sup>1</sup> An allergy project supported by the National Allergy Strategy, Australasian Society of Clinical Immunology and Allergy, Allergy & Anaphylaxis Australia, and Tick-induced Allergies Research and Awareness.

## Overview and summary

Ticks are parasites that feed off animal and human blood. Globally, ticks, along with mosquitoes, are recognised as the most important vectors in the transmission of bacterial and viral pathogens to humans and animals. Ticks transmit the most diverse array of infectious agents of any blood-feeding arthropod and have the potential to pose public health and biosecurity risks.

Globally, there are almost 900 species of tick, distributed into two main families: soft ticks (Argasidae) and hard ticks (Ixodidae). Of these nearly 900 tick species, only 28 species globally are recognised to transmit human pathogens, which include organisms such as bacteria, viruses and protozoa.

Hard ticks have a hard, flat body and elongated mouthparts with rows of backward pointing teeth. This group includes the most important species that bite humans. Hard ticks favour habitats with areas of vegetation, such as forests and fields where females lay eggs on the ground, however, they may also be found in urban areas if there are unoccupied patches of grass.

Soft ticks have a wrinkled leathery appearance. Only a few species of this type are found in Australia, and they rarely come into contact with people. Soft ticks generally favour sheltered habitats and will hide in the nests of hosts or areas where hosts rest.

While ticks and tick-borne diseases are often limited to specific geographical regions, they may be potentially found anywhere in the world, with international travel from endemic regions to non-endemic regions by people, animals and cargo, potentially transporting ticks. In recent decades, ticks have been expanding their geographic ranges largely due to climate change.

## Australian ticks and tick-borne illnesses

In Australia, there are over 70 species of tick, 66 of which are endemic to Australia. Five species were introduced by humans with domestic animals ('exotic' ticks), which result in economically important diseases restricted to domestic animal hosts. None of the exotic ticks typically bite or feed on humans.

Of the tick species endemic to Australia, 17 may attach and feed on humans, but only six of these ticks are able to act as competent vectors for the transmission of pathogens to humans. Apart from the occasional local bacterial infection at the tick bite site (eschar) the only two systemic infections that are definitely known to be transmitted by tick bites in Australia are rickettsial infections from infection with *Rickettsia* spp. (Queensland tick typhus (QTT), Flinders Island spotted fever (FISF), and Australian spotted fever (ASF)), and Q fever (*Coxiella burnetii*).

Two additional species of *Rickettsia* (other than those that cause QTT, FISF and ASF) have been identified in Australian ticks and may be considered potential pathogens, although their presence in febrile patients has yet to be confirmed. These new species are *Rickettsia gravesii* and *Candidatus Rickettsia tasmanensis*.

The species of Australian ticks known to bite humans and transmit bacterial infection are:

- the **Australian paralysis tick** (*Ixodes holocyclus*), which is endemic on the east coast of Australia and causes QTT due to *Rickettsia australis* and causes Q fever due to *C. burnetii*



- the **common marsupial tick** (*Ixodes tasmani*), which occurs in New South Wales, Queensland, South Australia, Western Australia, Tasmania and Victoria and causes QTT due to *R. australis* and causes ASF due to *Rickettsia honei* subsp. *marmionii*
- the **southern paralysis tick** (*Ixodes cornuatus*), which occurs in New South Wales, Victoria and Tasmania and causes QTT due to *R. australis*
- the **ornate kangaroo tick** (*Amblyomma triguttatum*), which occurs throughout much of the central, northern and western Australia and causes Q fever due to *C. burnetii*
- the **southern reptile tick** (*Bothriocroton hydrosauri*), which occurs mainly in south-eastern Australia and causes FISF due to *R. honei*
- the *Haemaphysalis novaeguineae* tick (no common name), which causes ASF due to *R. honei* subsp. *marmionii*.

Three of the 66 species endemic to Australia are well-known for biting and feeding on humans - the Australian paralysis tick (*I. holocyclus*), the ornate kangaroo tick (*A. triguttatum*), and the southern reptile tick (*B. hydrosauri*).

In Australia, most tick bites pose no medical problems if the tick is safely removed. Tick bites can lead to a variety of illnesses in patients, with the most common being allergic reactions. The Australian paralysis tick is the most medically significant tick in Australia and is responsible for over 95% of tick bites in humans in eastern Australia and for most tick-borne illnesses in Australia. The Australian paralysis tick can cause several illnesses, severe allergic reactions (anaphylaxis), mammalian meat allergy (MMA), paralysis, and death.

While tick bites in Australia can lead to a variety of illnesses in patients, as indicated above, much about Australian ticks and the [non-allergic] medical outcomes following tick bites remains unknown and requires further research.

Australian research and reviews on Australian ticks have investigated and reported on potential pathogens and tick-borne diseases including anaplasmosis, babesiosis, ehrlichiosis, bartonellosis, *Borrelia* and *Francisella*. Only one case of human babesiosis has been described in Australia. While this case was thought to be a locally-acquired infection, there have been no subsequent cases of babesiosis diagnosed in Australia and the origin of the aetiological agent remains unknown. In Australia, no definite tick-borne viral infections of humans are known, although a new tick virus has recently been isolated (Graves, unpublished).<sup>2</sup>

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<sup>2</sup> Unpublished at the time of publication of this Guidance Note. Provided by Graves, S. R., April 2021.

# Introduction to ticks, tick-borne diseases globally and public health significance

Ticks are obligate haematophagous ectoparasite arthropods of various animals including humans (Hall-Mendelin et al., 2011; Šimo et al., 2017). More simply, ticks are parasites that feed off animal and human blood and require blood for subsistence and reproduction (Australian Government Department of Health, 2015; New Zealand Ministry of Health, 2015).

Ticks feed off a range of hosts including mammals, reptiles, birds and amphibians and have the potential to pose public health and biosecurity risks as they can carry and transmit human and animal diseases (New Zealand Ministry of Health, 2015).

Worldwide, ticks (and mosquitoes) are recognised as the most important vectors in the transmission of bacterial and viral pathogens to humans and animals (Collwell et al. (2011) in Dehhaghi et al., 2019). Ticks are the major vectors of disease-causing agents to humans, companion animals and wildlife, and transmit the most diverse array of infectious agents of any blood-feeding arthropod (Sonenshine, 2018; Wikel, 2018), including the agents for Lyme disease, Rocky Mountain spotted fever, human granulocytic anaplasmosis, human monocytic anaplasmosis, tick-borne encephalitis (TBE), babesiosis, theileriosis, ehrlichiosis and many others. It is important to note that not all species of tick are capable of transmitting these pathogens and often only a limited number of species are capable of doing so.

Additionally, tick bites can cause substantial blood loss [in animals], severe toxic reactions and death due to tick paralysis (Sonenshine & Roe (2014) in Sonenshine, 2018). Tick saliva is secreted in varying amounts during the feeding process and this can cause local or systemic allergic reactions and/or paralysis (Cabezas & Valdés (2014) in Taylor et al., 2019). Nearly 70 species of tick globally are capable of inducing paralysis (Gothe & Neitz (1991) in Hall-Mendelin et al., 2011).

The remarkable success of ticks as vectors of disease is mainly related to their longevity, high reproductive potential and broad host spectrum for several species, along with their capacity to imbibe a very large quantity of blood over a relatively long period of time (Šimo et al., 2017).

Worldwide, there are almost 900 species of tick, distributed in two main families:

- Argasidae (soft ticks)
- Ixodidae (hard ticks) (Guglielmone et al. (2010), and Barker et al. (2014) in Dehhaghi et al., 2019).

Hard ticks have a hard, flat body and elongated mouthparts with rows of backward pointing teeth. This group includes the most important species that bite humans (Australian Government Department of Health, 2015). Hard ticks are more readily identifiable than soft ticks and also spend more time attached to their hosts than soft ticks, which feed for a shorter period of time (New Zealand Ministry of Health, 2015). Hard ticks favour habitats with areas of vegetation, such as forests and fields where females lay eggs on the ground, however, they may also be found in urban areas if there are unoccupied patches of grass (New Zealand Ministry of Health, 2015).

Soft ticks have a wrinkled, leathery appearance. Only a few species of this type are found in Australia and they rarely come into contact with people (Australian Government Department

of Health, 2015). Soft ticks generally favour sheltered habitats and will hide in the nests of hosts (New Zealand Ministry of Health, 2015) or areas where hosts rest.

Among these almost 900 species of tick, only 28 species of ticks globally are recognised to transmit human pathogens, which include organisms such as bacteria, viruses and protozoa (Rodríguez et al., 2018).

While ticks and tick-borne diseases are often limited to specific geographical regions, they may be potentially found anywhere in the world, with international travel from endemic regions to non-endemic regions by people, animals and cargo, potentially transporting ticks (Dehhaghi et al., 2019).

Tick species with very broad (and expanding) geographic and host ranges include:

- the **black-legged (deer) tick** (*Ixodes scapularis*) which is found in North America
- the **castor bean or sheep tick** (*Ixodes ricinus*), which is closely related to the black-legged tick and which is found mostly throughout Europe, the United Kingdom and localities in North Africa
- the **taiga tick** (*Ixodes persulcatus*), which is found in eastern Europe and northern Asia (Sonenshine, 2018).

In recent decades, ticks have been expanding their geographic ranges largely due to [but not limited to] climate change, while tick populations in many areas of their past and even newly established localities have increased in abundance (Molaei et al., 2019; Semenza & Suk, 2017; Sonenshine, 2018). Such dynamic changes present new and increasingly severe public health threats to humans, livestock and companion animals in areas where ticks were previously unknown or were considered to be of minor importance (Molaei et al., 2019; Sonenshine, 2018).

## Overseas-acquired tick-borne diseases diagnosed in overseas travellers, in Australia

Human infections transmitted by ticks seen in overseas travellers visiting or living in Australia include:

- **African tick bite fever**, seen in persons returning from Africa, often having visited game parks and being bitten by an infected tick. The bacterium is *Rickettsia africae* (Wang et al. (2009) in Graves & Stenos, 2017)
- **Mediterranean spotted fever**, seen mainly in persons returning from the Indian sub-continent. This tick-transmitted infection is caused by *Rickettsia conorii* (Graves (2002), and Punj et al. (2013) in Graves & Stenos, 2017)
- **ehrlichiosis**, caused by *Ehrlichia chaffeensis*, seen following the bite from an infected tick in the United States (US) (Burket et al. (2015) in Graves & Stenos, 2017)
- **Lyme disease**, from the bite of an infected tick in Europe or North America, is caused by a spirochaete bacterium, *Borrelia burgdorferi* (and related species) (Subedi et al. (2015) in Graves & Stenos, 2017). Graves & Stenos advised that all confirmed cases in Australia to date have been in returned travellers (Graves & Stenos, 2017)
- a case of **Siberian (North Asian) tick typhus**, which has been diagnosed in an overseas traveller, in Australia (Graves, unpublished).<sup>3</sup>

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<sup>3</sup> Unpublished at the time of publication of this Guidance Note. Provided by Graves, S. R., April 2021.

## Human tick-borne diseases acquired in the United States

In the US, the Tick-borne Disease Working Group's 2018 report to the US Department of Health and Human Services and Congress advised diseases transmitted by ticks are a serious and growing public health concern with tick-borne illnesses possibly causing severe health complications and often being difficult to diagnose (Aucott et al., 2017). The Centers for Disease Control and Prevention (CDC) currently recognises 13 unique human tick-borne illnesses caused by 18 different pathogens in the US, with seven of these being nationally notifiable (Aucott et al., 2017).

The tick-borne illnesses found in the US, profiled on the CDC website, include: anaplasmosis; babesiosis; *Borrelia miyamotoi* disease; Colorado tick fever; ehrlichiosis; Heartland and Bourbon virus diseases; Lyme disease; Powassan virus disease; Rocky Mountain spotted fever; *Rickettsia parkeri* rickettsiosis; tick-borne relapsing fever; and tularaemia (Centers for Disease Control and Prevention, 2020d).

In the US, reported cases of bacterial and protozoan tick-borne illness have doubled between 2004 and 2016 (Molaei et al., 2019). Ticks are responsible for nearly 95% of vector-borne diseases reported annually in the US (Eisen et al., 2017 in Sonenshine, 2018). Lyme disease is the most common tick-borne illness with approximately 300,000 new cases diagnosed in the US each year (Hinckley et al., 2014 and Nelson et al., 2015 in Aucott et al., 2017).

The overall public health threat posed by ticks and tick-borne illness in the US is steadily increasing to include new human populations as major vector ticks are expanding their geographic ranges (Eisen et al. (2016), Springer et al. (2014), Paddock & Goddard (2015), Sonenshine (2018), and Molaei et al. (2019) in Eisen, 2020) and as new native tick-borne human pathogens are discovered (Eisen et al. (2017), Rosenberg et al. (2018), and Eisen & Eisen (2018) in Eisen, 2020).

Within North America, the black-legged tick (*Ixodes scapularis*) (see [Figure 1](#) overleaf) is the primary vector for a greater variety of tick-borne illnesses than any human- or animal-biting tick, including the bacteria causing Lyme disease, human granulocytic anaplasmosis, tick-borne relapsing fever, human babesiosis, ehrlichiosis and the virus causing Powassan illness (Centers for Disease Control and Prevention, 2020b; Sonenshine, 2018).

**Figure 1: Adult female black-legged (deer) tick (*Ixodes scapularis*) (left), with eggs (right) (Public domain)**



Public domain: Photo courtesy of the Agricultural Research Service, the research agency of the United States Department of Agriculture.

Photo by Scott Bauer

Image Number: K8002-3, {{PD-USGov-USDA-ARS}}

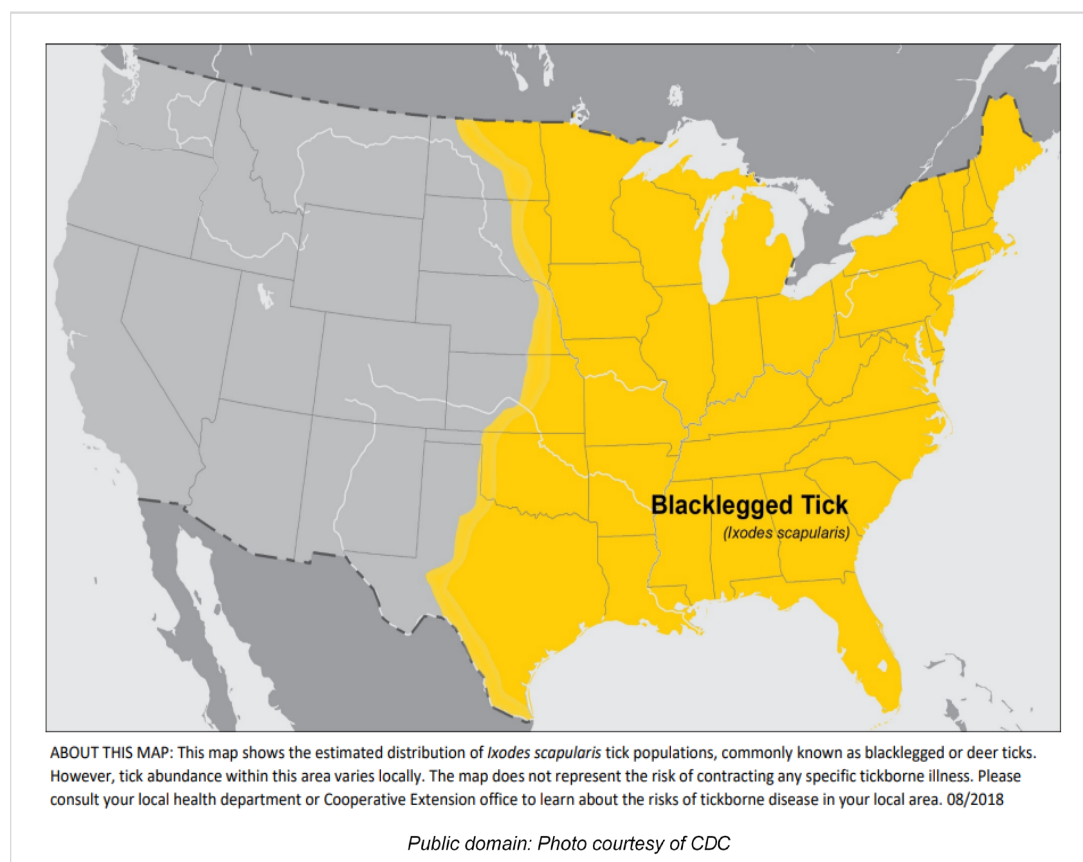
[https://commons.wikimedia.org/wiki/File:Adult\\_deer\\_tick.jpg](https://commons.wikimedia.org/wiki/File:Adult_deer_tick.jpg)



Public domain: CDC / Sue Partridge (2017)

*I. scapularis* is widely distributed across the eastern US (see [Figure 2](#) overleaf) (Centers for Disease Control and Prevention, 2020b). This tick has largely spread throughout most of the eastern US and into southern Canada during the 20<sup>th</sup> century, following the reforestation and reintroduction and proliferation of white-tailed deer (Randolph (2014) in Sonenshine, 2018). There is broad consensus that the white-tailed deer has been the main driver for the substantial increase in *I. scapularis* ticks in the northern parts of the eastern US over the past 40 years (Stafford (2007), Eisen & Dolan (2016), Spielman (1994) and Telford (2017) in Eisen, 2020). See *Overseas-acquired tick-borne diseases: Lyme disease* Guidance Note for more information about *I. scapularis*.

