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Beyond diversity loss and climate change: Impacts of Amazon deforestation on infectious diseases and public health

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Abstract

Amazonian biodiversity is increasingly threatened due to the weakening of policies for combating deforestation, especially in Brazil. Loss of animal and plant species, many not yet known to science, is just one among many negative consequences of Amazon deforestation. Deforestation affects indigenous communities, riverside as well as urban populations, and even planetary health. Amazonia has a prominent role in regulating the Earth's climate, with forest loss contributing to rising regional and global temperatures and intensification of extreme weather events. These climatic conditions are important drivers of emerging infectious diseases, and activities associated with deforestation contribute to the spread of disease vectors. This review presents the main impacts of Amazon deforestation on infectious-disease dynamics and public health from a One Health perspective. Because Brazil holds the largest area of Amazon rainforest, emphasis is given to the Brazilian scenario. Finally, potential solutions to mitigate deforestation and emerging infectious diseases are presented from the perspectives of researchers in different fields.

Keywords: Amazon rainforest, biodiversity, emerging infectious disease, deforestation, pathogens, public health.

INTRODUCTION

The Amazon Basin is the largest river system in the world, encompassing more than 7 million square kilometers distributed between Brazil, Bolivia, Colombia, Ecuador, French Guiana, Guyana, Peru, Suriname, and Venezuela. With enormous biodiversity, most of Amazonia is located in Brazil, representing the largest biome of a country known by its thriving nature (Garda et al. 2010, Peres et al. 2010, Latrubesse et al. 2017, Metzger et al. 2019).

Amazonia is a unique biome in many aspects, with importance in different spheres of life. This biome's huge diversity of animal and plant species is *per se* a strong justification for its preservation. In addition, many benefits to human life come from direct or indirect interactions with Amazon ecosystems. Indigenous and traditional peoples live and preserve ecosystems and their cultures through the forest. For urbanized communities, among other benefits, the Amazon forest is a source of food, chemical compounds for the development of medicines, and raw materials for a wide variety of industries. The Amazon rainforest is also crucial for maintaining planetary health due to its pivotal role in regulating the Earth's climate. In a broader perspective, protecting Amazon ecosystems is essential for biodiversity preservation, climate regulation, energy production, food and water security; it is also important for pollination, natural/biological control of pests, the region's economy and human health, not forgetting to mention its aesthetic and cultural value. Amazon ecosystems have an important role for the dynamics and control of zoonotic diseases and vector-borne infections, a very important, although sometimes neglected, point which will be discussed in detail throughout this article (Suffredini et al. 2004, Alho 2012, Bieski et al. 2015, Baker and Spracklen 2019, Metzger et al. 2019, Moraes et al. 2019, Valli and Bolzani 2019).

Global warming is an aspect of climate change that has consequences for the spread of human infections (Shuman 2010, Watts et al. 2018). "Climate change" refers to changes in climate properties (temperature, precipitation, extreme events, and wind patterns) that persist for a long period of time (decades or longer) (Liang and Gong 2017). The Earth's average temperature is increasing at least in part due to anthropogenic actions, such as the emission of greenhouse gases from industries and extensive use of fossil fuels (Levitus et al. 2001, Huber and Knutti 2012, Powel 2015, Letcher 2019).

A robust body of evidence shows that deforestation of Amazon forest is a fundamental driver of climate change (Shukla et al. 1990, Werth and Avissar 2002, Malhi et al. 2008, Khanna et al. 2017, Lovejoy and Nobre 2018, Baker and Spracklen 2019). About 20% of the original Amazon forest cover in Brazil has already been deforested (INPE 2019). Recently, policies, laws, agreements, funds, and practical actions focused on Amazon protection have been weakened in Brazil, encouraging deforestation (Carvalho et al. 2019, Ferrante and Fearnside 2019, Pereira et al. 2019, Seymour and Harris 2019). It is evident that, after a period when conservation policies were intensified in Brazil, which resulted in positive impacts on Amazon protection (West et al. 2019), deforestation in the region started to grow again (Artaxo 2019, Fearnside 2019). Along with environmental problems and the weakening of environment-related policies, lack of science funding will also cause economic losses for the country (Magnusson 2019). The current degradation status of the Amazon rainforest is already very serious, but, if this situation is not appropriately handled, the forest and climate situation on Earth will become increasingly worrying.

