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Haemorrhagic Fevers Transmitted by Vectors in the Neotropics

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1. Introduction

During the past 20 years there has been a dramatic emergence and re-emergence of epidemic of haemorrhagic vector-borne-disease (VBD) that have been caused by viruses believed to be under control such as dengue, yellow fever, Venezuelan equine encephalitis, Saint Louis Virus, Arenavirus, hantavirus or viruses that have extended their geographic distribution such as West Nile and Rift Valley fever. Bacteria like *Leptospira* and *Rickettsia* have also re-emerged.

Many reports have demonstrated the changing global and tropics epidemiology. The population growth, urbanization, human activities, and even climate variability all help to a continual fluctuation in the epidemiology of several haemorrhagic fevers transmitted by vectors in the tropics.

Haemorrhagic fevers produced by bacterial or virus share many general features. Those infectious agents are arthropod-borne cause many haemorrhagic fevers. For some viral haemorrhagic fevers, person-to-person transmission may occur through direct contact with infected blood or secretions. Infectious agents are transmitted by arthropod like mosquitoes and ticks. Animal reservoirs are usually wild rodents, however, pets, domestic livestock, urban mice, monkeys, and other primates may also provide as intermediate hosts.

The term viral hemorrhagic fever describes a potentially fatal clinical syndrome characterized by an insidious onset of nonspecific signs followed by bleeding manifestations and shock. The haemorrhagic fever syndrome is also characterized by a combination of a capillary leak syndrome and bleeding diathesis. The clinical manifestations and even histopathological findings are pretty similar and difficult to make a differential diagnosis

(Table 1, Figure1). In the tropics where endemic haemorrhagic fevers are frequent that is a big concern.

This chapter gives an overview of the epidemiology and ecology of haemorrhagic fevers transmitted by vector taking place exclusively in the neotropics, hence it shows the principal clinical syndromes associated to vectors.

Figure 1. Clinical diagnostic challenges of the haemorrhagic fevers in the tropics

Disease	Leptospirosis	Dengue Fever	Enteric fever	Yellow fever	Severe <i>P. vivax</i> malaria	Acute viral hepatitis	Hantavirus	Rocky Mountain spotted fever
Infectious agent	<i>Leptospira</i> sp.	Dengue virus	<i>Salmonella typhi</i> and <i>S. paratyphi</i>	Yellow fever virus	<i>P. vivax</i>	Hepatitis E virus, A, B	Hantavirus (different species)	<i>Rickettsia rickettsii</i>
Incubation period	(2 – 26) Average 10	7–10 days	7–14 days (range, 3–60 days)	incubation period of 3 to 6 days,	14 days (10 to 30) (occasionally months)	15 to 60 days, 45 to 180 (HBV)	14 to 17 days (range 9 to 33)	7 days (range, 2 to 14 days)
Clinical presentation	Abrupt onset of fever, rigors	Acute febrile disease	Non-specific febrile illness, often with an insidious onset.	Acute febrile disease	Abrupt onset of fever, rigors	Non-specific febrile illness, often with an insidious onset.	Fever, chills and myalgias, which can be severe in many cases	Acute febrile disease
Headache	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Musculoskeletal pain	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nausea - vomiting	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Abdominal pain	Occasionally	Occasionally	Yes	Yes	Rare	Yes	Yes	Yes
Diarrhea	No	Occasionally	Occasionally, antecedent of diarrhea at infection time	No	rare	Occasionally	Occasionally	yes
Cough	No	No	No	No	No	No	Occasionally	No
Physical examination								
Rash	Rare	yes after the third day of illness	Yes, rose spots	No	No	Occasionally (urticarial rash)	No	Yes after the fifth day of illness
Jaundice	Yes	rare	rare	yes	yes	Yes, cas definition	No	Yes
Hepatomegaly	Yes	Only in severe ill patient	yes	occasionally	rare	Yes	Only in severe ill patient	Only in severe ill patient
Splenomegaly	Yes	No	Yes	No	Yes	Rare	No	no
Ocular involvement	Yes, conjuntival suffusion	No	No	Conjunctivitis	No	No	No	conjunctivitis
Muscle tenderness	Yes	Yes	No	No	Rare	Occasionally	No	Only in severe ill patient
Hemorrhagic manifestations, such as petechiae, purpura	Only in severe ill patient	Yes	Only in severe ill patient	Only in severe ill patient	Only in severe ill patient	Only in severe ill patient	Only in severe ill patient	Only in severe ill patient
Abdominal pain	Yes	Only in severe ill patient	Yes	Yes	Yes	Yes	Yes	Yes
Other findings								Unlike other tickborne rickettsial diseases, the presence of inoculation eschar is rare in RMSF

