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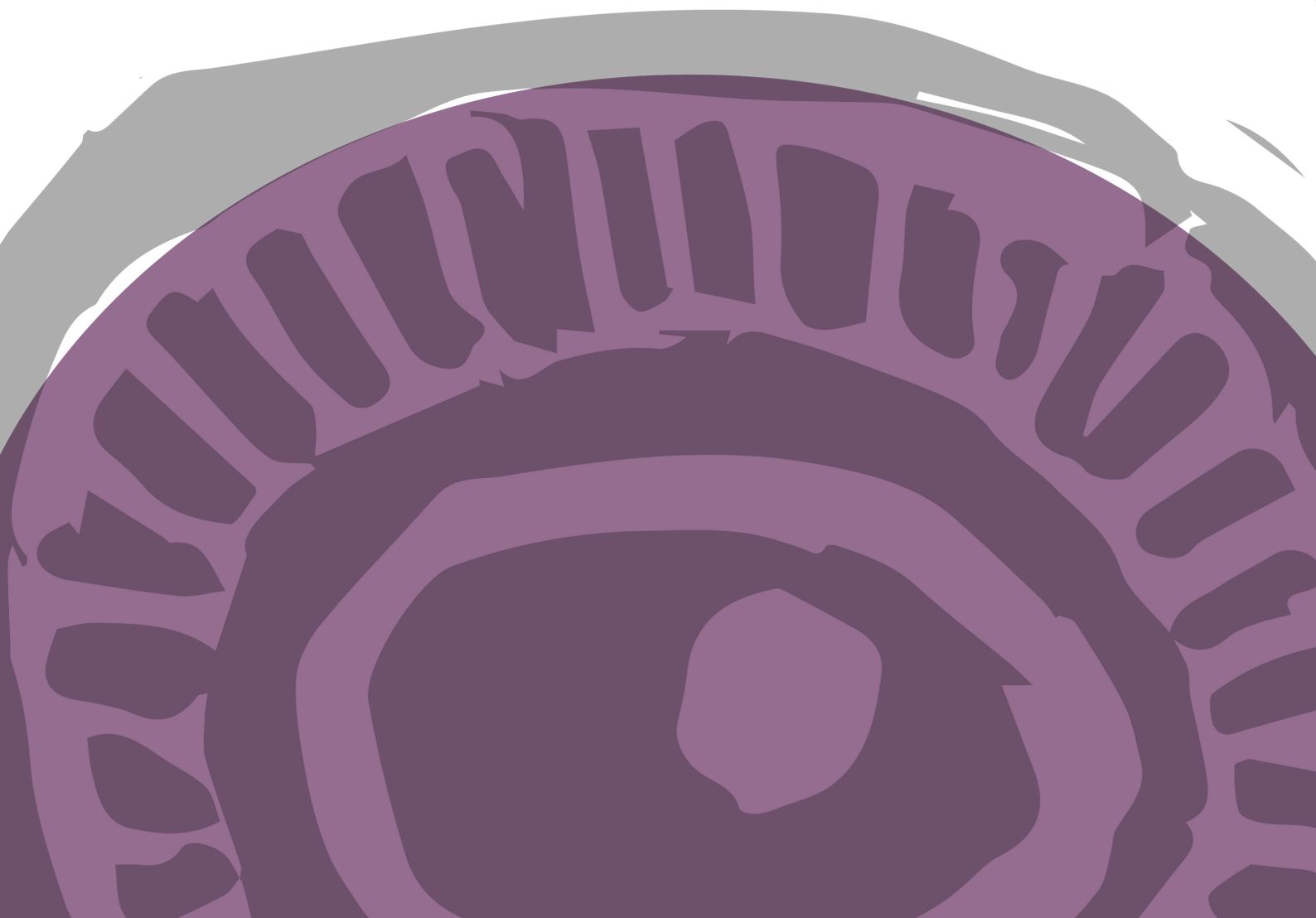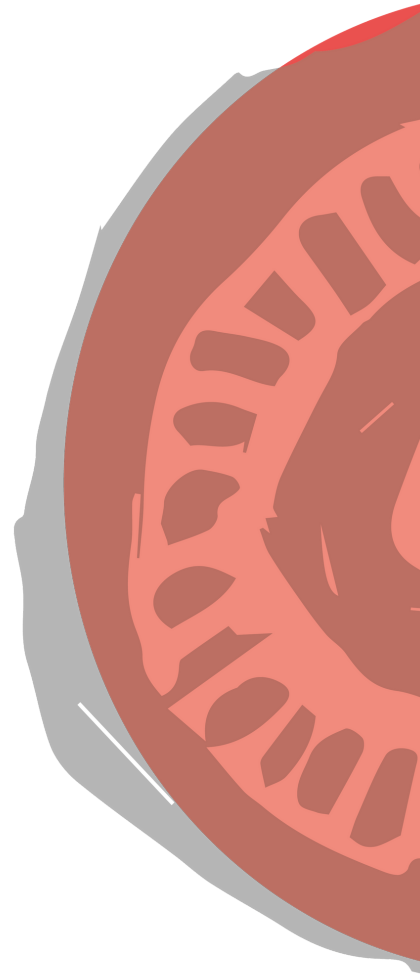## Animal Management in Rural and Remote Indigenous Communities