The association between anthropogenic action in the Amazon rainforest, climate change, alterations in vector dynamics, human migration, genetic changes in pathogens and the poor social and environmental

conditions in many Latin-American countries can give rise to the “perfect storm” for the emergence and re-emergence of human infectious diseases in Brazil and other Amazonian countries. The recent Zika virus epidemic and the spread of dengue, chikungunya and yellow fever cases are just a few examples of diseases that affect countries in the Amazon region and even other regions of the globe (Ellwanger and Chies 2016, Lima-Camara 2016, Schuler-Faccini et al. 2016, Donalisio et al. 2017, Goldani 2017, Gregianini et al. 2017). Amazonian fauna hosts a huge diversity of well-known pathogens, as well as many other potential new or even unknown pathogens (Vasconcelos et al. 2001, Abrahão et al. 2010, Dornas et al. 2014, Bonato et al. 2015, Soares et al. 2015, Barros et al. 2018, da Silva et al. 2018, Fernandes et al. 2018, Farikoski et al. 2019, Franco Filho et al. 2019, Medeiros and Vasconcelos 2019). Although several of these pathogens may have low epidemic potential in humans, this abundance of microorganisms in the Amazon region indicates that emergence of new infections from the forest is a constant threat to human health.

The link between “environmental imbalances” and “emerging infectious diseases” is already well established in the literature (Daszak et al. 2001, Weiss and McMichael 2004, Jones et al. 2008). However, descriptions and discussions regarding the factors involved in the emergence of infectious diseases due to deforestation specifically in the Amazon region are still scarce. As an attempt to foster this discussion, we review problems and activities associated with the Amazon deforestation and their impacts on the dynamics of infectious diseases and on human/public health.

Many examples cited in this article refer to the Brazilian context. However, such examples can be, at least in part, extrapolated to other countries in the Amazon region due to the similarity of social and environmental aspects. Finally, a problem as complex as the impact of Amazon deforestation on infectious diseases needs to be addressed using the One Health concept, in which characteristics of human, environmental, and animal health are considered in a unified way to detect, understand, and solve public health problems (Lee and Brumme 2013, Halliday et al. 2015, Ellwanger et al. 2017, Destoumieux-Garzón et al. 2018). This article therefore approaches Amazon deforestation and the impacts on infectious diseases from different fields and perspectives, such as genetics, human health, microbiology, veterinary medicine, public health, and ecology (Table I). The selection of the studies included in Table I respected the authors’ suggestions, which were based on each author’s background in a given field of study. Following this approach, the studies in Table I exemplify, from different disciplines, how the Amazon deforestation can impact different aspects of infectious diseases.

