Cell PRESS

Ticks and tick-borne diseases: a One Health perspective

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Tick-borne diseases are common occurrences in both the medical and veterinary clinical settings. In addition to the constraints related to their diagnosis and clinical management, the control and prevention of these diseases is often difficult, because it requires the disruption of a complex transmission chain, involving vertebrate hosts and ticks, which interact in a constantly changing environment. We provide a contemporary review of representative tick-borne diseases of humans and discuss aspects linked to their medical relevance worldwide. Finally, we emphasize the importance of a One Health approach to tick-borne diseases, calling physicians and veterinarians to unify their efforts in the management of these diseases, several of which are zoonoses.

Vector-borne diseases on the rise

Ticks were the first arthropods to be established as vectors of pathogens and currently they are recognized, along with mosquitoes, as the main arthropod vectors of disease agents to humans and domestic animals globally [1,2]. Moreover, the incidence of tick-borne diseases (TBDs) is increasing worldwide [3–5]. For instance, more than 250 000 human cases of Lyme borreliosis were reported from 2000 to 2010 in the United States (see http://www.cdc.gov/lyme/stats/chartstables/reportedcases_statelocality.html), and the disease is also increasing in Europe, where over 50 000 cases are reported each year in humans [5]. Hence, the need for a comprehensive approach towards a better management of these diseases is evident. In this article, we provide a contemporary review on some of the most important TBDs of humans. In particular, we discuss the general aspects of these diseases and present a list of tick species found on humans around the world, highlighting their relevance in terms of pathogen transmission. Finally, we emphasize the importance of a One Health approach (see Glossary) to TBDs, calling physicians and veterinarians to better unify their efforts in the management of these zoonoses.

The expanding world of tick-borne diseases

The spectrum of TBDs affecting domestic animals and humans has increased in recent years; many important zoonotic TBDs, such as anaplasmosis, babesiosis, ehrlichiosis, and Lyme borreliosis are increasingly gaining more attention from physicians and veterinarians. With the development of molecular biology, new species, strains, or genetic variants of microorganisms are being detected in ticks worldwide [6,7], and the list of potential tick-borne pathogens continues to increase [8–11]. Some of these agents, such as *Rickettsia slovaca*, *Rickettsia parkeri*, and *Rickettsia massiliae*, were identified in ticks, decades before these were associated with human diseases [12]. Other tick-borne pathogens, including many flaviviruses (e.g., Omsk hemorrhagic fever virus, Powassan encephalitis virus, and Kyasanur forest disease virus) have been implicated in human disease in new geographical regions (Table 1) [5,13]. Despite the enormous contribution of molecular biology to the discovery of new species or strains of tick-borne pathogens, genetic data must be interpreted with caution. For instance, the evaluation of partial 16S rRNA gene sequences amplified from the castor bean tick *Ixodes ricinus* revealed a plethora of *Rickettsia* sequences,

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Keywords: ticks; diseases; One Health; parasites; humans; control.

Glossary

Amplifying host: a host in which the level of pathogen can become high enough that a vector (e.g., a tick) that feeds on it will probably become infectious.
Anamnesis: the complete history recalled and recounted by a human patient.
Anaplasmosis: a tick-borne disease caused by rickettsiae of the genus *Anaplasma*.
Anthropophilic: from Greek *anthropos* (human) and *philein* (to like); usually said of parasites that prefer human beings to animals.
Babesiosis: a tick-borne disease caused by protozoa of the genus *Babesia*.
Control measures: actions or measures (e.g., elimination of reservoirs and vectors) adopted to restrain or reduce the prevalence of individual disease.
Ehrlichiosis: a tick-borne disease caused by rickettsiae of the genus *Ehrlichia*.
Entomopathogenic fungus: a fungus that can act as a parasite of insects, killing or seriously disabling them.
Hard ticks: hard ticks (family Ixodidae) are so-called because they have a dorsal scutum in all developmental stages (larva, nymph, and adults).
Lyme borreliosis: a tick-borne disease caused by bacteria of the genus *Borrelia*.
One Health approach: an interdisciplinary approach for combating threats (e.g., tick-borne diseases) to the health of animals, humans, and the environment they share on Earth.
Petechiae: a small purplish spot on skin or mucous membrane.
Preventive measures: actions or measures (e.g., vaccination, use of repellents) adopted to reduce the incidence of a disease or infection.
Reservoir host: an individual or a population of animals that is chronically infected with the causative agent of a disease and can act as a source of further infection.
Sentinel animal: an animal that may be used as an indicator of the presence of a pathogen.
Soft ticks: soft ticks (family Argasidae) are so-called because they lack a dorsal scutum in the nymphal and adult stages; larvae may present a dorsal plate, which is of taxonomic relevance.
Transmission time: time frame occurring from the initiation of feeding by an arthropod vector and the inoculation of an infectious agent in the host. It may vary widely according to vectors and pathogens.
Vector competence: the intrinsic ability of a vector to become infected with, to replicate, and to transmit a pathogen to receptive hosts.

