DISTRIBUTION OF RICKETTSIOSES IN OCEANIA: PAST PATTERNS AND IMPLICATIONS FOR THE FUTURE

ABSTRACT

Rickettsioses present a threat to human health worldwide, but relatively little is known on their epidemiology and ecology in Oceania. These bacteria are the cause of potentially fatal febrile illnesses in humans (categorized into scrub typhus, typhus group and spotted fever group rickettsioses). They are transmitted by arthropod vectors such as ticks, mites, fleas and lice, which are associated with vertebrate host animals including rodents and companion animals. We conducted a search in the scientific and grey literature of Rickettsia spp. *and* Orientia tsutsugamushi *within the Oceania region. Human case reports, human serosurveys and PCR-based testing of vectors and host animals reviewed here highlight the widespread distribution of these pathogens in the region, with the majority of human serological and vector surveys reporting positive results. These findings suggest that rickettsioses may have a significantly higher burden of disease in Oceania than is currently appreciated due to diagnostic challenges. Furthermore, consideration of the ecology and risk factors for rickettsioses reported for Oceania suggests that their importance as a cause of undifferentiated acute febrile illness may grow in the future: environmental and social changes driven by predicted climate change and population growth have the potential to lead to the emergence of rickettsioses as a significant public health problem in Oceania.*

KEYWORDS: Rickettsia; Orientia; Typhus; Scrub typhus; Murine typhus; Vector-borne diseases; Oceania; Pacific; Australia; New Zealand; Ticks; Fleas; Mites; Epidemiology; Environmental health; Emerging infectious diseases; infectious diseases; rickettsial infections; rickettsioses; acute undifferentiated fevers.

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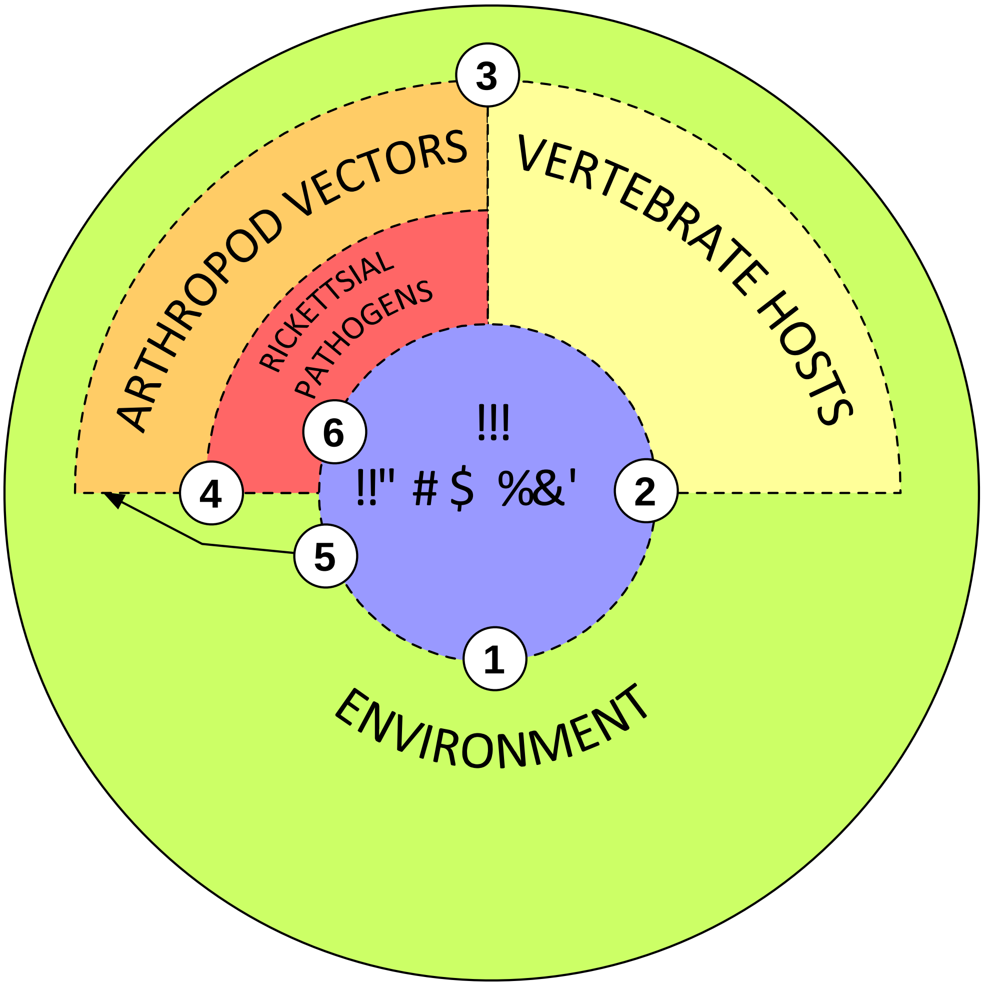
INTRODUCTION

Rickettsia is a genus of bacteria causing febrile illness in humans and other mammals. Belonging to the Class Alphproteobacteria, *Rickettsia* are small, obligate intracellular endosymbionts or parasites of eukaryotic cells (Weinert et al. 2009). To date, at least 16 of 25 known *Rickettsia* species are recognized human pathogens (Fournier and Raoult. 2009), with ticks, fleas, lice and mites acting as vectors and also reservoirs. Historically, *Rickettsia* species were serologically classified into typhus, spotted fever and the scrub typhus groups (Weinert et al. 2009). Formerly known as *Rickettsia tsutsugamushi*, the causative agent of scrub typhus has been reclassified into the *Orientia* genus (also a member of the Rickettsiaceae family) (Weinert et al. 2009). Other causative agents of rickettsioses include *Anaplasma* spp. and *Ehrlichia* spp. of the Anaplasmataceae family (Order Rickettsiales), and Q fever, caused by the morphologically similar but genetically and ecologically distinct bacterium *Coxiella burneti*.

In this review, we focus on illness caused by species of the *Rickettsia* and *Orientia* genera within Oceania, and summarise reports of rickettsia and rickettiosis that have been identified using the diagnostic tools available at the time of the study, but acknowledge that misidentification and misdiagnosis are possible. Prior to the 1990s, identification of rickettsial species relied on morphological, metabolic and antigenic characteristics, resulting in highly unreliable phylogenies (Fournier and Raoult. 2009). Conventional serological identification of rickettsial isolates has generally been limited to reference laboratories since it requires a laboratory equipped for the culture of rickettsia and a large panel of specific antisera (La Scola and Raoult. 1997). Serological methods may be limited by factors such as the cross-reactivity of human sera with *Rickettsia* spp. within and between biogroups, and also with other bacteria such as *Legionella* and *Proteus* spp. Cross-absorption reactivity will vary depending on the technique used. Even microimmunofluoresence assays, the current reference method for rickettsial serodiagnosis, do not provide conclusive evidence that a patient's illness was caused by the rickettsial species used as the antigen in the assay (Parola et al. 2013). Over the past three decades, new identification techniques, particularly molecular methods and DNA sequencing, have enabled rapid, convenient, sensitive and more accurate identification of rickettsial species, their intricate taxonomic relationships (La Scola and Raoult. 1997) and also that of their arthropod host/vectors (Latrofa et al. 2013). Due to serological cross-reactivity, only isolation and molecular identification of the etiologic agents allows for the unequivcocal recognition of rickettsial diseases in regions where they were not previously identified, or for the delineation of a new species (La Scola and Raoult. 1997).

