Emerging and Reemerging Diseases in Brazil: Data of a Recent History of Risks and Uncertainties

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This article discusses the emergence and reemergence of infectious diseases on the basis of a review of the literature. It shows the critical situations faced worldwide and in special Brazil's susceptible position due to its complexity, mostly represented by the mega-biodiversity of the country and its socio-economic problems directly affecting public health. It approaches the discussions around the issue with emphasis to the recommended investments in the health sector, directed to surveillance and to strengthening the epidemiological, laboratorial and clinical bases and centered on preventive and control measures in the affected areas including Biosafety.
Key-Words: Emerging and reemerging infectious diseases, epidemiology, public health, biosafety.

Brazil reached the XXI century still facing serious social problems directly reflecting on public health. As Luna [1] emphasized: "…great part of the conditions and factors related to the emergence and reemergence of infectious and parasitic diseases are present and the process of emergence and reemergence continues". Brazil responds therefore, together with other developing countries and due to the complexity of its social and environmental conditions and its rich biodiversity, for a considerable part of cases of emerging and reemerging infectious diseases in the world, a fact increasing the responsibility of the government in the sense of implementing policies for surveillance and epidemiological, laboratorial and clinical bases oriented to control and preventive measures.

Navarro et al. [2] pointed to the "expressive industrialization of the southwestern region while keeping the poorer regions on levels of underdevelopment that determine and worsen the already precarious public health structures and contribute to a logic of living together with the great endemic diseases and their "public management". One of the symptoms of this development strategy and the priorities it establishes is the fact that actions for containing outbreaks or investigations on emergence/reemergence of diseases in general only are carried out when these are directly threatening the great urban centers. By inducing an intense and unordered urbanization process, this model creates extremely unhealthy social and physical environments, favoring chaotic nets of infections of epidemic character and the dissemination of diseases formerly confined to endemic 'niches'. And there is one more factor contributing to this complexity: Brazil is neighbor of countries with the same serious problems, that is, a deficient public health system, emergence of new viruses and total lack of laboratory infrastructure for surveillance, control and research activities. Today this context is translated into the real threat of emergence of new viruses such as the Junin virus (*Arenaviridae*), causing agent of hemorrhagic fever in Argentina, and Machupo, causing agent of hemorrhagic fever in Bolivia. The occurrence of Oropouche virus, causing agent of encephalitis, also reveals a preoccupying reality. Recent data showed contamination of about 500 thousand individuals in areas involving the Amazon region and urban centers in Panama and Peru. It must be emphasized here that such occurrences are being recorded since 1960 [3].

The Oropouche virus illustrates very well the complex interaction of factors leading to emergence and reemergence of diseases. This virus of the serological group Sumbu is one of the arboviruses of greater importance, causes encephalitis and only loses to dengue virus infection in terms of numbers of notified cases. The virus has caused large and explosive epidemics of febrile disease of great economical and social impact [4,5] in cities and villages of the Amazon region and at the "*Planalto Central*". With the deforestation activities for the construction of the Belém-Brasília highway and the cacao plantations in the region, after a few years the mosquitoes (*Culicoides paraensis*) began to reproduce in the plantations and disseminated the virus all over the region, a fact demonstrating the complex interaction between the pathogen and its environment, where human activity (colonization and agriculture) with the resulting environmental alterations led to the proliferation of the vector and its contact with the man. It is noteworthy that one and the same species of mosquito can transmit different arboviruses and infect different species of vertebrates including man. One single virus also can infect and be transmitted to different species of mosquitoes of different genera [4]. This is important for the understanding of the complex relations existing between these arboviruses and the environment, besides being helpful for explaining the dynamics of their ecology, epidemiology and their life cycle in nature. The interference of man in nature, as occurring in the Amazon region, or the dislocation of great masses of individuals populating wide regions, opening new fields to economy, compromises the integrity of great forest areas and gives way to "accidental" infection through human interference in the ecological niches of these viroses. Once the link is established, the propagation of these agents is unavoidable. The poor health conditions in some regions, the habit to eat wild animals and the diminution of distances thanks to the modern means of transport contribute to the risk of

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emergence or reemergence of these diseases, which can establish themselves according to the ecological conditions of the etiologic agent and the biotic communities that shelter the reservoirs, hosts and vectors.