PROBLEMS AND ACTIVITIES ASSOCIATED WITH AMAZON DEFORESTATION AND THEIR IMPACTS ON INFECTIOUS DISEASES

Climate change and extreme weather events

The Amazon rainforest plays a pivotal role in regulating Earth’s climate (Bonan 2008, Malhi et al. 2008). In this sense, Amazon deforestation leads to regional and global average temperature rise (Baker and Spracklen 2019, Cohn et al. 2019, Prevedello et al. 2019), and changes in the Amazon biome are associated with an increase in the frequency of extreme weather events, such as droughts, altered rain patterns, heat waves, cold waves, and severe storms (Nepstad et al. 2008, Sena et al. 2014, Wu et al. 2016, Stoy 2018, Leite-Filho et al. 2019). Deforestation also facilitates forest fires, since degraded areas are naturally more susceptible to combustion. Intentional fires are a frequent problem in the Amazon region (Alencar et al. 2006, Nepstad et al. 2008, Alencar et al. 2015, Escobar 2019). Pollutants resulting from deforestation and agricultural fires represent a serious health threat in a broad perspective. Particulate matter emitted from the burning of biomass in the Amazon region exposes humans to an increased risk of DNA damage, gene mutations, inflammation, and cancer (de Oliveira Alves et al. 2017, de Oliveira Galvão et al. 2018). Not surprisingly, the incidence of respiratory diseases in the southern portion of the Amazon region increased substantially in 2019 (Barcellos et al. 2019). Fires and extreme weather events cause damage to the forest ecosystem, creating a cycle of destruction.

The most recent assessment report of the Intergovernmental Panel on Climate Change (IPCC) estimates that under the most likely scenario in the absence of dramatic mitigation actions (scenario RCP8.5) global average temperature would increase by 4.8°C at the end of this century as compared to the 1996-2005 period, while in the Amazon during the dry months from June to August the average increase would be 6-8 °C (IPCC 2013, p. 1343). This would have significant impacts on human health, including the worsening of chronic health conditions, as well as the spread of infections (Balbus et al. 2016, Hacon et al. 2018). Climate change resulting from deforestation of the Amazon rainforest and other tropical forests may favor the emergence of parasitic, fungal, viral and bacterial infections through the following basic mechanisms: first,

by climate-derived ecological disturbances interfering with the maintenance of pathogens in their natural environments and hosts; second, by favoring the presence, distribution and proliferation of disease vectors in forest and urban areas, and third, by changes in temperature and rainfall patterns favoring pathogens' survival and reproduction and/or their ability to infect the human host. Changes in temperature also modify the ability of pathogens to infect vectors and to replicate in these animals (Patz et al. 2000, Hales et al. 2002, Vittor et al. 2006, Barcellos et al. 2009, Altizer et al. 2013, Confalonieri et al. 2014, Carvalho et al. 2015, Flahault et al. 2016, Samuel et al. 2016, Wu et al. 2016, Lorenz et al. 2017, Nava et al. 2017, Casadevall et al. 2019, Duarte et al. 2019a; Duarte and Giatti 2019, Khan et al. 2019, Rao et al. 2019, Silva et al. 2019). For example, if the average temperature of a given region increases, the spread of disease vectors, such as mosquitoes, could be favored, and this spread could lead to the colonization of new geographical areas previously inaccessible to these vectors. Favorable temperatures for replication of pathogens in vectors also contribute to increase vectorial capacity, resulting in greater spread of infections in humans. Moreover, the rise of temperatures and the intensification of extreme rain can contribute to higher survival and spread of pathogens that cause successive diarrheal diseases among humans (Checkley et al. 2000, Duarte et al. 2019a). This is a particularly worrying scenario given the rapid unplanned urbanization and the lack of basic sanitary conditions in the Amazon region (Freitas and Giatti 2009). Also, humans who enter habitats of pathogens and become infected with a certain pathogen may subsequently introduce the infection into urban environments.

The dynamics of soil-transmitted helminths is also strongly influenced by deforestation and climate change (Weaver et al. 2010; Hernandez et al. 2013; Confalonieri et al. 2014; Seo et al. 2016; Blum and Hotez 2018). Helminth diseases are important problems in the Amazon region (Souza et al. 2007; Hotez et al. 2008; Confalonieri et al. 2014; Gonçalves et al. 2016).

Extreme weather events have substantial economic consequences and destabilize the order and functioning of affected human communities, especially in developing countries. This destabilization causes multiple problems in terms of environmental sanitation, creates social instability, and weakens the public health system. This is aggravated by the fact that public health facilities in Amazonian countries are precarious even before a climate disaster occurs. Together, these consequences contribute to the emergence and spread of zoonotic diseases, new human infections, and proliferation of endemic diseases (Epstein 2001, Mirza 2003, Hendrix and Salehyan 2012, Scheffran et al. 2012, Maystadt and Ecker 2014, Watts et al. 2015, Ma and Jiang 2019, Ridde et al. 2019).