Tick-borne rickettsial agents are transmitted to humans by tick salivary excretions during the process of tick biting. Rare cases of transmission by organ transplant have also been reported (Barrio et al. 2002). Flea and louse borne pathogens are transmitted through contact of broken skin or mucosal surfaces with crushed vectors or their faeces (Azad and Beard. 1998). Flea-borne rickettsioses can also be acquired by inhalation or by inoculation of the conjunctiva with these infectious materials (Eremeeva and Dasch. 2014). Clinical symptoms of rickettsioses commonly appear 1-2 weeks after inoculation and vary between the different pathogens. Clinical presentations are non-specific and rickettsioses are frequently difficult to distinguish clinically from other common etiologies of undifferentiated fever in the Pacific including dengue, leptospirosis, and typhoid fever. Characteristic symptoms and signs include fever, headaches, myalgia, eschars at the inoculation site, rash (petechial, macular, or maculopapular), and lymphadenopathy, and can be accompanied by gastrointestinal, respiratory and occasionally neurological symptoms (Parola and Raoult. 2006). Severity of infection varies significantly between individuals, and ranges from mild self-limiting illness to to fatal cases. Treatment with specific antibiotics (usually doxycycline) is highly effective, particularly if initiated early in the clinical course (Parola and Raoult. 2006). However, many first-line antibiotics commonly used for empirical treatment of undifferentiated fever (e.g. penicillins and cephalosporins) are ineffective for rickettsioses. Some cases progress to severe disease and death despite appropriate antibiotic treatment (e.g. Currie et al. (1996), Sexton et al. (1990)).

While some rickettsioses, such as epidemic, murine or cat flea typhus, are widespread throughout the world, most are restricted to specific areas of endemicity (Azad and Beard. 1998, Parola and Raoult. 2006). Such variation in distribution reflects that of their respective arthropod vector species, which require particular environmental conditions and the presence of appropriate vertebrate hosts for survival (Azad and Beard. 1998),(Parola and Raoult. 2006). Humans are at risk of infection by direct exposure to vectors, which is also a mechanism of indirect exposure when in proximity to or contact with vertebrate hosts. Infection risk is therefore partly determined by living conditions and occupational or recreational exposures. Risk can also vary with life stage of the vector, for example the larval stages of trombiculid mites carrying *O. tsutsugamushi* are found on grasses where they wait to attach themselves to a passing vertebrate hosts. The emergence of human rickettsioses thus reflects a potentially complex evolution in disease ecology (Frances. 2011), encompassing changing dynamics between multiple components of exposure pathways (fig. 1).



1) Humans alter environment through land use change, biodiversity loss, climate change and human exposure to environment is shaped by human and environment factors (e.g. choice of occupational and recreational activities shaped by socioeconomic status and physical environment).

2) Abundance, distribution and behaviour of vertebrate hosts shaped by environmental niche requirements (e.g. climatic conditions, food availability) and by human factors (e.g. animal husbandry, pets, creating food sources for wild animals from agriculture or domestic waste).

3) Arthropod vector/reservoir abundance, distribution, behaviour shaped by environmental conditions (e.g. climatic, vegetation types) and by vertebrate host availability and abundance.

4) Arthropod abundance determine vertical transmission of bacteria between vector/reservoirs and prevalence of the pathogen in that vector population. Environmental conditions may also determine infectivity of the pathogen.

5) Human activities and behaviours determine exposure to arthropod vectors by contact with environments and hosts required for lifecycle completion.

6) Bacterial and human immune factors determine pathogenicity.

Figure 1. The ecology of vector-borne rickettsioses. Disease risk to humans is determined by the overlap and interactions between humans, the environment, vertebrate hosts, arthropod vectors and rickettsial pathogens.

The region of Oceania encompasses the Australian continent and island nations and territories within Melanesia, Micronesia and Polynesia. With the exception of New Zealand and the southern portion of Australia, all of these nations and territories fall within the tropics. Oceania hosts a population of 38.5 million people, with Australia (23.1 million), Papua New Guinea (6.4 million) New Zealand (4.4 million) and Hawaii (1.4 million) as the only nations/territories with populations exceeding 1 million (CIA World Factbook. 2013). The nations and territories of Oceania represent a broad range of economies and living conditions. Poverty, remoteness and tropical climate all contribute to vulnerability to and significant burden of infectious diseases in this region (Lau. 2014). Worldwide, little is known about the ecological, epidemiological and clinical characteristics of tropical rickettsioses (Parola and Raoult. 2006), and Oceania is no exception (Eldin et al. 2011, Parola et al. 2013). The lack of knowledge is compounded by under-diagnosis, poor medical awareness, non-specific symptoms that overlap with many other tropical infectious diseases, and poor access to advanced laboratory diagnostic facilities in developing countries (Parola and Raoult. 2006). Here, we review scientific and grey literature to summarise reports of rickettsioses caused by *Rickettsia* spp. and *O. tsutsugamushi* within Oceania (see Parola et al.(2013) for a recent, global review of the distribution of tick-borne rickettsioses). We suggest that, like in other tropical regions, rickettsioses are under-diagnosed in Oceania and more widespread than current literature suggests. Alongside dengue, leptospirosis, typhoid, and malaria, rickettsioses may be a significant, serious and emerging cause of undifferentiated, potentially serious, acute febrile illnesses in this region.

METHODS

Searches of published scientific literature and grey literature reporting the occurrence of rickettsioses caused by *Rickettsia* spp. and *Orientia tsutsugamushi* within Oceania were conducted using Google and Google Scholar as search engines. Search terms used in addition to 'typhus', 'rickettsia' and 'spotted fever' are listed in Appendix 1. ProMed (ProMed, 2013), websites of government health departments and other relevant administrative bodies of Pacific Island Territories, as outlined in Appendix 2, were also searched using the terms 'typhus' and 'rickettsia' and 'spotted fever'. Reports of rickettsioses in the context of international travel were also searched for in two leading travel medicine journals. Relevant hits were manually searched for reports of Rickettsioses within the Pacific region. Relevant citations within these publications were also investigated where possible.

Reports indicating presence of *Rickettsia* spp. and *Orientia* sp. found using these search methods described either human cases of illness, human seroprevalence, or infection of arthropod vectors/reservoirs, or their vertebrate hosts. Vector studies were classified by vector species. Human case reports and serostudies were classified by group: scrub typhus, spotted fever group rickettsioses or typhus-type rickettsioses.

RESULTS & DISCUSSION

Scrub Typhus in Oceania

The presence of scrub typhus and/or its etiological agent *Orientia tsutsugamushi* was reported on several occasions in Papua New Guinea (PNG), the Torres Strait Islands and across northern Australia, the Solomon Islands, northern Vanuatu and Palau (see fig. 2 & table 1). The disease was widely reported in soldiers during World War II, and one case was reported in 1975 in Vanuatu. Since the 1990's, individual cases have been reported regularly, such as to the Australian National Notifiable Disease Surveillance System (NNDSS. 2013). Documented clusters of cases have occurred on Darnley Island (Torres Strait Island) with 10 cases in one year from 2000-2001, and in Palau with 15 cases over 2 years from 2001-2003. A cluster of 20 cases occurred in March 2005 in northern Queensland.

