Vector-Borne Diseases & Treatment

Chapter 3

The Occurrence of Two Different *Rickettsial* Pathogens in Eastern Texas

***Robert J Wiggers*[1]*; *Sarah Canterberry*[1]**

[1]*Department of Biology, Stephen F. Austin State University, Nacogdoches, TX 75901*

***Correspondence to: Robert J Wiggers,** Department of Biology, Stephen F. Austin State University, Nacogdoches, TX 75901.*

Email: rwiggers@sfasu.edu

1. Introduction

Zoonotic diseases are defined as diseases that are transmitted from vertebrate animals to humans, either by direct contact with an infected animal or via a vector [1,2] The pathogenic organism may be part of the commensal flora of the animal, causing no apparent disease, but can be detrimental to animal or human populations that have had no previous exposure [1]. Changes in human behavior, ecologic issues, and economic issues, have lead to the emergence of new, and the reemergence of existing, infectious diseases [3]. Many zoonotic agents are viruses, but bacteria and parasites have also been implicated in key food and waterborne outbreaks [4].

Domestic animals, such as pets and farm animals, are the most frequent sources of zoonotic diseases [1]. In the US, over 160 million dogs and cats are kept as pets (Humane Society Website), and more than 30 human diseases can be acquired from them although none are common [1]. Other domestic animals can be reservoirs for zoonotic diseases like brucellosis (cattle, sheep, pigs, and goats), anthrax (cattle and sheep), and salmonellosis (chickens, turkeys, rodents, and reptiles) [1]. Developments in disease control have led to a decrease in the number of cases of some zoonotic diseases, such as rabies. All states have some minimal requirement that pets be vaccinated [5] and numerous techniques exist to control the spread of rabies in populations of feral animals as well [6]. The US documents about 5 cases per year, but it is estimated that there may be almost 60,000 human cases per year worldwide [7]. In this paper we examine the occurrence of two different arthropod borne zoonotic pathogens – *Rickettsia typhi* (causal organism, murine typhus and *Rickettsia parkerii* (causal organism,

Tidewater fever) in east Texas. Both of these diseases are caused by members of the Rickettsia genus. Many members of the genus Rickettsia are pathogenic in humans and are generally divided into three broad groups: the Spotted Fever Group (SFG), the Typhus Group (TG), and the Scrub Fever Group (SF). With a world-wide distribution, these pathogenic bacteria cause a number of febrile illnesses with varying degrees of severity.

2. Murine Typhus

Rickettsia typhi is a small (0.4x1.3 μm), Gram-negative, obligate intracellular bacterium that causes murine typhus [8]. Because the symptoms of murine typhus are very much like those of "an array of other infectious diseases" [8], it is frequently unrecognized and / or misdiagnosed. It has been misdiagnosed as dengue fever [9], Brazilian spotted fever [10], and sub-acute meningitis [11]. Many times murine typhus is unreported [12] due to misdiagnosis; it has been said that for every person who is reported to have murine typhus, at least four other cases are unreported. This leaves the actual number of cases that occurs a mystery [8].

The incubation period of murine typhus is six to fourteen days [8]. The clinical profile of the disease includes a high fever (40 to 41 o C), headache, general pain, weakness, and sometimes, a rash on the trunk [8]. Respiratory difficulties also occur, but decrease as soon as the convalescent period starts.In rare cases, mild central nervous system manifestations can appear [11]. Murine typhus is normally mild, but the disease can be serious or fatal [12]. Old age, delayed diagnosis, pre-existing hepatic or renal dysfunction, or pre-existing pulmonary compromise are correlated with the severity of murine typhus. About 10% of patients are hospitalized [13] and 3% to 4% of patients die [12].

Murine typhus is one of the most common rickettsial infections of man; it occurs on every continent, except Antarctica, and in a range of environmental conditions [8]. It was first described in the US in 1913, and was most prevalent in the southeastern states [14]. Today, murine typhus is only endemic in southern California, Texas – where Nueces county and Corpus Christi have the greatest reported cases [15, 16] and Hawaii [17].