Habitat loss and pathogen spillover

Deforestation and uncontrolled urbanization are linked to habitat fragmentation and lack of adequate supplies of food and water. This ecological situation induces wildlife migration to alternative habitats, which can include both urbanized and de-urbanized environments. Human activities in forest areas put humans in close contact with wildlife (Mackenstedt et al. 2015, Wilkinson et al. 2018). As a consequence, humans have closer interactions with wild species and their pathogens, facilitating the occurrence of classic zoonotic diseases and the "jump" or "shift" of new pathogens between different host species, an event called "spillover."

Pathogen spillover can introduce new infections in the human population. In this process, many physical, molecular and ecological barriers must be overcome by the pathogen during the jump between different hosts. In other words, spillover is a complex event that depends on the phylogenetic distance between hosts, the frequency and intensity of contacts between species, and genetic factors of both pathogens and hosts, among other factors. Although complex, this phenomenon is common in the history of humankind; accordingly, most human infectious diseases originate from wild animals, which served as sources of pathogens (Taylor et al. 2001, Kruse et al. 2004, Olival et al. 2017, Plowright et al. 2017, Ellwanger and Chies 2018a, Ellwanger and Chies 2019). Following spillover, if the pathogens encounter favorable conditions, the infection is disseminated among humans (Morse 1995).

Some pathogens are capable of infecting a broad host range and can easily adapt to new hosts, including humans. This kind of adaptation will be more common with generalist than with specialist pathogens. Specific characteristics, such as the RNA genome (high mutation rates) or transmission by vectors, give pathogens a greater plasticity to infect new hosts and find new ecological niches (Nichol et al. 2000, Johnson et al. 2015). However, not all pathogens establish sustained transmission among humans following a spillover event. The characteristics that make a pathogen transmissible between different species may differ, at least in some aspects, from those that increase transmissibility among humans. Regarding viral infections, human-to-human transmission occurs more easily a) with pathogens showing the capacity to

cause chronic and non-lethal infections, b) with airborne/respiratory viruses, and c) by non-segmented, non-enveloped, and non-vector-borne viruses (Geoghegan et al. 2016; Walker et al. 2018). However, vector-mediated transmission can sustain viral epidemics among humans; the endemicity of dengue in Brazil, malaria in the Amazonian region, and Zika virus in Latin America illustrate this aspect.

Habitat loss and the related invasion of wild animals and/or its vector-associated fauna to urban areas lead to domestic animals such as dogs and cats encountering wild species more often and may serve as “bridges” for the circulation of pathogens between wild animals and humans (Ellwanger and Chies 2019). Close contact between wildlife, humans and domestic animals will occur more intensely in urban areas near the forest (Whiteman et al. 2007, Ellwanger and Chies 2019). For example, bat-transmitted human rabies occurs frequently in the Amazon region (da Rosa et al. 2006, Mendes et al. 2009, Gilbert et al. 2012, Vargas et al. 2019). These cases are probably associated with deforestation, livestock and agricultural expansion in the region and the associated increase of the contact of humans with wildlife (Schneider et al. 2001, Dantas-Torres 2008). Therefore, the current Amazonian landscape, characterized by rainforest, environmental degradation, and close contact of humans and domestic animals with wild species, is quite favorable for pathogen spillover.