**Figure 2: Reported populations of the black-legged (deer) tick (*Ixodes scapularis*) (Public domain)**



Additionally, the lone star tick (*Amblyomma americanum*) is an important emerging health threat to humans, domesticated animals and wildlife (Molaei et al., 2019). While lone star ticks have been established in the southern US for well over a century, the lone star tick has expanded into the upper midwestern and northeastern US and Canada (Stafford et al. (2018) and Nelder et al. (2019) in Molaei et al., 2019). The lone star tick may be recolonising areas where it thrived historically, with the resurgence of this tick linked to increased populations of deer, eastern coyotes, and wild turkeys (Molaei et al., 2019). Lone star ticks have been associated with several human diseases and medical conditions including tularaemia (*F. tularensis*), ehrlichiosis (*E. chaffeensis*, *E. ewingii*, and Panola Mountain *Ehrlichia*), Heartland virus disease, southern tick-associated rash illness (STARI) (pathogen unknown) and mammalian meat allergy (MMA) after tick bite (known in the US as alpha-gal syndrome) and are probably also associated with Bourbon virus disease (Stafford et al. (2018) in Molaei et al., 2019). While lone star ticks do not transmit the principal bacterium that causes Lyme disease in North America, symptoms of STARI and early Lyme disease are similar, with STARI potentially being misdiagnosed as Lyme disease in areas with both lone star ticks and black-legged ticks (Molaei et al., 2019).

## Human tick-borne diseases acquired in Europe and other countries (excluding Australia)

The information below is a summary based on information from the CDC. More information is available in other Guidance Notes on overseas ticks and tick-borne diseases.

The CDC advises a number of tick-borne illnesses can be contracted abroad [outside of the US] (Centers for Disease Control and Prevention, 2019a). The information from the CDC on tick-borne diseases that can be contracted abroad [outside of the US] is briefly provided below:

- **African tick bite fever (ATBF).** Transmitted by *Amblyomma hebraeum* and *Amblyomma variegatum* ticks, ATBF is the most commonly diagnosed rickettsial disease among returning international travellers. ATBF is found in Sub-Saharan Africa, the Caribbean (French West Indies), and Oceania (Centers for Disease Control and Prevention, 2019a). ATBF is the most commonly reported travel-related tick-borne disease. While the CDC notes ATBF is found in Oceania, the ticks that transmit ATBF (*A. hebraeum* and *A. variegatum*) are not found in Australia or recognised as ticks that cause human tick-borne diseases in Australia (Dehhaghi et al., 2019).
- **Lyme disease (Europe and Asia).** Outside of North America, Lyme disease is transmitted through the bite of infected *I. ricinus* and *I. persulcatus* ticks. In Europe, Lyme disease is endemic from southern Scandinavia into the northern Mediterranean countries of Italy, Spain, Portugal, and Greece and east from the British Isles into central Russia. Incidence is highest in Central and Eastern European countries. In Asia, infected ticks occur from western Russia through Mongolia, northeastern China, and Japan, however, human infection appears to be uncommon in most of these areas (Centers for Disease Control and Prevention, 2019a). See *Overseas-acquired Lyme disease* Guidance Note for more detail on Lyme disease.
- **Tick-borne encephalitis (TBE).** Transmitted through the bite of infected *I. ricinus* and *I. persulcatus* ticks, TBE is endemic in focal areas of Europe and Asia, extending from eastern France to northern Japan and from northern Russia to Albania. The highest disease incidence has been reported from western Siberia, Slovenia, and the Baltic States. Asian countries with reported cases or virus activity include China, Japan, Kazakhstan, Kyrgyzstan, Mongolia, and South Korea. TBE may also be acquired by ingestion of unpasteurized dairy products from infected goats, sheep, or cows (Centers for Disease Control and Prevention, 2019a).

In addition to the advice on ATBF, Lyme disease and TBE, the CDC also included the following information (see [Table 1](#) overleaf) on selected travel-associated tick-borne illnesses under the tick-borne diseases abroad advice.



**Table 1: Selected travel-associated tick-borne illnesses (Centers for Disease Control and Prevention, 2019a)**

Disease & Etiologic Agent(s)	Geographic Location and Additional Risk Factors
Mediterranean spotted fever (also known as boutonneuse fever)	Europe (Mediterranean basin), Middle East, Indian subcontinent, and Africa. Caused by <i>Rickettsia conorii</i> , symptoms include fever, headache, muscle pain, eschar (usually single), and rash. It is typically a moderately severe illness and can be fatal.
Crimean-Congo hemorrhagic fever <i>CCHF virus</i>	Asia, Africa, and Europe. May also be acquired by contact with infected blood or saliva or inhalation of infected aerosols.
Omsk hemorrhagic fever Omsk hemorrhagic fever virus	Southwestern Russia. May also be acquired by direct contact with infected muskrats.
Kyasanur Forest disease	Southern India, Saudi Arabia (aka Alkhurma disease in Saudi Arabia). Typically associated with exposure while harvesting forest products.

**Figure 3: Starved, female castor bean tick (*Ixodes ricinus*) (Public domain)**



Within Europe, the castor bean or sheep tick (*I. ricinus*) (see Figure 3 below) is the primary vector for Lyme disease and TBE, the most important tick-borne diseases in Europe (Semenza & Suk, 2017). This hard-bodied tick transmits a large variety of pathogens of medical and veterinary importance including *Borrelia burgdorferi* s.l. causing Lyme disease, *Anaplasma phagocytophilum* causing human granulocytic anaplasmosis, *F. tularensis* causing tularaemia, *Rickettsia helvetica* and *Rickettsia monacensis* causing spotted fever rickettsiosis, *Babesia divergens* and *Babesia microti* responsible for babesiosis, *Neoehrlichia mikurensis* causing TBE virus, Louping ill virus and TBE virus (Medlock et al., 2013).

Lyme disease is the most prevalent tick-borne disease of humans in the Northern Hemisphere with the incidence having increased in at least nine European countries over the last decade (Hofhuis et al. (2006), Hubalek (2009), and Rizzoli et al. (2011) in Medlock et al., 2013), with one plausible cause being the changing geographical distribution, density and activity of the principal vector tick *I. ricinus*, and/or changed activity that bring people into contact with ticks (Medlock et al., 2013). The distribution of *I. ricinus* is known to be changing in Europe, at extremes of altitude and latitude as well as within its prior range (Medlock et al., 2013). See *Overseas acquired tick borne diseases: Lyme disease* Guidance Note for more detail about *I. ricinus*.

## No human tick-borne diseases currently acquired in New Zealand

In New Zealand, endemic ticks are host-specific, infest mainly birds, and generally do not transmit diseases to humans. New Zealand also has an introduced species of tick, the brown cattle tick (*Haemaphysalis longicornis*), which can infest warm-blooded mammals such as cattle or humans (New Zealand Ministry of Health, 2015). The cattle tick is known as a vector of animal and human diseases such as tick-borne fever, Japanese (Oriental) spotted fever, Russian spring-summer encephalitis, however these diseases are not present in New Zealand. The New Zealand Ministry of Health notes that since travellers could introduce tick-borne diseases to New Zealand, there is a risk (albeit a very low one) that the ticks currently present in New Zealand could spread introduced diseases (New Zealand Ministry of Health, 2015).

## Tick biology and ecology – an overview

Ticks can feed on various hosts and transmit or receive pathogenic bacteria, protozoa, helminths and viruses to/from their host animals and humans (Dehghani et al., 2019). The majority of vector ticks have a well-defined geographic range: they are constrained by their adaptations to local abiotic environmental factors such as relative humidity, temperature variations, microenvironmental factors such as soil moisture and soil permeability and biotic factors such as dense vegetation, humid leaf litter, and forests providing dense shade. Additionally, many species are constrained by host-parasite associations, especially host-specificity relationships that have evolved over thousands or millions of years (Randolf et al. (2014) in Sonenshine, 2018). In Europe, high incidence of tick-borne disease has been reported to be linked with moderate winters and humid warm summers in Sweden, Slovakia, and Hungary, however the incidence may also be affected by the influence of climate on recreational activities (Ostfeld & Brunner (2015) in Semenza & Suk, 2017).

Tick-borne infections of humans are zoonoses (infections transmitted from animals to humans) of wildlife origins similar to tick-transmitted diseases of companion and domestic animals (Baneth (2014) in Wikel, 2018). Zoonotic tick-borne infections occur when humans encroach into natural environments where ticks, their wildlife reservoir hosts and their microbial communities co-exist within well defined (and long evolved) ecologies (Irwin et al., 2018), with these complex interactions sometimes referred to as tick-borne pathogen guilds (Telford & Goethert (2008) in Irwin et al., 2018).

Dynamic interactions among biotic and abiotic elements influence tick-borne disease epidemiology and ecology (Wikel, 2018). Changes in tick distribution and abundance, along with emergence, resurgence and geographic spread of tick-borne infections, are influenced by factors including tick and tick-borne pathogen demography, micro- and macro-climate changes, human behaviours, travel, land use and habitat modification (agricultural, residential, recreational), economics, politics, population growth and movement, and intrinsic changes in ticks and tick-borne pathogens (Pfäffel et al. (2013), Baneth (2014), and Dantas-Torres (2015) in Wikel, 2018).

Ticks spend most of their life cycle off their hosts, limited only by their ability to survive many months or even years without feeding due to their extremely low resting metabolic rates (Lighton & Fieldon (1994) in Sonenshine, 2018) and diapause.<sup>4</sup>

### Tick life cycle

Most ticks go through four life stages: egg, six-legged larva, eight-legged nymph, and eight-legged adult (male and female) (Centers for Disease Control and Prevention, 2020c). The larva, nymph and adult female (egg-producing) stages require a blood meal from a vertebrate animal to metamorphose into the next life stage (Graves & Stenos, 2017) or in the case of adult females, lay eggs (Public Health England, 2018). Ticks that require this many hosts can take up to three years to complete their full life cycle, and most will die because they don't find a host for their next feeding (Centers for Disease Control and Prevention,

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<sup>4</sup> A period of suspended development in an insect, especially during unfavourable environmental conditions.

2020c). However, in Australia, the complete life cycle of *I. holocyclus* takes about one year to complete (Doggett, 2004).

Nymphs and adult females are the stages that most often cause problems to humans (Graves & Stenos, 2017).

## How ticks bite, feed and transmit infection

The tick feeding process makes ticks very good at transmitting infection (Centers for Disease Control and Prevention, 2020a). The different components of the mouthparts of hard ticks (Ixodidae) enable these parasites to penetrate the host's skin, secrete saliva, embed, and suck blood, with the tick's mouthparts representing a key route for saliva-assisted pathogen transmission as well as pathogen acquisition from the blood meal during the tick feeding process (Vancová et al., 2020). Tick salivary glands represent a key route in transmission of tick-borne diseases and play multiple essential functions during periods when ticks are on and off hosts (Šimo et al., 2017).

Depending on the species of tick and type of pathogen, a tick needs to be attached to a human for different amounts of time (minutes to days) to infect a person with that pathogen (Centers for Disease Control and Prevention, 2019b). Transmission time for tick-borne disease varies by pathogen but is generally at least 24 hours post attachment (Eisen (2018) in Taylor et al., 2019).

For example, with Lyme disease, the duration of tick attachment is one of the most important predictors of subsequent disease, with infection more likely the longer a tick is attached to the skin (Borchers et al., 2015; Mackenzie, 2013; National Institute for Health and Care Excellence, 2018; Lantos et al., 2020). Unfed (that is, flat) and recently attached ticks do not pose a significant risk for *B. burgdorferi* infection (Lantos et al., 2020).

In most cases, the tick must be attached for 36 to 48 hours or more before the Lyme disease bacterium can be transmitted (Centers for Disease Control and Prevention, 2020a). The risk of subsequent Lyme disease may exceed 20% when a tick has been attached for  $\geq 72$  hours (Sood et al. (1997) in Lantos et al., 2020). However, research indicates the risk of infection following a tick bite in Europe is different than in the US. A number of reports have shown people in Europe became infected after a tick attachment of  $\leq 24$  hours (Huegli et al. (2011), Fryland et al. (2011), and Strle et al. (1996) in Borchers et al., 2015; Hofhuis et al. (2013), and Wilhelmsson et al. (2016) in Lantos et al., 2020), particularly in Russia (Korenberg et al. (1996) in Borchers et al., 2015). It is unclear whether differences in the tick or *Borrelia* species may be responsible for the faster transmission rate and that the travel history may therefore inform anticipatory guidance (Lantos et al., 2020). See Overseas-acquired tick-borne diseases: Lyme disease Guidance Note for more information on time to infection following tick bite.

Depending on the tick species and its stage of life, preparing to feed can take from 10 minutes to 2 hours (Centers for Disease Control and Prevention, 2020a). When the tick finds a feeding spot, it grasps the skin and cuts into the surface (Centers for Disease Control and Prevention, 2020a). The tick then inserts its feeding tube. The feeding tube can have barbs,<sup>5</sup> which help keep the tick in place. Ticks also can secrete small amounts of saliva with anaesthetic properties so that the animal or person cannot feel that the tick has attached

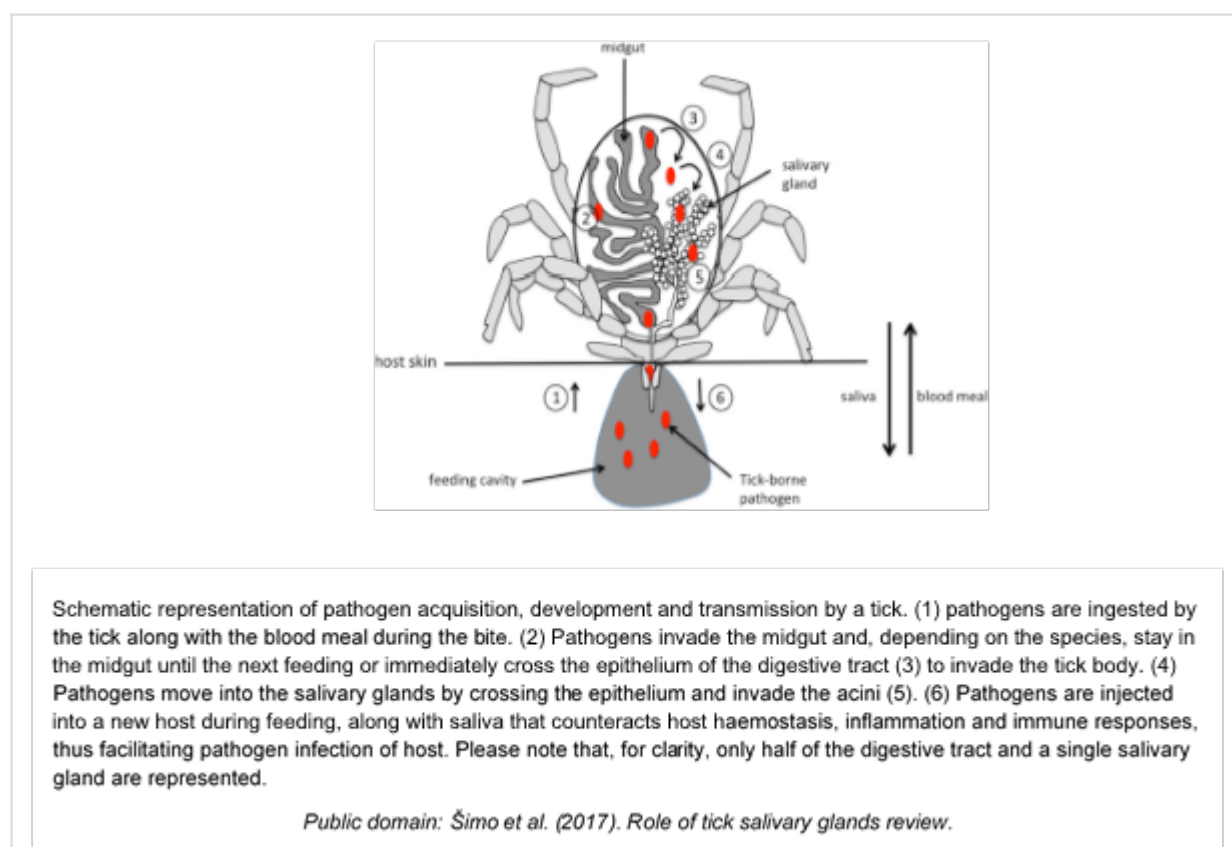
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<sup>5</sup> *I. holocyclus* has barbs.

itself. If the tick is in a sheltered spot on the body, it can go unnoticed (Centers for Disease Control and Prevention, 2020a).

In contrast to other blood-sucking arthropods, ticks are pool feeders in that they ingurgitate all of the fluids that are exuded into the haemorrhagic pool generated by the bite (Šimo et al., 2017; Vancová et al., 2020). Essentially they use their mouthparts to cut and tear into the host's skin, cause damage to blood and dermal tissues, secrete saliva that compromises their host's haemostatic processes, cement themselves to the skin and gorge on blood oozing around their mouthparts (Vancová et al., 2020). For most tick-borne pathogens, transmission to the vertebrate host occurs via the saliva, with both the salivary glands and saliva involved in the transmission process. During feeding, ticks inject saliva and absorb their meal in an alternating pattern through the same canal. Tick-borne pathogens are ingested by ticks during their feeding on infected hosts. From the midgut, tick-borne pathogens cross the digestive epithelium and invade the haemocoel (feeding cavity) from which they can penetrate the salivary gland epithelium to invade the salivary gland. Thereafter, tick-borne pathogens can be transmitted to a subsequent host via saliva injected during a subsequent blood meal (Šimo et al., 2017). Figure 4 below demonstrates diagrammatically how ticks feed and is reproduced from Šimo et al., 2017.

**Figure 4: How ticks feed (Public domain)**



The detection of a potential human pathogen in a tick does not mean it can be transmitted to a person when bitten, as the microbe must be present in the tick's salivary glands to be transmitted (Graves & Stenos, 2017). During the feeding process, ticks extract the blood of their host and regurgitate excess water from the blood back into the wound, this process enabling diseases to be transmitted between a tick and its host (New Zealand Ministry of Health, 2015). Disease transmission does not occur immediately following a tick bite; usually the infected tick does not begin to transfer diseases until it has been attached and fed for 24

hours or more (New Zealand Ministry of Health, 2015); however, time from tick attachment to transmission of infection can differ depending on the tick, as discussed above.

