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A review on rickettsiosis

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Abstract

Rickettsial genera contain several species that are pathogenic to man and animals. Members of the genus *Rickettsia* are transmitted by ticks, lice fleas etc. These organisms are responsible number of important zoonotic diseases in humans such as Q fever, Rocky Mountain Spotted Fever etc. This review discusses the main aspects of rickettsiosis and the prevention and control of the same.

Keywords: rickettsia, epidemiology, prevention

1. Introduction

Rickettsial infections are caused by various bacterial species from the genera *Rickettsia*, *Orientia*, *Ehrlichia*, *Neorickettsia*, *Neoehrlichia*, and *Anaplasma*. *Rickettsia* spp. are classically divided into the typhus group and spotted fever group (SFG). *Orientia* spp. makes up the scrub typhus group. The rickettsial pathogens most likely to be encountered during travel outside the United States include *R. africae* (African tick-bite fever), *R. conorii* (Mediterranean spotted fever), *R. rickettsii* (known as both Rocky Mountain spotted fever and Brazilian spotted fever), *O. tsutsugamushi* (scrub typhus), and *R. typhi* (murine or fleaborne typhus).

2. Transmission

Most rickettsial pathogens are transmitted by ectoparasites such as fleas, lice, mites, and ticks. Organisms can be transmitted by bites from these ectoparasites or by inoculating infectious fluids or feces from the ectoparasites into the skin. Inhaling or inoculating conjunctiva with infectious material may also cause infection for some of these organisms. The specific vectors that transmit each rickettsial pathogen are listed in Table 1. Transmission of some rickettsial diseases after transfusion or organ transplantation is rare but has been reported.

3. Epidemiology

All age groups are at risk for rickettsial infections during travel to endemic areas. Both short and long-term travelers are at risk for infection. Transmission is increased during outdoor activities in the spring and summer months when ticks and fleas are most active; however, infection can occur throughout the year. Because of the 5- to 14-day incubation period for most rickettsial diseases, tourists often do not experience symptoms during their trip, and disease onset may coincide with their return home or develop within a week after returning. Although the most commonly diagnosed rickettsial diseases in travelers are usually in the spotted fever or typhus groups, travelers may acquire a wide range of rickettsioses, including emerging and newly recognized species (Table 1).

Tickborne spotted fever rickettsioses are the most frequently reported travel-associated rickettsial infections. Those who go on safari—especially those walking in the bush, game hunters, and ecotourists in southern Africa—are at risk for African tick-bite fever, which consistently remains the most commonly reported rickettsial infection acquired during travel. Mediterranean spotted fever is less commonly reported but occurs over an even larger region, including much of Europe, Africa, India, and the Middle East. Rocky Mountain spotted fever (also known as Brazilian spotted fever and other local names) is reported throughout much of the Western Hemisphere, including Canada, the United States, Mexico, and several countries in Central and South America including Argentina, Brazil, Colombia, Costa Rica, and Panama.

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Clusters of illness may be reported in families or in geographic areas. Contact with dogs in rural and urban settings and outdoor activities such as hiking, hunting, fishing, and camping increase the risk of infection.

Scrub typhus, which is transmitted by trombiculid mites encountered in high grass and brush, is endemic in northern Japan, Southeast Asia, the western Pacific Islands, northern Australia, China, maritime areas, and several parts of south-central Russia, India, and Sri Lanka. More than 1 million cases occur annually. Most travel-acquired cases of scrub typhus occur during visits to rural areas in endemic countries for activities such as camping, hiking, or rafting, but urban cases have also been described.

R. typhi and *R. felis*, which are transmitted by fleas, are widely distributed, especially throughout the tropics and subtropics and in port cities and coastal regions with rodents. Humans exposed to flea-infested cats, dogs, and peridomestic animals while traveling in endemic regions, or who enter or sleep in areas infested with rodents, are at most risk for flea-borne rickettsioses. Murine typhus has been reported among travelers returning from southeastern Asia, Africa, and the Mediterranean Basin. In the United States, most cases are reported from Hawaii, California, and Texas.

R. akari, the causative agent of rickettsialpox, is transmitted by house-mouse mites, and circulates in mainly urban centers in Ukraine, South Africa, Korea, the Balkan states, and the United States. Outbreaks of rickettsialpox most often occur after contact with infected rodents and their mites, especially during natural die-offs or exterminations of infected rodents that cause the mites to seek out new hosts, including humans. The agent may spill over and occasionally be found in other wild rodent populations.

Epidemic typhus caused by *R. prowazekii* infection is rarely reported among tourists but can occur in impoverished communities and refugee populations where body lice are prevalent. Outbreaks often occur during colder months.