Disease	Leptospirosis	Dengue Fever	Enteric fever	Yellow fever	Severe <i>P. vivax</i> malaria	Acute viral hepatitis	Hantavirus	Rocky Mountain spotted fever
Laboratory findings								
Hemogram	normal	normal	normal	normal	Yes, also severe anaemia < 70 g/dl	normal	normal	Normal
White blood cell (WBC)	counts are generally less than 10,000/mm ³ but may range between 3,000 and 26,000/microL; a shift to the left is seen in about two-thirds of patients	leukopenia with lymphopenia,	either leukopenia or leukocytosis; leukocytosis is more common in children	Leukopenia with a relative neutropenia,	Usually normal	Neutropenia, lymphopenia and atypical lymphocytes may occasionally be observed	Leukocytosis (as high as 90,000 cells/microL) and the appearance of immunoblasts are more pronounced in those patients with severe forms of illness	may be low, normal, or elevated
Thrombocytopenia	Only in severe ill patient	Yes	Rare	Yes	Frequent	Rare	Rapid decline in the platelet count	yes
Blood chemistry								
Liver function tests	High bilirubin level despite minimal to moderate elevations of hepatic transaminases (usually <200 IU/L)	Moderate elevation of hepatic transaminases	Moderate elevation of hepatic transaminases	Important liver necrosis with high transaminases and bilirubin	High bilirubin level despite minimal to moderate elevations of hepatic transaminases (usually <200 IU/L)	Peak levels of ALT vary from 1000 U/L to 2000 U/L at the onset	Increase in serum levels of LDH, which often occurs early, and elevations in hepatocellular enzymes and lactate	Jaundice, only in severe ill patients
Hypoalbuminemia-albuminuria	Uncommon	Uncommon	Uncommon	Yes	frequent		Uncommon	Uncommon
Renal function test	Acute renal failure in 16–40 % of severe ill patients	ARF uncommon	ARF uncommon	ARF is frequent with albuminuria	Acute renal failure and hemoglobinuria	Only in severe ill patients	Only in severe ill patients	ARF in < 20% of cases
Creatine kinase	Elevation is found in approximately 50 percent of patients	Normal	Occasionally elevated	Occasionally elevated	Frequently elevated	Normal	Normal	Normal
Coagulation analyses	Normal	Normal	Normal	Prolonged clotting, and increased prothrombin time are common.	normal	Prolonged clotting	Coagulopathy with hemorrhage common in infections due to Andes virus	

Disease	Leptospirosis	Dengue Fever	Enteric fever	Yellow fever	Severe <i>P. vivax</i> malaria	Acute viral hepatitis	Hantavirus	Rocky Mountain spotted fever
Imaging								
Chest radiographs	May show small nodular densities, which can progress to confluent consolidation or a ground glass appearance	No contributive sometimes pleural effusion	No contributive	No contributive, sometimes pleural effusion	compatible with acute lung injury and non cardiogenic pulmonary edema	No contributory	Radiologic changes such as bilateral interstitial infiltrates compatible with acute lung injury and non cardiogenic pulmonary edema	Radiologic changes such as alveolar infiltrates, interstitial pneumonia, and pleural effusion occurs only in severe disease
Diagnosis								
Serologic test	Gold standard MAT (microscopic agglutination test) a single titer of >1:800 is strong evidence of current or recent infection with leptospira in a endemic area >1:200 in a non endemic area Serology may be insensitive, particularly in early acute-phase specimens. Delayed seroconversions are common, with up to 10% of patients failing to seroconvert within 30 days of the clinical onset	The most commonly used test for the diagnosis of dengue is the IgM capture ELISA, but this test is negative early in the course of the disease, should be performed only four to five days after the onset of symptoms, and gives only a probable diagnosis	Diagnosis of enteric fever requires the isolation of <i>S. typhi</i> or <i>S. paratyphi</i> from blood, bone marrow. The sensitivity of blood culture is only 40% to 80%, probably because of high rates of antimicrobial use in endemic areas and the small quantities of <i>S. typhi</i>	ELISA IgM The assay is more than 95% sensitive when serum specimens obtained between 7 and 10 days after the onset are tested	Gold standard: Detection of parasites on Giemsa-stained blood smears by light microscopy	Gold standard ELISA IgM	By the time symptoms are evident, patients uniformly have antiviral antibodies of the IgM class In the United States, those state health departments that offer hantavirus diagnostic testing use IgG and mu-capture IgM ELISAs developed and distributed by the CDC	indirect fluorescent antibody (IFA) test Antibodies typically appear 7 to 10 days after the onset of the illness