Because the tick injects local anaesthetic into the skin, most people are unaware when they are being bitten by a tick, however, once it starts to feed, it becomes noticeable, enlarging as it fills with blood and eggs. 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 (Graves & Stenos, 2017). Most people, when bitten by ticks, experience no problems arising from this abnormal host-ectoparasite feeding interaction (Graves & Stenos, 2017), although they may have negative influences on human health and quality of life (Dehhaghi et al., 2019).

## Tick saliva and its effects on the host

Tick saliva is a venom containing hundreds of functionally versatile proteins, injected through a bite and secreted in varying amounts throughout the feeding process (Cabezas-Cruz & Valdés (2014) in Taylor et al., 2019). Ticks, like vampire bats, secrete saliva proteins that have anaesthetic, anticoagulant, vasodilatory, anti-inflammatory and immunosuppressant properties designed to avoid host detection and optimise blood pool-feeding (Šimo et al., 2017; Cabezas-Cruz & Valdés (2014) in Taylor et al., 2019), and their saliva also contains allergens (Padula (2008), and Dorey 1998 in van Nunen, 2018). The venom of ticks, like bees, wasps and scorpions, can cause local or systemic allergic reactions and/or paralysis (Cabezas-Cruz & Valdés (2014) in Taylor et al., 2019).

Vertebrates, including humans, react to skin injury inflicted by a tick bite by forming a haemostatic plug, vasoconstriction, inflammation and tissue modelling related to wound healing (Šimo et al., 2017). If this reaction remained unchecked, these processes would cause rejection of the tick and/or disrupt feeding and arrest the tick's further development. Therefore, to facilitate the flow of blood and assure feeding, ticks have evolved a complex and sophisticated pharmacological armament that blocks pain and itch, inhibits haemostasis, and modulates innate and adaptive immune responses, angiogenesis and wound healing in their hosts (Šimo et al., 2017).

Regarding the effect of tick saliva on **host haemostasis**:

- ticks secrete vasodilators into the site of tissue injury to counteract host-derived vasoconstrictors (for example, non-proteinaceous lipid derived substances such as prostacyclin and prostaglandins) (Šimo et al., 2017)
- ticks target primary haemostasis (platelet activation and aggregation at the site of vascular injury) by various manners (Francischetti (2010) in Šimo et al., 2017)
- in secondary haemostasis (blood coagulation), different coagulation factors are countered by multiple tick salivary components, of which Kunitz-type proteinase inhibitors are the most abundant class (Koh & Kini (2009), and Chmelar et al. (2012) in Šimo et al., 2017)
- tick salivary components may display fibrinolytic activity (Šimo et al., 2017).

Regarding the effect of tick saliva on **host immune response**:

- ticks produce salivary components that degrade bradykinin and sequester histamine to mitigate itch and pain (Šimo et al., 2017)
- tick saliva strongly suppresses recruitment of blood-borne innate immune cells and notably neutrophils (Šimo et al., 2017)

- tick saliva quells inflammation at the bite location by diminishing or enhancing secretion of pro- and anti-inflammatory cytokines, respectively (Šimo et al., 2017)
- tick saliva restricts wound healing and angiogenesis (Francischetti (2010), and Hajnicka et al. (2011) in Šimo et al., 2017). Hard tick salivary molecules are able to bind to the transforming growth factor (TGF)- $\beta$ 1, the platelet-derived growth factor (PDGF), the fibroblast growth factor (FGF)-2, and the hepatocyte growth factor (HGF) depending on the tick species (Hajnicka et al. (2011), and Slovak et al. (2014) in Šimo et al., 2017)
- tick saliva inhibits the alternative pathway in the host's complement system (Šimo et al., 2017)
- tick saliva is also able to suppress the initiation of adaptive immunity by interfering with the capacity of macrophages and dendritic cells to present antigen to T cells and prime appropriate Th responses (Cavassani et al. (2005), Mejri & Brossward (2007), Oliveira et al. (2008), Skallova et al. (2008), and Carvalho-Costa et al. (2015) in Šimo et al., 2017).

For further detail on tick saliva and tick salivary gland physiology, see Šimo et al. (Šimo et al., 2017) and *Tick-induced allergies: tick anaphylaxis and mammalian meat allergy/anaphylaxis, and tick paralysis* Guidance Note.



# Australian situation

## Overview of Australian ticks

While tick bites in Australia can lead to a variety of illnesses in patients, including allergies, infection, paralysis, and post-infection fatigue, much about Australian ticks and the [non-allergic] medical outcomes following tick bites remains unknown with further research required in these areas (Graves & Stenos, 2017).

There have been two major studies of Australian ticks which have defined their number and variety (Roberts (1970) and Barker & Walker (2014) in Graves & Stenos, 2017). These studies defined over 70 species of ticks in Australia with a mixture of endemic and exotic ticks. Endemic species of ticks comprise the majority of ticks in Australia, with 66 species of ticks being reported as endemic (Barker & Barker, 2018). In Australia there are soft-bodied and hard-bodied ticks, with the majority being hard-bodied ticks. Only a few species of soft-bodied ticks are found in Australia and they only occasionally come into contact with people (Australian Government Department of Health, 2015; Geary et al., 2021).

Reviews consistently report 14 species of soft ticks (family Argasidae) (Barker et al. (2014) and Ash et al. (2017) in Barker & Barker, 2018; Barker et al. (2014), Ash et al. (2017), and Kwak et al. (2018) in Dehghani et al., 2019; Barker et al. (2014) in Graves & Stenos, 2017).

The number of hard ticks (family Ixodidae) varies slightly, with numbers reported as 56 (Barker et al. (2014) in Graves & Stenos, 2017), 57 (Barker et al. 2014; Ash et al. 2017 in Barker & Barker, 2018), and 58 (Barker et al. (2014), Ash et al. (2017), and Kwak et al. (2018) in Dehghani et al., (2019).

Five of the tick species known to be in Australia were introduced by humans with domestic animals (dogs, cattle and poultry) (Barker & Barker, 2018; Irwin et al., 2018). These 'exotic' ticks are:

- the **poultry tick** (*Argas persicus*)
- the **spinose ear tick** (*Otobius megnini*), a recent introduction, probably in the ears of horses
- the **bush tick** (*Haemaphysalis longicornis*), which occurs in much of Asia
- the **brown dog tick** (*Rhipicephalus sanguineus*), which is found worldwide
- the **Australian cattle tick** (*Rhipicephalus (Boophilus) australis*) (Barker & Barker, 2018).

The five exotic tick species result in economically important diseases including: canine and bovine babesiosis and anaplasmosis; bovine borreliosis; bovine theileriosis; and avian spirochaetosis that are restricted to domestic animal hosts and have been well studied internationally and in Australia (Irwin et al., 2018). While none of the exotic ticks typically bite or feed on humans (Barker & Barker, 2018; Barker et al. (2014) in Graves & Stenos, 2017) a 2021 study of arthropod samples, submitted for identification (after having been removed from a human) to the Department of Medical Entomology (the New South Wales reference laboratory for arthropods of medical importance) between 1988-2017, reported a very small number ( $n=11$ ) of the brown dog tick (*R. sanguineus*) had been identified (Geary et al., 2021). The total number of arthropod specimens submitted for identification over this period was 5,655. The authors advised the majority of samples were submitted by health professionals and pathology services from within New South Wales. Numerous samples were also received from interstate. Furthermore, environmental health officers, pest control



companies, veterinarians, schools, various government and industry organisations, as well as members of the public sent in samples for identification (Geary et al., 2021).

Of the tick species endemic to Australia and that mainly feed off wildlife, 17 species may attach and feed on humans and domestic animals whereas the remaining ticks mainly feed on birds, wild reptiles and wild mammals (Dehhaghi et al., 2019).

Of the 17 human biting ticks known in Australia, only six are able to act as competent vectors for the transmission of pathogens to humans. These ticks are:

- the Australian paralysis tick (*I. holocyclus*)
- the common marsupial tick (*I. tasmani*)
- the southern paralysis tick (*I. cornuatus*)
- the ornate kangaroo tick (*A. trigutattum*)
- the southern reptile tick (*B. hydrosauri*)
- the *Haemaphysalis novaeguineae* tick (no common name) (Barker & Walker (2014) in Dehhaghi et al., 2019; Graves & Stenos, 2017).

Ticks are present mainly on the east coast of Australia, however, there are also populations of ticks in several non-coastal areas (Australasian Society of Clinical Immunology and Allergy, 2019).

The tick season in Australia is often considered to range from July to December, when adult ticks are more prevalent. However, the risk of exposure to ticks exists throughout the year (Australasian Society of Clinical Immunology and Allergy, 2019).

The most medically significant tick in Australia is *I. holocyclus* (the Australian paralysis tick). Over 95% of tick bites in humans in eastern Australia are due to the Australian paralysis tick (Australian Government Department of Health, 2015; Geary et al., 2021; Taylor et al., 2019; van Nunen (2018) in van Nunen & Ratchford, 2021), and most tick-borne illnesses in Australia are due to this species (Australian Government Department of Health, 2015).

Table 2 below is reproduced from Dehhaghi et al.'s (2019) review of human tick-borne diseases in Australia.

**Table 2: Human-biting ticks of Australia with their habitats and main hosts (as in Table 1. Dehhaghi et al. 2019)**

Species	Australian Name	Region	Main Host in Australia	References
<b>Family Argasidae</b>				
<i>Argas persicus</i>	Fowl or poultry tick	All states in Australia except Tasmania	Fowl	Roberts (1970) in Dehhaghi et al., 2019
<i>Argas robertsi</i>	Robert's bird tick	Lake Cowal, NSWa; Southwestern Qldb	Fowl, Great cormorant	Roberts (1970) in Dehhaghi et al., 2019
<i>Ornithodoros capensis</i>	Seabird soft tick	Along the coast from Perth, WAc to Sydney, NSW; Off-shore islands, particularly	Seabirds, particularly terns, gulls, penguins	Barker & Walker (2014) in Dehhaghi et al., 2019

Species	Australian Name	Region	Main Host in Australia	References
		coral cays of the Great Barrier Reef, Qld		
<i>Ornithodoros gurneyi</i>	Kangaroo soft tick	Desert area of Australia, Malchi, Gracemere, and Brisbane, Qld	Eastern gray and red kangaroos, wallaroos	Doube (1975) in Dehhaghi et al., 2019
<i>Octobius megnini</i>	Spinose ear tick	WA	Domestic horses	Barker & Walker (2014) in Dehhaghi et al., 2019
<b>Family Ixodidae</b>				
<i>Amblyomma triguttatum</i>	Ornate kangaroo tick	Northern NSW; Qld; WA; Yorke Peninsula, SA	Kangaroos	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Bothriocroton auruginans</i>	Wombat tick	Armidale, Burrawang, and Tooloom, NSW; Benalla, Dargo (Gippsland), Healsville, Melbourne, Omeo, and Orbost, Vic; Flinders Island, Deloraine, Gretna, and Tarraleah, Tasmania	Dogs, wombats	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Bothriocroton hydrosauri</i>	Southern reptile tick	Jenolan Caves and along the narrow state border with Vic, NSW; Eyre Peninsula and southeastern SA; Along the coast from Bremer Bay to Albany and Margaret River area as well as along the coast from Cape Naturaliste to Cape Leeuwin, WA; Vic; Tasmania	Reptiles	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Haemaphysalis bancrofti</i>	Wallaby tick	Eastern coast of Australia, Vic	Kangaroos, wallabies and their kin	Roberts (1970) and Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Haemaphysalis longicornis</i>	Bush tick	A coastal area between Walpole and Denmark, WA; Buderim, Maleny, and Tamborine, Qld; Narrow coastal strip of eastern coast of Australia; Taree-Wauchope region, NSW; Vic	Cattle, horses, sheep	Roberts (1970) and Barker & Walker (2014) in Dehhaghi et al., 2019

Species	Australian Name	Region	Main Host in Australia	References
<i>Haemaphysalis novaeguineae</i>		Eastern half of Australia	Mammals	Unsworth et al. (2007) in Dehhaghi et al., 2019
<i>Ixodes cornuatus</i>	Southern paralysis tick	Brownlee, NSW; Bullengarook, Daylesford, Donvale Warragul District, Lakes Entrance, Mallacoota, Noojee Neerim North, Orbost, Silvan, and Leongatha, Vic; Tasmania	Wide range hosts	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Ixodes hirsti</i>	Hirst's marsupial tick	Sub-coastal areas of southern Australia	Kangaroos and their kin, domestic dogs and cats, some birds	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Ixodes holocyclus</i>	Paralysis tick	Narrow coastal strip of eastern Australia; Normanton, Qld	Mammals (mainly bandicoots), Birds	Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Ixodes tasmani</i>	Common marsupial tick	Central eastern NSW; Qld; southeastern SA; southwestern WA; Tasmania; Vic	Australian marsupials, monotremes, rodents, domestic animals and humans	Roberts (1970) in Dehhaghi et al., 2019
<i>Rhipicephalus australis</i>	Australian cattle tick	Broad coastal band from northeastern NSW to northeastern WA	Cattle	Arundel (1988) and Barker & Walker (2014) in Dehhaghi et al., 2019
<i>Rhipicephalus sanguineus</i>	Brown dog tick	Most common in north of latitude 30°S; Occasionally as far south as Sydney, NSW and Melbourne, Vic	Dogs	Roberts (1965) in Dehhaghi et al., 2019

<sup>a</sup> New South Wales; <sup>b</sup> Queensland; <sup>c</sup> Western Australia; <sup>d</sup> South Australia; <sup>e</sup> Victoria.

While Dehhaghi et al. (2019) reported the region of the tick *Haemaphysalis novaeguineae* as being 'eastern half of Australia', Unsworth et al. reported that seven cases of ASF were widely distributed throughout eastern Australia, including cases on the eastern seaboard of Australia (including the Torres Strait), Tasmania and South Australia (Unsworth et al., 2007). Five of the seven cases of ASF were in Queensland (Darnley Island, Queensland (2 patients); Yam Island, Queensland; Innisfail, Queensland; Iron Range, Queensland (Unsworth et al., 2007).

## Biology and ecology of Australian ticks

While much is known about tick-borne pathogen guilds in other parts of the world, relatively little is known in Australia about host preferences and ecologies of Australian ticks, with even less being understood about the communities or organisms within these arthropods (Irwin et al., 2018).

Many different bacteria have been detected in Australian tick species (Murrell et al. (2013), Vilcins et al. (2009), Goffton, Oskam et al. (2015), Goffton, Doggett et al. (2015) and Graves et al. (2016) in Graves & Stenos, 2017) mostly using molecular techniques. While some are known human pathogens or are closely related phylogenetically to known human pathogens, others are unique bacteria that are part of the tick biome (Graves & Stenos, 2017).

Irwin and colleagues have investigated the tick microbiome using next generation sequencing (Greay et al. (2018) and Goffton et al. (2015) in Irwin et al., 2018). Metagenomic analysis has revealed the microbiomes of Australian ticks comprise diverse genera and, similarly to northern American ticks, possess a rich and varied microbiome, with the tick species found to be the main factor influencing microbial composition (Irwin et al., 2018).

To date, in Australia, no known Northern Hemisphere bacterial pathogens have been discovered but phylogenetic analysis has revealed multiple organisms that are related to but distinct from known pathogens overseas, and their zoonotic potential remains unknown (Irwin et al., 2018). While Northern Hemisphere ticks have been detected in Australia on a number of occasions, they have not become established (Geary et al., 2021).

Studies and reviews on Australian endemic and exotic ticks have not shown tick vectors responsible for causing Lyme disease in the Northern Hemisphere to be present in Australia (Dehhaghi et al., 2019). Despite multiple studies which have searched for it in Australian ticks and patients, the organisms that cause Lyme disease have not, to date, been identified in Australian ticks (Australian Government Department of Health, 2018; Beaman, 2016; Chalada et al., 2016; Collignon et al., 2016; Dehhaghi et al., 2019; Goffton, Doggett, et al., 2015; Goffton, Oskam, et al., 2015; Graves & Stenos, 2017; Harvey et al., 2019; Irwin et al., 2017; Loh et al., 2016, 2017; Mackenzie, 2013), nor any other vector that could transmit the disease to humans (Australian Government Department of Health, 2018; Graves & Stenos, 2017). It is for this reason that the Australian medical profession does not support the diagnosis of locally-acquired Lyme disease in Australia (Australian Government Department of Health, 2018).

## Australian ticks well-known for biting humans

Three tick species endemic to Australia are well-known for biting and feeding on humans (Barker & Barker, 2018; Graves & Stenos, 2017), with these ticks known to sometimes transmit human pathogens to people when they bite. These ticks are briefly described below.

- The **Australian paralysis tick** (*I. holocyclus*) is the most notable human-biting tick on the east coast of Australia. *I. holocyclus* causes QTT due to *R. australis* and Q fever due to *C. burnetii* (Graves & Stenos, 2017) and is capable of causing the most severe effects on humans – anaphylaxis and paralysis (Australian Government Department of Health, 2015; Taylor et al., 2019; van Nunen, 2015, 2018). Over 95% of tick bites in humans in eastern Australia are due to *I. holocyclus* (Australian Government Department of Health, 2015; Geary et al., 2021; Taylor et al., 2019; van Nunen (2018) in van Nunen & Ratchford, 2021). Further, *I. holocyclus* was the most common (708 *I. holocyclus*

specimens submitted/5655 total specimens) specimen of all arthropods submitted to an Australian Medical Entomology Department for identification between 1988-2017, with 98.3% of *I. holocyclus* specimens submitted from New South Wales, with many from the south coast of New South Wales, and a small number ( $n=10$ ), were from Victoria (Geary et al., 2021). Additionally, of the *I. holocyclus* specimens submitted, Geary et al. reported that specimens from patients aged zero to nine years predominated and were more than twice as frequent as any other age class, even with population-adjusted data. Age classes were described as 'in 10 year intervals' (Geary et al., 2021). The samples were mostly submitted by health professionals and pathology services from within New South Wales but also received from interstate, environmental health officers, pest control companies, veterinarians, schools, various government and industry organisations, as well as members of the public (Geary et al., 2021). See section on '[The Australian paralysis tick \(\*I. holocyclus\*\) – the most medically significant tick in Australia](#)' for more details about this tick.