According to Vasconcelos et al. [6], Brazil has a variety of arboviruses maintaining themselves in enzootic cycles in the Amazon region and able to infect man when getting in contact with the bush. Important investigations were carried out in the Amazon region in the 60s and 70s, during the construction of the Transamazonian highway and in the cities Altamira and Tucurí during and after the construction of the hydroelectric station, for establishing a possible occurrence of these types of viruses and their relevance for public health. As a result, new viruses, members of the family *Buynyaviridae* and *Reoviridae,* were isolated and also other viruses whose group could not be established. Deforestation for cattle production was one of the factors that favored the reemergence of diseases and the increase in the number of registered cases in Brazil in the last years [4]. As already pointed out, the cases of infection with Mayare and Oroupoche viruses are also related to this practice [5,7]. Data from research institutions registered the identification of 187 different species of arbovirus, 157 of them isolated for the first time in Brazil and, this is important, 87 of them new in the world. Thirty-two are pathogenic for man, four are relevant for public health for causing severe diseases of epidemic extent and considerable economic and social impacts including cases of death (as observed with dengue and yellow fever) [4,6].

Dengue fever is considered one of the most important arboviroses affecting man in terms of morbidity and mortality. The disease was reintroduced to the country in Boa Vista, state of Roraima, in 1981, possibly brought from Venezuela. In 1986, dengue virus type 1 reemerged, in 1970 type 2, and in the end of 2000 type 3, all of them in the region of Rio de Janeiro. The infection is transmitted by the bite of the mosquito *Aedes aegypti*. Dengue fever is considered the greatest emerging disease, with three types of viruses circulating simultaneously, causing successive epidemics and severe and even fatal cases of the disease practically all over the country. Sequential infection by different serotypes of the virus is the most important risk factor for dengue hemorrhagic fever. Its incidence has increased in the country, with more than 175 thousand reported cases in 1966. This fact notwithstanding, the cases of hemorrhagic dengue fever are still few but they increased in the last years (575 notified cases in 2001, with a total of 28 deaths per 127 cases and 14 deaths in the period of 1994 to 1998) [8,9]. With more than 1 million and a half notified cases since 1986, Brazil participates with more than 70% in all cases notified in the Americas during the last ten years [1].

There was no case of urban yellow fever in Brazil since 1942 when, after a number of successive campaigns, the disease was considered eradicated during several decades. We emphasize here the work of the Brazilian scientist Oswaldo Cruz in the beginning of the XX century, internationally recognized mainly with regard to the combat of the mosquito *Aedes aegypti*, urban vector of the disease. The reemergence of yellow fever in Brazil is another good example for the factor that can determine the emergence or reemergence of infectious diseases. The disease, up to this moment only identified in its sylvan form, is maintaining its cycle in mosquitoes and among animals, especially in non-human primates of the tropical forests. Men, when invading the transmission areas, acquire the virosis through the infected mosquito of the genus *Hemagoggus*. Vaccination and implementation of more efficient environmental policies are considered the most effective forms of prevention and control of the disease. Cases of wild yellow fever occur every year. Between 1993 and 1996, 102 cases were notified in seven states: Amazonas, Goiás, Maranhão, Minas Gerais, Mato Grosso do Sul, Pará e Roraima [9]. In 2000 the disease reemerged with an outbreak in the Central West that expanded to São Paulo and Bahia, returned in 2001 with a new outbreak in Minas Gerais [1], and again in 2003 in Minas Gerais, Mato Grosso and Pará, when 64 cases of the disease with 23 deaths were recorded, 58 of which in Minas Gerais [10]. Although the urban form of the disease was eradicated, the risk of reemergence remains due to the increasing re-infestation of the transmitting mosquito in some cities as a result of the migration of infected individuals from the country to cities where *Aedes aegypti* is present, and due to the increase of ecotourism in endemic regions [11].

