ISSN 0001-6012/2013/55/3/7-10
Acta Médica Costarricense, © 2013
Colegio de Médicos y Cirujanos
de Costa Rica

Conferencias Magistrales

Enfermedades rickettsiales: ¿Un problema de salud pública en América Latina?

(Rickettsial diseases: a public health problem in Latin America?)

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Resumen

Para que una enfermedad sea considerada un problema de salud pública, los parámetros epidemiológicos son magnitud, vulnerabilidad y trascendencia. Si se considera sólo magnitud y vulnerabilidad basadas en la incidencia de las enfermedades rickettsiales en América Latina y en la ausencia de una vacuna efectiva contra esta clase de enfermedades, se puede decir que las enfermedades rickettsiales no son una prioridad ni un problema de salud pública. Sin embargo, si se investigan otros parámetros epidemiológicos se puede tener otra visión acerca de estas enfermedades. El objetivo de este trabajo es analizar mediante un estudio histórico retrospectivo, los factores de riego epidemiológicos en las enfermedades rickettsiales, para confirmar nuestra hipótesis sobre su relevancia en salud pública.

Descriptores: salud pública, rickettsiosis, epidemiología.

Abstract

The epidemiologic parameters for a disease to be considered a public health problem are magnitude, vulnerability and transcendence. If you consider only magnitude and vulnerability based on incidence of rickettsial diseases in Latin America and in the absence of an effective vaccine against these kind of diseases, you can say that rickettsial diseases are not priority and are not a public health problem. If you investigate other epidemiologic parameters we can have another vision about the rickettsial diseases. The objective of this paper is to analyze the epidemiologic risk factors in rickettsial diseases by an historic retrospective in Latin America, to confirm our hypothesis of the public health relevance of rickettsial diseases.

Keywords: Public Health; rickettsioses; epidemiology.

In Latin America, human cases of infection by the genus *Rickettsia* have been described in several countries in the last twenty years. The increase of notification of this kind of rickettsial diseases is the result of implementation of epidemiologic surveillance and too due to the modifications in the environment changing the spatial distribution of these diseases. The introduction of molecular biologic techniques in the investigation of rickettsial diseases has permitted the detection of new species of the genus *Rickettsia* in vectors, humans and animals. The sequence of conserved genes from amplified regions by PCR permitted the identification of Rickettsiae not cultivated yet. With this strategy was possible to identify new species as the *Rickettsia felis*. The description of *R. felis* human cases in Latin America by 2000s opened new perspectives for comprehension of the role performed by new species of *Rickettsia* in the epidemiology of rickettsioses. In 2000 only three species of *Rickettsia* were known in South America. In the beginning of this century more seven species were related in this continent, confirming the importance of the introduction of these techniques in rickettsiology area.[1] The use of molecular biology helps too to understand better about the geographic distribution of rickettsioses and about the association vector-rickettsia.[2]

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Some countries, such Brazil, have a long history of rickettsioses, while others such as Argentina, have only recently detected these diseases. In Brazil, *Rickettsia rickettsii* has been described as the agent of Brazilian spotted fever (BSF) transmitted by the tick *Amblyomma cajennense* since the 1920s.[3] In the last 20 years, cases of BSF have been confirmed by immunofluorescence serology and more recently by molecular techniques in the states of Minas Gerais, São Paulo, Rio de Janeiro and Espírito Santo.[4] Between 1990 and 2011, Brazil registered 269 deaths due to BSF. During this period the number of confirmed cases in southeast region reached 747 cases, representing 77.2 % of the total of cases of this country. São Paulo was responsible for 45.7 % of these cases and Minas Gerais for 20.2%.[5] Cases of cat flea-associated rickettsiosis caused by *Rickettsia felis* were reported too in Minas Gerais state, [6] with the detection of this bacterium in *Ctenocephalides* genus fleas by PCR.[7]

Spotted fever caused by *R. rickettsii* were identify too in Mexico, Panama, Costa Rica, Colombia and Argentina.[2,8] The Argentine cases were described in Jujuy Province in 1999, when six children with fever, rash and a history of recent tick bite were evaluated for rickettsial infections and immunohistochemistry staining of tissues obtained by \ autopsy from one fatal case.[9] In Panama the description of *R. rickettsii* re emergence occurred in 2007 after more than fifty years without the description of spotted fever cases.[10] In Mexico the first case of spotted fever caused by *R. rickettsii* was described in 1930. From 1930 to 1950 many cases of this disease were reported in many states.[11] The same phenomenon that was seen in Panama was observed too in Mexico with an epidemiologic silence occurred from 1950 till 2005, when new cases of this re emergent disease initiated to happen again.[10] Costa Rica registered the first outbreak of *rickettsii* spotted fever in 1975. After this date several cases were described in this country.[12] In Colombia nothing was known or published about rickettsioses since 1937 when a report of an epidemic caused by *R. rickettsii* was related and named as "Fiebre de Tobia". In 2007 two fatal cases of *R. rickettsii* spotted fever were related near the same locality were the disease was reported in the 1930s.[13, 14] Peru has a long history of epidemic typhus caused by *Rickettsia prowazekii* (transmitted by body lice), [15] isolated cases of murine typhus, and the detection of *R. felis* in *Ctenocephalides canis* fleas, indicating the possibility of human cases of this rickettsiose.