Table 1. Causative agents, vectors, and distribution of representative tick-borne diseases of humans

Diseases	Pathogens	Proven or putative vectors[a]	Distribution	Refs
African tick bite fever	*Rickettsia africae*	*Amblyomma hebraeum, A. variegatum*	Africa, West Indies	[1,5]
Human granulocytic anaplasmosis	*Anaplasma phagocytophilum*	*Haemaphysalis concinna, H. punctata, Ixodes ricinus, I. pacificus, I. scapularis, Rhipicephalus bursa*	Europe, North America	[1,5]
Human monocytic ehrlichiosis	*Ehrlichia chaffeensis*	*Amblyomma americanum*	North America	[1,5]
Lyme borreliosis	*Borrelia burgdorferi* sensu lato	*Ixodes hexagonus, I. pacificus, I. persulcatus, I. ricinus, I. scapularis*	Asia, Europe, North America	[1,5]
Mediterranean spotted fever	*Rickettsia conorii*	*Rhipicephalus sanguineus, R. turanicus*	Africa, Asia, Europe	[1,5,18]
Q fever	*Coxiella burnetii*	Many species of different genera	Africa, Asia, Australia, Europe, North America	[1,5]
Relapsing fever	*Borrelia* spp.	*Ornithodoros* spp.	Africa, Asia, Europe, North America	[1,5,66]
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Amblyomma americanum, A. aureolatum, A. cajennense, Dermacentor andersoni, D. variabilis, R. sanguineus*	North, South and Central America	[1,5,36,67]
Tularemia	*Francisella tularensis*	Many species of different genera	Asia, Europe, North America	[1,5,64,68,69]
Babesiosis	*Babesia divergens, B. microti*	*Ixodes ricinus, I. scapularis*	Europe, North America	[1,5]
Colorado tick fever	Coltivirus	*Dermacentor andersoni*	Western North America	[1,5]
Crimean–Congo hemorrhagic fever	Naiovirus	*Amblyomma variegatum, H. punctata, Hyalomma anatolicum, H. marginatum, H. truncatum, R. bursa*	Africa, Asia, Europe	[1,5]
Kyasanur forest disease	Flavivirus	*Haemaphysalis spinigera, H. turturis*	Indian subcontinent	[1,5]
Louping ill	Flavivirus	*Ixodes ricinus*	Western Europe	[70]
Omsk hemorrhagic fever	Flavivirus	*Dermacentor marginatus, D. reticulatus, I. persulcatus*	Asia	[5]
Powassan encephalitis	Flavivirus	*Dermacentor andersoni, Haemaphysalis longicornis, I. cookei, I. scapularis*	Asia, North America	[13,70]
Tick-borne encephalitis	Flavivirus	*Ixodes persulcatus, I. ricinus, H. concinna, H. punctata*	Asia, Europe	[5,70]

[a]The list of potential vectors may actually be longer.

including the first report of *Rickettsia australis* in Europe [14]. However, a meticulous analysis of these data revealed that 16S rRNA sequences of *Rickettsia helvetica* were most likely misinterpreted as *R. australis* [15].

Ticks and wildlife are the main reservoirs of tick-borne pathogens of medical and veterinary concern. Nonetheless, the expanding spectrum of tick-borne pathogens affecting domestic animals and humans will require new studies on the epidemiology, diagnosis, and ecology of these newly recognized diseases. For example, *R. massiliae*, a bacterium firstly isolated from brown dog ticks (*Rhipicephalus sanguineus*) in France, has been implicated in human cases of spotted fever in Europe and South America [16,17]. A laboratory study also suggested the potential of the tick *Rhipicephalus turanicus* in the transmission of *R. massiliae* [18]. In a human case recently diagnosed in Argentina, the patient exhibited no antibodies against *Rickettsia conorii*, and the definitive diagnosis of infection by *R. massiliae* was achieved by amplification and sequencing of bacterial DNA from a skin sample. Importantly, this patient was successfully treated with doxycycline [17], which is the drug of choice for the treatment of tick-borne rickettsioses [19].

Wildlife may serve as reservoirs or amplifying hosts of several human pathogens; the vast majority of TDBs are from wildlife reservoirs [2,4,5]. However, tick-borne pathogens traditionally associated with disease in domestic animals may also eventually emerge as human pathogens.