The classic vector for murine typhus is the rat flea (*Xenopsylla cheopis*) that parasitize roof rats (*Rattus rattus*) and Norway rats (*R. norvegicus*). In southern California and south central Texas, this host/vector system was reassessed following epidemiological studies that implied a change had occurred [13]. In Texas and California, R. typhi is now maintained in oposums, *Didelphis virginiana*, and the vector is the cat flea, *Ctenocephalides felis* [13]. In Hawaii, the classic rodent – flea cycle is still suspected [17]. In one study by Wiggers and Stewart from east Texas, almost 16% of individuals were seropositive for R. typhi; none had ever reported being officially diagnosed with murine typhus [18]. A very similar rickettsial organism, *Rickettsia felis*, is also implicated in causing a disease clinically indistinguishable from classic R. typhi murine typhus [19]. *R. felis* has been found in the same host / vector system as *R. typhi*

and is, in fact, more common in this system than *R. typhi* [20]. Desipte this, another study by Wiggers and Stewart found that of those same 16% of individuals seropositive from the first study [19], none were seropositive when tested against a recombinant antibody specific for *R. felis* [21].

Over the past decade the number of reported cases in Texas has climbed dramatically from under 100 in 2004 to over 500 in 2017 [22]. When looking distribution by county, in 2003, cases of murine typhus were restricted to nine counties in southern Texas, with Nueces county (Corpus Christi) having the most cases [23]. By 2013, cases had been reported in 41 counties [23]. Southern Texas, again specifically Nueces county still accounted for the most cases, but new emerging hot spots were seen moving up in to central and west central Texas, including Travis county (Austin), southeastern Texas, including Harris and Galveston counties (Houston and Galveston, respectively) [23]. The data collected by Wiggers and Stewart [18] indicated that, although not officially diagnosed, residents of counties in north and central east Texas (Smith, Nacogdoches, and Angelina) were also being exposed. In short, murine typhus has expanded in Texas beyond its traditional endemic area of southern Texas. It's new range now includes not only central Texas but east Texas as well.

The reasons for this spread are not clear. In Houston the homeless population has been found to have a high seropositive rate to primarily *R. typhi* but also *Rickettsia prowazekii* [24]; it has been suggested these individuals, by virtue of living outdoors, are exposed far more frequently to Rickettsia positive vectors. Others have suggested that the "new" expansion of murine typhus may not be new but reflects better recognition and diagnosis by physicians [23]. Another possibility involves the changing host / vector ecology of murine typhus: with the cat flea becoming the primary vector, many more people may find themselves exposed via their pets.

3. Tick Borne Rickettsioses

In the United States, Spotted Fever rickettsioses, a broad group that includes Rocky Mountain Spotted Fever, are reported to the CDC. By 2013 almost 3200 suspected cases of Spotted Fever rickettsioses were reported [25]. Over the past number of years, it has become apparent that a number of pathogenic *Rickettsial* species, potentially causing SFG type clinically illness, are circulating within the tick populations of the United States. *Rickettsia parkerii*, a known human pathogen, has been found in much of the southeastern U.S., including Texas [26]. Ticks in Texas have also been found to carry *Rickettsia monacensis*, the causal organism of Mediterranean Spotted Fever. Another *rickettsia*, of currently unknown pathogenicity, Candidatus *R. andeanae*, has been found widely distributed in ticks [27,28]. Choosing to focus on *R. parkerii*, causal organism of Tidewater Fever, we initially collected a large number of ticks from Nacogdoches county in east Texas. Utilizing PCR to detect both Rickettsia sp in general

and R. parkerii in particular, almost 71% of ticks were found to be positive for the presence of a rickettsial species [29]. Additionally, of those ticks identified as *Amblymomma maculatum* (the only known host of *R. parkerii*), 17% were PCR positive for *R. parkerii* [29]. Based upon these results, we concluded that if a person encounters a tick in east Texas, it is most likely carrying some kind of *Rickettsia* and a person that presents with a febrile illness AND reports an encounter with a tick, they should be presumptively treated with antibiotics without waiting for confirmatory laboratory results. Additional data for eastern Texas is lacking and would present fertile ground for an epidemiological study.

