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Vector Borne Diseases Related with Companion Animals in Panama: A Review

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ABSTRACT

Zoonoses are, in a broad sense, diseases transmitted to humans through direct or indirect contact with animals (vertebrates or invertebrates), their environment or by-products. There are different concepts, definitions and classifications of zoonoses according to different criteria. There are different concepts, definitions, and classifications of zoonoses following several criteria. Vectors are transmission vehicles that carry etiological agents between different animal species, including man, or between the environment and these species. The Republic of Panama is an interoceanic isthmus that meets all the basic conditions for the development of vector-borne diseases. This review provides a chronological analysis of the vectorial zoonoses related to companion animals or those that have a close relationship with humans. The history of studies on Trypanosomiasis, Leishmaniasis, Babesiosis, Hepatozoonosis, Rickettsiosis, Ehrlichiosis, Anaplasmosis, Bartonellosis, Borreliosis, Equine Encephalitis, Dirofilariasis and Dipylidiasis in Panama shows that environmental, socioeconomic, cultural, evolutive, investigative and educational factors have a direct influence on the success or failure in the control and prevention of these vectorial zoonoses. For this reason, major efforts are needed in relation to research and work that provide real data to support control programs for these diseases.

Keywords: Anaplasmosis, babesiosis, bartonelosis, borreliosis, companion animals, dipylidiasis, dirofilariasis, disease, ehrlichiosis, encephalitis, hepatozoonosis, leishmaniosis, panama, rickettsiosis, trypanosomiasis, vector, zoonoses.

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I. Introduction

Zoonoses are, in a broad sense, diseases transmitted to humans through direct or indirect contact with animals (vertebrates or invertebrates), their environment or by-products. These animals may constitute their natural reserve, since they can play a vital role in their biological cycle, playing a fundamental role for their maintenance in nature; however, on other occasions, vertebrate animals and humans are affected by the same sources of contagion such as water, soil, or invertebrate animals, among others, suffering to a greater or lower degree the effects of infectious agents, without participating in their life cycle. There are different concepts, definitions, and classifications of zoonoses following several criteria, as is the case of Anthropozoonoses or zoonoses themselves that characterize the direction of infection, where the causative agent has adapted to vertebrate or invertebrate animals and humans participate as the final link in a chain that suffers the consequences of the etiological agent, as in the case of Dirofilariasis. However, there are also diseases transmitted from humans to animals, the so-called Zooanthroponoses or Anthroponoses, which shows the reverse pathway with animals being the final victims of the infectious cycle, as in the case of Tuberculosis.

Vectors are transmission vehicles that carry etiological agents between different animal species, including man, or between the environment and these species. These have certain fundamental characteristics that closely relate them to the causal agent and to the animals and may be linked to the former in a mandatory way, since they may be part of their life cycle, or in a casual way by the simple fact of sharing the same environment or ecosystem, where their habits are vital, among them, hematophagy. In Latin America they are commonly small invertebrates, arthropods that live in close contact with animals and humans, very often through parasitism or adapted to their habits, ways and environments.

In complete review on the occurrence of vector-borne diseases transmitted to domestic animals in Latin America, the incidence of Leishmaniasis, Trypanosomiasis, Anaplasmosis, Ehrlichiosis and Rickettsiosis in Panama is reported [1]. On the other hand, the first report of canine Dirofilariasis in Panama was made in 2021 [2]. The same year, a study on bacteria and hematozoa found in ticks of the genus Ixodes in the highlands of the Panamanian isthmus highlights the importance of these mites in the enzootic cycles of pathogens such as *Anaplasma, Rickettsia, Borrelia, Babesia* and *Hepatozoon* [3].

The Republic of Panama is an inter-oceanic isthmus that meets all the basic conditions for the development of vector-borne diseases, due to its commercial characteristics that allow economic/tourist exchange with various countries of

the world, and geographical characteristics, which provide the country with the appropriate biotic and abiotic conditions for the development of the various agents that make up this vast group of pathologies. This country has also suffered, like the rest of the planet, with climatic changes in recent decades and has had a visible technological, urban and socioeconomic development, which has allowed adaptive modifications in the vectors to facilitate their coexistence. On the other hand, the etiological agent/vector/animal/human relationship is directly affected by changes in ecosystems that are constantly being modified due to population growth, climate change and global warming, deforestation, urbanization and agriculture, the movement of individuals and the increasingly easier trade between nations, as well as changes in the habits and traditions of human beings, thus the occurrence of other vector-borne diseases in the country is of very high risk. The increase in the world population, which is accompanied by an increase in the number of domestic animals that surround us either for company, food or work, has a significant effect on the probability of the appearance of zoonotic diseases, which is why it is vital to know the real role of domestic animals in the cycle and perpetuation of these pathologies. Back in 2011, the introduction of ectoparasites into the country through their vertebrate hosts was reported, and it was concluded that this fact makes it necessary to improve sanitary controls to minimize the importation of diseases into Panama [4]. The purpose of this article is to address some vectorial zoonoses that are plaguing, with greater or lesser impact on the Panamanian population, mainly those related to vectors of easy development in the country and associated with domestic animals of great importance to humans, regardless of their participation, whether biological or casual, in the disease cycle, such as canine dirofilariasis and equine encephalitis, respectively. However, other vectorial zoonoses such as those transmitted only by arthropods where the domestic animal does not play a predominant role or where the natural reserve is wildlife, as in the case of malaria, will not be addressed.

II. Vector-Borne Zoonotic Diseases Caused by Protozoa

A. Trypanosomiasis

Trypanosomiasis or Chagas disease is an anthropozoonoses first described in Brazil between 1907 and 1909. This disease is caused by a flagellated protozoan called *Trypanosoma cruzi*. This intracellular parasite shares its life cycle in two biological phases, one within vertebrate hosts and the other within its insect vectors. In the blood circulation of the vertebrate host, it assumes the trypomastigote form, invades the cells of the endothelial reticulum system and takes the amastigote form which reproduces inside the cell, destroying it. Within the insect vector the trypomastigote form, acquired from the circulation of the vertebrate host, passes to the epimastigote stage and from there to the metacyclic trypomastigote form. Among domestic mammals, the most affected are dogs, cats and guinea pigs, in which, as well as in humans, they are most frequently located in the spleen, liver, lymph nodes and myocardium.

The vectors transmitting this zoonoses are commonly known as bedbugs, insects belonging to the triatomine group. In Panama, the two species most commonly associated with the disease are *Rhodnius pallescens* and *Triatoma dimidiata*, arthropods closely related to palm cultivation areas, areas of rural and precarious social conditions with houses with adobe walls and thatched roofs, and forest areas. The life cycle of the parasite in the insect vector occurs in the intestine, where the metacyclic trypomastigote stages, infective for humans and animals, leave together with the bed bug's feces. The most common form of transmission of the parasite is by contamination of the wound, caused by the bite of the insect, with its feces, which occurs very easily due to the itching sensation at the wound and to the fact that, when the insect feeds on the blood of the vertebrate host, it also defecates. There are other forms of transmission less frequent than vectorial transmission, such as transplacental transmission, through blood transfusions or organ transplants and by accidental ingestion of the vector. Symptomatology in mammals is very variable and will depend on the organ affected.