Travelers at most risk for epidemic typhus include those who may visit areas with large homeless populations, impoverished areas, refugee camps, and regions that have recently experienced war or natural disasters. Active foci of epidemic typhus are known in the Andes regions of South America and some parts of Africa (including but not limited to Burundi, Ethiopia, and Rwanda). Louseborne epidemic typhus does not regularly occur in the United States, but a zoonotic reservoir occurs in the southern flying squirrel, and sporadic sylvatic typhus cases are reported. Tick-associated reservoirs of *R. prowazekii* have been described in Ethiopia, Mexico, and Brazil, but the role of ticks in the natural transmission of *R. prowazekii* has not been characterized.

Ehrlichiosis and anaplasmosis are tickborne infections most commonly reported in the United States. A variety of species are implicated in infection, but *E. chaffeensis* and *A. phagocytophilum* are most common. Infections with various *Ehrlichia* and *Anaplasma* spp. have also been reported in Europe, Asia, and South America. *Neoehrlichia mikurensis* is a tickborne pathogen that occurs in Europe and Asia and perhaps in Africa. Sennetsu fever, caused by *Neorickettsia sennetsu*, occurs in Japan, Malaysia, and possibly other parts of Asia. This disease can be contracted from eating raw infected fish.

4. Clinical Presentation

Rickettsioses are difficult to diagnose, even by health care providers experienced with these diseases. Most symptomatic

rickettsial diseases cause a moderately severe illness, but some, such as Rocky Mountain spotted fever, Mediterranean spotted fever, scrub typhus, and epidemic typhus, may be life threatening and can be fatal in 20%–60% of untreated cases, so prompt treatment is essential.

Clinical presentations vary with the causative agent and patient; however, common symptoms that typically develop within 1–2 weeks of infection include fever, headache, malaise, rash, nausea, and vomiting. Many rickettsioses are accompanied by a maculopapular, vesicular, or petechial rash or sometimes an eschar at the site of the tick bite. African tick-bite fever is typically milder than some other rickettsioses, but recovery is improved with treatment. It should be suspected in a patient who presents with fever, headache, myalgia, and an eschar (tache noir) after recent travel to southern Africa. Mediterranean spotted fever is a potentially life-threatening rickettsial infection and should be suspected in patients with rash, fever, and eschar after recent travel to northern Africa or the Mediterranean. Rocky Mountain spotted fever is frequently characterized by fever, headache, nausea, and abdominal pain; a rash is commonly reported, but eschars are not. Scrub typhus should be suspected in patients with a fever, headache, and myalgia after recent travel to Asia; eschar, lymphadenopathy, cough, and encephalitis may be present. Patients with murine or epidemic typhus usually present with a severe but nonspecific febrile illness, and approximately half will also present with a rash. Ehrlichiosis and anaplasmosis should be suspected in febrile patients with leukopenia and thrombocytopenia and mild to moderately elevated levels of hepatic transaminases.

5. Diagnosis

Diagnosis is usually based on clinical recognition and serology. Serologic testing provides stronger evidence when acute- and convalescent-phase serum samples are compared; a ≥ 4 -fold rise in titer is diagnostic. PCR assays and immunohistochemical analyses may also be helpful, but useful results are highly dependent upon the specimen submitted. If an eschar is present, a swab or biopsy sample of the lesion can be evaluated by PCR and provides a species-specific diagnosis. If ehrlichiosis or anaplasmosis is suspected, PCR of a whole-blood specimen provides the best diagnostic test. A buffy coat may provide presumptive evidence of infection if examined to identify characteristic intraleukocytic morulae. Contact the CDC Rickettsial Zoonoses Branch at 404-639-1075 for further information. Ehrlichiosis, anaplasmosis, and spotted fever rickettsiosis are nationally notifiable diseases.

6. Treatment

Treatment of patients with possible rickettsioses should be started when disease is suspected and should never await confirmatory testing, as certain infections can be rapidly progressive. Immediate empiric treatment with a tetracycline, most commonly doxycycline, is recommended for all ages. Almost all other broad-spectrum antibiotics are not helpful. Chloramphenicol may be an alternative in some cases, but its use is associated with more deaths, particularly for *R. rickettsii*. In some areas, tetracycline-resistant scrub typhus has been reported. Azithromycin may be an effective alternative. *Anaplasma phagocytophilum* infections may respond to rifampin, which may be an alternate drug for pregnant patients. Expert advice should be sought if alternative agents are being considered.

7. Prevention

No vaccine is available for preventing rickettsial infections. Antibiotics are not recommended for prophylaxis of rickettsial diseases and should not be given to asymptomatic people.

Travelers should be instructed to minimize exposure to biting arthropods during travel (including lice, fleas, ticks, mites)

and to animal reservoirs (particularly dogs) when traveling in endemic areas. The proper use of insect or tick repellents on skin or clothing, self-examination after visits to vector-infested areas, and wearing protective clothing are ways to reduce risk. These precautions are especially important for people with underlying conditions that may compromise their immune systems, as these people may be more susceptible to severe disease.