Rocio, a typically emerging virus, appeared in 1975 at the south coast of the state of São Paulo as a result of alterations in the natural environment and caused a severe epidemic of encephalitis, up to then restricted to wild animals. The outbreak resulted in more than 1,000 notified cases of encephalitis between 1973 and 1980, with 100 deaths and more than 200 cases with motor and neuropsychiatric sequela [12,13]. The virus, classified as belonging to the family Flaviviridae, probably circulated among birds and mosquitoes, mainly *Aedes scapularis* and *Psorophora ferox,* but since that time no more human cases were described. Antibodies against this virus were sporadically found in birds, small rodents and marsupials in different regions of the state of São Paulo and in the Amazon region, suggesting transmission through migrating birds [14].

The Sabiá virus is considered the example of highest risk up to now isolated in the country. It causes the Brazilian hemorrhagic fever, an extremely severe disease leading quickly to death due to the lack of specific treatment and immunoprophylaxis. It belongs to the family *Arenaviridae*. The virus was isolated in 1990 in a 25 years old female patient, the first known human case of the disease. The patient died on day four of the infection process, presenting with a picture of severe hemorrhagic fever. The contamination was verified in Cotia, Jardim Sabiá, in the neighborhood of Great São Paulo, which gave the name to the virus. Later, two laboratory infections with the same agent were described, one of them with febrile disease and another more severe one with symptoms resembling influenza. Both patients recovered without sequela. Similarly to other arenaviruses, the infection of the first patient seemed

to have occurred through contact with the urine of rodents although no data whatsoever were obtained with respect to the circulation in nature, maintenance, geographic distribution or epidemiology of this virus [15-17]. In December 2003, three individuals living in the rural area of Juquitiba, Vale da Ribeira, state of São Paulo fell ill. The serological diagnosis confirmed recent infection with hantavirus in its pulmonary form (HPS) [18]. Since then, the disease was detected mainly in the Southern region and in the states of São Paulo, Minas Gerais and Mato Grosso, and was associated with rodents. Until the year 2001, 167 cases were notified but more precise data about this disease are missing in the country [3]. According to the Oswaldo Cruz Foundation, 495 cases of the disease with 177 deaths were confirmed until 2004. Forty-seven of these cases were recorded in only two localities of the Federation, the State of Minas Gerais and the Federal District [19]. Wild rodents are the main natural hosts/reservoirs and man is most frequently infected through inhaling aerosols from contaminated excreta (feces, urine and saliva) of these animals. Hantavirosis is connected with precarious living and housing conditions and agricultural activities (harvesting and storage), favoring close contact between humans and rodents. Suburbanization, hunting, camping and other hobbies are favoring the transmission of the virus among other groups of individuals [20]. The mortality rate of this disease is of nearly 50% and no efficient treatment is available as yet [19].

AIDS is considered the most important emerging disease of the XX century. Its appearance in the 80s involves a variety of aspects concerning human relations. Its control and prevention are extremely difficult for implying in behavioral changes, use of preservatives, safe blood banks, disposable syringes, besides in investing in the development of low-cost immunobiological and pharmaceutical agents. In Brazil, this disease follows the same epidemiological trends observed worldwide: it extends to small cities, poorer places and does not spare women and consequently children. In Rio de Janeiro, until the end of 2001, 33,180 cases were notified [21]. This picture is aggravated by opportunistic infections as a result of immunosuppression, chemotherapy and use of corticoids or due to the infection itself.

The decline of tuberculosis observed in the 80s tends to become less perceivable. The number of notified cases of the disease in Brazil in recent years ranges between 80 and 90 thousand new cases per year. In 2000, the number of new cases was of 82,249, 38,690 in the Southeast, 23,196 in the Northeast, 9,281 in the South, 5,901 in the North and 3,522 in the Central-West [22].