The first records of Chagas disease in Panama were made in 1931, when the first three cases were reported, with the identification of a protozoan morphologically similar to *T. cruzi.* [5]. Some decades later, observations were made on the disease in the isthmus and a list of wild mammalian reservoirs of *T. cruzi* in the country was published. The author also commented that at that time there were approximately 40,000 infected people in Panama [6]. Studies on the prevalence of *T. cruzi* and *Trypanosoma rangeli* in Triatomine bugs in this country correlated with insects from four regions (Panama, Colon, Chiriqui and Bocas del Toro) observed that the most often found it vector was *R. pallescens* which also showed the highest levels of infection for *Trypanosoma* sp, 68.8%. The authors also commented that the Triatomine species *T. dimidiata* was found more frequently in the households of the province of Chiriqui, with 17.7% of this species being positive for *T. cruzi*. The study showed, after seven years, that there was an increase in the prevalence of this protozoan in the Triatomine collected [7]. For the first time, the relationship between *R. pallescens* and *T. dimidiata*, the most important vectors of Chagas disease in Panama, and the palm *Scheelea zonensis*, widely distributed in the central region of the Panamanian isthmus, has been recorded [8]. Epidemiological aspects of *T. cruzi, T. rangeli* and their vectors were studied in the Panama Canal zone, detecting risk factors for the disease in this area, since after the collection of 1110 triatomine in the zone, 100% of them were identified as *R. pallescens*, with 7.6% of the salivary glands and 45% of the rectal blisters of the insects being naturally infected with *Trypanosoma* sp, being 85.4%, *T. cruzi* and *T. rangeli* with 14.6% [9]. When evaluating the presence of anti-*T. cruzi* antibodies in residents of five rural communities in the districts of Chepo and Chiman located in the eastern part of Panama, a prevalence of 5.88% for *T. cruzi* and 5.88% for *T. rangeli* was detected. The authors also reported that the predominant Hemiptera species was *R. pallescens*, and that 17.8% of the insects were positive for *T. cruzi* and 17.8% were also positive for *T. rangeli.* The study concluded that the high prevalence of the parasite in the insect and the fact that insects were found in the domestic environment explains the high prevalence of human trypanosomiasis observed in

inhabitants of this region [10]. Evaluation of the association between changes in human land use and the increase of the *R. pallescens* vector in rural areas of the Panama Canal showed a higher proportion of palms infected by the vector in all habitats studied (77.1 to 91.4%); however, in habitats altered by humans, the prevalence of the insect was higher than in habitats with less human influence. On the other hand, although found in greater abundance in areas with greater human disturbance, these insects presented lower body condition when compared to insects from areas without as much human influence, suggesting that preserved forests can function as sources of *R. pallescens* populations when located within areas highly affected by human action [11]. The level of knowledge of habitants of two endemic areas for Chagas disease in Panama showed that 69.1% and 48.1% of the residents of these areas had limited knowledge about the disease, which complicates its prevention [12]. A chronological study of Trypanosomiasis in the isthmus provides a complete picture of the vertebrate hosts and reservoirs of *Trypanosoma* species in Panama. In their review, the authors describe the historical evolution of scientific research on the ecology and epidemiology of Chagas disease and detail a picture of the species of Triatominae found naturally infected and capable of transmitting *T. cruzi* and *T. rangeli.* The researchers conclude that the degradation of forest ecosystems is a study factor related to the emergence of Chagas disease and that the government should establish active monitoring programs, as a first step, to mitigate this serious public health problem [13]. The Hemiptera *R. pallescens*, collected in Attalea butyracea palms in the province of Veraguas, presented infection levels of 41.3% for *T. cruzi* and 52.4% for *T. rangeli* [14]. Recent results and current challenges in the ecology and control of Chagas disease vectors in Central America conclude that *R. pallescens* is considered the main vector of the disease in Panama, with *T. dimidiata* being the only Hemiptera species with domiciliary behavior, also found in the wild. On the other hand, Panstrongylus geniculatus is an insect species commonly found in houses in peri- and suburban environments, being repeatedly found infected with *T. cruzi.* However, Panama has never had a national program for the control of Chagas disease, being the country considered one of the four endemic countries for this pathology in Latin America. They also report that studies in moving identify a new subspecies of Triatominae as a potential vector for the disease, which means that this affectation may be more widely distributed in the country than previously considered [15].

B. Leishmaniasis

Leishmaniasis is a neglected disease and considered an emerging public health problem in Panama [16]. This is a zoonoses transmitted to humans from its vertebrate host, through the bite of mosquitoes of the *Lutzomyia genus*. The WHO (World Health Organization) considers it an emerging or re-emerging parasitic disease of high impact. There are three clinical forms of the disease, the visceral form, which causes lesions in internal organs and if not treated in time can cause death. The cutaneous form, which causes skin lesions; and the mucocutaneous form that develops from complications of the cutaneous form due to dissemination of the parasite to the respiratory system [17]. No human deaths have been reported in Panama from this disease, which was first reported in 1909 in Brazil, although since 2001 there has been a substantial increase of approximately 3,000 new cases per year in the isthmus [18]. Most of the reports come from the provinces of Bocas del Toro, Coclé, Comarca Ngabe Buglé, Panama Oeste and Darién.

Leishmania sp. is a protozoan that divides its life cycle into two stages, one within the insect vector and the other within the vertebrate host. The transmission cycle occurs when the insect ingests blood from the vertebrate host (human, dog) and inoculates the promastigote stage of the parasite in the skin, this stage is phagocytosed by macrophages where they are transformed into amastigote, which reproduce inside the cells of various tissues causing their death. The insect ingests host blood containing macrophages infected with the amastigote, this intercellular stage transforms into flagellated promastigotes in the vector's intestine, multiply and migrate to the insect's mouthparts, where they wait for a second feeding on the vertebrate to continue the cycle.

Leishmaniasis lesions can be confused, in many cases, with neoplastic changes in the skin, being reported diagnoses of carcinoma discarded by histopathological studies that confirm the absence of neoplastic lesion [19], [20]. Currently, it has become the second mosquito-borne parasite disease with the highest incidence in Panama, after Malaria [17].

The first record of the disease in Panama dates to 1910 [21]. Several cases have been reported in the literature since its initial discovery [22]-[24]. Natural cases of canine cutaneous leishmaniasis in Panama demonstrated that dogs could act as incidental hosts of human leishmaniasis and may participate as transporters of the disease between forests and communities [25]. The first report that related parasites, vectors and reservoirs of the disease in the isthmus was only published in 1984, where some variations regarding its pathogenicity were also detailed [26]. A study that investigated the epidemiological parameters of cutaneous Leishmaniasis in five communities: in the eastern region of Panama found that prevalence ranged from 3.8% to 77.3% among the communities. The authors also commented that the four mosquito species implicated as vectors of *Leishmania panamensis* in the country were *Lutzomyia panamensis, Lutzomyia ylephitelor, Lutzomyia gomezi* and *Lutzomyia trapidoi* [27]. Research using molecular epidemiology of American Tegumentary Leishmaniasis in Panama concludes that this method is a very effective alternative in the diagnosis and characterization of the different subspecies of Leishmania that participate in the disease cycle in this country [18]. The study of the diversity of Lutzomyia sandflies on the island of Barro Colorado in Panama observed Leishmania DNA in 43.3% of *Lu. trapidoi* and 26.3% in *Lu. gomezi* and pointed to an exotic Leishmania species, being that the DNA sequence of the protozoan was 93% similar to *Leishmania (viannia) naiffi,* an unknown species in Panama accused of causing cutaneous Leishmaniasis in northern and central South America [28]. The anthropogenic influence on the distribution and diversity of Cutaneous Leishmaniasis vector species in Panama is demonstrated by the reduction and fragmentation of forest areas, which affects the abundance and composition of the various species of insect vectors of the disease, mainly due to their adaptation to new habitats [29].