Canine Vector-Borne Diseases: The Zoonotic Potential of *Anaplasma platys* and *Ehrlichia canis* with a focus on these infections in Australia

A LITERATURE REVIEW BY EMERITUS PROFESSOR PETER IRWIN, COMMISSIONED BY AMRRIC
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Canine Vector-Borne Diseases: The Zoonotic Potential of *Anaplasma platys* and *Ehrlichia canis* with a focus on these infections in Australia
A Review of the Literature

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1. Background

Diseases transmitted by arthropod vectors are of major importance to the health of humans and animals globally. Canine vector-borne diseases (CVBD) result from infections by a heterologous group of organisms including viruses, bacteria, protozoa and helminths, that are transmitted to pet dogs (and wild canids) by a variety of invertebrate vectors including ticks, fleas, mosquitoes, lice, and mites. As well as impacting the health of the dogs, many of these infectious agents are recognised to have zoonotic potential, where the risk of humans infection arises from increased exposure to the vectors in the domestic environment.

As a result of improved diagnostic methods together with inadvertent importations, the list of CVBD in Australia has grown steadily over the last 20 years. In addition to canine babesiosis (*Babesia vogeli*), *Mycoplasma haemocanis*, and heartworm disease (*Dirofilaria immitis*), recent discoveries have included; anaplasmosis (*A. platys*) in 2001 (**Brown et al., 2001**), canine babesiosis caused by *B. gibsoni* was first reported in 2002 (**Muhlnickel et al., 2002**), canine leishmaniasis (*Leishmania infantum*) in 2014 (**Cleary et al., 2014**), and canine hepatozoonosis (*Hepatozoon canis*) in 2018 (**Greay et al., 2018**). Regrettably, the most serious of all CVBD has now been recognised in Australia, canine monocytic ehrlichiosis (*Ehrlichia canis*), prompting concerns across the country about the threat to canine health posed by this new disease.

Both *A. platys* and *E. canis* have been mooted as potentially zoonotic agents in other parts of the world. This review aims to provide an overview of anaplasmosis and ehrlichiosis with a specific focus on these two pathogens and their zoonotic potential, together with a brief review of the ubiquitous brown dog tick and its capacity to transmit disease to dogs and people.

2. The genera *Anaplasma* and *Ehrlichia*

2.1. The genus *Anaplasma* and the genus *Ehrlichia* are classified taxonomically within the family Anaplasmataceae (Class: Alphaproteobacteria; Order: Rickettsiales) – **Figure 1**. These two genera comprise **tick-borne** Gram negative obligate intracellular bacteria that reside within membrane-bound vacuoles ('morulae') in the cytoplasm of blood cells (neutrophils/granulocytes, monocytes or platelets), or endothelial cells of blood vessels.

2.2. *Anaplasma* spp. and *Ehrlichia* spp. are related to *Neorickettsia* spp. (transmitted to vertebrates by helminths), *Wolbachia* spp. (symbionts of invertebrates, mostly insects), and the recently discovered *Candidatus* Neoehrlichia spp. (also tick-associated) (**Figure 2**). Furthermore, these organisms are related to the true 'rickettsial bacteria' comprising three broad groups: Spotted Fever Group Rickettsia (SFGR), the Typhus Group, and the Scrub Typhus Group, each affecting humans.