- The **ornate kangaroo tick** (*A. triguttatum*) occurs throughout much of the central, northern and western Australia (i.e. Western Australia, at one place in South Australia, and in parts of Queensland (Barker & Barker, 2018; Graves & Stenos, 2017). The ornate kangaroo tick causes Q fever due to *C. burnetii* (Graves & Stenos, 2017). In Geary et al.'s study described above, the second most common tick submitted for identification after *I. holocyclus* was the kangaroo tick (*A. triguttatum*) with 23 specimens submitted (Geary et al., 2021). See section on '[The ornate kangaroo tick \(\*Amblyomma triguttatum\*\)](#)' for more details about this tick.
- The **southern reptile tick** (*B. hydrosauri*) bites humans and transmits infection (Barker & Barker, 2018; Graves & Stenos, 2017) but is not on the notorious biter list. The southern reptile tick occurs mainly in southeastern Australia and causes FISF due to *R. honei* (Graves & Stenos, 2017). The Tasmanian Department of Health reported in 2019 that confirmed cases have been acquired in Tasmania, including the Midlands of Tasmania (Willis et al., 2019). These locations included around Great Oyster Bay. The study was the first account including confirmed cases acquired in the Midlands of Tasmania (Willis et al., 2019). See section on '[The southern reptile tick \(\*Bothriocroton hydrosauri\*\)](#)' for more details about this tick.

In addition to the above ticks that are well-known for biting humans, *Ixodes (Endopalpiger) australiensis* (Kwak et al., 2018), endemic in Western Australia, has been confirmed as biting a human who then developed the tick-induced allergy mammalian meat allergy (MMA).

## Known Australian tick-associated bacterial infections

Apart from the occasional local bacterial infection at the tick bite site (eschar), the only two systemic infections that are definitely known to be transmitted by tick bites in Australia are rickettsial infections from infection with *Rickettsia* spp. (QTT, FISF, and ASF), and Q fever (*C. burnetii*) (Graves & Stenos, 2017).

The species of Australian ticks known to bite humans and transmit bacterial infection are:

- the **Australian paralysis tick** (*I. holocyclus*), which is endemic on the east coast of Australia
  - causes QTT due to *R. australis*
  - causes Q fever due to *C. burnetii*

- the **common marsupial tick** (*I. tasmani*), which occurs in New South Wales, Queensland, South Australia, Western Australia, Tasmania and Victoria  
causes QTT due to *R. australis*  
causes ASF due to *R. honei* subsp. *marmionii*
- the **southern paralysis tick** (*I. cornuatus*), which occurs in New South Wales, Victoria and Tasmania  
causes QTT due to *R. australis*
- the **ornate kangaroo tick** (*A. triguttatum*), which occurs throughout much of the central, northern, and western Australia  
causes Q fever due to *C. burnetii*
- the **southern reptile tick** (*B. hydrosauri*), which occurs mainly in southeastern Australia  
causes FISF due to *R. honei*
- the *Haemaphysalis novaeguineae* tick (no common name)  
causes ASF due to *R. honei* subsp. *marmionii* (Barker & Walker (2014) in Dehhaghi et al., 2019; S. R. Graves & Stenos, 2017).

## Tick-related medical illnesses and diseases in Australia

In Australia, most tick bites pose no medical problems if the tick is safely removed. Tick bites can lead to a variety of illnesses in patients, with the most common being allergic reactions. In some cases, people can experience severe allergic reactions (anaphylaxis) or mammalian meat allergy/anaphylaxis, and, rarely, tick-induced paralysis (Australasian Society of Clinical Immunology and Allergy, 2019; Australian Government Department of Health, 2015; Graves & Stenos, 2017; Rappo et al., 2013; Taylor et al., 2019; van Nunen, 2018). In Australia, tick-related medical illnesses include allergies, infection, paralysis, and post-infection fatigue (Graves & Stenos, 2017). The following information is a brief overview of tick-related medical illnesses. For further detail relating to tick-borne diseases in Australia see *Australian endemic tick-borne diseases* Guidance Note. For further detail relating to tick allergy, anaphylaxis and paralysis, see *Tick-induced allergies: tick anaphylaxis and mammalian meat allergy/anaphylaxis, and tick-associated toxicosis and paralysis* Guidance Note.

## Allergic reactions after tick bite

- Mammalian meat allergy (MMA) and tick anaphylaxis are the most serious tick-induced allergies; they are often severe and are largely avoidable through prevention of tick bites and safe management of tick bites. Severe allergic reactions (anaphylaxis) to the Australian paralysis tick have been reported. Anaphylaxis ONLY occurs when the tick is disturbed, as this may cause the tick to inject more allergen containing saliva (Australasian Society of Clinical Immunology and Allergy, 2019; Tick-induced Allergies Research and Awareness, n.d.).
- Anaphylaxis, including tick anaphylaxis, is a **potentially life threatening**, severe allergic reaction that requires **immediate treatment with adrenaline** (epinephrine). **Anaphylaxis should always be treated as a medical emergency** (Australasian Society of Clinical Immunology and Allergy, 2021b).
- **Tick anaphylaxis is only seen with bites from adult ticks, and only when the adult tick is disturbed** by inappropriate handling (van Nunen (2015), van Nunen (2014), Rappo et al. (2013), Gauci et al. (1988), Broady (2013), Dorey (1998), Padula (2008),



Commins & Platts-Mills (2011), Kemp (1986), Brown & Hamilton (1998), and van Nunen (2014) in van Nunen, 2018).

- Allergic reactions in humans are now considered more significant, and are far more common, than paralysis (Rappo et al. (2013), and van Nunen (2018) in Sukkanon et al., 2019). Life-threatening allergic reactions to ticks are much more common than similarly severe reactions to bees or wasps (Tick-induced Allergies Research and Awareness, n.d.) in regions where ticks are common.
- Allergic reactions can result in swelling of the throat, and may lead to breathing difficulties and collapse (Australian Government Department of Health, 2015) and even death (Brown & Hamilton (1998) in Graves & Stenos, 2017). Anaphylactic reactions to tick bites have been fatal, though fatalities are rare (Tick-induced Allergies Research and Awareness, n.d.). Tick anaphylaxis was responsible for four deaths in Australia between 1997 and 2013 (Mullins et al. (2016), and McGain et al. (2016) in van Nunen & Ratchford, 2021).
- Tick-related allergies are the reason many people present to hospital emergency departments (ED) in regions where ticks are hyper-endemic (van Nunen & Ratchford, 2021). A two-year survey of a New South Wales hospital ED found over 500 presentations of tick bite, with 34 tick bites resulting in anaphylaxis, and over 75% of these requiring adrenaline use (Rappo et al., 2013).
- MMA (also called  $\alpha$ -gal or alpha-gal syndrome (AGS), alpha-gal allergy, or red meat allergy) is a **serious, potentially life-threatening allergic reaction** which may occur after people eat red (mammalian) meat or are exposed to other products containing alpha-gal, and occurs after tick bite. The allergen associated with these allergic reactions is present in the saliva of certain species of ticks (Centers for Disease Control and Prevention, 2020e; Fischer et al. (2020) in van Nunen & Ratchford, 2021).
- In Australia, the locations of previous reports of MMA after tick bite have correlated with the distribution of *I. holocyclus* (Kwak et al., 2018; van Nunen, 2015). With the more recent description of *Ixodes (Endopalpiger) australiensis* as the second tick species as a cause of MMA in Australia, potential exposure of the Australian population to ticks associated with MMA has increased to about 60% (Tick-induced Allergies Research and Awareness, 2019).
- This syndrome has also been described overseas (Australian Government Department of Health, 2015; van Nunen, 2018). Worldwide, Australia has the highest proportion of its population affected by MMA and tick anaphylaxis.
- A local allergic reaction to ticks is not uncommon and may take the form of an urticarial lesion or induration (due to allergy to a component of tick saliva), scrub itch (due to infestations of nymphs) or rash (Pearce & Grove (1987), Storer et al. (2005), and Doggett (2004) in Graves & Stenos, 2017).
- Mild allergic reactions to ticks appear as large local swelling and inflammation at the site of the tick bite - this can last for several days (Australasian Society of Clinical Immunology and Allergy, 2019).

## Infections

- As noted in the section on '[Known Australian tick-associated bacterial infections](#)' above, apart from the occasional local bacterial infection at the tick bite site (eschar), the only two systemic infections that are definitely known to be transmitted by tick bites in

Australia are: rickettsial infections from infection with *Rickettsia* spp. QTT, FISH, ASF; and Q fever (*C. burnetii*) (Graves & Stenos, 2017). There are other possible microbial pathogens and possibly as yet unknown infections (Graves & Stenos, 2017).

- QTT, FISH and ASF have similar clinical and serological characteristics (Dehghani et al., 2019), with the *Rickettsia* spp. that cause each respective disease being members of the alpha subclass of proteobacteria (S. R. Graves, n.d.). The clinical presentation of these rickettsial infections in Australia include eschar, fatigue, fever, headache, myalgia and rash (macular, papular, vesicular) although the severity and duration of rickettsial diseases vary considerably (Dehghani et al., 2019). Early clinical features are often non-specific, making diagnosis challenging (Stewart et al., 2017a). Additionally, symptoms may overlap with other infectious diseases including those that are transmitted by non-tick vectors, as well as a number of chronic diseases.
- QTT is an emerging public health threat (Dehghani et al., 2019; Stewart et al., 2017a) and an increasingly recognised important cause of community-acquired acute febrile illness in eastern Australia (Stewart et al., 2017a). Stewart et al. noted acute *R. australis* infection is likely to be under-recognised with recent evidence showing its increased disease burden with increased recognition of severe disease including death (Derne et al. (2015), Laboratory Australian Rickettsial Reference (2015), Baird et al. (1992), and Unsworth et al. (2007) in Stewart et al., 2017a).
- While FISH is often described as a mild illness (Heymann (2015) in Willis et al., 2019), Willis et al. noted the infection can be severe and rare deaths have been reported, with the death of a middle-aged woman due to acute infection of *R. honei* described in Queensland (Graham et al. (2017) in Willis et al., 2019).
- Q fever is a nationally notifiable disease in Australia (Australian Government Department of Health, 2021) with a Q fever laboratory case definition (Public Health Laboratory Network, 2017), and it is included in the Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Units (Communicable Diseases Network Australia, 2018).
- In Australia, Q fever is the most commonly reported zoonotic disease (Eastwood et al., 2018).
- *C. burnetii* (Q fever) is not a true Rickettsia, despite being tick-transmitted, but is a member of the gamma proteobacteria (S. R. Graves, n.d.). Q fever is acquired via various modes of transmission, a minority of which are tick-borne.
- Transmission of infections by ticks in Australia is less common than allergic reactions to tick bites (Australasian Society of Clinical Immunology and Allergy, 2019).
- Tick-borne disease is of far less concern in Australia than in Europe or the US, with the tick-borne diseases that exist in Australia (Q fever and the spotted fever rickettsial diseases) being associated with less morbidity and mortality, and usually responding quickly to oral antibiotics (doxycycline and azithromycin) (Graves & Stenos (2017) in Taylor et al., 2019).

## Tick-associated toxicosis and paralysis

- Various forms of tick toxicosis affect humans and other animals and in their most severe form result in paralysis of the infested host (Hall-Mendelin et al., 2011). In Australia, tick paralysis is largely attributable to holocyclotoxin from *I. holocyclus*, although other species of ticks globally are capable of inducing paralysis (Hall-Mendelin et al., 2011).



Holocyclotoxins are small, cyclic polypeptides similar to botulinum toxin (Graves & Stenos, 2017).

- Paralysis is induced by a toxin that is transmitted to the host in the saliva of a female *I. holocyclus*, when the tick takes a blood meal (Hall-Mendelin et al., 2011). To cause host paralysis, a tick must be attached to its host for four to five days (Hall-Mendelin et al., 2011; Hall-Medelin et al. (2011) in Taylor et al., 2019). The toxins produced by *I. holocyclus* inhibit acetylcholine release at the neuromuscular junction (Chand et al., 2016), and tend to cause more severe neurological impairment than the toxins from ticks in North America (Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011).
- Paralysis can extend even after the tick has been removed (Dehhaghi et al., 2019; Grattan-Smith et al. (1997) in S. R. Graves & Stenos, 2017). The progress of paralysis continues for 24-48 hours after removal of *I. holocyclus*, in contrast to the short duration seen with North American ticks (Dehhaghi et al., 2019).
- Tick paralysis is rare in humans, as a tick must be attached for several days to inject enough toxin (Australasian Society of Clinical Immunology and Allergy, 2019).
- The most commonly affected group is children one to five years of age (Grattan Smith et al. (1997) in Dehhaghi et al., 2019; Grattan-Smith et al. (1997), and Inokuma et al. (2003) in Hall-Mendelin et al., 2011). Doggett noted that occasional cases of tick paralysis do still occur, mainly in children, with these rare cases often unrecognised or misdiagnosed (Doggett, 2004). Guillain-Barré syndrome (GBS) may be commonly confused with tick paralysis (Hall-Mendelin et al., 2011).
- Tick paralysis caused by Australian paralysis tick (*I. holocyclus*), while rarely severe, can be fatal (Hall-Mendelin et al., 2011). In Australia, between 1914 and 1942, 20 human fatalities were attributed to tick bite, with all but three fatalities being children (Murray & Koch (1969) in Hall-Mendelin et al., 2011), with about 70% of these fatalities being in children under four years of age (Sutherland & Tibballs (2001) in Doggett, 2004).
- In Australia, there have not been human deaths due to tick paralysis for many decades (since 1945) (Dehhaghi et al., 2019; Doggett, 2004; Grattan-Smith et al. (1997) in Graves & Stenos, 2017; Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011; Barker & Walker (2014) in Taylor et al., 2019). Deaths from the bite of *I. holocyclus* are now rare due to the addition of intensive care-units in regional hospitals and expert medical treatment [advances in intensive care treatment] (Barker & Barker, 2018), and an antivenene.
- Untreated tick paralysis can be fatal in humans (Hall-Mendelin et al., 2011).
- Tick paralysis, while rare, is usually seen in children rather than adults (Australian Government Department of Health, 2015). Occasional cases of tick paralysis still occur, mainly in children, with these rare cases often unrecognised or misdiagnosed (Doggett, 2004).
- **Untreated tick paralysis can be fatal in humans** (Hall-Mendelin et al., 2011).

## Post-infection fatigue

Post-infection fatigue is a well-known consequence of several infections (e.g. Ross River virus infection, Q fever, Epstein-Barr virus infection), although the antecedent infection may not be clearly identified by the patient (Graves & Stenos, 2017). While post-infection fatigue is not yet widely recognised as a problem following rickettsial infection, it has been suggested by a study involving two large cohorts of fatigued and non-fatigued patients

(Unsworth et al. (2008) in Graves & Stenos, 2017) and a case report (Watts et al. (2008) in Graves & Stenos, 2017).

## Autoimmunity

Autoimmunity was not included above under tick-related illness in Australia but is included here, as one report of Graves' disease developing in a patient bitten by an unknown species of Australian tick in Western Australia was published in 2015 (Marangou et al. (2015) in Graves & Stenos, 2017). Graves and Stenos noted that 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 (Graves & Stenos, 2017).

The article by Marangou et al. (2015), noted by Graves and Stenos above, was included in a recent review of international evidence on tick-borne diseases and autoimmunity (Rodríguez et al., 2018). Under the section 'Autoimmune thyroid disease', Rodríguez et al. commented of the Australian study by Marangou et al. (2015) that 'interestingly' the authors offer a compelling hypothesis for molecular mimicry in this entity; they had demonstrated homology between rickettsial proteins and TSH receptor, and furthermore they had ascertained that these homologous segments presented binding motifs for HLA-DRB1\*0301 (Marangou et al. (2015) in Rodríguez et al., 2018). Of the evidence reviewed on tick-borne diseases and autoimmunity, Rodríguez et al. noted that molecular mimicry appears to be the main mechanism associated with tick-borne diseases and autoimmunity (Woolley et al. (2017) in Rodríguez et al., 2018). The authors noted tick-borne diseases may present acute clinical pictures that resemble those of autoimmune disease such as musculoskeletal symptoms, neurologic impairment, cutaneous involvement, renal failure (Murray & Shapiro (2010), and Rebaudet & Parola (2006) in Rodríguez et al., 2018). Additionally, in some cases, infection is considered a triggering factor for autoimmunity, such as in rheumatoid arthritis, autoimmune thyroid disease, vasculitides, multiple sclerosis, Guillain-Barré syndrome, through "mechanisms of bystander activation, epitope spreading, molecular mimicry and original antigenic sin" (Arvikar et al. (2017), and Shapiro (1998), and Blander et al. (2012) in Rodríguez et al., 2018). Apoptosis induced by bacteria promoting self-peptides presentation by antigen-presenting cells likely due to enhanced Th17 responses have also been demonstrated to trigger autoimmunity (Campisi et al. (2016) in Rodríguez et al., 2018). As such, Rodríguez et al. advised clinicians should consider tick-borne diseases among the differential diagnoses when approaching autoimmune-like signs in areas of tick infection (Rodríguez et al., 2018). The DSCATT Clinical Pathway advises autoimmune diseases including inflammatory arthritis, motor neurone disease, and multiple sclerosis should be considered as a differential diagnosis when tick-borne disease has been considered and is not suspected (Australian Government Department of Health, 2020).