The finding of Lutzomyia longipalpis was recorded in the domiciliary area of Limón, Capira District, one of the oldest endemic transmission areas of Cutaneous Leishmaniasis in Panama, which, according to the authors, may indicate that this insect species is adapting to new habitats and may be playing an important role in the transmission of the disease in this country [30]. The close relationship between cutaneous Leishmaniasis rates and the number of *Lu. gomezi, Lu. panamensis* and *Lu. trapidoi* flies in intradomiciliary environments in Trinidad de las Minas, Panama was observed through the 6% increase in the probability of the disease for each *Lu. gomezi* found inside the domiciles in this region [31]. A historical review of entomological studies of *Lutzomyia* species was conducted in Panama and indicates that the increase in cases in recent years is also due to the increase in diagnostic tools for the disease and that future research is fundamental to be able to reach a holistic view of the problem generating information that facilitates the integrated control of vector species [32]. The variation in the cycles of cutaneous Leishmaniasis in Panama, between years, is affected by the natural phenomenon El Niño which increases its prevalence, in addition, seasonal variations affect the disease cycle due to changes in temperature and humidity within the same year, which alters the population density of the vectors [33]. A seroprevalence of 47% was observed among dogs in Panama without the observation of skin lesions suggestive of the clinical presence of the disease, which casts further doubt on the role and participation of the pet in the Leishmaniasis cycle [34]. Macro ecological patterns of American Cutaneous Leishmaniasis transmission and the increase in the rainy period are associated with the increase in the incidence of the disease [35]. Evaluation of the different ways of diagnosing cutaneous Leishmaniasis showed that the various methods tested on positive patients revealed a variation in effectiveness from 50% to 100%, providing efficient tools for mapping the disease in the region [36]. The correlation between *Leishmania* spp. infection rates and the feeding patterns of its vectors in hyperendemic areas for cutaneous disease in Panama, shows that the parasite is present in the two groups of vectors studied, anthropophilic and zoophilic, being that *Lu. trapidoi* is the main vector species of the disease for humans in the country, in addition, this species of insect is strongly associated with humans and domestic animals such as dogs [37]. The evaluation of the genetic diversity of *Lu. longipalpis* and its implications in the transmission of Leishmaniasis in Panama concludes that it is possible that the Panamanian populations of the insect participate in a set of transmitting species, in addition there is scientific evidence on the genetic structure of the populations of *Lu. longipalpis* useful for the development of control strategies adjusted to the Panamanian reality [38]. The disease has become a public health issue in the Darien region since this area has become a huge challenge for the control of this pathology due to the high frequency of cases reported, and not all Leishmania species related to the disease have been identified in this region. The study indicates that although *Leishmania (vianna) panamensis* is the only species isolated from skin lesions, reservoirs and vectors, other species have been isolated only from patients or only from reservoirs, such as *Leishmania (vianna) colombiensis* and *Leishmana (leishmania) amazonensis* [17]. Molecular identification of the parasites that cause cutaneous Leishmaniasis in Panama was performed by genetic testing of 475 human patients diagnosed positive for the disease and it was observed that 78.1% were *L. (v.) panamensis*, 18.9% were *Leishmania (vianna) guyanensis* and 3.0% were *Leishmania (vianna) brasiliensis* [16].

III. Vector-Borne Diseases Caused by Protozoa with Zoonotic Potential to Develop in Panama

Babesiosis is a zoonoses caused by intraerythrocytic protozoa of the genus *Babesia*, including *Babesia bovis*, *Babesia bigemina, Babesia canis, Babesia microti* and *Babesia divergens*, among others. These are transmitted by ticks of the Ixodidae group, with which they have a biological relationship of dependence. Panama has no records of human Babesiosis and the disease in animals is poorly studied, however, there has been an increase in cases of Malaria in recent years, a disease with very close symptomatological picture due to the similarity of the etiological agents, besides being very common in areas where cattle, dogs and humans have close contact, and among them: ticks. Hepatozoonosis is a disease caused by protozoa of the genus Hepatozoon, which causes disease in canines and very few accidental cases in humans. Within this genus we have *Hepatozoon canis* and *Hepatozoon americanum,* transmitted mainly by the ingestion of ticks of the species *Rhipicephalus* and *Amblyomma*. This is a parasite that colonizes leukocytes causing mild disease, usually associated with other hemoparasites. There are no records of human disease in this country and the prevalence of the disease in dogs is not well defined.

Both genders are described in America and Panama [3]; and apparently may be associated with immunological predispositions in humans, which is why it is essential to clarify the real importance and incidence of these species in the Panamanian isthmus.

IV. Vector-Borne Zoonoses Caused by Bacteria

A. Rickettsiosis

Rickettsiosis is one of the most aggressive, dangerous, and underestimated vectorial zoonoses in Panama. It is an inflammatory, febrile, hemorrhagic, immunosuppressive disease that causes severe alterations in the vascular endothelium of the respiratory system and in various organs and can often lead to death due to late diagnosis and treatment. It is caused by an intercellular bacterial group that belongs to the Rickettsiaceae family and is divided into two main groups. The Typhoid Group (TG) is composed of two species, *Rickettsia prowazekii* which is transmitted mainly by contact with feces of infected people and *Rickettsia typhi* which is responsible for Murine Typus and transmitted by fleas and lice. The other group, which is the focus of the present review due to its relationship with companion animals, is composed of a larger number of species and is the group of Spotted Fever or Rocky Mountain Spotted Fever or Maculosa Fever (SFG). Within this group we have *Rickettsia rickettsii, Rickettsia parkeri, Rickettsia felis, Rickettsia amblyommatis, Rickettsia belli, Rickettsia rhipicephali,* etc.