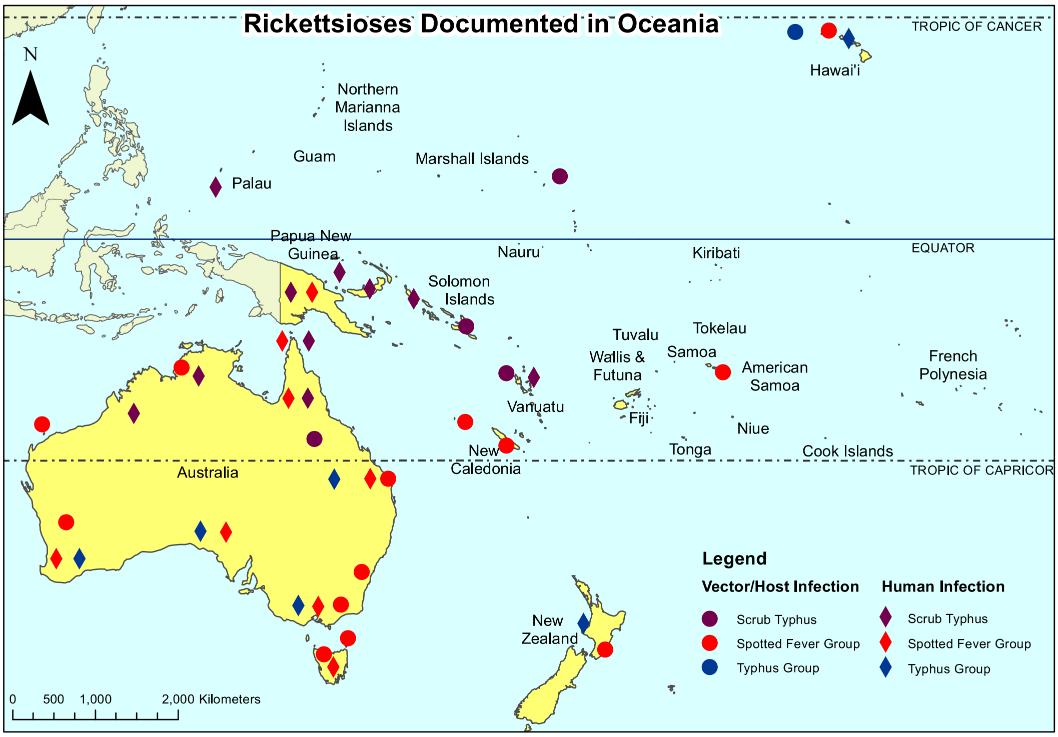


Figure 2. Map of rickettsioses in Oceania. Approximate locations of human rickettsial infections and presence in arthropod hosts/vectors or vertebrate hosts published in the scientific literature, colour-coded by type. Data from the Australian National Notifiable Disease Surveillance System not shown because they may have included infections acquired overseas.

Table 1. Human infection by *O. tsutsugamushi*, causative agent of scrub typhus in Oceania.

Country/ Territory	Time, Place, Source	Cases Reported/ Seroprevalence	Risk Factors, notes of interest
Palau	Sonsoral Island & Tobi Island (South Western Islands) October 2001-October 2003. (Durand et al. 2004)	6 cases[1] and 7 probable cases.	Temporality: No clear seasonality.
	All of Palau in 1995. South West Islands, Echang hamlet and other hamlets on Koror Island,	SW Islands: 50/59 (85%) seropositive. Echang hamlet: 44/52 (80%) seropositive. Other Koror hamlets:	Exposure: Higher seropositivity in areas where recreational and occupational lead to frequent exposure to outdoor environment and rodents.

	December 2003 and April 2005. (Demma et al. 2006)	7/99 (7%) seropositive. General Palau sample, 1995: 34/635 (5.4%) seropositive.	Possible driver: Change in unique host and environmental factors and occurrence, or increased recognition of an established disease. Disease endemic throughout Palau. All cases reported in SW but Koror has potential for emergence.
Papua New Guinea	Raubaul, East New Britain, July 1930. (Sinclair. 1930)	1 case.	
	Wau, Morobe District. Early 1936. (Von Derborch. 1937)	14 cases.	Exposure: All patients lived or worked on river/creek banks. 11 male cases had been clearing vegetation there, 3 female cases lived adjacent to bush land.
	Various locations. 1936- 1938. (Von Derborch. 1937, Gunther. 1938)	6 cases Sepik District. 1 case from Kar Kar Island. 1 case from Morobe District.	Listed as 'endemic typhus' (murine typhus), but clinical symptoms and location consistent with scrub typhus.
	Various locations. 1931- 1940. (Gunther. 1940)	105 cases, including 20 fatal cases. 69 cases from Morobe District. 3 cases from New Britain Island. 2 cases from Madang District. 1 case from Western Islands. 13 cases from Sepik District.	Listed as 'endemic typhus' (murine typhus), but clinical symptoms and location consistent with scrub typhus.
	Bat Island, Purdy Island Group. March- April 1944. (Philip and Kohls. 1945)	26 cases (out of 41 exposed people), including 2 fatal cases.	Exposure: Cases were soldiers. Possible drivers: High native rat population, vegetated by secondary vegetation, coconut plantation and coarse grasses.
	Various locations. 1942-1943. (Blake et al. 1945)	809 cases in American Troops.	Exposure: Cases in Dobadura area associated with camping in previously occupied areas, vegetated by Kunai grasses and adjacent to jungle (compared to areas of primary vegetation).
	Various locations, 1942- December 1945. (Williams et al. 1944, Frances. 2011)	2840 cases in the Australian Army. 2100 of those cases occurred between March 1942 and December 1943, with a 9% fatality rate.	
	Port Moresby & Samberigi area of Southern Highlands, October 1997. (Kende and Graves. 2003)	Port Moresby: 3/93 (3.2%) seropositive. Samberigi: 0 /98 seropositive.	Possible driver: Environmental differences between coastal grasslands of Port Moresby and dense rainforest of Smaberigi may account for presence and absence of rickettsioses.

	Stickland Gorge Area, Southern Highlands and West Sepik Provinces, October 2000. (Spicer et al. 2007)	39/140 (28%) seropositive.	
Solomon Islands	Northern Solomon Islands. May 1944. (Anderson and Wing. 1945)	49 cases in US troops.	Exposure: 700 soldiers camped for several days at a disused village site, with a meadow of coarse grass extending from riverbank to jungle. Most soldiers reported mite bites, using repellent inconsistently whilst camping there. No cases in 200 soldiers camping nearby on beachhead.
	Eastern Solomons Islands, December 1971-January 1972, plus 1 case in 1975. (Miles et al. 1981)	Total sample number: 335, including serum from 1 clinical case. Guadalcanal: 21% seropositive. Makira: 44% seropositive. Ugi: 48% seropositive. Ndende: 82% seropositive.	Possible driver: Endemic foci of disease were usually in areas of secondary vegetation following human activities e.g. milled forests, neglected coconut plantations.
Vanuatu	Espiritu Santo, 1942-1945. (Philip, 1964. in Miles et al. (1981))	3 cases in US soldiers.	
	Banks Islands, Northern Vanuatu, 1973. (Miles et al. 1981)	Banks Islands, Vanuatu: 13/72 (18%) seropositive.	Risk factor: Endemic foci of disease were usually in areas of secondary vegetation following human activities e.g. milled forests, neglected coconut plantations.
Australia	Northern Queensland, 1942-1945 (Frances. 2011)	Unspecified number of cases in soldiers during WWII.	Risk factor: Cases occurred in locations with high yearly rainfall (>1500mm).
	Litchfield Park, Northern Territory, August 1996. (Currie et al. 1996)	1 fatal case[1]. 7 previously reported cases in the park.	Exposure: Patient had been constructing walking paths for the park. Temporality: All cases reported during winter months (tourist season).
	Torres Strait Islands, mainly Darnley Island, March 2000-2001 (Faa et al. 2006), and April 2003 and May 2004 (Unsworth et al. 2007a).	10 cases[1,2] in 2000-2001 (7 from Darnley Is., 1 from Murray Is., 2 location not specified). 2 of these 10 cases showed positive PCR results. Mention of 2 additional local cases in the 1950's. 2 cases[1,2,3] in 2003 &	Exposure: Densely vegetated areas close to most domestic dwellings on the island. Temporality: 7/12 cases occurred during Jan, Feb, March.

		2004 (from Darnley Is.)	
	Cowley Beach, North Queensland, March 2005. (Likeman. 2006)	20 cases in soldiers[1,2.] 3 of 20 seropositive patients also had positive PCR results.	Exposure: Training exercises in dense vegetation.
	Kimberley region, Western Australia, 1993 or earlier (Quin et al. 1993 in Graves et al. (1999))	1993: 1 case[1] 1996 Serostudy: 37/920 (4%) seropositive.	
	1996-2011, various states. (NNDSS. 2013)	1996: 13 cases, 1997: 26 cases,1999: 2 cases, 2000: 11 cases. 2004: 64 cases in SA, 1 in VIC, 2 in WA. 2005: 71 cases in SA. 2006: 25 cases in SA, 1 in VIC, 26 in WA. 2007: 2 case in SA 2008: 1 case in NT, 2 in SA. 2009: 2 cases in SA 2010: 1 case in QLD, 1 in TAS, 2 in VIC, 4 in WA. 2011: 1 case in NSW, 1 in QLD.	