Disease	Leptospirosis	Dengue Fever	Enteric fever	Yellow fever	Severe <i>P. vivax</i> malaria	Acute viral hepatitis	Hantavirus	Rocky Mountain spotted fever
Severe forms								
Hepatic involvement	Frequently, but is not associated with hepatocellular necrosis, and liver function returns to normal after recovery	Serum aminotransaminases are increased in most cases (60%–80%) and can be accompanied by symptoms of acute hepatitis including right upper quadrant pain, hepatomegaly, and jaundice.	Only, moderate elevation of hepatic transaminases	Frequently, with severe hepatocellular necrosis	Jaundice (high levels of bilirubin direct and indirect), in infrequently hepatocellular necrosis	Liver failure	No	Only, moderate elevation of hepatic transaminases
Renal involvement	Intrinsic renal failure (interstitial nephritis)	Only pre-renal failure	Glomerulonephritis (rare)	Intrinsic renal failure with characterized by oliguria, azotemia, and very high levels of protein in the urine	Acute renal failure (acute tubular necrosis)	Rare	Rare, associated with Oran virus	rare
Pulmonary involvement	Severe pulmonary hemorrhage syndrome	Only pleural effusion	No	No	ARDS, acute noncardiogenic pulmonary edema	Rare	ARDS, acute noncardiogenic pulmonary edema	Occasionally, interstitial pneumonia, pulmonary non cardiogenic edema
CNS involvement	Rare, meningoencephalitis	Rare, encephalitis	Rare, meningitis	Metabolic encephalopathy by hepatic dysfunction	Cerebral malaria: coma, multiple convulsions (more than two episodes in 24 h)	Hepatic encephalopathy	No	Frequently Meningoencephalitis
Hemorrhagic manifestations	Rare	Frequently, case definition DHF	Rare, CID	Frequently, hepatic-induced coagulopathy, with gastrointestinal bleeding	Rare, only in severe ill patients	Only in severe ill patients	Coagulopathy with hemorrhage common in infections due to Andes virus	Rare

Table 1. Clinical characteristics of some tropical infections with hemorrhagic manifestations presents in tropical South America

Disease	Leptospirosis	Dengue Fever	Enteric fever	Yellow fever	Severe <i>P. vivax</i> malaria	Acute viral hepatitis	Hantavirus	Rocky Mountain spotted fever
Other	Uveitis, myocarditis		Intestinal perforation, gastrointestinal bleeding		hypoglycaemia (blood glucose <2.2 mmol/l or <40 mg/dl) metabolic acidosis (plasma bicarbonate <15 mmol/l) Spontaneous splenic rupture		Lactic acidosis associated with poor prognosis. Marked reduction of left ventricular ejection fraction at ecocardiography	Gangrene, Hyponatremia
Treatment	For hospitalized adults with severe disease, we suggest intravenous therapy with penicillin (6 million units daily), doxycycline (100 mg twice daily), ceftriaxone (1 g every 24 hours), or cefotaxime (1 g every six hours)	A rise in the hematocrit of 20 percent indicates considerable plasma loss, and patients with this condition require intensive care with intravenous replacement of fluids with cristaloids	For treatment of drug-susceptible typhoid fever, fluoroquinolones are the most effective class of agents Ceftriaxone, cefotaxime, and oral cefixime are effective agents for treatment of multidrug-resistant enteric fever	Ideally a severely ill patient is admitted to the intensive care unit (ICU) and provided with vasoactive medications, fluid resuscitation, and ventilator support.	Intravenous (IV) artesunate should be used in preference to quinine for the treatment of severe malaria in adults	Supportive, severe cases liver transplantation	Ideally a severely ill patient is admitted to the intensive care unit (ICU) and provided with vasoactive medications, fluid resuscitation, and ventilator support. The use of ribavirin off protocol cannot be recommended for established HCPS	Doxycycline is currently considered the drug of choice for nearly all patients with RMSF, including young children

2. Common VBD in the tropics transmitted by arthropods and rodents

Etiological agents of HF affect humans on all continents. Most but not all agents causing HF are arboviruses, with transmission to humans resulting from an arthropod bite. However, animal reservoirs are generally rats and mice, but domestic livestock, monkeys, bats and other primates may also serve as intermediate hosts. Population growth, urbanization, human activities, and even climate change all contribute to a continual flux in the epidemiology of many HF transmitted by vectors arboviruses.