These are bacteria that parasitize eukaryotic cells, normally related to invertebrates but capable of infecting vertebrates, such as man and other mammals, through the bite of blood-feeding arthropods, mostly ticks, but also fleas. This bacterial group (SFG) is commonly found circulating among wild animals of various species that function as its host. In Panama, transmission of the disease has been confirmed through the bite of ticks of the genera *Amblyomma* and *Rhipicephalus*. In cases such as this disease, the dog plays a fundamental role, functioning as a satellite host between forests and urban environments, and is mainly responsible for the perpetuation of the vectors in peri-domestic and domestic areas. The first reports of Rickettsiosis in Panama were observed in the early 1950s [39]-[41] when the authors identified the etiological agent, reported the first clinical symptoms and also identified its first vector in this country. In the early 1990s, a summary of the history of *R. rickettsii* and other tick-borne animal diseases in Panama was published, from its beginnings until the end of the 1980s [42]. At the end of 2004, a fatal case of *R. rickettsii* occurred in a 4-year-old girl from a rural area of western Panama, the first after those observed in the 1950s. The authors report the clinical picture, the severity of symptoms and the main organic alterations found at necropsy [43]. A complete review of the SFG group was published in 2007, showing details related to the etiological agent and other *Rickettsia* species including *Rickettsia conorii* and *R. felis*, their hosts and vectors, epidemiology and clinical manifestations in humans, and concluding that the diagnosis of SFG is a dilemma due to the limitations of diagnostic tools, mainly in the initial stage of the disease [44]. A study that investigated Rickettsiae in ticks from peri-domestic environments in Panama observed that 61% presented *Rickettsia amblyommii* DNA, however, no *R. rickettsii* DNA was found [45]. With the intention of detecting and identifying rickettsial agents in ticks from domestic animals in Panama, 280 adult ticks and 9 nymphs were collected between June and December 2007 in the Darien region and Comarca Kuna Yala, of which 108 (37.4%) showed presence of DNA of Rickettsiae of the spotted fever group, but only 56 specimens were sequenced at the species level, with one specimen positive for DNA of *R. rickettsii* and 55 for *R. amblyommii.* The authors also observed that 29 adult specimens of *A. cajennense* collected from horses and one from a dog, as well as all nymphs of this species, collected from pigs and dogs, had *R. amblyommii* DNA. The assay also found low levels of SFG DNA in Amblyomma ovale and Amblyomma oblongoguttatum and only one specimen of A. ovale showed the presence of *R. amblyommii* DNA, with the tick *R. sanguineus* showing the lowest prevalence of SFG Rickettsial DNA [46]. When evaluating the presence of *Rickettsia* spp. in ectoparasites of horses and dogs in Valle de Anton, Panamá, it was reported that *R. amblyommii* DNA was found in 36.7% of *Amblyomma cajennense*, 27.4% of *Dermacentor nitens* and 12.3% of *Rhipicephalus sanguineus* studied, while *Ctenocephalides felis* showed 35% of infection by *R. felis*. The authors also reported finding antibodies to *R. ambyommii, R. rickettsii, R. belli, R. rhipicephali, R. parkeri* and *R. felis* in horses and dogs, with the most common species for both vertebrate hosts being *R. amblyommii* and the less common being *R. felis* [47]. A critical and retrospective review of the scientific situation of the genus Rickettsia in Latin America considered accounts involving human and animal hosts, as well as their associated vectors, in addition to a taxonomic review of the different groups that form this genus, such as the TG and SFG, however, others considered more recent such as the Transitional Group TRG, the Belli group and other basic groups. The authors group the different Latin American countries, the various *Rickettsia* species found and their reported vectors [48]. A fatal outbreak of *R. rickettsii* in three members of the same family who died in 2007, coming from a semi-rural environment of the country and with the presence of domestic dogs, was reported and the diagnosis confirmed through the sequencing of bacterial genes found in tissues of the victims' organs collected as a result of autopsies [49]. The detection and identification of bacteria of the genus *Rickettsia* from ectoparasites of domestic and wild animals from Darien between April 2007 and March 2010 revealed genetic material of *R. amblyommii* in *A. cajennense* and *D. nitens* ticks collected from horses and *R. sanguineus* collected from dogs, as well as *Amblyomma* spp. collected from humans. *R. felis* was also observed in *C. felis* collected from cats and dogs and in *A. cajennense* collected from horses [50]. The study of tick-borne Rickettsioses in America found that the role of *R. amblyommii* as a pathogen is not yet well understood, but that it can certainly cause high seroprevalence rates for the SFG group even causing subclinical or asymptomatic infections [51]. Serological evidence of the presence of human infection by Rickettsia was demonstrated in three locations in Panama, showing that, of 97 volunteers in the study, 38 (39%) presented a positive reaction to at least one of the diagnostic tests performed, showing antibodies against Rickettsiae of the SFG group [52]. In a review of *R. felis* in Latin America, the variability of the symptomatology present in the clinical pictures of patients from different countries of the continent was highlighted, with different clinical manifestations without an evident common pattern, being fever the only one with the highest occurrence [53]. The identification of a new case of human Rickettsiosis in Panama, from serological and clinical evidence, highlighted that the affected patient's dog showed no evidence of infection, which led the authors to conclude, due to the case history, that it was possible that this was the first case of Spotted Fever acquired within a wild area in Panama [54]. The epidemiology of the disease has always been associated with the reservoir-vector-human interaction, in which social practices, the environment, the geographical situation and the political and social circumstances of each country play an important role [55]. When ticks were collected from the vegetation of protected areas and grazing areas near the Panama Canal, between 2009 and 2012, DNA of Candidatus *Rickettsia amblyommii* was observed in *Amblyomma mixtum (*formerly *Amblyomma cajennense), Haemaphysalis juxtakochi* and immature stages of *Amblyomma* spp. and the first report of Candidatus *R. amblyommii* in free-living ticks in nature in Central America was reported [56]. The distribution of Rickettsiae of the SFG group in hard ticks from urban and rural environments in Panama, between 2007 and 2013, was studied through the collection of ticks from 63 locations, 13 urban and 50 rural, and it was observed that five specimens of *A. mixtum* presented DNA of *R. rickettsii,* while 138 *A. mixtum*, 14 *R. sanguineus* and one *A. ovale* presented DNA of Candidatus

R. amblyommii. The authors also report a list of hosts parasitized by *A. mixtum* and *R. sanguineus*, mapping the distribution of these vectors in the country [57]. The comparative analysis between elevation, human population size, vegetation coverage and changes in land use patterns and the risk of tick-vector-borne disease in Chiriqui (Panama province), was performed by collecting ticks of four species (*R. sanguineus, Rhipicephalus microplus, A. ovale* and *Ixodes boliviensis*, observing that 97% of all ticks collected were *R. sanguineus*, and relating locations of low elevation and decreased vegetation cover, with the highest rates of ticks on dogs [58]. When evaluating the potential of synanthropic mammals as hosts of tick-borne pathogens in Panama, it was found that one coyote and 27 opossums showed seroreactivity for SFG Rickettsiae, 11 of which were seroreactive for Candidatus *R. amblyommii*. The authors report that ticks and tick-borne diseases are largely neglected by health care providers and the scientific community [59]. The review of the genus Rickettsia in Central America highlighted the pathogenic species for animals and humans, their taxonomic grouping, and *R. amblyommi* and Candidatus *R. amblyommi* are considered as *Rickettsia amblyommatis*, being this the most detected Rickettsia species in these countries. The authors also conclude that rickettsioses may be an underestimated problem due to the absence of more demanding diagnostics in cases of indeterminate febrile presentations [60]. The clinical and pathological characterization of two fatal cases of Rickettsiosis in humans in Panama in 2017, one in the Valle de Anton and the other in the capital, details the clinical and hematological presentation of each case and provides epidemiological data such as the detection of *R. rickettsii* DNA in *R. sanguineus* collected from the walls of the property of one of the cases. The authors pointed to the high pathogenicity of *R. rickettsii*, the late diagnosis of the disease due to the suspicion of other more prevalent etiologies and the lack of knowledge of the epidemiology of the SFG group and its vectors in Panama as the causes of the severity of the cases [61]. A complete synthesis of R. rickettsii Spotted Fever cases in Panama between 1950 and 1951; and between 2004 - 2017, with their clinical and paraclinical characteristics, was published, listing epidemiological data of each case and pointing as hypothesis of the high mortality to two main factors, lack of initial diagnosis and early therapeutics [62]. The need of research work on Spotted Fever and the lack of incentives for research in Latin America are factors that complicate the understanding of the disease [63]. In 2019, 10 cases were reported in a family of *R. rickettsii* exanthematous febrile syndrome in the region of Comarca Gnäbe Buglé, Panama, of which five died at the early stages of the outbreak [64]. An approach on bacteria found in ticks of the genus *Ixodes* in the highlands of the Republic of Panama, emphasizes the importance that this genus may have in the maintenance of undescribed pathogens, whose potential pathogenicity is unknown, and also makes the first report of *Rickettsia* spp. in species of *Ixodes* in Panama [3]. Recently, two pediatric cases of Rickettsiosis occurred in 2021 in Panama, the first was diagnosed as *Rickettsia* spp. and the patient was dead 10 days after hospital admission; the second was diagnosed as *R. rickettsii*, in which the patient presented nasal and oral hemorrhage and died with a rapid and aggressive course of the disease, showing multiorgan failure. The authors conclude that wrong diagnostic suspicions induced by incomplete clinical histories significantly delay the treatment of the disease [65].