Vector dynamics

In some specific macro- and micro-regions around the world, climate change may decrease the presence of disease vectors, especially mosquitoes. Extreme temperatures can be detrimental to the development of mosquitoes, and extreme weather events, such as droughts, can limit mosquito-breeding sites. However, in most cases, deforestation, the increase in global average temperature and other climate changes will favor the proliferation of disease vectors (for example, *Aedes aegypti* and *A. albopictus*) in different regions of Brazil and in other Amazonian countries. These changes can facilitate the transmission of arboviruses, such as Chikungunya, Dengue, Yellow fever, Oropouche, Mayaro, Rocio, Saint Louis, West Nile, and Zika virus infection (Hales et al. 2002, Lima-Camara 2016, Wu et al. 2016, Burkett-Cadena and Vittor 2018, Lorenz et al. 2017, Hacon et al. 2018, Klitting et al. 2018, Sakkas et al. 2018, Tesla et al. 2018, Khan et al. 2019, Kraemer et al. 2019, Rao et al. 2019). As an example, yellow fever is a disease traditionally associated to the forest, but it can easily adapt to the urban environment and the risk of re-emergence of yellow fever in urban areas is therefore of concern, especially in cities near forest areas. In South America mosquitoes of the genera *Haemagogus* and *Sabethes* are involved in the sylvatic cycle of yellow fever, and *A. aegypti* is involved in the urban cycle of transmission of this disease (Cardoso et al. 2010, Klitting et al. 2018).

As a counterpoint to the restrictions discussed above, higher temperature and rainfall may shorten the development time of mosquito larvae, favoring their proliferation (Lima-Camara 2016, Wu et al. 2016). Moreover, an increase in the frequency of extreme weather events, such as severe storms and floods, will favor the introduction and dissemination of disease vectors specifically in urban environments due to an increase in mosquito breeding sites, thus aggravating the transmission of infectious diseases (Lima-Camara 2016, Wu et al. 2016, Khan et al. 2019, Rao et al. 2019). The effects of climate change on vectors can be minimized or exacerbated according to human activities, such as those concerning land use and urbanization (Mordecai et al. 2019).

When recent data are compared with those from 1990, climate change has already increased vectorial capacity for dengue transmission by 3% for *A. aegypti* and by 5.9% by *A. albopictus*. These data suggest that continuous climate change may aggravate the epidemiological situation of arboviruses (Watts et al. 2018). Vectors of parasitic diseases such as malaria and leishmaniasis may also be affected by climate change (Githeko et al. 2000, Carvalho et al. 2015, Peterson et al. 2017) and deforestation. In this regard, Amazon deforestation has been associated with a higher human-biting rate of *Anopheles darlingi*, an important malaria-transmitting vector (Vittor et al. 2006); consequently, malaria transmission is linked to Amazon deforestation (MacDonald and Mordecai 2019). Leishmaniasis is caused by parasites of the genus *Leishmania* and is another disease strongly associated with the forest environment. Notably, human entry into the forest for deforestation exposes humans to sandfly (phlebotomine) bites, which transmit leishmaniasis (Desjeux 2004, Alvar et al. 2006, Palatnik-de-Sousa and Day 2011).

When addressing malaria, deforestation and climate change can either increase or decrease the spread of the infection, depending on the amount of forest cover, rainfall patterns, temperature ranges, and landscape characteristics (Githeko et al. 2000, Olson et al. 2009, Tucker Lima et al. 2017, Laporta 2019). Looking specifically at the deforestation factor, the initial process of deforestation generally increases human contact with malaria vectors, causing higher rates of infection. However, after an advanced stage of

deforestation is reached, human contact with the vectors can decrease, reducing opportunities for disease transmission (Tucker Lima et al. 2017). Finally, urbanization and peri-urbanization of transmission cycles of malaria are also affected by deforestation and climate change, representing common issues in the Amazon region (Takken et al. 2005; Taulli 2006; Costa et al. 2010; Oliveira-Ferreira et al. 2010; Olson et al. 2010; Padilla et al. 2015; Almeida et al. 2018).