While illnesses associated with ticks in Australia, such as those above, are currently known, much about Australian ticks and the [non-allergic] medical outcomes following tick bites remains unknown with further research required in these areas (Graves & Stenos, 2017).

## Symptoms and clinical signs of tick bites in Australia

In Australia, most tick bites pose no medical problems if the tick is safely removed. Tick bites can lead to a variety of illnesses in patients, with the most common being allergic reactions. In some cases, people can experience severe allergic reactions (anaphylaxis) or mammalian

meat allergy/anaphylaxis, or rarely, tick-induced paralysis (Australasian Society of Clinical Immunology and Allergy, 2019; Australian Government Department of Health, 2015; Graves & Stenos, 2017; Rappo et al., 2013; Taylor et al., 2019; van Nunen, 2018).

The most common serious medical complaints caused by ticks are allergic reactions to their bites, with allergic reactions to ticks ranging from mild, with swelling and inflammation at the site of a tick bite, to severe anaphylaxis (Australasian Society of Clinical Immunology and Allergy, 2019; Tick-induced Allergies Research and Awareness, n.d.).

Large local reactions to tick bites are the “least severe form” of tick-induced allergy (van Nunen, 2018; van Nunen & Ratchford, 2021). Mild allergic reactions to tick bites appear as a large local swelling and inflammation restricted to the site of the tick bite that typically extends from the bony joint above the bite to the bony joint below the bite, and can last for several days (Australasian Society of Clinical Immunology and Allergy, 2019b; Tick-induced Allergies Research and Awareness, n.d.-b; van Nunen, 2018; van Nunen & Ratchford, 2021).

Tick bites are also responsible for the development of mammalian meat allergy (MMA) (Australasian Society of Clinical Immunology and Allergy, 2019; Tick-induced Allergies Research and Awareness, n.d.; van Nunen, 2015, 2018; van Nunen & Ratchford, 2021). MMA symptoms often do not commence until a few weeks after the tick bite(s). While clinical findings range from angioedema or gut symptoms alone to life-threatening anaphylaxis, severe allergic reactions are more common at 65.5% (Fischer et al. (2016), and Kennedy et al. (2013) in van Nunen, 2018).

Allergic reactions can result in swelling of the throat, and may lead to breathing difficulties or cardiovascular collapse, which are life-threatening conditions and must be treated as medical emergencies (Australasian Society of Clinical Immunology and Allergy, 2019; Australian Government Department of Health, 2015; Tick-induced Allergies Research and Awareness, n.d.).

Symptoms of a severe allergic reaction (anaphylaxis) include any acute onset illness which evolves rapidly over minutes immediately after removing only an adult tick. Symptoms include skin reactions such as welts or swellings, difficulty breathing, closing over of the throat, tongue swelling, impending loss of consciousness (faintness), sense of impending doom, or loss of consciousness.

### **Anaphylaxis is a medical emergency**

Anaphylaxis, including tick anaphylaxis, is a potentially life threatening severe allergic reaction, that requires immediate treatment with adrenaline (epinephrine). Anaphylaxis should always be treated as a medical emergency. Call an ambulance (000 in Australia), immediately after giving an adrenaline autoinjector (EpiPen®, Anapen®) (Australasian Society of Clinical Immunology and Allergy, 2021).

A range of short videos including on ‘Signs and symptoms of allergic reaction’, ‘EpiPen® administration’, and ‘Anapen® administration’, from A&AA are available at this link <https://allergyfacts.org.au/resources/videos-from-a-aa>.

It is important for people to summon medical attention quickly if such symptoms occur. If people have had similar symptoms in the past after being bitten by a tick, then it is good practice to always be prepared (Australian Government Department of Health, 2015), with an Australasian Society of Clinical Immunology and Allergy Anaphylaxis Action Plan and an adrenaline auto-injector available.

The Australian paralysis tick needs several days of engorgement on their host before signs of paralysis become obvious (Hall-Mendelin et al., 2011).

Early symptoms of tick paralysis may include:

- rashes, headache, fever, influenza-like symptoms, tenderness of lymph nodes, unsteady gait, intolerance to bright light, increasing weakness of the limbs, and partial facial paralysis (Australian Government Department of Health, 2015; Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011)
- loss of appetite and slurred speech (Grattan-Smith et al. (1997), and Edlow & McGillicuddy (2008) in Hall-Mendelin et al., 2011)
- children becoming subdued, refusing food, and sleeping for excessive periods (Grattan Smith et al. (1997) in Dehaghhi et al., 2019)
- difficulty in reading due to double vision [as a result of eye muscle weakness], nystagmus (repetitive uncontrollable eye movements), or photophobia in older children and adults (Sutherland & Tibballs (2001), and Barker & Walker (2014) in Dehaghhi et al., 2019)
- laboured breathing (Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011).

Over 24 hours the paralysis will continue to involve the arms and the muscles involved in swallowing (Doggett, 2004).

More clinically, the toxins of *I. holocyclus* 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 (Graves & Stenos, 2017; Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011).

The progress of paralysis continues for 24-48 hours after removal of *I. holocyclus* (Dehaghhi et al., 2019). **It is crucial to carefully observe an affected patient during this period. If the affected patient's condition worsens during this period seek medical attention quickly.** There has not been a death from tick paralysis in Australia since 1945, but it **can be fatal in humans if left untreated.**

See *Australian endemic tick-borne diseases* Guidance Note for more information on the symptoms of rickettsial diseases (QTT, FISH and ASF), and Q Fever. See *Tick-induced allergies: tick anaphylaxis and mammalian meat allergy/anaphylaxis, and tick-associated toxicosis and paralysis* Guidance Note for more information on symptoms associated with these tick-borne illnesses.

## Guidance for medical practitioners

The incidence of the individual conditions within the entire spectrum of tick-related medical problems in Australia is not completely known.

In regards to allergic conditions, a large survey of 566 tick bite presentations to an Australian ED has been very informative of the incidence in hyper-endemic regions (Rappo et al., 2013). Moreover, the prevalence of mammalian meat allergy after tick bite is known to be 113/100,000, again in a tick hyper-endemic area (Fischer et al. (2016) in van Nunen, 2015).

Appropriate diagnostic tests are not always available [for the tick-transmitted infectious diseases] and, of the tick-borne infectious diseases, only Q fever is nationally notifiable (Australian Government Department of Health (2010) in Graves & Stenos, 2017).

As so little is known about the non-allergic 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. This advice was highlighted in the Australian Government Department of Health DSCATT Clinical Pathway (Australian Government Department of Health, 2020).

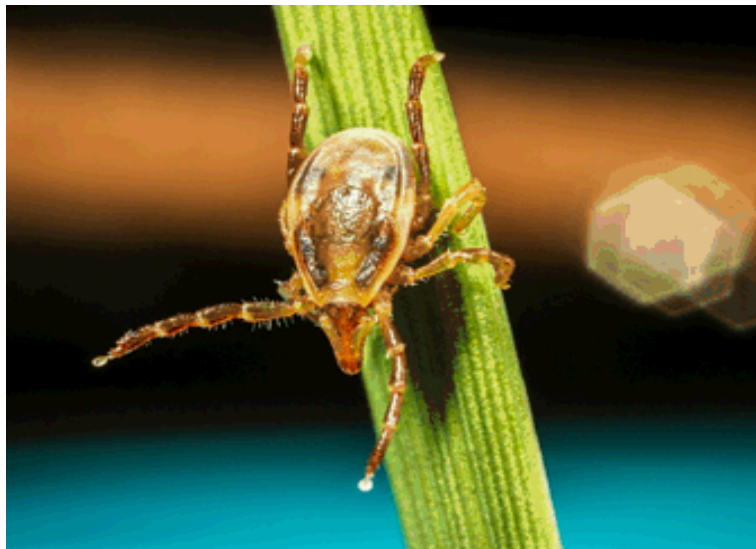
If the tick bite is recent (e.g. within 4 weeks) and the patient is symptomatic, an EDTA blood sample should be sent to a diagnostic laboratory for microbial polymerase chain reaction testing and culture, accompanied by a serum sample for antibody testing. This acute serum should be stored by the laboratory 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 (Graves & Stenos, 2017).

Further information about the microbiology laboratory techniques used for the diagnosis of human infections transmitted by ticks and the difficulties in interpreting serology results can be found in *Laboratory diagnosis of human infections transmitted by ticks, fleas, mites and lice in Australia* (Stenos & Graves, 2018). Additionally, the Australian Rickettsial Reference Laboratory provides information on the types of tests available, including tests the laboratory performs (Australian Rickettsial Reference Laboratory, n.d.). However, other NATA-accredited laboratories can also perform these tests.

For further guidance on Australian tick-borne diseases see *Australian endemic tick-borne diseases* Guidance Note and the DSCATT Clinical Pathway (Australian Government Department of Health, 2020). For further guidance on allergy, anaphylaxis and paralysis see *Tick-induced allergies: tick anaphylaxis and mammalian meat allergy/anaphylaxis, and tick-associated toxicosis and paralysis* Guidance Note.

## The Australian paralysis tick (*I. holocyclus*) – the most medically significant tick in Australia

Figure 5: Questing female Australian paralysis tick (*Ixodes holocyclus*) (Public domain)



Public domain: Doggett, S. L., Department of Medical Entomology, New South Wales Health Pathology

<https://www1.health.gov.au/internet/main/publishing.nsf/650f3eec0dfb990fca25692100069854/ea2fa455f96f36f1ca257c3700786bcb/WebPageBody/0.5510?OpenElement&FieldElemFormat=gif>

The most important and medically significant tick in Australia is *I. holocyclus* (the Australian paralysis tick) (see Figure 5 below) (Australian Government Department of Health, 2015; Taylor et al., 2019; van Nunen, 2018). It is the most common tick that causes tick paralysis in domestic animals, humans and wildlife in Australia (Dehghani et al., 2019). Over 95% of tick bites in humans in eastern Australia are due to the Australian paralysis tick (Australian Government Department of Health, 2015; Geary et al., 2021; Taylor et al., 2019; van Nunen (2018) in van Nunen & Ratchford, 2021) and most tick-borne illnesses are due to this species (Australian Government Department of Health, 2015). Further, *I. holocyclus* was the most common (708 *I. holocyclus* specimens submitted/5655 total specimens) specimen of all arthropods submitted to an Australian Medical Entomology Department for identification between 1988-2017, with 98.3% of *I. holocyclus* specimens submitted from New South Wales, with many from the south coast of New South Wales, and a small number ( $n=10$ ) from Victoria (Geary et al., 2021). This tick can attach to various sites of the body, including the conjunctiva, making removal of the tick very challenging (Teong et al. (2015) in Sukkanon et al., 2019).

While the official common name is the Australian paralysis tick, it is often referred to as the grass tick (larvae), seed tick (larvae) and bush tick (nymphs and adults) depending on its stage of development (Australian Government Department of Health, 2015; Doggett, 2004). In Queensland, *I. holocyclus* is also known as the scrub tick, particularly in North and Far



North Queensland, with the name echoing the tick's predilection for edges of wet forests (scrub) (Barker & Barker, 2018).

The Australian paralysis tick is the most medically significant tick in Australia for several reasons including the following:

- It has a geographical distribution along the eastern seaboard of Australia from Cape Tribulation in the north to the Australian Capital Territory and Victoria in the south, matching the distribution of a large proportion of Australia's population (Barker & Walker (2014) in Taylor et al., 2019; van Nunen, 2018).
- It commonly bites humans as well as other mammals, although its main host is thought to be the bandicoot (Barker & Walker (2014) in Taylor et al., 2019). However, observation in urban environments have found rabbits (Taylor et al., 2020) and rats (Lydecker et al., 2014) to be hosts in regions where tick-induced allergies are most prevalent (the northern beaches of Sydney's north shore).
- It is capable of causing anaphylaxis (Australasian Society of Clinical Immunology and Allergy, 2019; McKay (1940) in Taylor et al., 2019; Tick-induced Allergies Research and Awareness, n.d.; Rappo et al. (2013), McKay (1940), Trinca (1964), Banfield (1966), Kemp (1986), and Brown & Hamilton (1998) in van Nunen, 2018) – one of the most severe effects on humans.
- It is capable of causing paralysis (Graves & Stenos, 2017; Stone (1986) in Hall-Mendelin et al., 2011) – also one of the most severe effects on humans.
- It causes mammalian meat allergy (Australian Government Department of Health, 2015; van Nunen et al. (2007), van Nunen (2018), and Graves & Stenos (2017) in Taylor et al., 2019; van Nunen & Ratchford, 2021).
- It can transmit tick-borne diseases Q fever (rarely) and QTT (Australian Government Department of Health, 2015; Graves & Stenos, 2017 in Taylor et al., 2019).

### Toxicity of *I. holocyclus* saliva

The saliva of *I. holocyclus* is the most toxic of all tick salivas globally (Sutherland & Tibballs (2001) in Barker & Barker, 2018). It is capable of inducing allergic reactions, including fatal anaphylaxis, paralysis, and death (Australian Government Department of Health, 2015; Brown & Hamilton (1998) in S. R. Graves & Stenos, 2017; B. W. P. Taylor et al., 2019; van Nunen, 2015, 2018), although allergic reactions in humans from the bite of *I. holocyclus* are now considered far more common than paralysis (Rappo et al. (2013), and van Nunen (2018) in Sukkanon et al., 2019).

*I. holocyclus* injects a mixture of neurotoxins known as holocyclotoxins – small, cyclic polypeptides similar to botulinum toxins – into its host when it bites, (Graves & Stenos, 2017). The role of these toxins for the tick is uncertain, but they often have a profound impact on the host animal and can affect native animals, family pets and occasionally humans, especially if the host is small (Grattan-Smith et al. (1997), and Miller (2002) in Graves & Stenos, 2017). A single *I. holocyclus* tick is capable of killing a large dog (Stone & Wright (1981) in Hall-Mendelin et al., 2011) or a sheep (Sloan (1968) in Hall-Mendelin et al., 2011). Paralysis is induced in the host by these toxins when transmitted in the saliva of a female *I. holocyclus* when the tick takes a blood meal. However, paralysis is not instantaneous. Hall-Mendelin et al. noted the interesting clinical phenomenon of *I. holocyclus* is that this tick needs several days of engorgement on their host before signs of paralysis manifest (Hall-Mendelin et al., 2011). During feeding, toxicity in the salivary glands of *I. holocyclus*

increases, peaking after four to five days of engorgement (Goodrich & Murray (1978) in Hall-Mendelin et al., 2011), As such, to cause host paralysis, a tick must be attached for four to five days (Hall-Mendelin et al., 2011; Hall-Medelin et al. (2011) in Taylor et al., 2019). The toxins produced by *I. holocyclus* inhibit acetylcholine release at the neuromuscular junction (Chand et al., 2016), and tend to cause more severe neurological impairment than the toxins from ticks in North America (Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011).

Tick paralysis caused by the *I. holocyclus* (Australian paralysis tick), while rarely severe, can be fatal (Hall-Mendelin et al., 2011). In Australia, between 1914 and 1942, 20 human fatalities were attributed to tick bite, with all but three fatalities being children (Murray & Koch (1969) in Hall-Mendelin et al., 2011). About 70% of these fatalities were in children under four years of age (Sutherland & Tibballs (2001) in Doggett, 2004).

Paralysis caused by the holocyclotoxin in the saliva of *I. holocyclus* has resulted in higher human mortality than either the red-back or funnel-web spiders (Sutherland & Tibballs (2001) in Barker & Barker, 2018; Nicholson et al. (2006), and Miller (2002) in Taylor et al., 2019).

In Australia, there have not been human deaths due to tick paralysis for many decades (since 1945) (Dehghani et al., 2019; Doggett, 2004; Grattan-Smith et al. (1997) in S. R. Graves & Stenos, 2017; Grattan-Smith et al. (1997) in Hall-Mendelin et al., 2011; Barker & Walker (2014) in Taylor et al., 2019) Deaths from the bite of *I. holocyclus* are now rare due to the introduction of intensive care-units in regional hospitals and expert medical treatment [advances in intensive care treatment] (Barker & Barker, 2018), and an antivenene. Occasional cases of tick paralysis still occur, mainly in children, with these rare cases often unrecognised or misdiagnosed (Doggett, 2004). Doggett noted in his 2004 paper that in a case at Westmead Hospital, the cause of a mysterious coma in a young patient was found serendipitously when a nurse discovered the tick while stroking the child's head (Doggett, 2004).

While *I. holocyclus* ticks generally appear to be consistently toxic, Hall-Mendelin et al. noted there is some evidence of variation in toxin potency in this species (Alexander (1986), Curtin (1986), Jones (1986), Pursell (1986), and Atwell & Fitzgerald (1994) in Hall-Mendelin et al., 2011).