B. Ehrlichiosis

Ehrlichiosis is a zoonoses caused by intercellular bacteria of the genus *Ehrlichia* sp., transmitted to its hosts through the bite of infected ticks of various genera, affecting canines, humans and wild animals, among others. This bacterium belongs to the Anaplasmataceae family, colonizes leukocytes and platelets, and multiplies in liver, spleen and lymph nodes, resulting in a febrile, anemic, hemorrhagic and immunosuppressive disease, with symptoms such as anorexia, lethargy, epistaxis, uveitis, generalized inflammation, corneal edema, petechiae and vomiting in its initial stage. It is also capable of causing neuritis and myocarditis. However, recurrent or non-curable secondary infections and afebrile disease are common after this stage, and if not treated in time can cause severe consequences mainly in the pancreas, liver and kidneys, and can, in its chronic stage, affect the bone marrow, leading to bone marrow hypoplasia, compromising the production of blood cells and the patient's recovery and survival. Various wild vertebrates function as its natural reservoirs and play a fundamental role in the preservation and dissemination of the disease. This bacterial group is very common in warm countries due to the constant presence of its vectors most of the year, and Panama does not escape from this condition, especially nowadays with the population growth and the increasingly aggressive invasion of forests and preservation areas.

There are several species of *Ehrlichia* and with them variations in their pathogenicity [46]. When detecting and identifying Rickettsial agents in ticks of domestic animals in the Darién region of Panama, it was observed that 2.1% of the ticks were positive for the presence of *Erlichia chaffeensis* DNA, etiological agent of Human Monocytic Ehrlichiosis. When investigating Rickettsiae*, Ehrlichia* and *Anaplasma* in ticks from peridomestic environments in Panama, it was detected that 40% of the ticks collected had DNA from the Anaplasmataceae group, with *Erlichia chaffeensis* and *Erlichia ewingii*, as well as other species of *Ehrlichia* sp. that could not be identified due to their similarity within the group [45]. The first characterization of canine Ehrlichiosis in Panama observed a prevalence of 64.2% for *Ehrlichia canis* among the canines studied [66]. Clinical and serological evidence of dogs with the disease, from rural and urban areas in Panama, showed, through immunochromatography, that 63% (14) of the canines had antibodies against *E. canis*/*E. chaffeensis* and that 13% (3) had *Ehrlichia*/*Anaplasma* co-infection. The authors also relate that patient from rural environments showed the highest rates of *Ehrlichia* sp infection [67].

The first case of human infection caused by *Ehrlichia canis* in Panama occurred in the province of Chiriqui in 2013. The authors report the case of a 14-year-old immunocompetent boy who developed severe disease, showing high fever, general illness, lymphadenopathy, thrombocytopenia and alterations in liver and kidney function. The seriousness of the condition was since these symptoms can be confused with

other etiologies such as Dengue, Malaria, *Leptospira*, and even *Rickettsia* and other species of *Ehrlichia* sp. For this reason, and because of the wide distribution of the vectors and their participation in the transmission of *E. canis*, the differential diagnosis of these pathologies in Panama is of crucial importance [68].

V. Vector-Borne Diseases Caused by Bacteria with Zoonotic Potential to Develop in Panama

Anaplasmosis is a disease caused by intracytoplasmic bacteria of the same group as *Ehrlichia*, family Anaplasmataceae, genus *Anaplasma*, transmitted to vertebrate hosts, including man, through the bite of various species of ticks of the Ixodidae group. It causes febrile, anemic, debilitating and inflammatory disease, capable of causing convulsion and damage to various organs. The presence of DNA from *Anaplasma phagocytophilum*, the causative agent of Human Granulocytic Anaplasmosis, and *Anaplasma marginale* protozoan commonly found in cattle is reported [45], [46]. Already, molecular studies with this group in the isthmus, observed a prevalence of 21.4% for *Anaplasma platys* [66]. When studying canines from rural and urban areas in Panama, it was observed that 9% of the patients were positive for *A. platys* and *A. phagocytotophilum* and that only canines from rural areas showed positivity, through immunochromatography, for *Anaplasma* sp [67]. Recently, the presence of *A. phagocytophilum* DNA was detected in ticks of the *Ixodes tapirus* species from highlands in the Republic of Panama [3]. No human cases have been reported in this country. Bartonellosis is a disease caused by Gram-negative bacteria of the genus *Bartonella sp.* belonging to the Rickettsiae family, the most common of which is *Bartonella henselae*, which has developed in coexistence with cats. It is transmitted from cat to cat through the feces of their fleas containing the bacteria, and in humans causes the disease called Cat Scratching Sickness, whose transmission occurs when the cat causes a skin lesion in humans, with their claws contaminated with the feces of their own fleas, therefore inoculating the bacteria. This bacterium parasitizes red blood cells, most frequently from immunocompromised patients, with greater sensitivity in children. A comprehensive review of Bartonellosis, its several species, its zoonotic potential and its vectors, includes Veterinarians as a risk group for the disease due to the probability of being bitten by fleas and lice [69]. Since this bacterial group is of worldwide distribution and Panama has a high density of vertebrate hosts and their vectors, the possibility of this etiological agent showing its zoonotic potential in this country certainly exists. Borreliosis is a zoonotic infectious disease caused by the spirochete *Borrelia burgdorferi*, transmitted to humans by the bite of ticks of the genus *Ixodes* and perpetuated in the environment by wild animals such as deer and mice. It causes inflammatory joint disease in humans called Lyme disease. The update of this disease, carried out in Mexico in 2014, indicates that it is the most frequent vector-borne disease in the United States and is on the rise worldwide. The authors list the clinical stages of the disease, outlining its symptoms, diagnostic techniques and treatment [70]. The first report of canine Borreliosis, in a mid-altitude region in Medellín, Colombia, concludes that the disease moves through high altitude and urban areas, and that an increase in the incidence of bacterial vector-borne diseases is possible due to the growth of tick distribution because of climatic changes [71]. The first report of the *B. burgdorferi* complex found in ticks of the genus Ixodes in Central America and Panama highlights the importance of further studies with this genus of ixodids to understand their real importance in the ecology and epidemiology of vector-borne diseases [3].

VI. Vector-Borne Zoonoses Caused by Viruses

A. Equine Encephalitis

Although the horse is considered a working animal, its increasingly close relationship with humans, including children, due to sport, its use as a transport animal in ecological excursions, and even its therapeutic use in various pathologies, mainly of locomotive background, for this reason I include it in this review. **Equine encephalitis** is a vector-borne zoonosis caused by viruses of the family Togaviridae of *Alphavirus* genus. There are three variants of the disease, Eastern, Venezuelan and Western Equine Encephalitis, of which the first two have been reported in Panama. The reservoir agents of these diseases are birds, rodents and horses, and their vectors are mosquitoes of the genus *Culex* sp., *Aedes* sp. and *Culiseta* sp. The symptoms are those of an encephalitis, varying from headache, fever, weakness, pain, nausea, stiff neck, reflex alterations, vomiting, anorexia, in severe cases it can lead to death or have after-effects such as mental retardation, convulsions and paralysis. 6 confirmed cases of Eastern and/or Venezuelan Equine Encephalitis were described in 2019 in patients ranging from 1 to 35 months of age from the province of Darien, Panama, detailing symptomatology and diagnostic methods. Due to the severity of the pathology, the author recommends vector control and the development of vaccines for humans and animals against the disease [72].