Agricultural intensification and land-use change

Agriculture and land-use change are extensive phenomena in Amazonia. The intensification of these activities has promoted significant alterations in the region. In Brazil, the supervision of agricultural activities in Amazonia is flawed and allows intensified conversion of forest to agriculture and cattle pasture (Barona et al. 2010, Machovina et al. 2015, Carvalho et al. 2019, Seymour and Harris 2019).

Agricultural practices are associated with the emergence of viral, bacterial, and parasitic infections since these activities can, among other mechanisms, affect the maintenance of pathogens in their natural hosts, alter the dynamics and population number of vectors and increase the ecological contact of humans with pathogens (Patz et al. 2000, Patz et al. 2004, Foley et al. 2005, Wilcox and Ellis 2006, Jones et al. 2013, Gottdenker et al. 2014). Incidence of malaria has been linked to extractive activities and agricultural settlements in the Amazon forest. Malaria in some areas is closely associated with deforestation and unplanned development of new agricultural settlements (Guimarães et al. 2016, Souza et al. 2019). We can speculate that deforestation for pasture and agriculture is the main factor contributing to the emergence of infectious diseases in the Amazon region. These land-use transformations occur on a large scale and are directly linked to various known drivers of infectious diseases, such as habitat loss and human insertion in forest environments. Lack of sanitation and health facilities add complexity to this situation.

Mining

Mining is another major driving force of deforestation in Amazonia and is also a constant source of conflicts between indigenous populations and invaders. The Amazon region is well known for its mineral resources, which include copper, tin, nickel, bauxite, manganese, iron and gold. Mining has a great impact on the environment; besides deforestation resulting from the mining activities within mining lease areas, extensive deforestation also occurs off-lease as a consequence of population growth, urban expansion, infrastructure construction, industrial growth and other factors associated with greater economic activity (Sonter et al. 2017).

Informal mining is associated with water and soil pollution. Also, people living near mining sites or working in informal mines are more exposed to mosquitoes. The disease burden associated with mining includes mercury intoxication, respiratory diseases, diarrhea, vector-borne diseases such as malaria and other infectious diseases (Bauch et al. 2015, Terças-Trettel et al. 2019).

Rainfall, flooding, and water contamination

Altered rainfall patterns and floods are consequences of extreme weather events associated with Amazon deforestation and climate change. Climate change is associated with current and projected extreme hydrological events in the Amazon region (Marengo and Espinoza 2016, Sorribas et al. 2016).

The risk of infection and the spread of malaria in the Amazon region are influenced by rainfall patterns and river water levels (Olson et al. 2009, Wolfarth-Couto et al. 2019). The presence of pathogens in water (considering quantity and diversity) is modified by hydrological events, modulating the exposure of humans to such pathogens. As a result, many infectious diseases spread during rainfall, periods of high river levels and floods, including leptospirosis and gastroenteritis, which are important public health problems not only in the Amazon region but also in other parts of Brazil (Gracie et al. 2014, Rodrigues et al. 2015, Nava et al. 2017, Vieira et al. 2016, Vieira et al. 2017, Duarte et al. 2019b, Duarte and Giatti 2019, Naing et al. 2019, Péres et al. 2019).

Rapid population growth from migration to urban areas is associated with poor sanitation and water pollution, which are common in Amazon cities (Goveia et al. 2019, Mendes et al. 2019). This scenario contributes to the transmission of various water-borne diseases, including gastroenteritis and viral hepatitis. These diseases have very important economic impacts in the Amazon region because, in addition to directly affecting the health of infected individuals, water-borne diseases also overload the public health system and cause workday losses (Constenla et al. 2008, Braga et al. 2009, Machado et al. 2013, Prado and

Miagostovich 2014, Duarte et al. 2019b). Water-related issues in the Amazon region also facilitate the spread of mollusks that are part of the schistosomiasis transmission cycle (Goveia et al. 2019).