[1] Clinical diagnosis of rickettsial infection confirmed using serological methods.

[2] Clinical diagnosis of rickettsial infection confirmed using Polymerase Chain Reaction.

[3] Clinical diagnosis of rickettsial infection confirmed by culture..

Whilst recorded in a wide range of ecological conditions, scrub typhus has long been associated with disturbed habitats which have been repopulated with secondary vegetation (Traub and Wisseman. 1974, Kelly et al. 2002). Scrub and grasses which dominate as secondary vegetation appear to provide optimal conditions for trombiculid mite vector/reservoirs of *O.* t*sutsugamushi*; possibly as a platform for the parasitic larval stage to attach to passing ground-dwelling vertebrate hosts (Traub and Wisseman. 1974). Furthermore, we speculate that disturbed areas may attract more hosts for the mites (with lessened endemic biodiversity permitting the proliferation of generalist rodents). For tick-borne Lyme disease, smaller fragments of forest habitat have been associated with higher human disease incidence, as lowered mammal diversity leads to greater densities of white-footed mice (ecological generalists who are highly competent reservoirs of the pathogen) and higher densities of infected tick vectors (Allan et al. 2003). In addition, humans are more likely to spend time in disturbed or fragmented areas, since land clearing is generally associated with human activities.

Accordingly, reports of scrub typhus cases and clusters within Oceania are commonly associated with areas of secondary vegetation (table 1). During World War II, over half of 931 American troops infected with scrub typhus in the Vogelkop Peninsula in Dutch New Guinea were thought to have been bitten by chigger mites in village and garden areas, or overgrown coconut groves (Griffiths. 1945). In the Solomon Islands, Anderson & Wing (1945) report a cluster of scrub typhus cases in soldiers camping at a disused village site vegetated with coarse grasses, and an absence of cases from soldiers camping at a nearby beach head. In a serostudy in the Eastern Solomon Islands and Banks Islands of Northern Vanuatu, Miles et al. (1981) observed that endemic foci of the disease were usually found where secondary vegetation had grown back after human modification. More recently, densely vegetated areas close to domestic dwellings on Darnley Island (Unsworth et al. 2007a) were thought to have been sites of transmission for 12 cases reported between 2000-2004. The association between re-vegetated areas and disease risk is also supported by a study that sampled over 800 mammal hosts from multiple sites throughout mainland PNG. *Leptotrombidium deliensis* mite, the most common vector of *Orientia tsutsugamushi*, was more abundant in disturbed habitats (either scrub, secondary forest or areas otherwise altered by human activities) (Goff. 1979).

Rainfall is also an important limiting factor for this predominantly tropical disease. In Australia, distribution of published scrub typhus cases and seropositivity appears to be restricted to areas receiving more than 1500 mm of precipitation annually ((Campbell and Domrow. 1974, Currie et al. 1996, Frances. 2011). Concordantly, a Thai study found that trombiculid mite larvae were more abundant on hosts in the wetter months than the drier months (Frances et al. 1999). However, in contrast to this tropical distribution, positive serology to *O. tsutsugamushi* has been reported in large numbers by Australia's national disease surveillance (NNDSS) in the sub-tropical to temperate states South Australia between 2004-2011, and in small numbers in Victoria, New South Wales and Tasmania (NNDSS. 2013)(table 1). The interpretation of case data from the NNDSS require caution, especially since information on where infections may have been acquired is not provided.

Scrub typhus risk is also determined by the nature of human activities leading to exposure. The disease is infamous for having killed and disabled thousands of soldiers during World War II in the Asia-Pacific region. Within Oceania, the largest cluster of scrub typhus cases occurred in Papua New Guinea during this time, with cases also recorded in Solomon Islands and Australia (including a 2005 cluster in soldiers during training) (table 1.). Activities such as patrolling, training and camping in mite habitat, i.e. outdoor environments such as forest and secondary vegetation, increase the risk of exposure and infection. In a serostudy in different localities of Palau, Demma et al. (2006) attributed the high prevalence of *O.* t*sutsugamushi* infection observed on certain islands to more frequent exposure to rodents and outdoor environments, from both recreational and occupational activities. In Litchfield National Park in northern Australia, cases of scrub typhus have occurred during the drier tourist season (Currie et al. 1996), contrary to expectations that risk would be higher during the wet season due to a greater abundance of mites. However, the dry season coincides with the tourist season, when more people engage in recreational (or occupational) pursuits in this environment, thus demonstrating the importance of the human-environment interaction in disease ecology and transmission dynamics.

Typhus Group Rickettsioses in Oceania

Murine typhus, found worldwide (Parola and Raoult. 2006), is the main representative of typhus-type rickettsioses documented in this region. Human cases and flea vectors infected with *Rickettsia typhi* have commonly been reported in subtropical or temperate areas in Australia (Jones et al. 2004, Graves and Stenos. 2009) and the north island of New Zealand (Roberts et al. 2001, Gray et al. 2007, Irwin et al. 2012, Lim et al. 2012)(Roberts et al. 2001, Gray et al. 2009, Lim et al. 2012, Irwin et al. 2013) (table 2). However, murine typhus is also considered endemic to tropical regions of Australia (ARRL. 2014). The Hawaiian archipelago, the third area to report Murine typhus cases (Manea et al. 2001, CDC. 2003), and vector infection (Eremeeva et al. 2008), lies immediately south of the Tropic of Cancer (fig. 2). Cases of murine typhus have been reported in Australia since the pathogen's discovery in the 1920's (Graves and Stenos. 2009) and since 1990 in New Zealand (Roberts et al. 2001), including an cluster of up to 12 cases over 5 months during 2006 in the Waikato region. Murine typhus in the Hawaiian archipelago was first documented in the 1930s, peaked at 186 cases in1944 and generally declined in subsequent years. However, 47 cases were reported in 2002, the highest annual number of recorded cases in 50 years (Manea et al. 2001, CDC. 2003).

Louse-borne epidemic typhus, caused by another member of the typhus group *Rickettsia prowazekii* was periodically introduced to Australia in the 1700's and 1800s by migrants from endemic areas of Europe and Asia who lived in crowded, unhygienic conditions, as convicts or gold miners. However, this species is not considered endemic to Australia or elsewhere in Oceania (Parola and Raoult. 2006, Graves and Stenos. 2009). Interestingly, the National Notifiable Disease Surveillance System of Australia reports serology of *R. prowazekii* at times large numbers from South Australia in 2004 to 2011, and also one case in Western Australia in 2006 and 6 cases in Victoria in 2009(NNDSS. 2013). Possible explanations for this discrepancy are that these cases were acquired overseas from *R. prowazekii* endemic regions, or that they indicate infection by another typhus group member which is known to be endemic to Australia, namely murine typhus (which is not listed in the surveillance reporting). The latter seems likely given that cross reactivity commonly occurs between *R. typhi* and *R. prowazekii* in serological testing (Jones et al. 2004).

Table 2. Human infection by Typhus Group rickettsial agents in Oceania. Unless otherwise stated, all illness are cases of murine typhus, caused by *Rickettsia typhus*.