VII. Vector-Borne Diseases Caused by Helminths with Zoonotic Potential to Develop in Panama

Dirofilariasis is a vector-borne zoonoses of worldwide distribution that affects dogs, cats and humans causing serious alterations in the heart and lungs of these companion animals but is also capable of causing granulomatous lesions in human lungs. This pathology is caused by a nematode called *Dirofilaria immitis* transmitted to humans and animals through the bite of mosquitoes of the genus *Aedes, Culex, Anopheles, Culiseta* and *Taeniorhynchus,* vectors with which it has a relationship of dependence since they are a vital part of its biological cycle. This disease was recently reported for the first time in domestic canines in the province of Chiriqui, Panama, and its incidence is increasing in this country [2]. No human cases have been reported in Panama. Dipylidiasis is a zoonotic disease of worldwide distribution, whose etiological agent is Dipylidium caninum, a parasite of the tapeworm group, which is transmitted to dogs, cats and children through the ingestion of dog and cat fleas of the genus *Ctenocephalides*, rarely human fleas *Pulex irritans* and dog lice *Trichodectes canis* [73]. Like all parasitosis, it causes

abdominal pain and gastrointestinal disorders, leading to nutritional and health imbalances. This parasite, as well as its vector, are very present in Panama; however, the absence of studies in this regard makes it difficult to evaluate the impact of this zoonoses on public health and veterinary medicine. No human cases have been reported in this country.

VIII. Concluding Remarks

From the review carried out we can group some considerations in agreement among the different vectorial zoonoses related to our pets. One of the main common factors is the increase in the vector population related to climatic changes and the rise in environmental temperature, which leads to a shortening of biological cycles with an increase in the number of arthropod populations within a time space. On the other hand, the frequent invasion of forests and woodlands by humans due to the increase in world population and therefore an upsurge in the demand for housing and food production, as well as the increasingly famous ecological tourism, which leads to the invasion of wild areas where humans and animals can function as vehicles of propagation to urban areas. At the same time, the ever-present adaptive evolutionary mechanism that allows the emergence of new species, originating from the co-evolution of etiological agents with new environments, climates, vectors and hosts. The increasingly common and alarming migration of human populations due to socioeconomic problems in the various countries of Latin America, which is favoring the transport and transmission of diseases between communities, including the reappearance of pathologies in regions where they were eradicated or controlled. The lack of public policies for the control of diseases and their vectors with real characteristics adapted to each region, as well as the absence of incentives for local and individualized research in each country. It is worth mentioning that the coexistence of pets with their owners has very positive effects for human beings with several immunological, ethological and psychological advantages and benefits, etc, once we have preventive control of the different diseases and the mapping of risk environments to avoid contact with the different vectors and thus protect our health and that of our pets, which are also victims of endemic areas and vectorial diseases. Finally, to stimulate the study and increase the knowledge of the population about these diseases, about the importance of preventive care of pets, about the importance and role of the veterinarian in public health, about the professions and activities at risk, and mainly, to stimulate, among the various professions involved, the habit of records, reports and publications that provide relevant data and information that help to clarify and draw the real situation of our country in relation to these diseases, since the absence of a pathogen in a region is very different from the lack of its diagnosis.

Conflict of Interest

Authors declare that they do not have any conflict of interest.

References

[1] Maggi GR, Krämer F. A review on the occurrence of companion vector-borne diseases in pet animals in Latin America. *Parasit Vectors*. 2019; 12(145): 1-37.

[2] Chacón SC, Candanedo PGC. Canine Dirofilariasis in Panama First Cases Report Immunochromatography and Necropsy Diagnosis. *J Appl Microb Res.* 2021; 4(1): 7-17.

[3] Bermúdez CSE, Félix ML, Domínguez AL, Kadoch N, Muñoz-Leal S, Venzal JM. Molecular screening for tick-borne bacteria and hematozoa in Ixodes cf. boliviensis and Ixodes tapirus (Ixodida: Ixodidae) from western highlands of Panama. *Curr Res Parasitol Vector Born Dis.* 2021; 1: 1-10.

[4] Bermúdez CSE, Miranda CRJ. De mascotas exóticas y turistas: nuevas oportunidades para la introducción de ectoparásitos en Panamá. *Bol Soc Ent Aragonesa.* 2011; (48): 491-492. Spanish.

[5] Miller JW. Chagas disease in Panama: Report of three cases. *Sth Med* J. 1931; 24(7): 645-647.

[6] Sousa OE. Anotaciones sobre la enfermedad de Chagas en Panamá. Frecuencia y distribución de Trypanosoma cruzi y Trypanosoma rangeli. *Rev Biol Trop.* 1972; 20(2): 167-179. Spanish.

[7] Sousa OE, Johnson CM. Precalence of Trypanosoma cruzi and Trypanosoma rangeli in triatomines (Hemiptera:Reduviidae) collected in the Republic of Panama. *Am J Trop Med Hyg.* 1973; 22(1): 18-23.

[8] Whitlaw Jr JT, Chaniotis BN. Palm trees and Chagas disease in Panama. *Am J Trop Med Hyg.* 1978; 27(5): 873-881.

[9] Vasquez AM, Samudio FE, Saldaña A, Paz HM, Calzada JE. Eco-epidemiological Aspects of Trypanosoma cruzi, Trypanosoma rangeli and their vector (Rhodnius pallescens) in Panama. *Rev Inst Med Trop S Paulo.* 2004; 46(4): 217-222.

[10] Calzada JE, Pineda V, Garisto JD, Samudio F, Santamaria AM, Saldaña A. Short Report: Human Trypanosomiasis in the Eastern Region of the Panama province: New Endemic Areas for Chagas Disease. *Am J Trop Med Hyg.* 2010; 82(4): 580-582.

[11] Gottdenker NL, Calzada JE, Saldaña A, Carroll CR. Association of Anthropogenic Land Use Change and Increased Abundance of the Chagas Disease Vector Rhodnius pallescens in a Rural Landscape of Panama. *Am J Trop Med Hyg.* 2011; 84(1): 70-77.

[12] Hurtado LA, Calzada JE, Pineda V, González K, Santamaria AM, Cáceres L, et al. Conocimiento y factores de riesgo relacionados con la enfermedad de Chagas en dos comunidades panameñas donde Rhodnius Pallescens es el vector principal. *Biomédica*. 2014; 34: 260-270. Spanish.

[13] Rodriguez IG, Loaiza JR. American trypanosomiasis, or Chagas disease, in Panama: A chronological synopsis of ecological and epidemiological research. *Parasit Vectors.* 2017; 10: 459:1-16.

[14] Saldaña A, Santamaria AM, Pineda V, Vásquez V, Gottdenker NL. A darker chromatic variation of Rhodnius pallescens infected by specific genetic groups of Trypanosoma rangeli and Trypanosoma cruzi from Panama. *Parasit Vectors.* 2018; 11: 423: 1-6.

[15] Peterson JK, Hashimoto K, Yoshioka K, Dorn PL, Gottdenker NL, Caranci A, et al. Chagas Disease in Central America: Recent Findings and Current Challenges in Vector Ecology and Control. *Curr Trop Med Rep.* 2019.