Table 1: Zoonotic diseases caused by members of family Rickettsiaceae

Genus	Group	Species	Disease (s)	Arthropod(s) involved	Animal Reservoir(s)	Distribution
Anaplasma		<i>Anaplasma phagocytophilum</i> <i>A. platys</i> <i>A. ovis</i> "A. capra"	Human anaplasmosis	Tick	Small mammals, rodents, deer Dogs Sheep Goats	Primarily United States, worldwide Venezuela Cyprus, Iran China
Ehrlichia		<i>Ehrlichia chaffeensis</i> <i>E. muris</i> <i>E. ewingii</i> <i>E. canis</i>	Human ehrlichiosis	Tick	Deer, wild and domestic dogs, domestic ruminants, rodents	Common in United States, possibly worldwide
Neoehrlichia		<i>Neoehrlichia mikurensis</i>	Neoehrlichiosis	Tick	Rodents	Europe, Asia
Neorickettsia		<i>Neorickettsia sennetsu</i>	Sennetsu fever, Neorickettsiosis	Tick	Fish	Japan, Malaysia, possibly other parts of Asia
Coxiella	Q fever	<i>C. burnetti</i>	Q fever	<i>Haemophysalis spinigera</i> , <i>H. turturis</i> , <i>H. kinneari</i> , <i>Rhipicephalus sanguineus</i> , <i>Hyalomma intermedia</i>		Worldwide
Orientia	Scrub typhus	<i>O. tsutsugamushi</i>	Scrub typhus	<i>Leptotrombidium deliense</i> (Larval mite)	Rodents	Asia-Pacific region from maritime Russia and China to Indonesia and North Australia to Afghanistan
Rickettsia	Typhus group	<i>R. typhi</i>	Murine typhus, flea-borne typhus	<i>Xenopsylla cheopis</i>	Rodents	Tropical and subtropical areas worldwide
		<i>R. prowazekii</i>	Epidemic typhus (Brillzinser disease), Sylvatic typhus	<i>Pediculus humanus corporis</i>	Humans, flying squirrels	Central Africa; Asia; Central, North and South America
	Spotted fever group (SFG)	<i>R. felis</i>	Cat flea rickettsiosis	<i>Ctenocephalides felis</i>	Domestic cats, rodents, opossums	Europe, North and South America, Africa, Asia
		<i>R. rickettsii</i>	Rocky mountain spotted fever, Brazilian spotted fever	<i>Dermacenter variabilis</i> , <i>D. andersoni</i> , <i>Rhipicephalus sanguineus</i>	Rodents	North, Central and South America
		<i>R. conorii</i>	Indian tick typhus, Israeli spotted fever, Mediterranean spotted fever, Artraskan spotted fever, Boutonneuse fever	<i>Rhipicephalus sanguineus</i> and other ticks mentioned in Q fever	Dogs, rodents	India, Southern Europe, Southern and Western Asia, Africa
		<i>R. akari</i>	Rickettsial pox	<i>Allodemyssus sanguineus</i>	House mice, wild rodents	South Africa, Korea, Turkey, United states, Balkan countries, Russia
		<i>R. arifraicae</i>	African tick bite fever	<i>Amblyomma hebraeum</i>	Ruminants	Sub Saharan Africa, West Indies
		<i>R. australis</i>	Queensland tick typhus	<i>Ixodes holocyclus</i>	Rodents	Australia, Tasmania
		<i>R. japonica</i>	Japanese tick typhus	<i>Haemophysalis longicornis</i>	Rodents	Japan
		<i>R. honei</i>	Finders island tick typhus, Thai tick typhus	Unknown	Rodents, reptiles	Australia, Thailand, Finders island (Tasmania)
		<i>R. sibirica</i>	North Asia tick typhus, Siberian tick typhus	<i>Dermacenter nuttalli</i>	Rodents	N. China, Pakistan, Siberia, Armenia
<i>Haemophysalis concinna</i>						
<i>R. sibirica</i>	Lymphangitis	<i>Hyalomma asiaticum</i> in	Rodents	Southern France,		

		<i>mongolotimonae</i>	associated rickettsiosis	1996		Portugal, China, Africa
		<i>R. slovacae</i>	Tickborne lymphadenopathy (TIBOLA)	<i>Dermacentor marginatus</i>	Lagomorphs, rodents	Southern and eastern Europe, Asia
		<i>R. heilongjiangensis</i>	Far eastern spotted fever	Tick	Rodents	Far east of Russia, Northern China, Eastern Asia
		<i>R. helvetica</i>	Aneruptive fever	Tick	Rodents	Central and Northern Europe, Asia
		<i>R. monacensis</i>	Mediterranean spotted fever-like illness	Tick	Lizards, possibly birds	Europe, North America
		<i>R. massiliae</i>	Mediterranean spotted fever-like disease	Tick	Unknown	Spain, Portugal, Switzerland, Greece, Mali, Argentina, Central Africa
		<i>R. parkeri</i>	Maculatum infection, tidewater spotted fever, American boutonneuse fever	Tick	Rodents	North and South America
		<i>R. raoultii</i>	Tickborne lymphadenopathy	Tick	Unknown	Europe, Asia

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