Country/ Territory	Time, Place, Source	Cases Reported	Risk Factors, environmental factors, notes of interest
Hawaii	Various Hawaiian Islands, 1933-1998 (Manea et al. 2001)	1 case in 1933 >5000 cases 1940-1949 186 cases in 1944 12 cases in 1950 <100 cases 1980-1989 33 cases in 1994-1998	Possible drivers: Rodents in houses, changes in agricultural practices, encroachment of houses onto agricultural land.
	South West Kauai, 1998 (Manea et al. 2001)	2 cases.[1] 3 probable cases.	Possible drivers: Recent habitat changes of peridomestic animals and their fleas.
	Various islands, 2002. (CDC. 2003).	47 total cases, 25 of which were confirmed [1/2 /3]: 35 cases from Maui 6 cases from Molokai	Exposure: 3 patients[1] whom were interviewed were exposed to rodents or to domestic animals and fleas. Temporality: 34 (72%) cases

		3 cases from Oahu 2 cases from Kauai 1 case from Hawaii	occurred during July—October (Summer/Spring). Largest number recorded annually since 1947. Demographic: The median age of the patients was 38 years (range: 1-68 years); 28 (60%) were male.
New Zealand	New Zealand, until 2009. (Lim et al. 2012)	47 cases ever recorded nation-wide as of December 2009.	
	Auckland, Northland & Waikato regions, 1990-2001. (Roberts et al. 2001)	9 cases [1].	Exposure: 8 of 9 patients lived rurally.
	Waikato region, May-October 2006 . (Gray et al. 2007)	6 cases[1] and 6 probable cases.	Exposure: All patients from rural areas. 11/12 patients saw rats or had more direct contact. 3 patients recalled flea bites.
	Waikato region, October 2009-October 2010. (Irwin et al. 2012)	4 cases [1,2] and 1 probable case. 2 of 4 seropositive cases confirmed by PCR.	Exposure: Infection associated with rural lifestyle.
Australia	South Australia, Western Australia, Queensland, Victoria, 1920's-2009 (Review by Graves et al. (1993)).	Not specified.	Exposure: Contact with rodents from handling grain, poor living conditions, mouse plagues.
	South Australia, 1932-1940. (Dwyer and Atkinson. 1940).	64 cases of 'typhus' (article title refers to 'endemic typhus').	
	Geelong, Victoria, 2002. (Jones et al. 2004)	1 case[1].	Exposure: Patient was hobby farmer, exposed to rats.
	Mid-North Coast of New South Wales, June 2010. (Simon et al. 2011)	1 case[1].	Exposure: Patient lived on a rural property, indirect contact with a pet rat.
	Various states, 1993-2011 (NNDSS. 2013)	Cases of R. *prowazekii* seropositivity . 1993: 1 case,, 2000: 2 cases. 2004: 102 cases in SA, 1 in WA. 2005: 161 cases in SA. 2006: 24 in SA. 2007: 1 case in SA. 2008: 1 case in SA, 6 in VIC 2009: 2 cases in SA 2010: 3 cases in SA 2011: 1 case in SA	

[1] Clinical diagnosis of rickettsial infection confirmed using serological methods.

[2] Clinical diagnosis of rickettsial infection confirmed using Polymerase Chain Reaction .

[3] Clinical diagnosis of rickettsial infection confirmed by culture methods.

The majority of documented murine typhus cases in Oceania are from individuals who spend time in rural environments such as farms (table 2). Many of these cases also report more direct contact with either fleas or rodent hosts (which also act as reservoirs). However, contact with rodents is not necessary for transmission of *R. typhi,* since the principal vector, the oriental rat flea (*Xenopsylla cheopsis*) is capable of remaining dormant in the environment for long periods of time and jumping large distances to seek blood meals (Bitam et al. 2010), and *R. typhi* may be transmitted to humans by inhalation of dust containing flea faeces (Manea et al. 2001). Risk of the disease is therefore largely dependent on the presence of peridomestic rodents and human interaction with them. In the past, murine typhus was associated with poor living conditions where rodents were not excluded from homes (Manea et al. 2001, Graves and Stenos. 2009). However, in the high-income areas of Australia, New Zealand and Hawaii, this risk factor has become less important.

Case clusters in Australia have occurred during rodent population booms (Graves and Stenos. 2009), perhaps because increased host populations support increased vector and *R. typhi* populations, or because higher rodent densities simply intensify human-rodent interactions. Similarly, on the Hawaiian island of Kauai, Manea et al. (2001) suggest that the general increase in murine typhus cases since the 1970s may have been driven by adoption of corn as a major crop, which supports larger rodent populations than the previously dominant sugarcane.

Spotted Fever Group Rickettsioses in Oceania

Rickettsia felis, etiological agent of cat flea typhus, appears to be the most widespread of spotted fever group rickettsiosis agents in Oceania, reflecting its worldwide distribution (fig. 2 & table 3). The bacterium has been found in the cat flea *Ctenocephalides felis* in the Australian states of Western Australia (Schloderer et al. 2006), Victoria (Williams et al. 2010), Queensland and the Northern Territory (Hii et al. 2013); New Caledonia (Mediannikov et al. 2011); the north Island of New Zealand (Kelly et al. 2004); and further east in American Samoa (Tuten et al. 2013)(table 4). *R. felis* has a range of flea vector species (table 4), having been found not only in its primary vector and reservoir species, the cat flea (Kelly et al. 2004, Schloderer et al. 2006, Mediannikov et al. 2011, Hii et al. 2013, Tuten et al. 2013) but also in the oriental rat flea (Eremeeva et al. 2008) and possibly sticktight fleas and rabbit fleas (Schloderer et al. 2006), as well as other flea species outside of Oceania (Parola and Raoult. 2006). Cats, dogs, and house mice in the case of the oriental rat flea, have been reported as hosts in the studies reviewed (table 4). Though *R. felis* has also been associated with wild hosts such as opossums and hedgehogs (Reif and Macaluso. 2009), these studies underline the importance of contact with flea-infested domestic animals as a risk factor, and of flea control in pets as a preventative measure. Seropositivity in 2 of

24 people sampled was recently reported near Wellington, New Zealand by Lim et al. (2012), though the infections may have been acquired during travel overseas. Illness in humans due to *R. felis* has only been documented once in Oceania; five cases occurred in a family in Victoria, Australia, in 2009 after contact with kittens (Williams et al. 2010) (table 3). However, three cases have been reported from within the tropics in southeast Mexico (Zavala-Velázquez et al. 2000), thus cat flea typhus may have the potential to emerge in tropical regions of Oceania.

Within Australia, Queensland tick typhus, caused by *Rickettsia australis* and first described in 1946, is found in coastal or near coastal regions from Northern Queensland south to Eastern Victoria (ARRL. 2014). Its distribution also extends northwards, with one clinical case from the Torres Strait (Unsworth et al. 2007a) and also seropositivity in central Papua New Guinea (Spicer et al. 2007) (table 3). Flinders Island Spotted Fever, first documented on this Tasmanian island in 1991 is caused by tick-borne *Rickettsia honei* and is endemic to south-eastern Australia (ARRL. 2014). Human illness caused by this species has also been reported outside Oceania, in Asia and Europe (Graves and Stenos. 2009, Murphy et al. 2011). *R. honei* is clinically and serologically similar to *R. australis* (Baird et al. 1992), emphasizing the importance of genetic characterization. Clinical cases of Australian Spotted Fever caused by the "marmionii" strain of *R. honei* have been reported as broadly as South Australia, Tasmania, northern Queensland and the Torres Strait Islands (Unsworth et al. 2007b).

Ixodes holocylcus, *I. tasmani* and *I. cornuatus,* the tick vector/reservoir species of *R. australis*, are found along the eastern Australian coast, and extend to northern Tasmania, though Queensland Tick Typhus remains restricted to mainland Australia (Sexton et al. 1991, ARRL. 2014). This suggests that temperate climates may be unsuitable for the pathogen. The restriction of Flinders Island Spotted Fever to southeastern Australia appears to match that of *R. honei*'s vector/reservoir, the reptile tick *Bothriocroton hydrosauri* (previously known as *Aponomma hydrosauri*) (Stenos et al. 2003). The combined distributions of *R. honei* "marmionii" tick vectors/reservoirs *Haemaphysalis novaeguinae* and *Ixodes tasmani* account for Australian Spotted Fever's broad latitudinal range. Unlike *R. felis* and *R. typhi*, which are largely associated with fleas of domestic and peridomestic animals, the principal hosts for these tick species are native mammals (Campbell and Domrow. 1974, Sexton et al. 1991) and reptiles (Stenos et al. 2003). The ecology of these tick-borne rickettsioses is therefore expected to depend on human interaction with wild ecosystems. Concordantly, several Australian cases reported were preceded by exposure to bush environments during activities such as gardening, living near bush land (McBride et al. 2007), military training exercises (Likeman. 2006), fishing and fieldwork (Unsworth et al. 2007b)(Unsworth et al. 2007).