Haemorrhagic fevers share many clinical common features. Infectious agents that are arthropod-borne (usually mosquitoes and ticks) cause many viral hemorrhagic fevers. Some viral hemorrhagic fevers, person-to-person transmission may occur through direct contact with infected patients, their blood, or their secretions and excretions.

3. Flaviviral hemorrhagic fevers

Dengue is the mainly significant arboviral disease of humans with over half of the world's population existing in areas of risk. The occurrence and scale of epidemic dengue have augmented considerably in the last 40 years as the viruses and the mosquito vectors have both extended geographically in the tropical regions of the world in particular across South-east Asia, Africa, Western Pacific and tropics areas of the Americas, (Figure 2).

Dengue and Yellow fever are the prototype virus of the *Flaviviridae*, Dengue is a mosquito-transmitted viral disease very common in tropical areas of South America. The virus is transmitted mainly by *Aedes aegypti*, this mosquito is peridomestic and breeds in artificial containers around human settlements. The vector has a great preference feed for humans, which is a reason for the success disease; Dengue mainly is an urban disease and has no social class preferences. Dengue has two clinical presentations: dengue fever and hemorrhagic dengue. There are four dengue serotypes classified as 1, 2, 3, 4.

Dengue fever is supposed to generate about 230 million infections worldwide every year, of which 25,000 are lethal. Worldwide incidence has increasing swiftly in new decades with some 3.6 billion people, over half of the world's population, currently at risk, primarily in cities and villages centres of the tropics and subtropics. Demographic and community changes, in particular urbanization, globalization, and augmented worldwide journey, are most important contributors to the get higher incidence and geographic extension of dengue infections.

In modern lifetimes, the proliferate of unprepared urbanization, with related unsatisfactory housing, overcapacity and weakening in water, sewage and waste management systems, has produced model circumstances for enlarged diffusion of the dengue virus in tropical urban areas. Age frequency of dengue has been distributed in a broad ages either in adolescents or adults. In addition, the advance of tourism in the tropics has led to a boost in the number of tourists who become infected, mainly adults.

Figure 2. Distribution of several hemorrhagic fevers in Latin America

Symptoms and risk factors for dengue haemorrhagic fever (DHF) and severe dengue differ between children and adults, with co-morbidities and incidence in more elderly patients associated with greater risk of mortality. Treatment options for DF and DHF in adults, as for children, centre round fluid replacement (either orally or intravenously, depending on severity) and antipyretics. Further data are still needed on the optimal treatment of adult patients.

Because Dengue is endemic in the most tropical countries, the disease is overdiagnosed, therefore, many other hemorrhagic fevers as leptospirosis, hantavirus, arenavirus, rickettsiosis, Venezuelan equine encephalitis, chikungunya virus and malaria are erroneously diagnosed as dengue. Those diseases are clinically indistinguishable from dengue and other vector borne diseases and confirmatory diagnosis needs the employ of proficient laboratory tests that are difficult to pay for developing countries. Consequently, the endemic diseases above mentioned in developing countries remains mostly unidentified. Recent surveillance suggests

that Venezuelan equine encephalitis, it may represent up to 10% of the dengue burden in neotropical cities, or tens-of-thousands of cases per year throughout Latin America.

On the other hand, yellow fever remains an important cause of mortality and morbidity in several South American countries like Colombia, Venezuela, Guyana, Ecuador, Peru, Bolivia and Brazil (Figure 2). The mosquitoes of *Haemagogus* and *Sabethes* are the main vectors in the rain forest, in contrast, *Aedes aegypti* in the urban areas cause YF.

YF has two different cycles: one endemic or sylvan cycle involving monkeys and epidemic urban cycle rare in South America. The frequented endemic sylvan YF constitutes to great source for introducing into urban environment. Despite the serious public health that YF represents, many South American countries abruptly discontinued YF campaigns.

4. Hantavirus

The hantaviruses are a group of emerging rodent-borne pathogens (family *Bunyaviridae*; Genus *Hantavirus*) that are etiologic agents for hemorrhagic fever with renal syndrome (HFRS) in Europe and Asia and hantavirus cardiopulmonary syndrome (HCPS) in the Americas. HFRS is associated with rodents of the family *Muridae*, subfamilies *Murinae* and *Arvicolinae*; HPS is associated with rodents of the subfamily *Sigmodontinae*. Since the identification of HCPS in USA in 1993, a huge number of cases of HPS and an rising number of hantaviruses and rodent reservoir hosts have been identified in Central and South America (Figure 2). Epidemiologic studies have demonstrated important differences in frequency of infection with hantaviruses in both human and rodent host populations. Antibody prevalences in rodent and human populations may vary from less than 1% to more than 40%. Currently, more than 1500 cases of HCPS have been reported and more than 15 genetically distinct variants of hantaviruses, all associated with sigmodontine rodents, have been identified throughout the Americas. Hantaviruses have been documented in South America from Argentina, Chile, Paraguay, Uruguay, Bolivia, Brazil, Peru, and Venezuela, and in Central America from Costa Rica and Panama.