2.3. Many of these organisms are pathogenic in domestic animals and some are zoonoses. **Table 1** provides an overview of the clinically important *Anaplasma* and *Ehrlichia* spp., however this literature review will focus specifically two species; *Anaplasma platys* and *Ehrlichia canis* and their zoonotic potential (refer to shaded boxes).
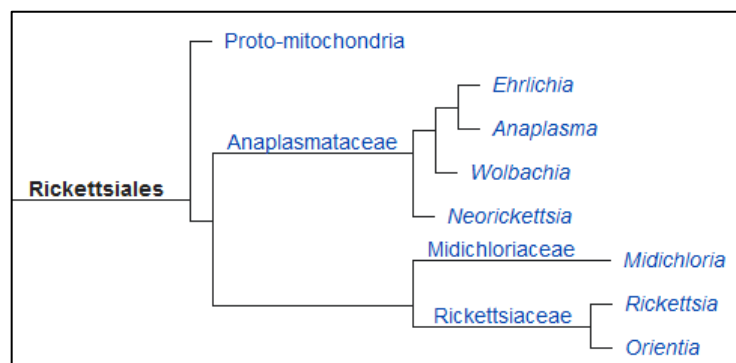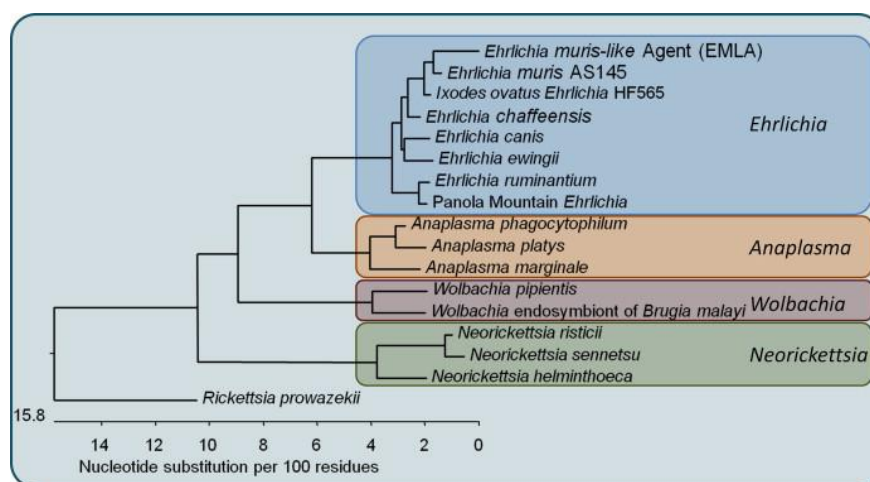
Figure 1

Figure 2

Table 1 – Characteristics of *Ehrlichia* and *Anaplasma* species (adapted from **Rar et al., 2011**)

Species	Infected cell line	Distribution	Primary vectors	Animal hosts	Diseases in animals and Zoonoses, with Comments
Anaplasma phagocytophilum	Granulocytes (neutrophils)	Worldwide (not reported in Australia)	*Ixodes* spp.	Rodents, ruminants, dogs, horses	Tick-borne fever of cattle, equine anaplasmosis, anaplasmosis of dogs and cats, human granulocytic anaplasmosis
*A. marginale**	Erythrocytes	Tropical and subtropical	*Dermacentor* app. *Rhipicephalus* spp.	Wild ruminants, cattle	Anaplasmosis of cattle (severe disease)
*A. centrale**	Erythrocytes	Tropical and subtropical	*Rhipicephalus simus*	Cattle	Anaplasmosis of cattle (mild disease, used as a vaccine vs. *A. marginale*)
A. ovis	Erythrocytes	Europe, USA	*Dermacentor* app. *Rhipicephalus* spp.	Wild ruminants, sheep, goats	Ovine anaplasmosis
*A. bovis***	Monocytes	Africa, S America, Asia	*Amblyomma* spp. *Rhipicephalus* spp. *Hyalomma* spp.	Cattle, buffaloes	Bovine anaplasmosis and infection in multiple other hosts
*A. platys**	Platelets	Worldwide	*Rhipicephalus sanguineus*	Wild canids, dogs	Canine infectious cyclic thrombocytopenia, reported in humans
*E. chaffeensis****	Monocytes	Worldwide	*Amblyomma americanum*	White-tailed deer	Ehrlichiosis in dogs, human monocytic ehrlichiosis
*E. canis**	Monocytes	Worldwide	*R. sanguineus*	Wild canids, dogs	Canine monocytic ehrlichiosis, reported in humans
E. ewingii	Granulocytes	USA, Africa, Asia	*A. americanum*	White-tailed deer, dogs	Ehrlichiosis in dogs and humans
E. muris	Monocytes, macrophages	Europe, USA	*Haemaphysalis* spp. *Ixodes* spp.	Rodents	Murine splenomegaly
E. m. eauclairensis		USA	*Ixodes* spp.	Deer	
E. ruminantium	Endothelial cells, white blood cells	Africa, Caribbean	*Amblyomma* spp.	Wild ruminants, cattle, sheep, goats	Heartwater in ruminants
Candidatus Neoehrlichia mikurensis	Endothelial cells	Eurasia	*Ixodes* spp.	Rodents	Reported in humans
C. N lotoris	Unknown	USA	Unknown	Raccoons	

* Only those with asterisk occur in Australia. ** Variants of *A. bovis* have been detected in Australian ticks (**Gofton et al., 2017** & Section 2.7). *** A case of *E. chaffeensis* infection was detected in a human in Australia, however travel history indicated they had resided in the USA where he was bitten by a tick (**Burke et al., 2015**). Travel history is critical.