The only known vector for *R. parkerii* is the Gulf Coast tick, *A. maculatum*. In 1936 it was suggeted that *A. maculatum* required high humidity and rainfall, typically associated with coastal habitats, to survive [30] however it is now well established that permanent populations of *A. maculatum* exist well inland in coastal states from Texas to Rhode Island as well in states with no coastline at all, including Arkansas, Tennessee, Oklahoma, Kansas, and Kentucky [31]. This suggests that the potential for exposure to *R. parkerii* is much greater than previously thought and would explain why cases were occurring in states that were not originally recognized as home to the vector as well as why *R. parkerii* was detected in east Texas, well away from a coastal habitat.

4. References

1. Yu, V.L. (1999) Zoonoses In: Microbial Disease, 3rd ed., M. Schaechter, N.C. Engleberg, B.I. Eisenstein & G. Medoff, eds. Baltimore, Lippincott Williams & Wilkins, p. 643-650.

2. Jaffry, K.T., Ali, S, Rasool, A., Raza, A., and Gill, Z.J. (2009) Zoonoses. International Journal of Agriculture and Biology. 11(2): 217–220

3. Azad A.F., Radulovic S., Higgins J.A., Noden B.H., and Troyer J.M. (1997) Flea-borne rickettsioses: ecologic considerations. Emerging Infectious Disease. 3(3):319-327.

4. Meslin, F.X. (1997) Global aspects of emerging and potential zoonoses: a WHO perspective. Emerging Infectious Disease. 3: 223-228.

5. AVMA. www.avma.org

6. Rosatte, R. (2011) Evolution of Wildlife Rabies Control Tactics. Advances in Virus Research. 79:397-419

7. World Health Organization. www.who.int/rabies/epidemiology/en/

8. Azad, A.F., (1990) Epidemiology of murine typhus. Annual Review of Entomology. 35: 553-569.

9. Zavala-Velaquez, J.E., Yu, X., and Walker, D.H. (1996) Unrecognized spotted fever group rickettsiosis masquerading as dengue fever in Mexico. American Journal of Tropical Medicine and Hygiene. 55:157-159.

10. Oliveria, R.P., Galvao, M.A.M., Mafra, C.L., Chamone, C.B., Calic, S.B., Silva, S.U., and Walker, D.H. (2002) Rickettsia felis in Ctenocephalides spp. fleas, Brazil. Emerging Infectious Disease. 8:317-319

11. Galanakis, E., Gikas, A., Bitsori, M. and Sbyrakis, S. (2002) Rickettsia typhi infection presenting as sub-acute men-

ingitis. Journal of Child Neurology. 17:456-457.

12. Dumler, J.S., Taylor, J.P., and Walker, D.H. (1991) Clinical and laboratory features of murine typhus in South Texas, 1980 through 1987. JAMA 266:1365-1370.

13. Schriefer, M.E., Sacci, J.B., Taylor, J.P., Higgins, J.A. & Azad, A.F. (1994) Murine typhus: updated roles of multiple urban components and a second typhus-like rickettsia. Journal of Medical Entomology. 31:681-685.

14. Adam, W.H., Emmons, R.W., and Brooks, J.E. (1970) The changing ecology of murine (endemic) typhus in southern California. American Journal of Tropical Medicine and Hygiene. 19:311-318.

15. Azad, A.F., Radulevic, S., Higgins, J.A., Noden, B.H. & Troyer, J.M. (1997) Flea-borne rickettsioses: ecologic considerations. Emerging Infectious Disease. 3:319-327.