Interestingly, a third tick-borne spotted fever group Rickettsia species of known pathogenicity, *R. africae,* has been documented for the first time in Oceania in islands off New Caledonia (Eldin et al. 2011). The infected *Ambylomma loculosum* ticks were found on humans working with marine birds (known hosts) which if migratory, may have introduced ticks from *R. africae* endemic areas of sub-Saharan Africa or the Indian Ocean (see Hubalek ((CDC. 2003, 2004)).

Finally, several studies in Australia, Papua New Guinea and the Marshall Islands have found serological evidence of spotted fever group rickettsioses which were not identified at a species level, either requiring further testing or signifying novel species. This work included human serostudies conducted in northern Western Australia (Graves et al. 1999, Abdad et al. 2010), southern Western Australia (Abdad et al. 2010), and Papua New Guinea (Faa et al. 2003, Kende and Graves. 2003, Spicer et al. 2007) (table 3). The species of *Rickettsia* found on rat mites and lice on Wake Island (Marshall Islands) may be *Rickettsia heilongjiangensis*, a known agent of human rickettsioses (Reeves et al. 2012b) (table 4). The spotted fever group species found by Abdad et al. (2010) in Australian workers on Barrow Island and recreational rogainers from the south of Western Australian is identified as an emergent species, *Rickettsia gravesii*, (Abdad. 2011), currently of unknown pathogenicity to humans. Work by Unsworth et al. (in (Graves and Stenos. 2009) and (Vilcins et al. 2008)) also identify a range of emerging tick-borne spotted fever group *Rickettsia* species of unknown pathogenicity, borne by ticks of native Australian mammals and reptiles. Finally, antibodies to spotted fever group rickettsiae were found in both domestic cats and dogs in Launceston, Tasmania in 2004 and 2005 (Izzard et al. 2010).

Table 3. Human infection by spotted fever group rickettsiae in Oceania.

Country/ Territory	Time, Place, Source	Cases Reported/ Seroprevalence	Risk Factors, notes of interest
Papua New Guinea	Port Moresby & Samberigi area of Southern Highlands, October 1997. (Kende and Graves. 2003)	Port Moresby: 4/93 (4.3%) seropositive for spotted fever group rickettsiae. Samberigi: 0 /98 seropositive for spotted fever group rickettsiae .	Possible driver: Environmental differences between coastal grasslands of Port Moresby and dense rainforest of Smaberigi may account for presence and absence of rickettsioses.
	Strickland Gorge Area, Southern Highlands and West Sepik Provinces, October 2000. (Spicer et al. 2007)	16 /140 (11 %) regional residents seropositive for *Rickettsia australis.*	
	Gazelle Peninsula, East New Britain, 2002-2003. (Faa et al. 2006).	19 /113 (17%) antenatal patients sampled were seropositive for spotted fever group rickettsiae .	
	Australia, July, 1998-December 1999. (O'Brien et al. 2001).	1 case[1] of spotted fever rickettsiosis in a traveller returned from Papua New Guinea.	

	Wellington. (Lim et al. 2012)	2/24 (8%) of volunteers (at an Environmental Research Agency) tested were confirmed to be *R. felis* seropositive.	Exposure: Contact with fleas, cat, rats, dog, possums, but had travelled overseas therefore infection may have not been local.
Australia	Coastal Eastern Australia- Northern QLD south to Flinders Island, Tasmania, 1946-1989 (Sexton et al. 1991).	62 cases [1,2] of Queensland tick typhus, (etiological agent of . the 23 cases from Flinders Island and Victoria not established- Flinders Island spotted fever since discovered). [1,2] 59 of 62 cases seropositive, 3 cases diagnosed by cell culture.	Exposure: 49% cases associated with outdoor occupational or recreational activities, and 22% were holidaymakers.
	Northern Queensland: Mossman, August 1989 (Sexton et al. 1990). Kuranda, Innisfail, Deeral, over 4 years 2007 or earlier (McBride et al. 2007).	1 fatal case[1] and 3 severe cases[1] of Queensland tick typhus (*R. australis*) at 4 different locations.	Exposure: Surviving patients bitten by ticks - one whilst gardening, another lived adjacent to bush land.
	Various locations in Eastern & Southern Australia. May 2002-June 2003. (Unsworth et al. 2007b)	7 cases [3] of Australian Spotted Fever (*R. honei* "marmionii" strain): 1 case from Port Willunga, South Australia. 2 cases from Darnley Is., Torres Strait. 1 case from Yam Is. Torres Strait. 1 case from Innisfail, North Queensland. 1 case from Lilydale, Tasmania. 1 case from Cape York, North Queensland.	
	Darnley Island, Torres Strait Islands March 2004 (Unsworth et al. 2007a)	1 case [2,3] of Queensland tick typhus (*R. australis*)	
	Cowley Beach, North Queensland, March 2005. (Likeman. 2006)	2 cases[1] of Queensland tick typhus (*R. australis*) in Australian soldiers.	Exposure: Training activities in dense vegetation.

	Perth area, Western Australia, 2006-2009. (Abdad et al. 2014).	23% (n=61) of recreational rogainers were seropositive for spotted fever group *Rickettsia* in 2.7% (n=47) of controls (Perth residents, no occupational or recreational bias) were seropositive for spotted fever group rickettsiae.26/920 (2.8%) seropositive for potted ever roup .	Exposure: Outdoor recreational activities were significant risk factors.
	Barrow Island & Perth area, Western Australia. 2010 or earlier. (Abdad et al. 2010)	23.1% (n=167) of recreational rogainers were seropositive for spotted fever group rickettsiae in 44.8% (n=67) of workers from Barrow Island (likely to be exposed to reservoir) were seropositive for spotted fever group rickettsiae. 1.7% (n=60) of controls (Perth residents, no occupational or recreational bias) were seropositive for spotted fever group rickettsiae.	Exposure: Outdoor recreational and occupational activities were significant risk factors.
	Kimberley region, Western Australia, 1996 (Graves et al. 1999)	26/920 (2.8%) seropositive for spotted fever group rickettsiae.	
	Brisbane, Queensland. 2013 or earlier. (Hanna et al. 2014)	1 case[1] of spotted fever group rickettsiosis.	Exposure: Patient frequently gardened.
	Melbourne & Lara, Victoria, April 2009. (Williams et al. 2010)	5 cases[1] of cat flea typhus (*R. felis*) Fleas from cats, but not patients, tested positive for *R.felis* DNA in PCR tests.	Exposure: Contact with cats from rural farm.
	Various states, 1992-2007 (NNDSS. 2013)	Cases of *R. australis* seropositivity: 1992: 8 cases, 1993: 3 cases, 1994: 3 cases, 1997: 10 cases, 1998: 2 cases, 2000: 2 cases. 2005: 1 case in Vic 2007: 1 case in Vic	
	Various states, 1992-2011 (NNDSS. 2013)	Cases of 'spotted fever group' seropositivity: 1992: 21 cases, 1995: 2 cases, 1999: 1 case, 2000: 44 cases. 2004: 232 cases in SA, 4 in	

		TAS 2005: 136 cases in SA, 3 in TAS 2006: 85 cases in SA, 2 in TAS 2007: 3 cases in NSW, 1 in QLD, 7 in SA, 1 in TAS, 8 in VIC 2008: 8 cases in NSW, 1 in NT, 24 in QLD, 6 in SA, 1 in TAS, 8 in VIC. 2009: 13 cases in NSW, 60 in QLD, 2 in SA, 1 in TAS, 7 in VIC. 2010: 10 cases in NSW, 30 in QLD, 8 in SA, 1 in VIC, 2 in WA. 2011: 8 cases in NSW, 15 in QLD, 4 in SA, 2 in TAS, 4 in VIC.	

[1] Clinical diagnosis of rickettsial infection confirmed using serological methods.