## Geographic distribution

The main distribution of the *I. holocyclus* tick is within 20 km of the coast along virtually the entire eastern seaboard of Australia (Barker & Walker (2014), and Hardy et al. (2014) in Stewart et al., 2017a; Tick-induced Allergies Research and Awareness, n.d.) (see [Figure 6](#) overleaf). However, it has been isolated in areas more than 100 km inland including the Bunya Mountains, Barcaldine, and Thargomindah in Queensland and the Lower Blue Mountains in New South Wales (Stewart et al., 2017a; Tick-induced Allergies Research and Awareness, n.d.). It can also be found in the Australian Capital Territory probably having travelled from the coast (Tick-induced Allergies Research and Awareness, n.d.).<sup>6</sup>

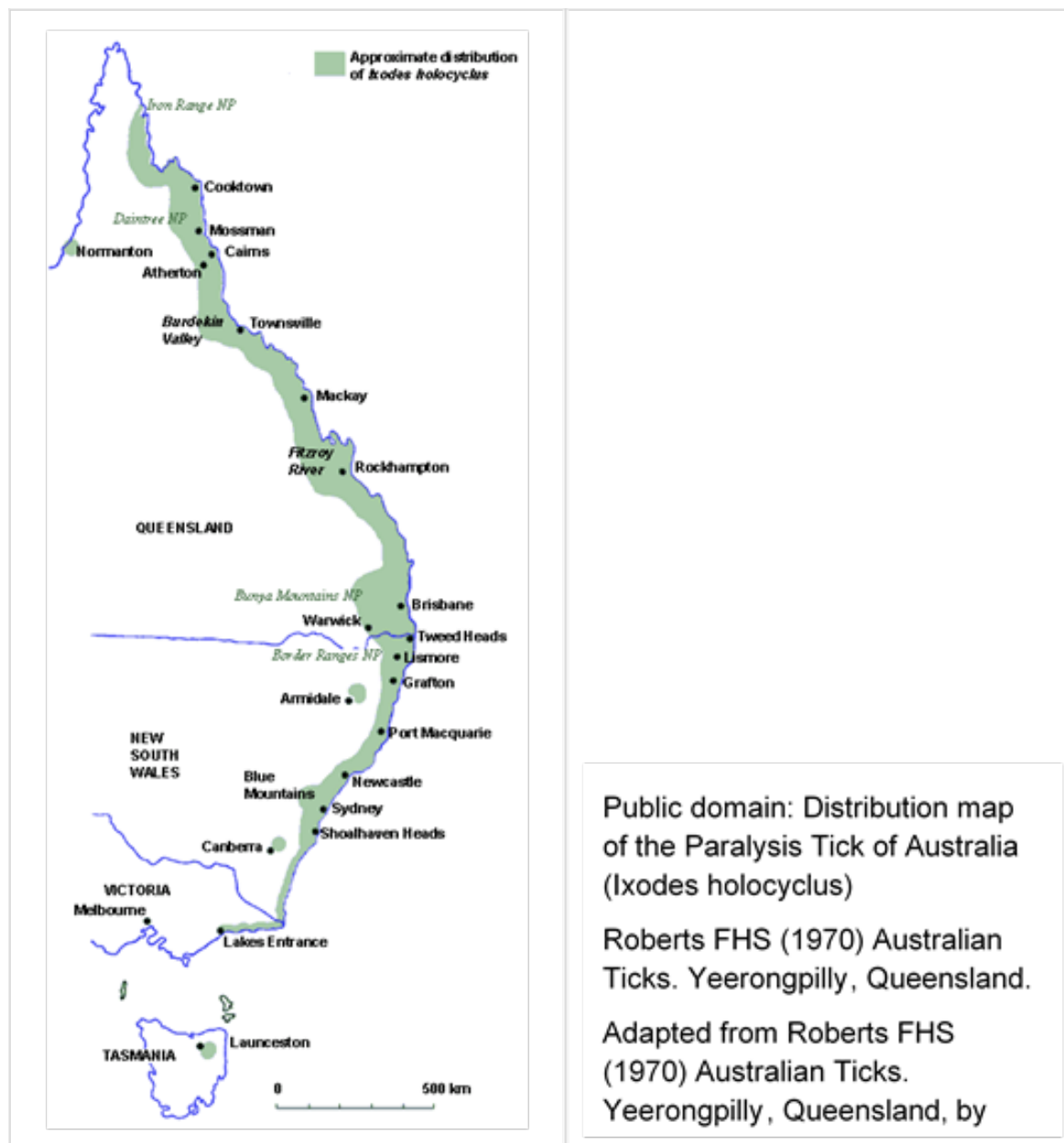
It is not known to occur in South Australia, Western Australia or the Northern Territory (Australian Government Department of Health, 2015).

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<sup>6</sup> Probably travellers from the south coast on people and their companion animals.



Figure 6: Approximate geographic distribution of Australian paralysis tick (*Ixodes holocyclus*) (Public domain)



## Habitat and hosts

*I. holocyclus* has a predilection for forested areas with annual rainfall over 1,000 mm and requires the presence of appropriate vertebrate hosts for its survival (Barker & Walker (2014), and Domrow & Derrick (1964) in Stewart et al., 2017a). Australian paralysis ticks are therefore found most commonly in wet sclerophyll forests and temperate rainforests (Tick-induced Allergies Research and Awareness, n.d.) and in moist, humid coastal areas with abundant native animals that serve as hosts for the tick (Australian Government Department of Health, 2015). Long grasses and bushland provide ideal environments for ticks, and if people live close to these areas, it is not uncommon for them to have paralysis ticks in their garden (Australian Government Department of Health, 2015).

*I. holocyclus* has been recorded from 34 species of mammals and seven species of bird (Barker & Walker (2014) in Barker & Barker, 2018) although whether it feeds successfully on all of these species is undetermined (Barker & Barker, 2018). Indeed, this tick has an extensive host range including, but not limited to, domestic animals such as dogs, cats, chickens and other fowl, as well as humans (Barker & Walker (2014) in Chalada et al., 2016) while in native animals, hosts include wallabies, kangaroos, bandicoots, possums and dingoes (Barker & Walker (2014) in Chalada et al., 2016).

Where it is abundant, *I. holocyclus* will be found on most of the species of mammals present, but in southeastern Queensland the bandicoots *Isodon macrourus* (Northern brown bandicoot) and *Perameles nasuta* (Long-nosed bandicoot) have been considered the principal hosts since at least 1975 (Doube (1975) in Barker & Barker, 2018). These bandicoots may carry many ticks (Barker & Barker, 2018). In southeastern Queensland it appears that reasonable numbers of *I. macrourus* and *P. nasuta* are required for populations of *I. holocyclus* to persist from one tick season to another (Doube (1975) in Barker & Barker, 2018), however, in other parts of the geographic range of *I. holocyclus*, where there seem to be large numbers of ticks but few, if any, bandicoots, this is probably not the case (Barker & Barker, (unpublished data) in Barker & Barker, 2018).

The Australian paralysis tick has also been found in urban environments, feeding on introduced pests (Lydecker et al., 2014; Taylor et al., 2020). A recent study (2020) that investigated the potential role of rabbits in the life cycle of Australian ticks, using rabbits collected from pest control programs in two urban forest remnants in Sydney, found the most abundant tick species on the rabbits was *I. holocyclus* (Taylor et al., 2020). A study by Lydecker that questioned whether urban bandicoots were solely to blame for tick concerns noted *I. holocyclus* has also been recorded feeding on the following urban pests: the wild rabbit, the house mouse, the brown rat, and the black rat (Lydecker et al., 2014).

## Life cycle, questing and feeding

The Australian paralysis tick has four stages in its life cycle; the egg, larvae (around 1 mm and light brown in colour when not full of blood, and can be hard to see), nymph (around 2 mm and pale brown) and the adults (4–5 mm in length, without blood) (Australasian Society of Clinical Immunology and Allergy, 2019; Australian Government Department of Health, 2015). The Australian paralysis tick needs to feed on blood to develop through its lifecycle from the larvae stage to a nymph and to an adult. The adult female takes blood to obtain protein [nutrients] for the laying of eggs. When fully engorged, the female tick is grey-blue in colour and up to about 1 cm in length (Australian Government Department of Health, 2015). Figure 7 shows a female *I. holocyclus* tick before and after feeding.

**Figure 7: Female Australian paralysis tick (*Ixodes holocyclus*) before and after feeding (Public domain)**



Public domain: Tørrissen, B. C. (2009) (CC BY 3.0)

[https://upload.wikimedia.org/wikipedia/commons/c/c0/Tick\\_before\\_and\\_after\\_feeding.jpg](https://upload.wikimedia.org/wikipedia/commons/c/c0/Tick_before_and_after_feeding.jpg)

The complete life cycle of *I. holocyclus* takes about one year to complete (Doggett, 2004). Adult female *I. holocyclus* ticks can lay up to 2500 eggs (Doggett, 2004). The tiny six-legged larvae that emerge do not move far in the vegetation from where they hatch; as such many larvae may be present in a small area and multiple larval bites numbering in the tens to hundreds are common (Doggett, 2004). The larvae search for a host by climbing the nearest vegetation and waiting until a warm-blooded animal brushes past. Larvae of *I. holocyclus* cannot feed on humans; if they do attach to humans, they usually cause not more than localised dermatitis (Dehhaghi et al., 2019). Multiple larval bites are common, particularly on the lower limbs and around the waist, which is often referred to as 'scrub-itch' (Doggett, 2004). In Geary et al.'s study of arthropod specimens sent to the Department of Medical Entomology at Westmead Hospital, Sydney, New South Wales, 1988-2017, there was a strong seasonality observed among the different stages of *I. holocyclus* sent to the Department for identification, with nymphs the predominant stage in the autumn (Geary et al., 2021).

Nymphs and to a greater extent female *I. holocyclus* frequently attach to humans and, after several days, can feed abundantly and engorge (Barker & Walker (2014) in Dehhaghi et al., 2019). Nymphs require a blood meal for five to seven days before moulting to the adult stage (Doggett, 2004). Adult male and female *I. holocyclus* ticks have marked differences in appearance and behaviour. Doggett notes that male *I. holocyclus* ticks are of little medical concern as they do not tend to blood feed on a host; rather searching for female *I. holocyclus* ticks in order to mate and feed on them (i.e. parasitising them) (Doggett, 2004). Adult female *I. holocyclus* blood feed for about eight days (up to 21 days in mid-winter) before dropping off to lay eggs, wither and die (Doggett, 2004).

Australian paralysis ticks are not particularly mobile, and rely on passing animals for a blood meal (Australian Government Department of Health, 2015). In searching for a host, the Australian paralysis tick displays a behaviour referred to as 'questing' (see [Figure 5](#)); whereby the tick climbs to the top of nearest vegetation and waves its forelegs to and fro

slowly, in the hope of contacting a prospective passing host (University of Sydney Department of Medical Entomology, 2003). The Australian paralysis tick undertakes this questing behaviour each time a host is required for blood. They rarely climb higher than 50 cm in their habitat, for risk of desiccation, so do not drop out of trees, despite this common belief (Australian Government Department of Health, 2015; Doggett, 2004; University of Sydney Department of Medical Entomology, 2003). However, after successfully making contact with and landing on a person or animal they wander over the host for some hours before attaching, often attaching to the head area (Australian Government Department of Health, 2015; Doggett, 2004) such as on the scalp behind the ear, or other areas where skin is thinner.

## Seasonality

The Australian paralysis tick has a distinct seasonality; the larval stage is most active during the autumn months, the nymph during winter and the adult during the spring (Australian Government Department of Health, 2015; Geary et al., 2021; Eppleston et al. (2013) in Sukkanon et al., 2019). Geary et al.'s 2021 study of arthropod samples sent to the Department of Medical Entomology at Westmead Hospital, in Sydney, New South Wales, between 1988-2017, showed strong seasonal trends for *I. holocyclus*, the most common (708 specimens submitted/5655 total samples submitted) of all arthropods sent to the Department for identification. In their study, larval *I. holocyclus* ticks peaked in autumn, nymphs peaked during winter and adult ticks peaked during spring (Geary et al., 2021). Adult female *Ixodes* spp. ticks (the vector for *R. australis*) are most abundant in Queensland from October to December (Barker & Walker (2014) in Stewart et al., 2017a).

This tick is most active during periods of high humidity, especially after rain, and this is when people should take particular care to avoid tick bites (Australian Government Department of Health, 2015). Any life stage, however, may be found at any time of the year.

## The ornate kangaroo tick (*Amblyomma triguttatum*)

While known as a kangaroo tick, *Amblyomma triguttatum triguttatum* will feed on humans and is one of four subspecies of *A. triguttatum* (Barker et al. (2014) in Barker & Barker, 2018).

The tick *A. t. triguttatum* is geographically distributed in two parts of Australia: eastern Australia and western Australia. While one of the 18 valid species of *Amblyomma* in Australia, only *A. triguttatum* has been regularly reported on domestic animals and has been taken from humans (Barker & Walker, 2014 in Dehhaghi et al., 2019).

While primarily a tick found on kangaroos (genus *Macropus*), it is also common on wild (feral) pigs in Australia (Guglielmone (1990) in Barker & Barker, 2018).

Banks and Hughes' review of black rat impacts in Australia noted the black rat in Australia carries several diseases known to affect native wildlife and humans and also carry a large diversity of ectoparasites, including ticks, mites and fleas that act as vectors for transmitting disease-causing agents between animals or humans (Breed (2007) in Banks & Hughes, 2012). With respect to ticks, Banks and Hughes noted rats may also harbour the tick *A. triguttatum* which is a natural host and vector for the *C. burnetii* bacterium which may cause Q fever in humans (Garner et al. (1997) in Banks & Hughes, 2012). However they have stated that the relative role of black rats as compared with other wildlife in spreading this disease is not known (Banks & Hughes, 2012).

## The southern reptile tick (*Bothriocroton hydrosauri*)

The southern reptile tick will feed on humans. *B. hydrosauri* was named the southern reptile tick as it may be found on all of the main types of reptiles in southern Australia, including lizards, snakes and terrestrial turtles (Barker & Walker (2014) in Barker & Barker, 2018). While the main host of *B. hydrosauri* in much of South Australia is the sleepy lizard (*Tiliqua rugosa*), this tick will attach to and feed on humans, cattle and horses, given the opportunity (Barker & Barker, 2018). The geographic distribution of *B. hydrosauri* is very well known, with the distribution in South Australia mapped to a scale of meters (Smyth (1973) and Bull & King (1981) in Barker & Barker, 2018).

## *Ixodes (Endopalpiger) australiensis*

In addition to the above ticks that are well-known for biting humans, *Ixodes (Endopalpiger) australiensis* (Kwak et al., 2018), endemic in Western Australia has been confirmed as biting a human who subsequently developed mammalian meat allergy after the tick bite.

## Potential, but not confirmed, human pathogens in Australian ticks

Two additional species of *Rickettsia* (other than those that cause QTT, FISF and ASF) have been identified in Australian ticks and may be considered potential pathogens, however, their presence in febrile patients has yet to be confirmed (Graves & Stenos, 2017). These new species are:

- *Rickettsia gravesii*, which was detected in ornate kangaroo ticks in Western Australia (Li et al. (2010) in Graves & Stenos, 2017), and Queensland (unpublished data in Graves & Stenos, 2017). Graves and Stenos noted a Western Australian study had found rogainers (orienteering-type sport) had a significantly higher seroprevalence to spotted fever group rickettsiae than controls who had had minimal bush exposure (Abdad et al. (2014) in Graves & Stenos, 2017), suggesting possible exposure to a possible tick-transmitted rickettsia.
- *Candidatus Rickettsia tasmanensis*. Graves and Stenos noted a Tasmanian study had found that 55% of *I. tasmani* ticks collected from Tasmanian devils contained rickettsial DNA, and that further molecular characterisation of the DNA had demonstrated sufficient divergence from previously described species to designate this new organism *Candidatus Rickettsia tasmanensis* (Izzard et al. (2009) in Graves & Stenos, 2017). Graves and Stenos advised that as *I. tasmani* is known to bite humans, this *Rickettsia* must be considered as a potential pathogen (Graves & Stenos, 2017).

## Tick-borne infections reported to have been found in Australian patients but not known to be acquired in Australia currently

The Senate Community Affairs References Committee Inquiry into *Growing evidence of an emerging tick-borne disease that causes a Lyme-like illness for many Australian patients* (Senate Community Affairs References Committee, 2016) reported that ticks are hosts and vectors of a number of parasites, bacteria and viruses, with the main organisms that are known to be transmitted by ticks but not yet associated with human disease in Australia being:



- *Anaplasma* – which causes disease in cattle (bovine anaplasmosis, or 'bovine tick fever') and dogs (canine anaplasmosis)
- *Babesia* – a significant cause of disease in cattle (bovine babesiosis) and dogs (canine babesiosis) (see section below on '[Babesiosis and the Australian situation](#)' that describes the one case in a human in Australia)
- *Bartonella* – there are Australian species found in domestic and wild animals, including cats and kangaroos. Some species are recognised as human pathogens (e.g. *Bartonella quintana* and *Bartonella henselae*) but others are not
- *Ehrlichia* – which causes disease in dogs worldwide. Cases of canine ehrlichiosis have recently been recorded in Australia
- *Francisella* – there are human pathogenic species (e.g. *F. tularensis*) but in Australia there are subspecies sometimes associated with sick native animals which are not yet confirmed to be human pathogens.

*Rickettsia* was also included in the list. The rickettsial infections known to cause disease in humans in Australia including QTT (*R. australis*), FISF (*R. honei*), and the variation of spotted fever now called ASF (*R. honei* subsp. *marmionii*) were discussed in the previous section on '[Known Australian tick-associated bacterial infections](#)'. See *Australian endemic tick-borne diseases* Guidance Note for more detail about QTT, FISF and ASF.

Several peer-reviewed papers have reported findings on organisms identified in Australian ticks. While the scope for the DSCATT Clinical Pathway focussed on known tick-borne infections in Australia (QTT, FISF, ASF, and Q fever), infections or organisms identified in Australian ticks where human infection has not been established was out of scope. The published research findings on organisms identified in Australian ticks are included below.