16. Holez, P. (2018) PLOS The rise of neglected tropical diseases in the “new Texas”. PLOS Neglected Tropical Diseases. 12(1)

17. Civen, R. and Ngo, V. (2008) Murine typhus: an unrecognized suburban vectorborne disease. Clinical Infectious Disease. 46(6):913-916.

18. Wiggers, R.J. and Stewart, R.S. (2002) Ownership of cats or dogs does not increase exposure to Rickettsia typhi. Texas Medicine. 98, 56-57.

19. Schriefer, M.E., Sacci J.B. Jr., Dumler, J.S., Bullen, M.G., and Azad, A.F. (1994) Identification of a novel rickettsial infection in a patient diagnosed with murine typhus. Journal of Clinical Microbiology. 32:949-954.

20. Boostrom, A., Beier, M.S., Macaluso, J.A., Macaluso, K.R., Sprenger D., Hayes J., Radulovic, S., and Azad, A.F. (2002) Geographic association of Rickettsia felis-infected opossums with human murine typhus, Texas. Emerging Infectious Diseases. 8:549-554.

21. Wiggers, R.J., Martin, M.C., and Stewart, R.S.(2005) Rickettsia felis infection in an east Texas population. Texas Medicine. 101:56-58.

22. Shuford, J., Hunt, P., and Mayes, B. (2018) Changing epidemiology of murine typhus in Texas. Open Forum Infectious Diseases. 5:S242.

23. Murray, K.O., Evert, N., Mayes, B., Fonken, E., Erickson, T., Garcia, M.N., and Sidwa, T. (2017) Typhus Grop Rickettsiosis, Texas, USA, 2003-2013. Emerging Infectious Diseases. 23(4):645-648.

24. Reeves, W.K., Murray, K.O., Meyer, T.E., Bull, L.M., Pascua, R.F., Holmes, K.C., and Loftis, A. (2008) Serological evidence of typhus group rickettsia in a homeless population in Houston, Texas. Journal of Vector Ecology. 33(1):205-207.

25. CDC. (2015) Summary of notifiable infectious diseases – United States, 2013. MMWR. 62:1-118.

26. Paddock C.D., Summer J.W., Comer J.A., Zaki S.R., Goldsmith C.S.,Goddard, J., McLellan, S.L.F, Tamminga, C.L., and Ohl, C.A. (2004) Rickettsia parkeri: A newly recognized cause of spotted fever rickettsiosis in the United States. Clinical Infectious Disease. 38: 805-811.

27. Fornadel CM, Zhang X, Smith JD, Paddock CD, Arias JR, and Norris, D.E. (2011) High rates of Rickettsia parkeri infection in gulf coast ticks (Amblyomma maculatum) and identification of “Candidatus Rickettsia andeanae” from Fairfax County, Virginia. Vector Borne Zoonotic Dis 11: 1535-1539.

28. Paddock C.D., Denison A.M., Dryden M.W., Noden B.H., Lash R.R., Abdelghani, S., Evans, A.E., Kelly, A. R., Hecht, J. A., Karpathy, S.E., Ganta, R.R., and Little, S.E. (2015) High prevalence of “Candidatus Rickettsia andeanae”

and apparent exclusion of Rickettsia parkeri in adult Amblyomma maculatum (Acari: Ixodidae) from Kansas and Oklahoma. Ticks and Tick-Borne Dis 6: 297-302.

29. Canterberry, S., Bennett, D., and Wiggers, R.J. (2015). The frequency of ticks carrying Rickettsia sp. Bacteria in eastern Texas. Archives of Medicine. 6:1-3.

30. Bishopp, F.C., and Hixson, H. (1936) Biology and economic importance of the Gulf Coast tick. Journal of Economic Entomology. 20:1068-1076.

31. Paddock, C., and Goddard, J. (2015) The evolving medical and veterinary importance of the Gulf Coast tick (Acari: Ixodidae). Journal of Medical Entomology. 52(2):230-252.