The excessively centralized health care system, the length of the currently available therapy (a minimum of six months), the increasing populational density in the outskirts of the big cities, people lacking adequate health conditions, poverty, negligence, inadequate diagnosis and treatment, the impact of HIV, all of them contribute to the complex epidemiology of emerging diseases in the developing countries. According to the WHO, tuberculosis and HIV constitute a calamity unprecedented in history [9,23]. According to Hijjar, Oliveira & Teixeira [2], in 1999, about one third of HIV infected individuals were also infected by Koch's bacillus and "the impact of this interrelation is alarming when considering that HIV constitutes today the greatest risk factor for developing tuberculosis in previously infected persons". According to the same authors, in the city of Rio de Janeiro, in 1995, 9.8% of HIV positive adults presented with tuberculosis. It must be emphasized that the AIDS control program of the Ministry of Health is considered very efficient and that the combined antiretroviral therapy is exerting a very positive impact upon the co-infection HIV/tuberculosis [4].

Malaria is a typical reemerging disease. In Brazil, as a result of the eradication campaign using pesticides like DDT and due to the access to synthetic antimalarial drugs, the disease was kept under control during a certain time but reemerged intensely in the 70s. Today, there is an important incidence of the disease because of the resistance of the parasites to these agents. Twelve point three percent of the Brazilian population live in risk areas. These areas are situated in the Amazon region, where the greater part of cases are registered (in 1996, 99.4% of a total of 444,049 cases). The states that registered the highest number of cases in 2002 were: Pará, Acre, Amapá, Tocantins, Rondônia, Roraima, Amazonas, besides the west of Maranhão and the north of Mato Grosso. Malaria shows seasonal cycles, increasing in the end of the rain period and beginning of the dry season. This is due to the creation of secondary breeding sites and demonstrates the usefulness of simple sanitation and draining measures. The main focuses of malaria are related to agricultural and mining activities, the construction of great hydroelectric stations and highways and are found in the periphery of cities as a consequence of the deterioration of urban structures and migration from rural areas to the cities [9,25,26].

Recently, more precisely in 2005, cases of maculous fever were notified in the state of Rio de Janeiro. This disease is transmitted by bites of infected tics, mainly of the genus *Ambyiomma,* occurring in nearly the entire national territory, transmitting *Rickettsia rickettsii*. The disease was described for the first time in 1929, in the states of São Paulo and Minas Gerais. One of the theories for explaining the incidence of this disease was a growth in the population of the natural reservoirs of rickettsia (protected by the hunting prohibition, principally for capybara) contributing to the infestation of infected ticks disseminating the disease around areas inhabited by humans and domestic animals [27]. During the period of 1995 to 2003, 241 cases were confirmed. The mean lethality rate was of 30%, increasing to 80% in case the disease was not treated in due time. In Brazil, cases were notified in the states of São Paulo, Minas Gerais, Rio de Janeiro, Espírito Santo and Santa Catarina. The disease occurs more frequently between April and October, when young forms of ticks are predominant. Being smaller than the adult insects, they are not so easily noticed and remain for a longer time attached to the skin of individuals, a fact increasing the possibility of infection [19].

Biosafety as a Tool for Facing Diseases

The extensive phenomena resulting from globalization turned the issue dissemination of emerging and reemerging diseases into one of the top concerns in the biosafety agenda of the countries. One of the strategies globally adopted for facing the quick dissemination of these diseases is the strengthening of biosafety. On national level, this area stands up for the formulation of policies including public investment in the construction of safety level 3 laboratories and advocates the implementation of at least one BSL4 facility for manipulating high-risk emerging microorganisms, thus establishing a hierarchic network in the country.

Biosafety is understood as an essential area for supporting epidemiological surveillance activities and ensuring conditions for facing the problem of emerging and reemerging diseases.