Patients with HCPS typically present a short febrile prodrome of 3-5 days. In addition to fever and myalgias, early symptoms include headache, chills, dizziness, non-productive cough, nausea, vomiting, and other gastrointestinal symptoms. Malaise, diarrhoea, and lightheadedness are reported by approximately half of all patients, with less frequent reports of arthralgias, back pain, and abdominal pain. The mean duration of symptoms before hospitalization is 5.4 days. Remarkable hematologic result included a high white-cell count with augmented neutrophils, myeloid precursors, and atypical lymphocytes.

Several characteristics distinguish Latin American HCPS cases from the classical HCPS described for the first time in the USA. These include a variation in severity of disease from moderate and self-limiting to severe, the demonstration of person-to-person transmission, and a somewhat higher incidence of extrapulmonary clinical manifestations in the South American form of HCPS. Nevertheless, hantaviruses in the Americas is still far from complete knowl-

odgement. The factors involved in the dynamics of these viruses in nature, their establishment and transmission within host populations and from hosts to humans, and the variable pathology of these viruses in humans are complex. It is likely that more hantaviruses will be described in the future, and much more data will be required in order to describe the diversity and evolution of this group of pathogens. Latin America, as the centre of diversity for *Sigmodontine* rodents and their hantaviruses is presented with the unique opportunity as well as the challenge of being center stage for continued studies of the dynamics of hantaviruses in natural host populations and the links of host and virus to human populations.

5. Arenavirus

The *Arenaviridae* is a miscellaneous RNA viruses and contains the etiologic agents of some emerging zoonoses that are characterized by high case-fatality rates. Rats and mice (murids) are the main reservoirs of the arenaviruses. So far, six arenaviruses are reported to produce human disease: Guanarito (causes Venezuelan hemorrhagic fever), Junin (Argentine hemorrhagic fever), lymphocytic choriomeningitis (lymphocytic choriomeningitis), Lassa (Lassa fever), Machupo (Bolivian hemorrhagic fever), and Sabiá (human disease from Brazil).

The recognized arenaviruses in the Americas are hosted by rodents of the family *Cricetidae*; with the exception may be hosted by a bat (genus *Artibeus*, family *Phyllostomidae*). Pichindé virus, hosted by *Oryzomys albigularis*, was described from animals in the Pichindé Valley near Cali, Colombia, Guanarito virus, is also hosted by *Zygodontomys brevicauda*, the short-tailed cane mouse, causes Venezuelan hemorrhagic fever in the Venezuelan state of Portuguesa. This state borders on Colombia, and *Z. brevicauda* is a common species in Caribbean Colombia.

6. South American hemorrhagic viruses

Four members of the Tacaribe complex produce acute disease in humans: Junin, Machupo, Guanarito, and Sabiá viruses. Junin virus, the mainly considerably studied of the South American hemorrhagic fever viruses, is the agent of Argentine hemorrhagic fever. The disease disproportionately affect men, probably because of the job-related risk linked with agricultural work. The mouse *Calomys musculinus* is recognized the primary host of Junin virus.

Guanarito virus, the agent of Venezuelan hemorrhagic fever, mainly affects rural populations and has a restricted geographic circulation. Venezuelan hemorrhagic fever has been described close to the Portuguesa province in northwestern Venezuela, an intensively agricultural area. In 1989, previous to its detection as a dissimilar an hemorrhagic disease, irregular cases of Venezuelan hemorrhagic fever were probably mistaken diagnosed as dengue fever. Remarkably, deforestation and human intrusion into rodent environment may have resulted in augmented human contact to infected rodents and a concurrent enhance in human illnesses. The reservoir of Guanarito virus is a short-tailed rodent called *Zygodontomys brevicauda* and *Sigmodon alstoni*.

Regarding Bolivian hemorrhagic fever, Machupo virus is considered the etiology agent, which it was discovered in 1962 during an outbreak of viral hemorrhagic fever. Outbreaks of Bolivian hemorrhagic fever have occurred in cities and towns, probably connected to factors that privileged the invasion of human dwellings by rodents. Good practices control of outbreaks was capable through execution of intensive rodent trapping and education programs. The reservoir of Machupo virus is a sunset mouse *Calomys callosus*.