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Prof. Peter Irwin: 15 October 2020

2.4. Most human ehrlichiosis and anaplasmosis cases worldwide are caused by *E. chaffeensis* **(human monocytic ehrlichiosis, HME)** and *A. phagocytophilum* **(human granulocytic anaplasmosis/ anaplasmosis)**, respectively (**Rar et al., 2011**). Whilst there is an increasing trend in recorded cases (**Heitman et al., 2016**), total numbers of human ehrlichiosis are approximately 1,000-1,500 annually (in the US), and three-to-four times this number reported for anaplasmosis (**CDC 2020a; 2020b**). *Ehrlichia ewingii* is currently the second most frequently reported form of ehrlichiosis in humans (also recognised, with *E. chaffeensis*, to infect dogs, **Gettings et al., 2020**) and a total of **218** cases of *E. ewingii* ehrlichiosis were reported to CDC from 2008–2018 (**CDC 2020a**). A recently detected form of ehrlichiosis caused by *E. muris eauclairensis* (formerly *E. muris*-like agent – EMLA) is emerging as a new zoonotic pathogen, with < 200 cases reported in the US to date (**CDC, 2020a**).

2.5. The vector ticks of the organisms described in 2.4 **do not exist in Australia** and there are no reliable reports of autochthonous human (or animal) infections with these species in Australia.

2.6. Two organisms, *A. centrale* and *A. marginale*, are known to be present in cattle in Australia, introduced to the continent with cattle and their ticks (*Rhipicephalus australis*, *Haemaphysalis longicornis*) during the last two centuries since European settlement.

2.7. Recent metagenomic analyses has revealed novel *Anaplasma* and *Ehrlichia* spp. in some of Australia's unique ticks (**Gofton et al., 2017**). Their ability (if any) to infect domesticated animals and humans is completely unknown.

3. *Anaplasma platys*

3.1. **Disease in dogs**

3.1.1. *Anaplasma platys* is a canine pathogen that infects host platelets and is the causative agent of canine infectious cyclic thrombocytopenia (CICT). *Anaplasma platys* has a worldwide distribution, closely associated with the geographical range of *Rhipicephalus sanguineus*, the brown dog tick, recently confirmed as its vector (**Snellgrove et al., 2020**). A high prevalence (~20-32%) of *A. platys* is reported in dogs where ticks are abundant (**Brown et al., 2006**).

3.1.2. Infection in dogs is typically subclinical or mild, associated with waxing and waning non-specific clinical signs including; anorexia, weight loss, lethargy, fever (**Little et al., 2010**). Low grade bleeding during surgical procedures and a tendency to bruise after venepuncture are also reported (**Irwin, 2001**). It has been proposed that geographic variations in strains of *A platys* may account, in part, for differences in reported pathogenicity; for example *A platys* infections in some countries appear to be more pathogenic than those seen in Australia (**Bouzouraa et al., 2016**).

3.1.3. The severity of *A. platys* infection is increased by co-infections with other haemotropic tick-borne organisms such as *Babesia vogeli* (**Brown et al., 2006**), *E. canis* (**Gaunt et al., 2010**) and *Hepatozoon canis*; this may explain some of the regional differences (3.1.2) in apparent virulence.

3.1.4. Diagnosis of *A. platys* infection is usually confirmed by a combination of PCR and serology; direct observation of morulae in platelets carries a very low sensitivity.

3.1.5. Treatment of *A. platys* requires doxycycline.

3.1.6. Prevention of canine infectious cyclic thrombocytopenia requires stringent tick prevention. Note: *A. platys* infection can be transmitted from one dog to another via blood transfusion and pre-screening donors for *Anaplasma* spp. (and *E. canis*) is recommended by the American College of Veterinary Internal Medicine (ACVIM) (**Wardrop et al., 2016**).