## Anaplasmosis and ehrlichiosis and the Australian situation

Human granulocytic anaplasmosis (HGA) was formerly known as human granulocytic ehrlichiosis. HGA is caused by the rickettsial bacterium *Anaplasma phagocytophilum*, previously known as *Ehrlichia phagocytophilum* (Dehghani et al., 2019). It is an acute febrile, non-specific, viral-like disease that presents within about two weeks of a tick bite with common early symptoms of fever, headache, myalgias, and laboratory abnormalities of elevated hepatic transaminase, leukopenia, and thrombocytopenia (Dehghani et al., 2019; Lantos & Wormser, 2014). While potentially fatal, the infection will be self-limiting in survivors regardless of whether they are treated (Lantos & Wormser, 2014).

Human monocytic ehrlichiosis (HME) is a rare infectious tick-borne infection caused by bacteria from the '*Ehrlichia*' family. There are several forms of human ehrlichiosis, each of which is caused by a different strain of the bacteria, and they are often carried by different species of tick.

Human ehrlichiosis is found in countries around the world, including the US.

### Australian research

Within Australia there are as yet no reports of HME or HGA, although a case of the former has been detected in a traveller from the US (Burket et al. (2015) in Graves & Stenos, 2017).

Cases of canine ehrlichiosis have recently been recorded in Australia. Further information on canine ehrlichiosis is available from the Department of Agriculture, Water and the

Environment (Australian Government Department of Agriculture, Water and the Environment, 2021).

There are three *Anaplasma* species occurring in Australia. These are *A. platys*, *A. marginale*, and *A. centrale*. None is a human pathogen. In 2013, Mackenzie noted that two *Anaplasma* species occur in Australia, *A. platys* which causes canine anaplasmosis (Brown et al. (2006) and Jefferies (2006) in Mackenzie, 2013) and *A. marginale* which is one of the causes of bovine anaplasmosis or bovine tick fever in northern and eastern Australia and is transmitted by the cattle tick *Rhipicephalus (Boophilus) microplus* (Rogers and Shiel (1979) and Jonnson et al. (2008) in Mackenzie, 2013). Mackenzie commented neither are known to infect humans (Mackenzie, 2013). *A. marginale* subsp. *centrale* also infects cattle. However, it is a less virulent subspecies than *A. marginale* and was detected by Sir Arnold Theiler, who recognised its potential as a vaccine against anaplasmosis; 100 years later this live vaccine is still in use in South Africa, Israel, South America, and Australia (Theiler (1911), and Aubry & Geale (2011) in Khumalo et al., 2016). The Australian Government Department of Agriculture mentions *A. centrale* in its report on tick-borne diseases in cattle, including that the competitive inhibition ELISA is a useful alternative to the card agglutination test for detection of *A. marginale* and *A. centrale* infection (Bock et al., 2006).

*Anaplasma* and *Ehrlichia* species have been detected in Australian paralysis ticks and ornate kangaroo ticks using bacterial profiling of 460 ticks from four species of Australian human-biting ticks (Dehhaghi et al., 2019; Gofton, Doggett, et al., 2015; Graves & Stenos, 2017). The study by Gofton, Doggett et al. (2015) surveyed the microbial communities harboured by human-biting ticks from across Australia in an attempt to identify bacteria that may contribute to the symptoms associated with DSCATT (Gofton, Doggett, et al., 2015). Of the 460 ticks included in the study, including *I. holocyclus*, *A. triguttatum*, *H. bancrofti* and *H. longicornus*, all were negative for *Borrelia* spp. However, a novel *Anaplasma* sp. was identified in 1.8% of *A. triguttatum* ticks, and a novel *Ehrlichia* sp. was identified in both *A. triguttatum* (1.2%) ticks and a single *I. holocyclus* (0.6%) tick, with further phylogenetic analysis of the novel *Anaplasma* and *Ehrlichia* suggesting these are new species. The authors commented that determining whether these newly discovered species cause disease in humans and animals, like closely related bacteria do abroad, is of public health importance and requires further investigation (Gofton, Doggett, et al., 2015).

Graves and Stenos (2017) advised certain species of these bacterial genera (for example, *E. chaffeensis*, *A. phagocytophilum*) are known to be human pathogens and commented there is thus a possibility that these Australian bacteria may also be human pathogens (Graves & Stenos, 2017). Dehhaghi et al. noted other studies have drawn attention to the competence of tick species *R. sanguineus* and *R. australis*, both of which are found in Australia, in transmission of *Anaplasma* spp. (Rogers and Shiel (1979) and Jonnson et al. (2008) in Dehhaghi et al., 2019). Dehhaghi et al. commented further investigation is required to determine whether these ticks or other ticks within Australia can act as a vector for *A. phagocytophilum* and subsequently transmit *Anaplasma* to humans or not (Dehhaghi et al., 2019).

A study of 14 persons who lived in an area of Australia endemic for the Australian paralysis tick *I. holocyclus*, and who were regularly involved in collecting and handling these ticks found none had antibodies to *Ehrlichia* or *Anaplasma*, suggesting they had not been exposed to these bacteria (Graves et al., 2016). Additionally, in a subset of 74 *I. holocyclus* ticks examined for DNA from *Anaplasma* spp. and *Ehrlichia* spp., none was positive. Graves et al. commented some of these recognised human bacterial pathogens associated with ticks may



not be present in this Australian tick species from northeastern New South Wales (Graves et al., 2016).

## Babesiosis and the Australian situation

Babesiosis is a malaria-like protozoal infection of erythrocytes, that is transmitted by *Ixodes* spp. ticks, particularly in the Northern Hemisphere (Dehhaghi et al., 2019; Lantos & Wormser, 2014). Several species of *Babesia* are capable of causing human disease, the most important of which are *B. microti* in the northeastern and Midwestern US and *B. divergens* in Europe (Lantos & Wormser, 2014). *Babesia* may also be acquired from blood transfusions (Dehhaghi et al., 2019; Lantos & Wormser, 2014). Lyme disease-*Babesia* co-infection has been well-established and may result in greater disease severity than Lyme disease alone (Lantos & Wormser, 2014; Mackenzie, 2013).

Clinical babesiosis is nearly always dominated by fever and characteristic laboratory abnormalities (Lantos & Wormser, 2014). Patients may also have haemolytic anaemia, influenza-like disease, and thrombocytopaenia, with asplenic patients typically more susceptible to severe life-threatening illness (Dehhaghi et al., 2019). *Babesia* infection can be atypically associated with rheumatoid muscular pains [not further defined by the authors] and nervous complications including incoordination of legs, hysteria, restlessness and nervousness, and it appears that *Babesia* is capable of mimicking Lyme-like syndrome (Chalada et al., 2016).

## Australian research

Babesiosis is a well-documented infection in domestic animals including cattle and dogs in Australia (Dehhaghi et al., 2019; Graves & Stenos, 2017; Mackenzie, 2013).

Only one case of human babesiosis in Australia caused by *Babesia microcoti* has been described. The 2012 case was a 56-year-old man from the south coast of New South Wales, who lived in close proximity to dogs, did not recall being bitten by a tick, had not travelled outside of Australia for nearly 40 years and had no history of blood transfusions (Dehhaghi et al., 2019; Graves & Stenos, 2017; Mackenzie, 2013; Senanayake et al., 2012). While this case was thought to be a locally-acquired infection, there have been no subsequent cases of human babesiosis diagnosed in Australia (Graves & Stenos, 2017). Mackenzie commented the origin of the aetiological agent is uncertain. Although it is most closely related to North American strains, the patient was either bitten by an imported tick, or a local tick might have transmitted an autochthonous infection presumably originating from one or more species of introduced rodent (Mackenzie, 2013).

Asymptomatic blood donors have been the index cases for transfusion-associated babesiosis, therefore patient infection could actually be subclinical or nonspecific (Lantos & Wormser, 2014). Dehhaghi et al. noted no information on the incidence rate for babesiosis is available in Australia or in the world, and highlighted that unlike several countries such as the US, blood products are not screened for *Babesia* in Australia, which they noted posed the [potential] danger of transmission through blood donation by unrecognised babesiosis patients (Ngo and Civen (2009) and Government (2018) in Dehhaghi et al., 2019). Dehhaghi et al. advised babesiosis may be suspected in Australia in patients with a history of overseas travel to an endemic area (with or without a documented history of tick bite), or with a history of blood transfusion. They also cited a recent study by Storey Lewis and colleagues which reportedly found no *B. microti* could be identified in the DNA extracted from 1,154 ticks that were collected from across Australia (Storey Lewis et al (2017) in Dehhaghi et al., 2019).

A 2013 paper by Dawood et al. described three cases of a novel *Babesia* in eastern grey kangaroos. In one case two adult ticks were removed from the kangaroo's skin and identified by the carer but were not formally submitted to a reference laboratory. In the second case ticks were collected but not submitted for identification, and in the third case, ticks were not collected for identification (Dawood et al., 2013). The authors commented their preliminary observations that *Haemaphysalis* spp. ticks were present in the captive area and suggest they may be the vector of *Babesia* to eastern grey kangaroos, however, further studies are required to confirm their supposition (Dawood et al., 2013).

## Bartonellosis and the Australian situation

The three most common diseases caused by the genus *Bartonella* are Carrion's disease, cat scratch disease and Trench fever, with the diseases transmitted when humans are scratched by domestic or feral cats or by contact with arthropods including body lice, fleas and sand flies (Dehghani et al., 2019). Symptoms and signs include a papule or pustule at the site of inoculation, abdominal pain, bone pain, fever, enlarged lymph nodes, headache, rash, bacillary angiomatosis (lesions in the skin, subcutaneous tissue, bone or other organs), bacillary peliosis (vascular lesions in the liver and spleen), severe anaemia and subacute endocarditis (Dehghani et al., 2019). Chalada et al. noted *B. henselae* is typically associated with isolated lymphadenopathy with fever and without any other symptoms, however, it has been associated with erythema marginatum rashes that may be mistaken for erythema migrans rash. Additionally, it is now recognised that *Bartonella* may cause a wide spectrum of atypical manifestations in immunocompetent patients and that atypical manifestations may mimic a Lyme-like illness including rheumatic manifestations, fibromyalgia and chronic fatigue syndrome, neurological disease and endocarditis (Chalada et al., 2016).

### Australian research

*Bartonella* species occur in both domestic and wild animals in Australia (Dehghani et al., 2019; Mackenzie, 2013). *Bartonella clarridgeiae* and *B. henselae*, the causative agents of cat scratch disease, are found in cats, fleas and humans in Australia (Dehghani et al., 2019; Mackenzie, 2013) with Mackenzie noting these two species are most frequently transmitted to humans by cat fleas rather than ticks (Flexman et al. (1995) and Barrs et al. (2010) in Mackenzie, 2013).

Gofton, Oskam et al. (2015) identified *B. henselae* in ticks in their gene profiling study of 196 *I. holocyclus* collected from mammalian and avian hosts and from the environment in various locations in New South Wales (Gofton, Oskam, et al., 2015). Several *Bartonella* species have been reported in ticks and fleas collected from marsupial hosts, including brush-tailed bettong or woylie, western barred bandicoots, yellow-footed antechinus, and eastern grey kangaroos as well as from various rodents as hosts, (Fournier et al. (2007), Saisongkroh et al. (2009), and Kaewmongkol et al. (2011) in Mackenzie, 2013) with the most frequent tick vectors being *Ixodes* spp. (including *I. australiensis*, *I. tasmani*, and *I. myrmecobii*).

Mackenzie commented it is uncertain whether these species of *Bartonella* can cause human disease, or whether the tick vectors bite humans. He also noted there has been no record of co-infection of *Bartonella* species with *B. burgdorferi* s.l. overseas (Mackenzie, 2013).

Dehghani et al. in 2019 reported three studies had identified novel *Bartonella* spp. in mammalian hosts in Australia (Dehio (2008), Gundi et al. (2009), and Kaewmongkol et al. (2011) in Dehghani et al., 2019) and at least eight *Bartonella* spp. are carried by some ticks within Australia (Vilcins et al. (2009) and Kaewmongkol et al. (2011) in Dehghani et al., 2019), with ticks collected from various animals including koalas, rodents, woylies, or yellow-

footed antechinus. Of these studies, Dehhaghi commented that “*despite these findings there is currently no convincing evidence that verifies tick-borne transmission of Bartonella infection to humans, in Australia*” (Dehhaghi et al., 2019).

## **Borrelia and the Australian situation**

*Borrelia* are the species of bacteria associated with Lyme disease which is endemic in parts of the US, Europe and Asia. Lyme disease is an infectious disease that can be transmitted to humans who are bitten by a tick carrying different species of *Borrelia* bacteria (spirochaetes) collectively known as *Borrelia burgdorferi* s.l. (Australian Government Department of Health, 2018; Mackenzie, 2013; National Institute for Health and Care Excellence, 2018; Royal College of Pathologists of Australasia, 2019). More than 18 spirochaete species comprise the *B. burgdorferi* s.l. complex. Four species are found only in North America, 11 species occur in and are restricted to Eurasia and three species occur in North America and Europe (Mackenzie, 2013).

## **Australian research**

In the quest to determine the cause or causes of DSCATT, a number of reviews of Australian studies along with studies designed to try to find the bacteria *B. burgdorferi* s.l. or other *Borrelia* in Australian ticks have been published. The literature review that supports the DSCATT Clinical Pathway provides a comprehensive overview of these reviews and studies (Allen + Clarke, 2020). The DSCATT Clinical Pathway advised that despite multiple studies which have searched for it in Australian ticks and patients, the organisms that cause Lyme disease have not, to date, been identified in Australian ticks (Australian Government Department of Health, 2018; Beaman, 2016; Chalada et al., 2016; Collignon et al., 2016; Dehhaghi et al., 2019; Gofton, Doggett, et al., 2015; Gofton, Oskam, et al., 2015; Graves & Stenos, 2017; Harvey et al., 2019; Irwin et al., 2017; Loh et al., 2016, 2017; Mackenzie, 2013) nor any other vector that could transmit the disease to humans (Australian Government Department of Health, 2018; Graves & Stenos, 2017). See section 3.5.7 of the literature review (Allen + Clarke, 2020) that supports the DSCATT Clinical Pathway (Australian Government Department of Health, 2020) for the review of these studies and papers.

Some of the more recent studies on *Borrelia* identified in Australian ticks and other research that was included and considered in reviews of the literature but not specifically covered in the literature review to support the DSCATT Clinical Pathway are included below.

In 2018 Gofton et al. published their genome-wide analysis of ‘*Candidatus Borrelia tachyglossi*’ (described above) and *Borrelia turcica*, noted by the authors as members of a recently described and rapidly expanding *Borrelia* clade<sup>7</sup> associated with reptile (*B. turcica*) or echidna (*B. tachyglossi*) hosts, transmitted by hard ticks and of unknown pathogenicity (Gofton et al., 2018). The analysis showed *B. turcica* and *B. tachyglossi* showed relapsing fever-like genomes with unique genomic links to Lyme disease *Borrelia*. The authors commented these genomes provide a valuable resource for future work and show the importance of including *Borrelia* species- even those with unknown human pathogenicity- into further studies exploring the evolution, pathobiology and ecology of this diverse bacterial genus (Gofton et al., 2018).

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<sup>7</sup> A group of organisms believed to comprise all the evolutionary descendants of a common ancestor.

In 2017, Irwin et al. in their canine sentinel study, used a combination of serological assays to test dogs living in tick 'hot spots' and exposed to the Australian paralysis tick, *I. holocyclus*, for evidence of exposure to *B. burgdorferi* s.l. antigens and other vector-borne diseases (Irwin et al., 2017). The rationale for this approach was that studies conducted in Europe and the US had used dogs as sentinels for tick-associated illness in people because dogs readily contact ticks that may harbour zoonotic pathogens. Irwin et al. found that, of the 555 dogs from four demographic regions recruited into the study, except for one dog presumed to have been exposed to *Anaplasma platys*, infection with *Anaplasma* spp., *B. burgdorferi* s.l., *Ehrlichia* spp., and *Dirofilaria immitis*, was not detected in the cohort of dogs. Irwin et al. commented:

*These results provide further evidence that Lyme borreliosis [disease] does not exist in Australia but that cross-reacting antibodies (false positive results) are common and may be caused by the transmission of other tick-associated organisms.* (Irwin et al., 2017)

Graves and Stenos, in their 2017 review, noted that although a *Borrelia* species had been detected by Loh et al. in the Australian echidna tick (*Bothriocroton concolor*), this bacterium belongs to a unique clade unrelated to the *Borrelia* species responsible for causing Lyme disease (Loh et al. (2016) in Graves & Stenos, 2017). They commented this tick is not known to bite humans therefore the bacterium is unlikely to be a human pathogen (Graves & Stenos, 2017). Of this study, the authors, Loh et al., reported that in addition to the finding that the novel *Borrelia* sp. identified in their study does not belong to the *B. burgdorferi* s.l. complex, the zoonotic potential and pathogenic consequences of this novel *Borrelia* sp. are unknown at the current time (Loh et al., 2016). Loh et al. reported that subsequent analyses confirmed that this novel species of the genus *Borrelia* is more closely related to, yet distinct from, the reptile-associated and relapsing fever groups. The authors proposed the name *Candidatus Borrelia tachyglossi*, and hypothesized that this species of the genus *Borrelia* may be endemic to Australia. Loh et al. commented the pathogenic potential of this bacterium is not yet known (Loh et al., 2016).

Additionally, Graves and Stenos noted that Carley and Pope had detected a *Borrelia* species in native rats that was not virulent for a human after experimental challenge (Carley & Pope (1960) in Graves & Stenos, 2017).