Regarding Brazilian hemorrhagic fever, Sabiá virus, is recognized as the etiologic agent. Sabiá virus was detected in 1994 from a Brazilian patient who was originally believed to have yellow fever, at that moment, a viral hemorrhagic fever was diagnosed. After that, no cases of acquired human disease caused by Sabiá virus have been reported. The reservoir of this virus is unknown, but is assumed to be a South American rodent. Sporadic cases of infections with Sabiá virus was been reported among laboratory workers in Brazil and the United States.

Arenavirus cases in Colombia have not been reported yet. However, we collected and tested 210 sigmodontine rodents of 3 species: 181 *Z. brevicauda*, 28 *Oligoryzomys fulvescens*, and 1 *Oecomys concolor*. Eleven serum samples, 10 from *Z. brevicauda* and 1 from *O. fulvescens*, had detectable arenavirus antibody. Three *Z. brevicauda* samples had antibody reactive to both Pichindé and Guanarito virus, and 7 more were positive for either Pichindé or Guanarito arenaviruses. The results demonstrated the presence of >1 arenaviruses circulating among common rodent hosts in Caribbean Colombia. We emphasize that many New World arenaviruses are likely cross-reactive to the antigens we used; recovery and sequencing of viral RNA will be essential to fully characterize these viruses. Hemorrhagic fever of arenaviral origin should be included in the differential diagnosis of tropical fevers, at least in studied region. As the human population of the rural Department of Córdoba and adjacent areas of the tropical Caribbean coast.

Besides the hemorrhagic South American virus described above, the principal old world arenavirus are the Lymphocytic choriomeningitis virus (LCMV) and Lassa virus. LCMV has a global spreading, which coincides with the geographic dispersion of its major host, the ever-present house mouse (*Mus musculus*). LCMV is a cause of acute aseptic meningoencephalitis and congenital malformations of the CNS and eye. People with a decreased immune system and women in the first or second trimester of pregnancy are at enlarged probability of developing severe disease. Mainly inhabitants are most likely to be infected by rodents in their homes; because population of *Mus musculus* are much larger in tropical countries, infections with LCMV in humans, may be frequent. Hence, deprived sanitation and other natural conditions facilitate mice incursion of human settlements.

In Europe and USA, peaks in the summer and fall are likely because more mice are entering homes. It is really unknown the incidence of infection in humans in different countries with lymphocytic choriomeningitis virus, but mainly experts believe the disease is not well known or underrecognized or underreported. The seroprevalence of lymphocytic choriomeningitis in different countries is between 0% and 60%. Vague clinical signs, demanding diagnostic problems, because require of knowledge on physicians and public health workers to put together recognition of lymphocytic choriomeningitis virus infections and its role diseases in humans.

Regarding Lassa fever is a significant cause of febrile disease in West Africa; it is projected about 100,000 to 300,000 cases and numerous deaths linked to Lassa virus. The cases are primarily reported from hyperendemic or endemic foci in the West African countries of Guinea, Liberia, Nigeria, and Sierra Leone.

7. Leptospirosis

It is a bacterial zoonotic disease that affects both humans and animals. Humans become infected through direct contact with the urine of infected animals or with a urine-contaminated environment. *Leptospira* is the bacteria belong to *Spirochetaceae* family transmitted directly or indirectly from animals to humans, who can suffer severe hemorrhagic, hepatic/renal and pulmonary disease. The bacteria enter the body through cuts or abrasions on the skin, or through the mucous membranes of the mouth, nose and eyes. Person-to-person transmission is rare. In the early stages of the disease, symptoms include high fever, severe headache, muscle pain, chills, redness of the eyes, abdominal pain, jaundice, haemorrhages in the skin and mucous membranes, vomiting, diarrhoea, and rash.

There are 20 known *Leptospira* species and hundreds of serovars, some of which belong to different species. Because there are pathogenic and non-pathogenic leptospira, it is basic to identify the pathogenic serovars of leptospires and their potential reservoirs to focus control strategies.

Pathogenic *Leptospira* spp are chronically maintained in renal tubules of a wide range of wild and domestic mammals and enzootic cycles are maintained by direct contact with infected urine or indirect contact with contaminated soil or water. More than 260 pathogenic serovars have been serologically identified and grouped in to 24 serogroups which have adapted to different animal species. Although some animal species may act as maintenance host for some serovars, they can also be incidental hosts from other serovars which may result in a range of clinical symptoms which is dependent upon the infecting strain, the geographical location and the hosts' immune response. Leptospirosis is a rural and occupational disease, which is considered to be an emerging zoonotic disease. In tropical and subtropical areas the transmission of leptospires is increased during heavy rainfall resulting in flooding, as well as poor sanitation and high host biodiversities, and has therefore become a major public health problem in these areas.