3.2. *Anaplasma platys* **in Australia**

3.2.1. *Anaplasma platys* infection was first detected in Australia in 2001, in blood samples collected from free-roaming dogs at an Indigenous community in the Tanami desert (**Brown et al., 2001; Irwin, 2001**). (Note that at the time of these reports *A. platys* was classified taxonomically as an ehrlichial species and named *Ehrlichia platys*. Re-description of the Anaplasmataceae family occurred in 2001 as described by **Dumler et al., 2001**).

3.2.2. Since 2001 there have been numerous studies reporting *A. platys* in dogs in Australia (**Brown et al., 2006; Hii et al., 2011; 2012; 2015; Barker et al., 2012; Irwin et al., 2017; Shapiro et al., 2017**), with or without coinfections of *Babesia vogeli*, haemotropic *Mycoplasma* spp. (haemoplasmas), and *Rickettsia felis*.

3.2.3. Cases of canine *A. platys* infection have been detected in the Northern Territory, Queensland, and northern regions of Western Australia and New South Wales, consistent with the distribution of *R. sanguineus* (**Roberts, 1970**). Most studies were located within Indigenous communities.

3.2.4. As noted in 3.1.2, the disease, if any, caused by *A. platys* infections alone in Australia appears to be mild, however infectious and non-infectious comorbidities may contribute risk factors for more severe pathology (**Hii et al., 2015**; **Shapiro et al., 2017**)

3.3. Zoonotic potential of *Anaplasma platys*

3.3.1. The scientific literature contains numerous publications about ***A. phagocytophilum* infections in humans**, however confirmed molecular detection of zoonotic *A. platys* has been the subject of only **three papers** to date (totalling 5 infected persons) (**Maggi et al., 2013**; **Breitschwerdt et al., 2014**; **Arraga-Alvarado et al., 2014**). All three studies originated from the same diagnostic and research facility in North Carolina, USA.

3.3.2. *Anaplasma platys* infection was first reported in a human in 2013 (**Maggi et al., 2013**):

- The patient was a 27-year-old female veterinarian who had worked with companion animals and wildlife in the West Indies (Grenada), South Africa and Ireland. She reported exposure to a variety of ectoparasites during her duties and had been bitten and scratched by several animal patients. Co-infection with *Bartonella henselae* (the cause of cat scratch disease) and *Candidatus* Mycoplasma haematoparvum was also detected in this person.

- The patient exhibited migraine headaches, seizures, including status epilepticus, and other neurological and neurocognitive abnormalities.

- The diagnosis was made by detection of *Anaplasma platys* DNA in blood samples prior to, but not following doxycycline treatment.

3.3.3. A 57-year-old physician and her 16-year-old daughter living in Chicago, USA tested positive to *A. platys* (DNA detection), as well as to two other tick-borne pathogens; *E. ewingii* and *E. chaffeensis*. The family dog was positive to the same three pathogens. Two other family members living in the same household but with less interaction with the dog were negative for these organisms (**Breitschwerdt et al., 2014**):

- Neither person testing positive had symptoms or laboratory abnormalities consistent with anaplasmosis or ehrlichiosis; the mother had reported intermittent subcutaneous oedema and the daughter developed upper body pain. The dog showed aggressive tendencies and each patient (but not other family members) had been bitten at some time prior to testing.

- The detection of three pathogens in these patients was essentially serendipitous since blood samples were submitted as part of a study into bartonellosis. In addition to molecular amplification, inclusions consistent with bacteria or morulae were observed in cell cultures made from the patients' blood samples (and not the other in-contact family), and the DNA of all three organisms was amplified from cultures.

- Cross-contamination of samples could explain these unanticipated findings, however the authors reported that all DNA extraction and PCR-negative controls remained negative throughout testing processes.

3.3.4. Another report of *A. platys* describes two people in Venezuela whose blood samples were positive for intraplatelet inclusions and *A. platys* DNA (**Arraga–Alvarado et al., 2014**):

- Both persons owned dogs with known tick exposure, and one patient reported having been bitten by these ticks (*R. sanguineus*). The dogs in one household were tested for vector-borne pathogens and noted to be seroreactive to *A. platys*.