[2] Clinical diagnosis of rickettsial infection confirmed using Polymerase Chain Reaction.

[3] Clinical diagnosis of rickettsial infection confirmed by culture.

Table 4. Tick, mite, flea and louse species tested for *Rickettsia spp*. or *Orienta tsutsugamushi* in Oceania. [a,b,c]

Arthropod vector or possible vector	Country/Territory tested in	Vertebrate Hosts	Rickettsial agent indentified in arthropod vector/host	Source
Ambylomma loculosum[1] Tick	New Caledonia (Chesterfield and Walpole Islands), 2001-2007	Sea birds	*Rickettsia africae*	Eldin et al. (2011)
Ambylomma triguttatum[1] Kangaroo tick	Western Australia (Barrow Island)	Marsupials	*R. gravesii* Unknown pathogenicity	Owen et al. (2006)
Ixodes holocyclus[2] Paralysis tick	Australia (South East Queensland), 1970-1972	Bush rats	*R. australis*	Campbell and Domrow (1974)
Ixodes tasmani[2] Marsupial tick	Australia (South East Queensland), 1970-1972	Bush rats	*R. australis*	Campbell and Domrow (1974)
Ixodes cornuatus[2] Tasmanian paralysis tick	Australia (Gippsland, Victoria) 1993 or earlier.	Dogs, bush rats	Spotted fever group *Rickettsia* species.	Graves et al. (1993)
Bothriocroton (Aponomma)	Australia (Flinders Island), 2001	Snakes, lizards	*R. honei*	Stenos et al. (2003)

hydrosauri[1] Reptile Tick				
Haemaphysalis novaeguineae[1] Tick	Australia (Northern Queensland)		*R. honei*	(Lane et al. 2005), Unsworth et al. (2007b)
Haemaphysalis longicornis[1] Cattle Tick	Vanuatu (Santos Island)	Cattle	No rickettsial DNA found.	Eldin et al. (2011)
Rhipicephalus sanguineus[2] Brown dog tick	Australia (Western Australia), 2006 or earlier.	Dogs, cats	None found	Scholderer et al. (2006)
	New Caledonia (Païta) 2001-2007 Marshall Islands (Kwajalein Atoll), 2010 Guam, 2010 American Samoa, 2012	Dogs	None found	Eldin et al. (2011), Reeves et al. (2012b) Reeves et al. (2012a), Tuten et al. (2013)
	Tahiti, French Polynesia, 2012.	Dogs, cattle	None found	Musso et al. (2014)
Laelaps nuttalli[1] Mite	Marshall Islands (Wake Island), 2010	Pacific rat	*R. heilongjiangensis* (or spotted fever group *Rickettsia* unknown species/strain).	Reeves et al. (2012b)
Leptotrombidium akamushi [d,2] Mite/Chigger	Solomon Islands (Ndende Island), 1975	Pacific rat	*Orienta tsutsugamushi*	Miles et al. (1981)
*Leptotrombidium deliense*s[2] Mite/Chigger	Bat Island, Purdy Islands, Papua New Guinea.	Native rats	*Orienta tsutsugamushi*	Philip and Kohls (1945)
	Vanuatu (Vanua Lava & Mota Lava Island), 1975	Rats-various species	None found	(Miles et al. 1981)
	Australia (North Queensland), 1974 or earlier	Bandicoots, bush rats	*Orienta tsutsugamushi*	Campbell and Domrow (1974)
Ornithonyssus bacoti[1] Mite	Guam, 2010	Black rat	None found	Reeves et al. (2012a)
Ctenocephalides felis[2] Cat Flea	American Samoa, 2012	Dogs	*Rickettsia felis* (or similar species)	Tuten et al. (2013)

	Guam, 2010	Dogs, cats	None found	Reeves et al. (2012a)
	Marshall Islands (Kwajalein Atoll), 2010	Cats	Spotted fever group *Rickettsia* species	Reeves et al. (2012b)
	New Caledonia (Paita), 2010 or earlier Australia (South East Queensland and Katherine Northern Territory), 2013 or earlier	Dogs	*R. felis*	Mediannikov et al. (2011), Hii et al. (2013)
	New Zealand (Palmerston North), 2003 Australia (Western Australia), 2005 or earlier	Dos, cats	*R. felis*	Kelly et al. (2004), Schloderer et al. (2006)
	Australia (Victoria), 2009	Cats	*R. felis*	Williams et al. (2010)
	Australia (Sydney, Melbourne & Brisbane), 2010 or earlier	Cats	*R. felis*	Barrs et al. (2010)
	Tahiti, French Polynesia, 2012	Dogs	No rickettsial DNA found.	Musso et al. (2014)
Xenopsylla cheopsis[2] Oriental rat flea	Hawaii- Oahu, 2004-2007 and Maui 1976	House mice Black, Brown and Pacific rats	*R. typhi* & *R. felis*	Eremeeva et al. (2008), Higa and Broadhurst (1976)
	Guam, 2010	Black rats	No rickettsial DNA found.	(Reeves et al. 2012a)
Echidnophaga gallinacean[1] Sticktight Flea	Australia (Western Australia), 2005 or earlier	Dogs, cats	*R. felis*	Schloderer et al. (2006)
Spilopsyllus cuniculi[1] Rabbit Flea	Australia (Western Australia), 2005 or earlier	Dogs, cats	*R. felis*, - equivocal indentification by PCR.	Schloderer et al. (2006)
Hoplopluera pacifica[2] Tropical Rat Louse	Marshall Islands (Wake Island), 2010	Pacific rat	*R. heilongjiangensis* (or spotted fever group *Rickettsia* unknown species/strain).	Reeves et al. (2012b)
Menopon gallinae[1]	Guam, 2010	Chickens	No rickettsial	Reeves et

Chicken Louse			DNA found.	al. (2012a)
Pediculus humanus capitis[2] Human Head Louse	Guam, 2010	Humans	No rickettsial DNA found.	Reeves et al. (2012a)

[a] If vector species included in this table have not tested positive for a *Rickettsia* species in the Oceania, they have been documented as rickettsial vectors or potential vectors elsewhere in the world.

[b] Published occurrences of vector species in the Pacific without testing for *Rickettsia* not included in this table.

[c] Newly discovered spotted fever group *Rickettsia* spp. found in ectoparasites of native Australian mammals not included in this table (see Unsworth et al. in (Owen et al. 2006), Graves and Stenos (2009), Owen et al. (2006) and Vilcins et al. (2008).

[d] *L.akamushi* is not known to occur in this region (being endemic to Japan), the mite reported is likely to be the congenic species *L.delienses*, since the two species names were used inconsistently to describe either species in the past (Traub and Wisseman Jr. 1968).

[1] Indicates that the arthropod species has not been experimentally shown to transmit rickettsial infection and is a possible vector.

[2] Indicates that the arthropod species has been experimentally shown to transmit rickettsial infection and is a known vector.

Implications of findings

Our review confirms the widespread presence of pathogenic *Rickettsia* spp. and *Orientia tsutsugamushi* within Oceania. Currently, Guam (Reeves et al. 2012a) and French Polynesia (Musso et al. 2014) are the only Pacific Island Countries or Territories where testing for *Rickettsia* spp. have not revealed the presence of the bacteria in at least one vector/reservoir species. Human case reports, at times describing serious illness or fatality, in Australia, New Zealand, Papua New Guinea, Hawaii, Palau, Solomon Islands and Vanuatu demonstrate the threat these pathogens pose to human health in the region. Furthermore, seroprevalence studies in humans and PCR testing of vector/reservoir species from these countries, as well as from New Caledonia, Solomon Islands, Marshall Islands and American Samoa indicate the presence of the pathogens and thus their potential for emergence as causes of human illness, given the right conditions for interactions between humans, bacteria, vectors, hosts, and the environment. Our findings are a cause for concern, and merit further investigation for two reasons.