Chalada et al. in 2016 reviewed veterinary evidence on *Borrelia* in introduced animals. While they noted two species of *Borrelia* were introduced to Australia via the agricultural industry in the 1900s, they commented that if Lyme disease was present in Australia it would be reasonable to expect that its presence would be prominent in livestock, domestic animals and particularly feral deer, as is the case with Lyme disease in the northern hemisphere (Chalada et al., 2016). Of the veterinary evidence reviewed Chalada et al. concluded that:

*Overall, the relative absence of reports of veterinary cases of Lyme or a Lyme-like disease in Australia suggests the absence of traditional Lyme Borreliosis [disease] causing agents in Australia.* (Chalada et al., 2016)

Regarding evidence for *Borrelia* in native animals, Chalada et al. noted reports of "*Borrelia* species" in Australian native animals appear to be localised to Queensland. They reviewed the study by Mackerras (1959) which identified a novel *Borrelia* species from spirochaetes observed in blood films of bandicoots in Brisbane and in blood films of kangaroos in Western Queensland (Mackerras (1959) in Chalada et al., 2016). Chalada et al. commented molecular characterisation methods were not available at the time and morphological appearance alone was used to classify these into the *Borrelia* genus (Chalada et al., 2016).

Along with other authors who reviewed evidence on *Borrelia* in native animals (and included in this section) Chalada et al. cited four studies by Carley and Pope (Pope & Carley (1956), Carley & Pope (1962), Carley & Pope (1957), and Carley & Pope (1958) in Chalada et al., 2016). Chalada et al. noted that spirochaetes isolated from one native rat out of 27 dead and dying rats tested in Richmond, northwestern Queensland was subsequently named *Borrelia queenslandica*; attempts to infect a human volunteer with this spirochaete were unsuccessful. Chalada et al. commented that due to loss of all isolates, whether *B. queenslandica* is part of the *B. burgdorferi* s.l., a relapsing fever group, or another genus of spirochaete cannot now be determined. However, the lack of pathogenicity in the human volunteer is counterintuitive to this organism being the causative agent of the Australian Lyme disease considered in their review paper (Chalada et al., 2016).

Chalada et al. also looked at the evidence of spread of *Borrelia* by migratory birds and noted most relevant to the Australian situation is the worldwide dispersal of seabirds and the seabird tick *Ixodes uraiae* (Chalada et al., 2016). Citing a 1995 study, Chalada et al. noted that *B. garinii*, a species known to cause Lyme disease, in addition to being detected in the northern hemisphere, had also been detected in southern hemisphere locations and that transhemispheric dispersal of *B. garinii* may not be just due to the spread of infected ticks, but also by seabirds acting as *B. garinii* reservoirs (Olsen et al. (1995) in Chalada et al., 2016). However, they also noted from this study by Olsen et al. (1995) that the theoretical spread of *B. garinii* from seabirds to humans and other birds and mammals was unlikely, as generally the seabirds and their ticks are restricted to the open sea, remote islands and peninsulas where contact with other animals is rare (Chalada et al., 2016). Chalada et al. did comment though that the ticks of seabirds along the Australian coast had, at the time of their review, not been investigated for *Borrelia* (Chalada et al., 2016).

Mackenzie, in his review of other *Borrelia* associated with disease, noted tick-borne relapsing fever is caused by various *Borrelia* species depending on geographic area, with soft ticks, usually *Ornithodoros* species being the vectors of the tick-borne relapsing fever group (Mackenzie, 2013). Tick-borne relapsing fever is found in Africa, parts of Asia and southern Europe and in North and South America, and is characterised by multiple episodes of fever, and frequently with nausea, malaise, headaches and body aches, and sometimes with skin rashes, hepatomegaly and jaundice. Mackenzie reported tick-borne relapsing fevers have not been reported in Australia (Mackenzie, 2013).

Regarding *Borrelia* species in Australia, Mackenzie also cited, as Chalada et al. (2016) had done, three older studies: (Mackerras (1959), Carley & Pope (1962), and Pope & Carley (1956) in Mackenzie, 2013) of two early reports of the detection of *Borrelia* species in rodents, native mammals and cattle, noting that Carley and Pope were able to culture a *Borrelia* species, *B. queenslandica* from *Rattus villosissimus* collected near Richmond in northwestern Queensland but were unable to maintain it in culture. Mackenzie also noted that while Wills and Barry (1991) had cultured spirochaetes morphologically similar and antigenically related to *B. burgdorferi* from the gut contents of *I. holocyclus* and *Haemaphysalis* ticks, the cultures were not sustainable and the results of Wills and Barry have not been able to be repeated from ticks collected more recently (Wills & Barry (1991) in Mackenzie, 2013). Mackenzie also cited the two studies by Russell (Russell et al. (1994) and Russell (1995) in Mackenzie, 2013) that had not found *Borrelia* spirochaetes or *Borrelia* species among the ticks tested.

In 2016, Graves et al. conducted a study of persons who lived in an area of Australia endemic for the Australian paralysis tick *I. holocyclus*, and who were regularly involved in

collecting and handling of these ticks. Graves et al. found none had antibodies to *Borrelia* (Lyme disease), suggesting they had not been exposed to these bacteria (Graves et al., 2016). Additionally, in the subset of 74 *I. holocyclus* ticks examined for DNA from *Borrelia* spp. none was positive (Graves et al., 2016).

In 2015, Gofton, Oskam et al., in their study of 196 individual specimens of *I. holocyclus* ticks collected from mammalian and avian hosts and from the environment to identify and characterise bacteria harboured by *I. holocyclus* ticks, found a *Borrelia* relapsing fever group sp. (Gofton, Oskam, et al., 2015). The authors commented *Borrelia* relapsing fever pathogens are being identified in new geographic regions throughout the world, their medical importance is well recognised and while the aetiological agent of Australian “Lyme-like” illness has been a source of unresolved debate for many years, the discovery of this *Borrelia* relapsing fever pathogen in Australian *I. holocyclus* ticks may provide insights in this medical conundrum (Gofton, Oskam, et al., 2015).

In Gofton, Doggett et al.’s (2015) study, in which they surveyed the microbial communities harboured by human-biting ticks from across Australia in an attempt to identify bacteria that may contribute to the symptoms associated with Lyme-like illness, the authors found that of the 460 ticks studied, including *I. holocyclus*, *A. triguttatum*, *H. bancrofti* and *H. longicornus*, all were negative for *Borrelia* spp. (Gofton, Doggett, et al., 2015).

## *Candidatus* Neoehrlichia mikurensis and the Australian situation

*Candidatus* Neoehrlichia mikurensis is a newly recognised human pathogen that has been found in other countries (Graves & Stenos, 2017; Mackenzie, 2013). It was first recognised as a human pathogen in 2010 (Wellinder-Olsson et al. (2010) in Mackenzie, 2013).

The pathogen has been shown to cause human infection in China, where it is found in ticks and rodents (Li et al. (2012) in Mackenzie, 2013); and co-infection of *I. ricinus* ticks in Sweden (Andersson et al. (2013) in Mackenzie, 2013), Denmark (Fertner et al. (2012) in Mackenzie, 2013), and Switzerland (Maurer et al. (2013) in Mackenzie, 2013). It has also been shown to be the cause of human disease in Germany (von Loewenich et al. (2010) in Mackenzie, 2013).

*Candidatus* Neoehrlichia mikurensis causes febrile illness and post-infection fatigue especially in immunocompromised patients. Chalada et al. reported symptoms from 11 human cases in Europe included fever, myalgia, arthralgia, neutrophilia and anaemia combined with vascular events such as transient ischaemic attacks and deep vein thrombosis, although all but one patient was actively immune suppressed, and most were asplenic. They also commented that while some of these symptoms may be confused with a “Lyme-like” illness, further work must be performed to determine the host range infectivity, and clinical presentation of the novel *Candida* Neoehrlichia species detected in Australian *I. holocyclus* ticks before these may be confirmed as potential Lyme-like candidates (Chalada et al., 2016).

### Australian research

Graves and Stenos noted that recent Australian studies (Gofton, Doggett et al. (2015) and Gofton, Doggett et al. (2016) in Graves & Stenos, 2017) had demonstrated the presence of *Candidatus* Neoehrlichia spp. in Australian paralysis ticks but their presence in Australian patients is yet to be shown (Graves & Stenos, 2017). The study by Gofton, Doggett et al. (2015) surveyed the microbial communities harboured by human-biting ticks from across Australia in an attempt to identify bacteria that may contribute to the symptoms associated with Lyme-like illness (Gofton, Doggett, et al., 2015). Of the 460 ticks included in the study, including *I. holocyclus*, *A. triguttatum*, *H. bancrofti* and *H. longicornus*, two novel “*Candidatus* Ehrlichia” spp. were identified in 12.9% of *I. holocyclus* ticks with further phylogenetic analysis of the novel “*Candidatus* Ehrlichia” suggesting this is a new species. The authors commented that determining whether this species (and other newly discovered species identified in their study- see *Anaplasma* and *Ehrlichia* above) cause disease in humans and animals, like closely related bacteria do abroad, is of public health importance and requires further investigation (Gofton, Doggett, et al., 2015).

The study by Gofton, Oskam et al. (2015) of 196 individual specimens of *I. holocyclus* ticks collected from mammalian and avian hosts and from the environment to identify and characterise bacteria harboured by *I. holocyclus* ticks, also identified a novel “*Candidatus* Neoehrlichia” spp. in Australia (Gofton, Oskam, et al., 2015). The authors commented *Candidatus* Neoehrlichia pathogens are being identified in new geographic regions throughout the world, their medical importance is well recognised and while the aetiological agent of Australian Lyme-like illness has been a source of unresolved debate for many years, the discovery of this novel “*Candidatus* Neoehrlichia” pathogen in Australian *I. holocyclus* ticks may provide insights into this medical conundrum (Gofton, Oskam, et al., 2015).



## Francisella and the Australian research

*Francisella* spp. are tick-transmitted bacteria that cause classic tularaemia (Dehhaghi et al., 2019; Graves & Stenos, 2017). Dehhaghi et al. noted tularaemia is re-emerging in many parts of the world and while there is no report of the frequency of this disease in Australia, it is currently considered an infrequent disease in the Southern Hemisphere. It persists in soil and water and ubiquitously occurs in arthropod vectors as well as wildlife, and where present, it is a highly contagious pathogen in domestic animals and humans. Tularaemia can be transmitted through direct contact, ingestion or inhalation, and indirectly through bites of infected deer flies, ticks or an infected animal. Symptoms may appear after three to five days after exposure and include cough, chest discomfort, chills, fatigue, fever, headache, sore throat, vomiting malaise, myalgia, abdominal pain and anorexia (Dehhaghi et al., 2019).

### Australian research

Mackenzie noted the first evidence of *Francisella* species in ticks in Australia was obtained from the Northern Territory (Vilcins et al. (2009) in Mackenzie, 2013) from a study using DNA from pools of *Amblyomma fimbriatum* hard ticks, although Mackenzie commented there is no evidence to suggest that these organisms are pathogenic for humans (Mackenzie, 2013). Additionally, this study, Graves and Stenos commented, had shown the tropical reptile tick from northern Australia (*Amblyomma fimbriatum*) contained DNA from this bacterium, but this tick is not known to bite humans (Vilcins et al. (2009) in Graves & Stenos, 2017).

Dehhaghi et al. reported two *Francisella* spp. (both *Francisella hispaniensis*) have been separately isolated from two infected women in Australia (Whipp et al. (2003) and Aravena Román et al. (2015) in Dehhaghi et al., 2019) and commented these studies proved the presence of *Francisella* spp. in New South Wales, Northern Territory, Tasmania and Western Australia since 2003 (Dehhaghi et al., 2019). Mackenzie also cited the study by Whipp et al. and commented this study was the first evidence of a *Francisella tularensis* subsp. *novicida* in Australia with the organism identified from an environmentally-acquired foot infection sustained in the Northern Territory (Whipp et al. (2003) in Mackenzie, 2013). MacKenzie noted that this low pathogenicity subspecies of *F. tularensis* is relatively rare, and that the study by Whipp et al. represented the first time it had been found in the Southern Hemisphere (Mackenzie, 2013). Mackenzie also noted a more recent study had reported on a second case of infection due to *Francisella tularensis* subsp. *holartica* with this occurring in a woman bitten by a ringtail possum in Tasmania (Jackson et al. (2012) in Mackenzie, 2013). Dehhaghi et al. also cited this 2012 study by Jackson et al. and then reported that six years later, in 2017, Eden et al. had isolated *F. tularensis holartica* from ringtail possums in Sydney (Jackson et al. (2012) and Eden et al. (2017) in Dehhaghi et al., 2019). Of the evidence, Dehhaghi et al. commented that in Australia, the ringtail possum is, so far, proven to be the only natural host of tularaemia (Dehhaghi et al., 2019). Graves and Stenos also cited this study by Jackson et al. 2012 and commented it is not yet clear whether tularaemia is a tick-transmitted infection in Australia (Graves & Stenos, 2017).

## Other selected *Ixodes* ticks in Australia

Kwak reported on the first record of human infestation and feeding by the native tick species *Ixodes (Endopalpiger) australiensis* in Australia (Kwak, 2018). The tick was found attached and feeding on the leg of a man bushwalking near the town of Denmark, Western Australia in October 2017, and subsequently identified as an adult female of *I. australiensis*. After the tick was removed the patient reported itchiness around the feeding site followed by pustular discharge, however, no [infectious] disease associated with the tick developed in the man, either during or after its removal (Kwak, 2018). The man was later reported to have developed mammalian meat allergy after tick bite (Kwak et al., 2018). Indeed, Kwak et al. reported in 2018 that *Ixodes (Endopalpiger) australiensis* had been established as a second tick species associated with MMA in Australia (Kwak et al., 2018).

Greay et al. reported on a survey of hard ticks (Acari: Ixodidae) of companion animals in Australia, which the authors commented was the first of its kind to be conducted in Australia, with the results contributing to the understanding of the species and distribution of ticks that parasitise dogs, cats and horses in Australia (Greay et al., 2016). The authors concluded the species that were most commonly found on these animals are well-known vectors of pathogens or cause neurological disease, however, the vector competency of several species identified had not been widely investigated. They commented such knowledge is required to better understand the risk of tick-borne disease transmission to pets and potentially to their owners (Greay et al., 2016).

## Tick-borne viruses and the Australian situation

While there are several viral infections associated with ticks in other parts of the world (e.g. TBE in Europe), three reviews of the literature concurred that currently there are no definite tick-borne viral infections of humans yet discovered in Australia (Dehhaghi et al., 2019; Graves & Stenos, 2017; Mackenzie, 2013). While no definite tick-borne viral infections of humans are known in Australia, a new tick virus has recently been isolated in Australia (Graves, unpublished).<sup>8</sup>

Dehhaghi et al. noted that more than 75 arboviruses (arthropod-borne viruses) have been identified in Australia, some of which are associated with human diseases, but these are almost exclusively mosquito-borne (Russell and Dwyer, 2000 and Smith et al. 2011 in Dehhaghi et al., 2019).

All three reviews discussed Australian evidence on viruses isolated from seabird ticks. Mackenzie concluded the role, if any, that these seabird-associated tick-borne viruses play in human disease is unknown except for the antibodies to Gadgets Gully virus in some residents of Great Barrier Reef islands (Mackenzie, 2013). Graves and Stenos cited two studies (Wang et al. (2014) and Gauci et al. (2015) in Graves & Stenos, 2017) on a phlebovirus present in an Australian bird tick (*I. eudyptidis*) and commented that human pathogenic viruses may be present in Australian ticks although there is currently no evidence of *I. eudyptidis* biting humans (Graves & Stenos, 2017).

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<sup>8</sup> Unpublished at the time of publication of this Guidance Note. Provided by Graves, S. R., April 2021.

Dehghani et al. noted that Saumarez Reef virus was isolated from *I. eudyptidis* associated with a dead silver gull in Northern Tasmania but as *I. eudyptidis* does not attach to and feed on humans, it was not considered further in their review (Dehghani et al., 2019).

A study reported on the virome of Australian ticks collected from two locations on the central east coast of Australia including metropolitan Sydney (Harvey et al., 2019). Harvey et al. noted that each year a growing number of individuals along the east coast of Australia experience debilitating disease following tick bites and, as there is no evidence for the presence of the causative agent of Lyme disease *B. burgdorferi* s.l. in Australian ticks, the aetiological basis for this disease syndrome remains controversial (Harvey et al., 2019). Harvey et al. used a metatranscriptomics approach and identified 19 novel RNA viruses from a diverse set of families. Harvey et al. commented that the majority of these viruses were related to arthropod-associated viruses, suggesting that they do not utilise mammalian hosts. They also reported that, notably, three of these viruses clustered with known mammalian viruses, including a novel coltivirus that was related to the human pathogen Colorado tick fever virus (Harvey et al., 2019).

## Research related to DSCATT

The Australian Government has acknowledged the need for, and is supporting, research to further investigate debilitating symptom complexes attributed to ticks. In January 2019, the National Health and Medical Research Council funded research to better understand the nature, prevalence and causes of these symptoms, with the longer-term aim to obtain evidence to guide development of treatments:

- Professor Peter Irwin of Murdoch University received funding for research to determine the causes of DSCATT, as a first step towards improving diagnostic outcomes for patients through the provision of accurate and evidence-based information about their illness.
- Professor Richard Kanaan of the University of Melbourne received funding for a project to develop a new treatment for DSCATT, that will include the development of a case definition, adapting the treatment approach for unexplained syndromes to the specifics of DSCATT, and then piloting a randomised controlled trial to test the effectiveness of the new therapy (Australian Government Department of Health, 2019).

Additionally, the Australian Government Department of Health funded the Commonwealth Scientific and Industrial Research Organisation (CSIRO) to progress two projects, both of which were completed in 2021 (Australian Government Department of Health and Aged Care, 2022) These projects included:

- a tick survey to better understand which bacteria, viruses and other pathogens are carried by ticks in Australia and their impact on human health
- a case study biobank to gather and analyse samples from DSCATT patients for possible biomarkers as possible indicators of disease.

Results of these projects are available on the Australian Government Department of Health and Aged Care website at this link: <https://www.health.gov.au/initiatives-and-programs/dscatt>.

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