> - One patient described poor appetite, generalized weakness, muscular pain, fatigue, and occasional headaches; the other patient reported muscular pain, arthralgia, headaches, chills, and insomnia.
> 3.3.5. No cases of human infections with confirmed (i.e. DNA positive) *A. platys* have been reported since 2014. However, no other publications report utilizing a molecular diagnostic strategy in order to specifically detect this organism.
> 3.3.6. A range of symptoms were reported in each of the case reports above, however the authors noted a direct cause-and-effect could not be attributed with certainty to *A. platys* in these people.
> 3.3.7. Assays for *Anaplasma* spp. antibodies often utilise *A. phagocytophilum* antigen (which is readily commercially available), however due to genetic similarity between *Anaplasma* species, serological cross-reactivity occurs between *A. phagocytophilum* and *A. platys* (**Kordick et al., 1999**); seropositivity in some individuals therefore may be attributed to infection with *A. platys* rather than *A. phagocytophilum*, as concluded by **Acosta-Jamett et al. (2020)** during a serosurvey of humans (n=1,105) living in low socio-economic conditions with dog contact in **Chile**, 9.4% of whom were seroreactive.

4. *Ehrlichia canis*

4.1. Disease in dogs

4.1.1. *Ehrlichia canis* causes canine monocytic ehrlichiosis (CME), a serious disease of dogs worldwide, especially in tropical and sub-tropical regions where the tick vector, *R. sanguineus*, is enzootic. Ehrlichiosis in dogs can also be caused by *E. chaffeensis* and *E. ewingii*, however these two agents have a relatively restricted geographical range compared with *E. canis* on account of their vector ticks (**Beall et al., 2012**). The prevalence of *E. canis* infections in dogs in certain environments (low socio-economic tropical urban developments) may be as high as 72% (**Diniz et al., 2008**).

4.1.2. The course of *E. canis* infection in dogs has been described experimentally to occur in three phases; acute, sub-acute and chronic (**Little, 2010**), however the phase of infection for a given canine patient is not generally clear in the field environment. The disease ranges in severity from subclinical to life-threatening, which is further compounded by variations in individual dog or breed-specific immune responses, differences in the dose and strain of pathogen transmitted, presence of coinfecting agents (**Rawangchue & Sungpradit, 2020**), and the overall health of the dog prior to infection (**Little, 2010**).

4.1.3. Clinical abnormalities include fever, anorexia, lethargy, splenomegaly, lymphadenomegaly and bleeding diatheses. Less commonly oedema, ocular lesions, neurological signs and myalgia are reported in dogs (**Little, 2010**). Thrombocytopenia, anaemia, leucopenia or leucocytosis, pancytopenia, hypoalbuminaemia and hyperglobulinaemia (polyclonal gammopathy) are typical clinicopathological abnormalities reported. Persistent pancytopenia in the chronic phase of disease is generally a terminal development, with affected dogs succumbing to sepsis or blood loss.

4.1.4. Diagnosis of *E. canis* infection is usually confirmed by a combination of PCR and serology; a range of in-clinic diagnostic test kits are available worldwide (not Australia) with varying sensitivity and specificity characteristics (**Stillman et al., 2014**). Direct observation of morulae in monocytes is diagnostic but carries a low sensitivity.

4.1.5. The treatment of *E. canis* involves doxycycline or minocycline, with rifampicin also recommended in cases of tetracycline failure (**Mylonakis et al., 2019**). Imidocarb dipropionate is no longer indicated in CME (**Eddlestone et al., 2006**).

4.1.6. Prevention of canine ehrlichiosis requires stringent tick prevention. *Ehrlichia canis* organisms are transmitted by the tick soon (<6 hours) after attachment, so acaricides with strong repellency properties are indicated (**Stanneck & Fourie, 2013**; **Jongejan et al., 2016**)

4.2. *Ehrlichia canis* in Australia

4.2.1. The Australian continent was believed to be free of *E. canis* until the discovery of a cluster of canine cases in Kununurra, Western Australia, in April-May 2020. Prior to this, and at the time of writing, serological testing (IFAT) is a mandatory pre-importation requirement for dogs entering Australia and canine monocytic ehrlichiosis is a notifiable disease in all states and territories.

1.1.1. The conclusions drawn by the authors of a 2001 study screening dogs (n=316) in northern Australia for CME was that "**no evidence of *E canis* infection was confirmed in any of the dogs examined**. **Northern Australia would appear to remain free of this obligate parasite**" (**Mason et al. 2001**). In their study one sample collected from Kununurra had a titre of 1:640. This dog, owned by a veterinarian, was healthy and had not previously exhibited a clinical syndrome indicative of infection with *E canis*. The dog was seronegative when re-bled 1 year later.

1.1.2. Official data about the number of dogs with confirmed CME is not publicly available at the current time, however multiple cases have been diagnosed in Western Australia (Port Hedland, Broome, Kununurra, Halls Creek, Fitzroy Crossing and Perth; and the Northern Territory (Alice Springs, Ti Tree, Katherine, Darwin).