Firstly, even where rickettsioses are known to be present or endemic, they are under-recognised, particularly in lower income areas with poor access to advanced diagnostic facilities (Parola and Raoult. 2006). Recent evidence from other tropical regions suggests that rickettsioses are a major cause of undifferentiated acute febrile illness. In hospital studies in Laos, Thailand and Nepal, rickettsial infections were found in up to 27% of patients presenting with acute febrile illness (Peacock and Newton. 2008). Similarly, in a Sri Lankan hospital, nearly a third of 58 consecutive patients diagnosed with Chikungunya Fever showed serological evidence of rickettsioses (Premaratna et al. 2011). Understanding of finer scale distribution and prevalence of rickettsioses in Oceania, both spatially and temporally, are needed for improving clinical diagnosis and also for identifying potential drivers of disease emergence.

Secondly, Oceania will increasingly face the combined pressures of climate change, population growth, urbanisation, and globalisation, leading to environmental change and consequent shifts in the ecological interactions underlying the transmission of rickettsioses (see figure 1). A direct relationship between pathogen infectivity and temperature was reported by Policastro et al. (1997), where *R. rickettsia* from ticks kept at 37°C infected guinea pigs, but failed to do so at lower temperatures. Altered climatic conditions are likely to directly affect vector life cycles and abundance. For example, warmer temperatures predicted in all areas of Oceania (Solomon. 2007) may affect vector behaviour, e.g. resulting in more aggressive host seeking and biting behaviours in ticks, as has been shown in the field and experimentally for *Rhipicephalus sanguineus* ticks in Southern France (Parola et al. 2008). In the Southern Pacific region, warming of conditions (Solomon. 2007) may extend the range of murine typhus by improving breeding conditions for flea vectors (Mellanby. 1933). Host abundances and their proximity to humans are also likely to be affected by climate change. Increased climatic variability could drive boom-bust cycles in rodents, as has been observed in ENSO affected regions of Chile (Lima et al. 1999). Tropical cyclones are predicted to become more frequent and intense, resulting in extreme rainfall events (Solomon. 2007). Flooding and natural disasters usually increase human interactions with rodent populations, and creation of disturbed habitats may increase scrub typhus risk well after the event.

The majority of countries and territories in Oceania exhibit a positive population growth rate (CIA World Factbook. 2013). Consequently, natural environments will be increasingly converted to urban and agricultural areas as more land is needed to accommodate and feed growing populations, creating disturbed, rodent-friendly environments and potentially increasing the risk of rickettsioses. The area of agricultural land needed to feed the population may rise not only absolutely, but on a per capita basis, as food security of small island states is diminished by unpredictable rainfall, natural disasters, and the loss of arable land by sea level rise and human activities (FAO. 2008). Population growth will also necessitate a return to subsistence farming (FAO. 2008), engaging a larger proportion of the population in activities where exposure to pathogens is high. Increased subsistence farming and commercial harvesting (e.g. of coconuts) is already being driven by pressure from global market economies (FAO. 2008). In addition, international trade and travel are likely routes of introduction of new pathogens into isolated island nations (Reeves et al. 2012a).

Conclusions

The literature reviewed here revealed that rickettsioses and their causative agents are widespread in Oceania, but possibly under-recognised as causes of potentially serious acute febrile illness. In light of the importance of ecological change on the emergence and transmission of rickettsial diseases, environmental and population changes predicted for Oceania may plausibly increase infection risk. The scenario presents a strong case for gaining a better understanding of the prevalence and drivers of rickettsioses within this region. Continuing human and vector surveys which monitor prevalence more consistently through space and time should accompany the raising of awareness amongst clinicians, as well as an increase in testing of cases of acute febrile illness cases and improved reporting. These require the availability of local diagnostic laboratories and reliable surveillance systems. The reporting of confirmed cases also needs to be coordinated regionally in order to identify trends and drivers from a broad to fine scale approach. Elucidating ecological drivers of a specific rickettsiosis at a local scale calls for the monitoring of vector and host populations on vector-host-environment dynamics and environmental monitoring. Only with such knowledge will it possible to devise appropriately targeted public health interventions, and mitigate any potential emergence of rickettsioses in vulnerable regions such as Oceania.

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APPENDICES

Appendix 1. Search engines and search terms used to find reports of rickettsioses in Oceania.

Search Engine	Disease related search terms	Location or context related search terms used along side disease search terms (separate searches as shown by commas)
Google.com and Google Scholar	'Typhus' + 'Rickettsia' OR 'Spotted fever'	Pacific, Oceania, Micronesia, Melanesia, Polynesia, Australia, Papua New Guinea, Solomon Islands, Fiji, Vanuatu, Hawaii, New Zealand, Guam, New Caledonia, French Polynesia, Cook Islands, Marshall Islands, Palau, Kiribati, Samoa, Tonga, Tuvalu, Niue, Wallis Futuna, Nauru, Northern Marianna, Tokelau, Wake Island.
Google.fr	'Typhus' + 'Rickettsia' OR 'Fièvre pourprée'	Pacifique, Oceanie, Polynesie Française, Nouvelle Caledonie, Wallis et Futuna.
Google.com and Google Scholar	'Typhus' + 'Rickettsia'	Travellers+ Pacific, Travelers + Pacific
Google.com and Google Scholar	'Typhus' + 'Rickettsia'	Military + Pacific

Appendix 2. Resources and administrative bodies whose website were searched for reports of rickettsioses using the search terms 'Rickettsia' + 'Typhus' or 'Spotted Fever'.

Resource/Administrative Body	Website
ProMed	http://www.promedmail.org/
Sectretariat of the Pacific Community Public Health Division	http://www.spc.int/php/
Pacific Public Health Surveillance Network Inform'ACTION Publications	http://www.spc.int/phs/PPHSN/index.htm
Pacific Health Dialog and Pacific Health Voices	http://www.pacifichealthdialog.org.fj/ http://www.pacifichealthvoices.org/
World Health Organisation Western Pacific Region	http://www.wpro.who.int/en/

Annals of Tropical Medicine (Australasian College of Tropical Medicine)	http://www.tropmed.org/publications/annals/index.php
Australian Defence Force Journal	http://www.adfjournal.adc.edu.au/site/
ADF Health Journal	http://www.defence.gov.au/health/infocentre/journals/Topics/i-Infectious_diseases.html
Armée Française de Terre	http://www.defense.gouv.fr/terre
New Zealand Army	http://www.army.mil.nz/
Australia: National Notifiable Diseases Surveillance System 1991-2013	http://www9.health.gov.au/cda/source/cda-index.cfm
PNG Department of Health	http://www.health.gov.pg/
Solomon Islands Department of Health	http://www.pmc.gov.sb/
Government of Vanuatu Ministry of Health	http://www.governmentofvanuatu.gov.vu/index.php/government/health
Direction des Affaires Sanitaires et Sociales de la Nouvelle Caledonie	http://www.dass.gouv.nc/portal/page/portal/dass/observatoire_sante
Government of Guam	http://www.guam.gov/
Samoa Ministry of Health	http://www.health.gov.ws/
Centre for Communicable Disease Control (Hawaii & American Samoa)	http://www.cdc.gov
Republic of the Marshall Islands	http://www.rmigovernment.org/index.jsp
NZ Ministry of Health	http://www.health.govt.nz/
NZ Public Health Observatory	http://www.nzpho.org.nz/NotifiableDisease.aspx
Cook Islands Government	http://www.cook-islands.gov.ck/
L'Etat en Polynesie Francaise	http://www.polynesie-francaise.pref.gouv.fr/
Kiribati Ministry of Health and Medical Services	N/A
Government of Tonga Ministry of Health	http://www.health.gov.to/
Republic of Palau National Government Ministry of Health	http://www.palaugov.net/PalauGov/Executive/Ministries/MOH/MOH.htm
Government of Tuvalu	http://www.tuvaluislands.com/gov_info.htm
Government of Tokelau	http://www.tokelau.org.nz/
The Government of the Republic of Nauru	http://www.naurugov.nr/
Journal of Travel Medicine	http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1708-8305
Travel Medicine and Infectious Disease	http://www.journals.elsevier.com/travel-medicine-and-infectious-disease/