Outdoor and agricultural workers (rice-paddy and sugarcane workers for example) are particularly at risk but it is also a recreational hazard to those who swim or wade in contaminated waters. In endemic areas the number of leptospirosis cases may peak during the rainy season and even may reach epidemic proportions in case of flooding because the floods cause rodents to move into the city.

Prevention strategies of human leptospirosis include wearing protective clothing for people at job-related risk and evading of swimming in water that can be polluted. Leptospirosis control in animals dependent on the serovar and animal species, the management infection can be done by vaccination and rodent controls (24, 26).

8. Rickettsiosis

The genus *Rickettsia* includes bacteria Gram-negative in obligate association with eukaryote cells. A number of species have been identified in various terrestrial arthropods, and more recently in leeches and amoeba. Usually, pathogenic rickettsiae were classified into two groups: the typhus group (TG), composed of *Rickettsia prowazekii* and *Rickettsia typhi*, vectored by lice and fleas, respectively; and the spotted fever group (SFG), composed of more than 20 species mostly vectored by ticks. Other rickettsiae have shown antigenic and genetic particularities that preclude their inclusion in either the TG or SFG, such as *Rickettsia bellii* and *Rickettsia canadensis*, reported in ticks from the American continent.

Many *Rickettsia* species cause diseases in humans and animals, to which they are vectored by lice, fleas, ticks, or mites. Most of the recognized pathogenic *Rickettsia* species are classified into the SFG, which includes agents of spotted fever rickettsioses in humans in different parts of the world, vectored by ticks. During the last decades, there has been an increasing number of new *Rickettsia* species of unknown pathogenicity, mostly isolated from ticks. Some of them, previously considered non-pathogenic, were recently shown to be pathogenic to humans, such as the SFG *Rickettsia slovaca*, *Rickettsia aeschlimannii*, *Rickettsia massiliae*, and *Rickettsia monacensis* in Europe. In addition, *R. parkeri*, an 'old' SFG organism first reported in ticks in the 1939 was shown to be pathogenic 65 years later. These facts indicate that any novel described *Rickettsia* from invertebrate hosts, especially ticks, should be regarded as potentially pathogenic for humans.

In Latin America, several *Rickettsia* species (belonging mostly to the spotted fever group) pathogenic for humans or with unknown pathogenicity have been reported. *Rickettsia rickettsii*, the etiological agent of the most severe spotted fever in the world, has been reported in *Amblyomma cajennense* ticks in Brazil, Colombia, Panama, and Mexico and in *Amblyomma aureolatum* ticks in Brazil, (Figure 2).

In Colombia, Rocky Mountain Spotted Fever (RMSF) was first reported in 1937 by Patino. It was named Tobia fever because of the village where these cases occurred. The disease remained forgotten until 2003, when two fatal cases were identified and reported in Villeta, a locality next to Tobia. More recently, three outbreaks of RMSF have occurred in Colombia: in 2006 among military personnel in Necocli (Antioquia), in 2007 in a township of Los Cordobas (Colombia) and in 2008 in Altos de Mulatos (Antioquia). These reports defined the reemergence of the disease in Colombia and alerted the systems of surveillance across the country.

Eight *Rickettsia* species have been associated with human diseases in Latin America and Caribbean: *R. rickettsii* causing rocky mountain spotted fever in Mexico, Costa Rica, Panama, Colombia, Brazil and Argentina; *R. prowazekii* causing epidemic typhus in Argentina, Bolivia, Chile, Ecuador, Guatemala, Mexico, and Peru; *R. typhus* causing endemic typhus in Brazil, Colombia, Guatemala, Mexico, Panama, and Puerto Rico; *R. felis* causing flea spotted fever in Mexico and Brazil; *R. parkeri* causing spotted fever in Brazil, Uruguay, and Argentina; *R. africae* causing African tick bite fever in the Caribbean islands; *R. akari* causing

rickettsial pox in Costa Rica and Mexico; and *R. massiliae* causing spotted fever in Argentina. *R. massiliae* case was reported in a Spanish traveler presumed to have acquired the infection in Argentina, but suffered the disease after her return to Spain. The distribution of *R. felis*-infected fleas included seven countries (Costa Rica, Panama, Caribbean islands, Peru, Argentina, Chile, and Uruguay) where no human cases of infection have been reported so far.