1.1.3. The diagnosis of CME is based on clinical suspicion (4.1.2) and laboratory findings (4.1.3) together with PCR and serological testing through state and Commonwealth (Australian Centre for Disease Preparedness (ACDP), formerly AAHL, Geelong) laboratories. The clinical and clinicopathological abnormalities reported to date by Australian veterinarians are consistent with the range of severe signs and changes reported elsewhere in the world. There are no peer-reviewed publications detailing this outbreak at the current time.

1.1.4. Canine monocytic ehrlichiosis is notifiable in Australia.

1.1.5. Further information is available via State and Territory websites in Western Australia, the Northern Territory, Queensland, and the Commonwealth Government:

Zoonotic potential of *Ehrlichia canis*

1.1.6. To date, *E. canis* infections in people have been reported only from Central or South America.

1.1.7. The first report described the isolation of a microorganism referred to as *E. canis*-like and named as the cause of Venezuelan Human Ehrlichiosis (VHE) (**Perez et al., 1996**):

- The finding arose consequent to a retrospective study of 43 **healthy** (asymptomatic) adult humans living in **Venezuela** who were in contact with dogs exhibiting clinical signs consistent with CME. The degree of contact was not defined. Six out of 11 **dogs** tested by immune-fluorescent antibody test (IFAT) were seropositive to *E. canis* antigen and one of these was positive by PCR for *E. canis* DNA (buffy coat extract). Additionally, six children with febrile illness were tested (the study aimed to investigate ehrlichiosis in people).

- The **human** blood samples were screened by IFAT using antigens of *E. chaffeensis*, *E. canis* and *E. muris*. Only two adults were seropositive (no child tested positive).

- One asymptomatic adult (a 27-year-old female veterinarian - Subject 1) with a weak constant positive titre (1:160/320) to *E. chaffeensis* antigen over one year. This person also had a very low IFAT titre (1:10) to *E. canis* antigen on both occasions and was seronegative to *E. muris*. (The second patient – with higher IFAT titres (>1:1280) to *E. chaffeensis*, *E. canis* & *E. muris* – was lost to follow-up and not retested.)

- A blood sample from this person (Subject 1) was used to isolate and characterise the VHE organism through culture (using a dog-derived macrophage cell line DH82), Western blot (WB) analysis, electron microscopy, in-vivo (mouse) virulence testing, and by 16SrRNA gene PCR and sequence analysis.

- The VHE organism induced mild clinical signs in mice, was ultrastructurally like other *Ehrlichia* spp., and induced a WB reaction pattern similar to serum samples from *E. chaffeensis*-infected human patients in Oklahoma. When compared with data deposited on GenBank, a near-full length (1,434bp) sequence of the 16S rRNA gene of VHE demonstrated single-

nucleotide polymorphisms (SNPs) at positions 199 and 1264, and was determined to be most closely related to *E. canis* Oklahoma.

- On the basis of these observations, the authors suggested that VHE was a new strain or a subspecies of *E. canis* (**Perez et al., 1996**).

1.1.8. In a follow-up study (**Unver et al., 2001**) the Ohio-based team examined the relationship between *E. canis* isolated from dogs and ticks in Venezuela and the VHE isolate above (4.3.1). PCR analysis using *E. canis*-specific primers revealed that 17/55 dog blood samples (31%) and pools of *R. sanguineus* ticks were positive. An ehrlichial agent was isolated and propagated in cell culture from one dog sample and was further analysed to determine its molecular and antigenic characteristics. The 16S rRNA 1,408-bp sequence of the new isolate **was identical to that of the previously reported VHE**.

1.1.9. This same strain of *E. canis* (VHE) was also discovered in a dog with CME in **Southeastern Brazil** (São Paulo) (**Diniz et al., 2008**).

1.1.10. Ten years after the first report of VHE (4.3.1) the same research group (Ohio-based) published a study of 20 humans in Venezuela **showing illness** consistent with ehrlichiosis (fever >39°C, rash, malaise, headache, myalgia, arthralgia, & cytopenia) (**Perez et al., 2006**). Six patients (30%) tested positive by PCR, with the same SNP at position 199, described previously.

- With respect to concerns about the possibility of cross-contamination, the authors noted that their laboratories had not been working with the VHE strain for numbers of years and all negative controls were negative. The Ohio laboratory also ensured the samples being amplified were human specimens by sequencing human-specific DNA (**Perez et al., 2006**).