[16] Miranda AD, González KA, Samudio F, Pineda VJ, Calzada JE, Capitan-Barrios Z, et al. Molecular Identification of Parasites Causing Cutaneous Leishmaniasis in Panama. *Am J Trop Med Hyg.* 2021; 104(4): 1326-1334.

[17] Valderrama A, González M. Leishmaniasis: desafío para la salud pública en la región del Darién. *Rev Med Panama.* 2020; 40(2): 151-156.

[18] Miranda A, Carrasco R, Paz H, Pascale JM, Samudio F, Saldaña A, et al. Molecular Epidemiology of American Tegumentary Leishmaniasis in Panama. *Am J Trop Med Hyg.* 2009; 81(4): 565-571.

[19] Ramos A, Múñez E, Garcia-Dominguez J, Martinez-Ruiz R, Chicharro C, Baños I, et al. Mucosal leishmaniasis mimicking squamous cell carcinoma in a liver transplant recipient. *Transpl Infect Dis.* 2015; 17(3): 488-492.

[20] Prieto M, Uribe-Restrepo F, Arcos D, Vargas D. Case Report: Squamous Cell Carcinoma Referred for Mohs Surgery Found to be Cutaneous Leishmaniasis. *Am J Trop Med Hyg.* 2018; 99(6): 1537-1540.

[21] Darling ST. Autochthonous oriental sore in Panama. *Trans Soc Trop Med Hyg*. 1910; 4: 60-63.

[22] Calero CM, Johnson CM. Cutaneous leishmaniasis in the Republic of Panama. A report of twenty-five cases. *Am J Trop Med Hyg*. 1953; 2: 628-633.

[23] Hertig M, Fairchild GB, Johnson CM. Leishmaniasis transmisión reservoir project, in The 30th Annual Report of Gorgas Memorial Laboratory, Washington DC, US Goverment Printing Office. 1958.