A total of 10 *Rickettsia* species have been reported in both Spain and Portugal: *R. conorii*, *R. helvetica*, *R. monacensis*, *R. felis*, *R. slovaca*, *R. raoultii*, *R. sibirica*, *R. aeschlimannii*, *R. typhi*, and *R. prowazekii*. In addition, *R. rioja* has been reported in Spain, and *R. massiliae* has been reported to occur in Portugal. Amongst these *Rickettsia* species reported in Portugal and Spain, only *R. prowazekii*, *R. typhi*, *R. felis*, and *R. massiliae* have also been reported in Latin America.

9. Malaria

The etiologic agent of malaria is a parasite denominated *Plasmodium*, which is transmitted by means of the bites of infected *Anopheles* mosquitoes. The genus *Plasmodium* includes species of *malaria*, *vivax*, *falciparum*. Malaria is may be a main cause of morbidity and mortality in the tropics with *Plasmodium falciparum* responsible for the common of the disease burden and *P. vivax* being geographically most broadly circulated cause of malaria.

In the human body, the parasites reproduce in the liver, and then infect red blood cells. Symptoms of malaria consist of fever, headache, and vomiting, and usually show between 10 and 15 days after the mosquito bite. If not treated, malaria can rapidly turn into life-threatening by disturbing the blood provide to vital organs (30). In Africa and Latin America, the parasites have showed resistance to a several of malaria medicines. Means interventions to control malaria include: prompt and effective drug treatment; apply of insecticidal nets by people at risk; indoor residual spraying with insecticide to manage the vector mosquitoes, transgenic mosquitoes manipulated for resistance to malaria parasites and biological control of mosquitoes.

Malaria remains one of the world's serious health problems with 1.5 to 2.7 million deaths yearly; these deaths are mainly among children and pregnant women in sub-Saharan Africa. Of connotation, more people are dying from malaria today than 30 years ago. It seems to be the vector, the female anopheline mosquito is changing its behaviour or adapting to human activity such as creating new mosquito breeding sites. Hence, the impact of augmented population, and people displaced by violence can boost the incidence and proliferation of malaria. Furthermore, the difficulty of drug resistance by the parasites to almost all currently available antimalarial drugs.

Finally, most of the hemorrhagic tropical diseases describe above, can be also classified as neglected tropical diseases. Those represent some of the most common infections of the poorest

people living in developing countries. Because they primarily affect the marginalized poor as well as preferred indigenous populations and people of African descent, the tropical hemorrhagic diseases in the Latin American and African countries are predominantly ignored diseases.

There is also misdiagnosis of hemorrhagic diseases in the tropics, mainly because the weak epidemiology and public health system in developing countries. The maximum disease problem of hemorrhagic diseases, such as leptospirosis, rickettsiosis, malaria and hantavirus infections, have first require scale-up of accessible funds or the advance of new measures instruments in order to accomplish control (32). The total elimination is implausible in the tropics, for that reason require and inter-disciplines efforts as social services, community education and environmental interventions.

10. Conclusions

The tropical hemorrhagic fevers in the neotropics is a group of debilitating viral, bacterial and parasitic infections, that are very common aetiology of illness of the poorest people living in developing countries as Latin America. During the past 20 years there has been an intense emergence and re-emergence of epidemic of haemorrhagic vector-borne-disease (VBD) that have been produced by viruses supposed to be under control such as dengue, yellow fever, Venezuelan equine encephalitis, Saint Louis Virus, Arenavirus, hantavirus or viruses that have prolonged their geographic distribution such as West Nile and Rift Valley fever. Bacteria like *Leptospira* and *Rickettsia* have also re-emerged. Haemorrhagic fevers produced by bacterial or virus share many general features. Those infectious agents are arthropod-borne cause many haemorrhagic fevers. For some viral haemorrhagic fevers, person-to-person transmission may occur through direct contact with infected blood or secretions. Infectious agents are transmitted by arthropod like mosquitoes and ticks. Animal reservoirs are usually wild rodents, however, pets, domestic livestock, urban mice, monkeys, and other primates may also provide as intermediate hosts. Disease difficulties following from infection by these agents are common; the most tremendous manifestations include circulatory instability, augmented vascular permeability, and diffuse haemorrhages among them. Thus, the clinical manifestations and even histopathological findings are extremely comparable and challenging to make a differential diagnosis. Finally, in the Latin American the etiologic agents described in this chapter are disseminated in almost all countries, with exception of Uruguay.

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