The principal vectors of rickettsioses found in Latin America as in other parts of the world are arthropods like ticks, fleas, lices and mites. The transmission of *Rickettsia* by the vector is influenced by different factors, including physiologic and ecologic process. These last factors influence the intensity of *Rickettsia* transmission for humans and animals. Intrinsic and extrinsic factors can affect significantly the competency of these arthropods as agents of rickettsioses. The risk of occurrence of these diseases due to extrinsic factors includes the population level of the arthropods, the susceptibility of the preferential hosts to *Rickettsia*, the immunity of the host, the genetic variation determined by infectivity of the agent and the environmental relationships. The intrinsic factors related to the vectors are food, physiologic and compartment questions, transovarial and transstadial transformation, the presence of other organisms or pharmacology actives substances, and the time of permanence of the vector in the host.

The rates of vector infection can variety depending of pathogen virulence, *Rickettsia* susceptibility, the presence of co-infections and modulation of immune response at the host. The *R. rickettsii* maintains in general levels of infection lower than 1%.[1,16] Although some authors don´t consider difference between endemic and non endemic areas, asserting that the presence of infected ticks cannot be sufficient to produce human disease, the high infestations by ticks in the environment and in the animals can modify this relation.

Conclusions

To judge if rickettsial diseases are an important public health problem or not in Latin America we need to evaluate all these factors related. Summarizing all them by epidemiologic parameters they can be represented by magnitude, spreading potential, vulnerability and transcendence (measured by fatality, severity, social and economic relevance/spatial distribution of the diseases).

If you consider only magnitude and vulnerability based on incidence of rickettsial diseases in Latin America and the absence of an effective vaccine against this kind of disease, you can say that rickettsial diseases are not priority and are not a public health problem. But if you consider the other epidemiologic parameters we can have another vision about the importance of rickettsial diseases. We can try to do it discussing the situation of each rickettsiose of the genus *Rickettsia* in Latin America.

The spotted fever caused by *R. rickettsii* is the more severe rickettsiose among the rickettsial diseases in Latin America with a high case-fatality ratio.[1] The primary vectors for *R. rickettsii* in Latin American are ticks from *Amblyomma cajennense* specie (Mexico, Panama, Costa Rica, Colombia, Argentina e Brazil), *Amblyomma aureolatum* (Brazil), *Amblyomma imitator* (Mexico) and *Riphicephalus sanguineus* (Mexico).[8]

Rickettsia parkeri is considered an emergent pathogen in Latin America with suspected human cases related in Uruguay[17] and *Amblyomma triste* as vector.[18] Brazil also have suspected cases of this rickettsiose described in the south of the country.

The riquetsiose felis caused by *Rickettsia felis* has the fleas of *Ctenocephalides* genus as the principal vector. Although the symptoms of this disease are common in other rickettsioses (fever, myalgia, rash and abdominal pain) and can be synonym of mild cases, neurologic symptoms occurred in Brazilian and Mexican cases can traduce the possibility of severity of this disease in some cases.[19]

The occurrence of epidemic typhus in Latin America caused by *Rickettsia prowazekii* can be observed in Peru and Mexico.[15, 20] This disease is transmitted by the feces of *Pediculus humanus corporis*. The outbreaks of epidemic typhus are related to social

problems as absence of hygiene and extreme poverty. The case fatality ratio of cases without treatment can reach 30%, with a tax of 60% in elderly people.

Rickettsia typhi the agent of endemic typhus occurs in all Latin America having *Xenopsylla cheopis* as primary vector and *Rattus norvegicus* as host. The case fatality ratio is lower than 5%. The elimination of infected fleas with the use of insecticides has diminished the number of human cases and the importance of murine typhus as a public health problem.

The analysis presented of the epidemiologic situation of each rickettsiose help us to conclude that rickettsial diseases are an important public health problem in Latin America due their great social and economic impact. At the time the rickettsioses reach poor regions, the association of agglomeration of people to the potential dissemination of the vector originates an increase in the number of cases in a short period of time. The exemplification of this thesis can be demonstrated in Brazil with *R. rickettsii* and in Peru and Mexico with *R. prowazekii*. The phenomenon of familial clusters of *R. rickettsii* spotted fever rickettsiosis has been noted numerous times in Latin America.[21] In fact, the simultaneous occurrence of severe febrile illness in more than one patient generally suggests person-to-person or a point-source transmission of infection. Few physicians in USA may be aware that 4.4% of cases of Rocky Mountain spotted fever occur in the household of another case-patient with the disease, a situation that often lends further diagnostic confusion for this illness that can mimic other febrile exanthems, such as dengue, as well as gastrointestinal infection, other abdominal conditions, pneumonia, and meningoencephalitis.

We conclude with the affirmation that the analysis of the spatial distribution of rickettsial diseases besides social/economic impact is fundamental to understand the occurrence and the spread of these diseases in the present moment in Latin America. We can exemplify it affirmation by the re emergence of cases of Brazilian spotted fever in Minas Gerais state, Brazil since 1980 in urban areas. This occurrence suggests the invasion of natural focus of the disease by the man and an expansion of rickettsioses due to a new ecologic reorganization associated to the way of life of a population excluded in the social economic context.[22, 23, 24] The presence of ricketsioses focus in areas of urban expansion was first related in São Paulo by 1920, [25] but continues to be a reality now in Latin America as related in Brazil by 1980's and recently in Costa Rica.[26]

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