[24] Johnson CM. Personal communication. Gorgas Memorial Laboratory, PO Box 2016 Balboa Heights CZ. 1953.
[25] Herrer A, Christensen HA. Natural Cutaneous Leishmaniasis among dogs in Panama. *Am J Trop Med Hyg.* 1976; 25(1): 59-63.
[26] Christensen HA, Johnson CM, Vásquez AM. Leishmaniasis Cutánea en Panama. Un breve resumen. *Rev Med Panama.* 1984; 9(3): 182-187. Spanish.
[27] Christensen HA, Vasquez AM, Petersen JL. Short Report: Epidemiologic Studies on Cutaneous Leishmaniasis in Eastern Panama. *Am J Trop Med Hyg*. 1999; 60(1): 54-57.
[28] Azpurua J, De La Cruz D, Valderama A, Windsor D. Lutzomyia Sand Fly Diversity and Rates of Infection by Wolbachia and an Exotic Leishmania Species on Barro Colorado Island, Panama. *PLoS Negl Trop Dis.* 2010; 4(3): e627.
[29] Valderrama A, Tavares MG, Andrade Filho JD. Anthropogenic influence on the distribution, abundance and diversity of sandfly species (Diptera: Phlebotominae: Psychodidae), vector of cutaneous leishmaniasis in Panama. *Mem Inst Oswaldo Cruz.* 2011; 106(8): 1024-1031
[30] Valderrama A, Tavares MG, Andrade Filho JD. Report of Lutzomyia longipalpis (Lutz & Neiva, 1912) (Diptera: Psychodidae: Phlebotominae) in a cutaneous-leishmaniasis-endemic área of Panama. *Mem Inst Oswaldo Cruz.* 2011; 106(8): 1049-1051
[31] Saldaña A, Chaves LF, Rigg ChA, Wald C, Smucker JE, Calzada JE. Short Report: Clinical Cutaneous Leishmaniasis Rates Are Associated with Household Lutzomyia gomezi, Lu. panamensis, and Lu. trapidoi Abundance in Trinidad de Las Minas, Western Panama. *Am J Trop Med Hyg.* 2013; 88(3): 572-574.
[32] Dutari LC, Loaiza JR. American Cutaneous Leishmaniasis in Panama: a historical review of entomological studies on anthropophilic Lutzomyia sand fly species. *Parasit Vectors.* 2014; 7(1): 1-10.
[33] Chaves LF, Calzada JE, Valderrama A, Saldaña A. Cutaneous Leishmaniasis and Sand Fly Fluctuations Are Associated with El Niño in Panamá. *PLoS Negl Trop Dis.* 2014; 8(10): e3210.
[34] Calzada JE, Saldaña A, González K, Rigg Ch, Pineda V, Santamaría AM, et al. Cutaneous Leishmaniasis in dogs: is high seroprevalence indicative of a reservoir role? *Parasitol*. 2015; 142: 1202-1214.
[35] Yamada K, Valderrama A, Gottdenker N, Cerezo L, Minakawa N, Saldaña A, et al. Macroecological patterns of American Cutaneous Leishmaniasis transmission across the health areas of Panama (1980-2012). *Parasit Epidemiol Control.* 2016; 1: 42-55.
[36] González K, Calzada JE, Diaz R, Paz H, García V, Miranda A, et al. Performance of immunohistochemistry as a useful tool for the diagnosis of cutaneous leishmaniasis in Panama, Central America. *Parasitol Int.* 2019; 71: 46-52.
[37] Rigg ChA, Calzada JE, Saldaña A, Perea M, Chaves LF, Valderrama A. Leishmania spp. Infection Rate and Feeding Patterns of Sand Flies (Diptera: Psychodidae) from a Hyperendemic Cutaneous Leishmaniasis Community in Panamá. *Am J Trop Med Hyg.* 2019; 100(4): 798-807.
[38] Valderrama A, Santos M, Castro A, Andrade Filho JD. Cryptic Species Lutzomyia longipalpis (Diptera: Phlebotominae) and its Implications in the Transmission of Leishmaniasis in Panama. *Rev Med Panama.* 2019; 36(1): 2-7.
[39] Rodaniche EC, Rodaniche A. Spotted Fever in Panama; Isolation of the Etiologic Agent from a Fatal Case. *Am J Trop Med.* 1950; 30(4): 511-517.
[40] Calero MC, Nuñez JM, Goytía RS. Rocky Mountain Spotted Fever in Panama. Report of two cases. Medical Departments, Panama Hospital and Santo Tomás Hospital, and Instituto de Salubridad y Enfermedades Tropicales, Mexico, D.F. 1952: 631-636.
[41] Rodaniche EC. Natural Infection of the Tick Amblyomma cajennense, with Rickettsia rickettsii in Panama. *Am J Trop Med Hyg*. 1953; 2(4): 696-699.
[42] Obaldía N. Historia de las Enfermedades Animales Transmitidas por Garrapatas en Panamá. *Notas Veterinarias Ass Pan Med Vet.* 1992; 2(1): 15-17. Spanish.
[43] Estripeaut D, Aramburú MG, Sáez-Llorens X, Thompson HA, Dasch GA, Paddock ChD, et al. Rocky Mountain Spotted Fever, Panama. *Emer Infect Dis.* 2007; 13(11): 1763-1765.
[44] Dantas-Torres F. Rocky Mountain spotted fever. *Lancet Infect Dis.* 2007; 7: 724-732.
[45] Eremeeva ME, Karpathy SE, Levin ML, Caballero CM, Bermudez S, Dasch GA, et al. Spotted fever rickettsiae, Ehrlichia and Anaplasma, in ticks from peridomestic environments in Panama. *Eur Soc Clin Micro Infect Dis*. 2009; 15(suppl. 2): 12-14.
[46] Bermúdez SE, Eremeeva ME, Karpathy SE, Samudio F, Zambrano ML, Zaldivar Y, et al. Detection and Identification of Rickettsial Agents in Ticks From Domestic Mammals in Eastern Panama. *J Med Entomol. 2009*; 46(4): 856-861.
[47] Bermúdez CSE, Zaldívar AY, Spolidorio MG, Moraes-Filho J, Miranda RJ, Caballero CM, et al. Rickettsial infection in domestic mammals and their ectoparasites in El Valle de Antón, Coclé, Panama. *Vet Parasitol.* 2011; 177: 134-138.
[48] Labruna MB, Mattar VS, Nava S, Bermúdez S. Venzal JM, Dolz G, et al. Rickettsioses in Latin America, Caribbean, Spain and Portugal. *Rev MVZ Córdoba.* 2011; 16(2): 2435-2457.
[49] Tribaldos M, Zaldivar Y, Bermúdez S, Samudio F, Mendoza Y, Martinez AA, et al. Rocky Mountain spotted fever in Panama: a cluster description. Case Report. *J Infect Dev Ctries.* 2011; 5(10): 737-741.
[50] Bermúdez S, Miranda R, Zaldívar Y, González P, Berguido G, Trejos D, et al. Detección de Rickettsia spp. en ectoparásitos de animales domésticos y silvestres de la Reserva Natural Privada Cerro Chucantí y comunidades aledañas, Panamá, 2007-2010. *Biomédica*. 2012; 32: 189-195.
[51] Hidalgo M, Faccini-Martínez AA, Valbuena G. Rickettsiosis transmitidas por garrapatas en las Américas: avances clínicos y epidemiológicos, y retos en el diagnóstico. *Biomédica*. 2013; 33(Supl.1): 161-178. Spanish.
[52] Bermúdez SE, Lyons CR, García GG, Zaldívar YL, Gabster A, Arteaga GB. Serologic evidence of human Rickettsia infection found in three locations in Panamá. *Biomédica*. 2013; 33(Supl.1): 31-37.
[53] Zavala Castro JE. Rickettsia felis: un patógeno emergente en Latinoamérica. Conferencias Magistrales. *Acta Méd Costarric.* 2013. Spanish.
[54] De Lucas J, García E, García G, Castro A, Lyons C, Bermúdez CSE. Nuevo caso de rickettsiosis humana en Panamá, a partir de evidencia serológica y clínica. Informe de caso. *Rev Med Panama.* 2013; 33(2): 40-43. Spanish.
[55] Abarca K, Oteo JA. Aproximación clínica y principales rickettsiosis transmitidas por garrapatas presentes en Latinoamérica. *Rev Chil Infect.* 2014; 31(5): 569-576. Spanish.
[56] Castro DAM, García GG, Dzul-Rosado K, Aguilar A, Castillo J, Gabster A, et al. Questing Amblyomma mixtum and Haemaphysalis juxtakochi (Acari: Ixodidae) Infected with Candidatus "Rickettsia amblyommii" from the Natural Environment in Panama Canal Basin, Panama. *Tropical Medicine Health.* 2015; 43(4): 217-222.
[57] Bermúdez SE, Castro AM, Trejos D, García GG, Gabster A, Miranda RJ, et al. Distribution of Spotted Fever Group Rickettsiae in Hard Ticks (Ixodida: Ixodidae) from Panamanian Urban and Rural Environments (2007-2013). *EcoHealth. International Association for Ecology and Health.* 2016.
[58] Ferrell AM, Brinkerhoff RJ, Bernal J, Bermúdez SE. Ticks and tick-borne pathogens of dogs along an elevational and land-use gradient in Chiriquí province, Panamá. *Exp Appl Acarol.* 2017.
[59] Bermúdez SE, Gottdenker N, Krishnvajhala A, Fox A, Wilder HK, González K, et al. Synanthropic Mammals as Potential Hosts of Tick-Borne Pathogens in Panama. *PLoS ONE.* 2017; 12(1): e0169047.
[60] Bermúdez CSE, Troyo A. A review of the genus Rickettsia in Central America. *Res Report Trop Med.* 2018; 9: 103-112.
[61] Martínez-Caballero A, Moreno B, González C, Martínez G, Adames M, Pachar JV, et al. Descriptions of two new cases of Rocky Mountain spotted fever in Panama, and coincident infection with Rickettsia rickettsii in Rhipicephalus sanguineus s.l. in an urban locality of Panama City, Panama. *Epidemiol Infect.* 2018; 146: 875-878.
[62] Daza TC, Bermúdez CS. Clinical and para clinical characteristics of patients with fever spotted by Rickettsia rickettsii in Panama (1950-1951; 2004-2017). *Rev Med Panama.* 2019; 39(3): 79-84.
[63] Cuero C. Spotted fever, shortage of research papers and other matters. Rev Med Panama. 2019; 39(3): 78.
[64] TVN.COM. Personas (Fotografía). Identifican Bacteria que causó la muerte de cinco personas en la comarca Ngäbe Buglé. [Internet] 2019. Available from: https://www.tvn-2.com/nacionales/identifica-bacteria-muerte-personas-ngabe-bugle-minsa-garrapatas-rickettsia-rickettsii_1_1296705.html Spanish.
[65] Linero K, Serrano S, Florián D. Rickettsiosis: La importancia de realizar un diagnóstico y manejo precoz. Caso Clínico. *Pediátr Panamá.* 2022; 51(1): 30-38. Spanish.
[66] Santamaría A, Calzada JE, Saldaña A, Yabsley MJ, Gottdenker NL.Molecular Diagnosis and Species Identification of Ehrlichia and Anaplasma Infections in Dogs from Panama, Central America. Short Communications. Vector-Borne Zoo Dis. 2014; 14(5): 368-370.
[67] Petrucelli JV, Bermúdez S. Clinical and Serological Evidence of Canine Anaplasmosis and Ehrlichiosis in Urban and Rural Panama. Ann Clin Cytol Pathol. 2017; 3(1): 1050.
[68] Daza TC, Osorio J, Santamaría AM, Suárez JA, Hurtado A, Bermúdez S. Characterization of the First Case of Human Infection by Ehrlichia canis in Panama. Rev Med Panama. 2018; 38(3): 63-68.

[69] Breitschwerdt EB, Maggi RG, Chomel BB, Lappin MR. Bartonellosis: an emerging infectious disease of zoonotic importance to animals and human beings. J Vet Emerg Crit Care. 2010; 20(1): 8-30.
[70] Meléndez MEG, Taylor CS, Alanís JCS, Candiani JO. Enfermedad de Lyme: actualizaciones. Gac Med Mex. 2014; 150: 84-95.
[71] González-Dominguez MS, Villegas JP, Carmona S, Castañeda H. First report of canine borreliosis seroprevalence in a middle-altitude tropical urban área (Medellin-Colombia. Rev CES Med Zootec. 2014; 9(2): 348-354.
[72] De la Rosa AG. Equine encephalitis at Hospital del Niño Dr. José Renán Esquivel (Panama): Bibliographic and case review. Pediátr Panamá. 2019; 48(2): 23-28.
[73] Neira OP, Jofré ML, Muñoz SN. Infección por Dipylidium caninum en un preescolar. Presentación del caso y revisión de la literatura. Rev Chil Infect. 2008; 25(6): 465-471.