1.1.11. In a study of 280 **human blood donors** in **Costa Rica**, 10/280 (3.6%) samples yielded DNA with >99-100% genetic similarity to *E. canis* and 35/100 serum samples from the same donor pool were seroreactive to *E. canis* antigen by IFAT. Five donors had relatively high titres (1:1,024-1:8,192 and all five persons were positive for *E. canis* DNA (**Bouza-Mora et al., 2017**).

1.1.12. **Bouza-Mora et al., 2017** also cite a reference to a case of human ehrlichiosis in **Mexico** attributed to *E. canis* (**Silva et al., 2014** – not sighted as the journal is not readily available).

2. The brown dog tick (*Rhipicephalus sanguineus*)

2.1. Overview

2.1.1. The brown dog tick (*R. sanguineus*) is the most widespread tick in the world and a well-recognized vector of many pathogens affecting dogs and occasionally humans.

2.1.2. This tick can be found on dogs living in both urban and rural areas, being highly adapted to live within human dwellings and being active throughout the year not only in tropical and subtropical regions, but also in some temperate areas. Depending on factors such as climate and host availability, *R. sanguineus* can complete up to four generations per year.

2.1.3. Studies have demonstrated that ticks exposed to high temperatures attach and feed on humans and rabbits more rapidly. This observation suggests that the risk of human parasitism by *R. sanguineus* could increase in areas with warmer and/or longer summers, consequently increasing the risk of transmission of zoonotic agents (**Dantas-Torres, 2010**).

2.2. Distribution in Australia

2.2.1. The range of *R. sanguineus* in Australia was described by **Roberts (1970)** to include Western Australia, the Northern Territory and Queensland north of the Tropic of Capricorn (23°26′S).

2.2.2. Recent studies detected brown dog tick populations well to the south of this delineation, with sporadic reports from urban centres in southern Australia (**Greay et al., 2016**).

2.3. Potential role in zoonotic disease transmission

2.3.1. Although the preferred hosts for *R. sanguineus* are dogs, there are numerous reports of this tick biting humans, especially when tick burdens are high in domestic/indoor dwellings.

2.3.2. Zoonotic agents recognised to be transmitted by *R. sanguineus* worldwide include: *Rickettsia conorii*, *R. rickettsii*, *Coxiella burnetii*, *A. platys* and *E. canis* (**Dantas-Torres, 2010**). *Coxiella burnetii*, *A. platys* and (recently) *E. canis* are recognised in Australia.

2.3.3. One example of the role played by *R. sanguineus* in zoonotic disease transmission is the well documented outbreak of **Rocky Mountain Spotted Fever** (*R. rickettsii*) amongst Indigenous Native Americans in Arizona/Sonora, USA, where there was human exposure to heavy tick infestations (**Demma et al., 2006**).

Concluding Remarks

There is little doubt that the recent detection of *E. canis* in Australia will have significant ramifications for canine health in this country. Whilst the full extent of this outbreak is not understood at the time of writing, the continual movement of dogs around the country, travelling with their owners and via commercial or rescue operations, represents a significant risk for the widespread dissemination of CME. Additionally, the capacity of its vector tick to establish in many environments raises further concern about *E. canis* becoming endemic throughout Australia.

The implications of *E. canis* (and *A. platys*) for human health are more difficult to predict. As described in sections 3.3 and 4.3 of this review, the total number of confirmed cases of human ehrlichiosis and anaplasmosis attributed to these organisms number less than a dozen worldwide. Furthermore, there is evidence that for *E. canis* at least, cases in humans are restricted to Central and South America and appear to be associated with a strain of *E. canis* that differs genetically, albeit is a minor way, from most isolates found in dogs in other parts of the world.

We should not ignore the zoonotic potential of these organisms, however. The relative paucity of reported human cases associated with *E. canis* and *A. platys* should be considered with respect to the fact that these organisms are rarely, if ever, screened for by medical diagnostic laboratories, routinely or even during deeper investigations. The fact that most published cases have originated from just two research groups is very pertinent to this consideration. Whilst critics might consider these studies irrelevant or, worse, attribute them to laboratory failures such as contamination, we should be careful not to dismiss them. Increasingly, animal-associated pathogens have been recognised for their ability to cause illness in people – the recent case of a haemoplasma infection in Queensland, in a person with extensive animal contact is a case in point (**Alcorn et al., 2020**).

It would seem prudent to remain vigilant for unexplained febrile illnesses in people who live closely with dogs, especially where ectoparasite control measures are suboptimal, when tick burdens are consequently high.

References:

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[1] Not prophetic, the taxonomy of *A. platys* was at this time still attributed to the genus *Ehrlichia*.

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[2] The title of the paper refers to "a man", yet the results clearly describe Subject 1 as female.