In 2002, the Ministry of Health instituted the Biosafety Commission in Health, which since then is subsidizing the country with a number of guidelines in this field. In 2004, the Commission launched the "Directives for confined manipulation of biological agents", classifying "biological agents on the basis of the risk they pose" [28]. These directives contain a list of biological agents considered risk class 5, exactly for being exotic. This kind of classification however requires much flexibility and dynamism because a disease representing a high risk today may not do so tomorrow. To give an example for this group, we can mention bovine spongiform encephalopathy – BSE (a great worldwide concern not only because of the severe losses it causes for the British economy but also for its ability to cause human disease) and avian influenza (considering the enormous damage this disease causes to public health and the economical losses it may cause in Brazil, one of the greatest exporters of chicken meat in the world). Recently, the Ministry of Agriculture published a number of normative instructions, regulating the necessary import restrictions for animals and animal products from countries affected by these diseases. The import of cattle from the United Kingdom is prohibited since 1990, and since 1993 the same prohibition refers to ovines, caprines and wild ruminants, as well as cattle and sheep embryos and giblets, bone, blood and meat powder, glands and organic liquids for use in the pharmaceutical industry. In the beginning of 2006, the Ministry of Health created the "National Contingency Plan for facing an Influenza Pandemic" with the intent to guide the activities necessary for containing or at least delaying the introduction of the pandemic strain to Brazil and to minimize the impacts on the health of the population. Furthermore, the "Hemisphere Conference for Surveillance and Prevention of Avian Influenza" took place in Brasília, in December 2005. During this conference the present countries committed themselves to providing technical, political and budgetary support to national, regional and continental actions for facing the risk posed by the avian flu to animal and public health.

Final Considerations

The challenges for public health posed by the emergence and reemergence of infectious diseases are widely discussed, in terms of global concern, due to the reappearance of diseases and appearance of new infectious agents of great impact as factors contributing to calamities of worldwide extent.

The countries have to prioritize health actions enabling them to avoid or minimize the effects of the emergence or reemergence of these diseases, establishing policies directed to surveillance, the creation of epidemiological, clinical and laboratorial bases aimed at preventive and control measures. Among these measures we point out the following [1,29-32]:

a) Encourage communication and circulation of information about emerging and reemerging diseases as well as ensure the implementation of preventive strategies;
b) Establish a strategy based on an attitude of surveillance and alert, with a network of hierarchically organized laboratories, adequate equipment and supply of inputs and qualified human resources;
c) Strengthen the national capacity of developing preventive strategies against emerging and reemerging diseases;
d) Promote applied research for quick diagnosis and treatment of emerging and reemerging diseases and risk prevention;
e) Promote applied research integrating the laboratory and epidemiological survey systems;
f) Strengthen the communication between laboratories (research and diagnostic) and health services for improving the surveillance of infectious biological agents;
g) Maintain systematic survey of known vectors and reservoirs of emerging and reemerging diseases;
h) Systemize the survey of risk factors and environmental and climatic elements favoring epidemics;
i) Create a structure for integrated survey of causing agents and risk factors allowing for analyzing information quickly and efficiently and for taking opportune decisions with most well-founded confidence possible.

The prevention of epidemics, epizooties and pests as well as the appropriate decisions for minimizing their impact are not only responsibility of the specific governmental organisms normally in charge of these activities in the different countries. Many times these emergency situations require a multisectoral approach depending on the magnitude of the impact that these diseases exert on public health and on the economy, especially in developing and poor countries.

It is extremely difficult to propose guidelines for interventions due to the unforeseeability and consequent complexity of these diseases. According to Marques [33], "recognize the study of the complexity as being a central scientific challenge of our times" is primordial.

To conclude this review of the literature we refer to the thoughts of Dr. Lorenzo Pacheco Bautista when he said: "we must conceive globalization as Albert Einstein said: "the world is one or nothing". We inhabit a global village with about 6.100 billion individuals and a daily increase of 250 thousand new passengers coming on board. There are no borders for the air nor for the water nor for epidemics, all of us are passengers on the same ship and when the storm comes up there is no more color of the skin, richness, ethnicity, age or gender; we are simple human beings sharing a common destiny and trying to stay on board. This is exactly the situation of the big blue ship called Earth, in the beginning of the XXI century facing great economic, social, environmental, cultural and moral storms".

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