Human agglomeration, urbanization and de-urbanization

Historically, the expansion and clustering of population in towns, villages, and cities were factors that allowed the emergence of epidemics among humans (Waldman 2001, Bañuls et al. 2013, Zanella 2016). Currently, urbanization has critical importance for the emergence and maintenance of epidemics as well as the occurrence of zoonotic diseases. Increased interaction among humans from different places and the facilitated proliferation of vectors and pathogen reservoirs in the urban context explain, at least in part, how urbanization affects the spread of infectious diseases (Morse 1995, Neiderud et al. 2015, Zahouli et al. 2017, Li et al. 2014, Tian et al. 2018). Urbanization usually decreases forest cover and may increase the risk of infectious diseases. For example, reduced forest cover and urbanization were associated with higher rates of Zika virus infection and Zika-linked microcephaly cases in Brazil (Ali et al. 2017).

Urbanization represents a paradox concerning infectious diseases. Urban environments contribute to the spread of disease due to human agglomeration. On the other hand, urban areas provide better access to health services, which is a mitigating factor for the problems caused by infectious diseases, especially in high-income countries (Vlahov et al. 2005, Neiderud et al. 2015, Segurado et al. 2016). This tug-of-war can remain in relative equilibrium in areas with predominantly urban characteristics but may slide to one side at city/forest interfaces. In these areas, deforestation processes in association with poor health services contribute synergistically to the emergence of infectious diseases, especially in low-income countries.

Degradation of sanitation services and the abandonment of urban areas by the government, a phenomenon known as “de-urbanization” (Eskew and Olival 2018), strongly contribute to the proliferation of vectors and other pests. De-urbanized areas are ideal for the dissemination of infectious diseases (Pignatti 2004, Gulachenski et al. 2016, Eskew and Olival 2018). Urban slums are good examples of de-urbanized environments (Costa et al. 2017), although it can be argued that these communities were never urbanized enough for a de-urbanization process to occur.

Urbanization, de-urbanization, poor sanitation, and deficient healthcare services are common phenomena in Amazonia (Silva 2006, Giatti 2007, Viana et al. 2007, Carvalho-Costa et al. 2009, Gomes et al. 2009, Gorayeb et al. 2009, Giatti and Cutolo 2012, Johansen and do Carmo 2012, Brierley et al. 2014, Viana et al. 2016, Cardoso et al. 2017). Taken together, these factors create the perfect storm for the occurrence of outbreaks and epidemics in the human population living or working in the Amazon region, especially in cities near forest areas and that have deforestation-associated activities.

Hydroelectric dams, waterways and irrigation systems

Amazon deforestation and other perturbations in the forest landscape are fundamental consequences of the construction of hydroelectric dams, waterways and irrigation systems (Sanchez-Ribas et al. 2012, Tundisi et al. 2014, Fearnside 2015). A good example is the Belo Monte hydroelectric power plant, which significantly changed the landscape of the Xingu River in the Brazilian Amazon, flooding an area of 516 km² [228 km² (44%) corresponding to the original riverbed and seasonally flooded area] (ANA 2019). However, this flooded area is likely to become very much larger, considering the 6140-km² Babaquara (or Altamira) dam that, if built, would regulate the flow of the Xingu River to supply water to the Belo Monte hydroelectric power plant during the dry season (Fearnside 2017a). Two other examples of dams with large reservoir areas may be cited: The Marabá Dam, located on the Tocantins River, would have a total of 1115.4 km² of flooded area, and the Simão-Alba Dam, located on the Juruena River, would have more than a 1000 km² (Fearnside 2015).

The strongest effect of dam construction on the dynamics of infectious diseases concerns vector proliferation. Flooding of hitherto dry areas creates new breeding sites for disease vectors, especially mosquitoes, which contributes to the increase in the cases of various arboviral and parasitic infections (Sanchez-Ribas et al. 2012, Fearnside 2015, Brito et al. 2018).

Construction of hydroelectric dams is often associated with the relocation of communities from areas that will be flooded or significantly impacted by the construction. Both the displaced population and the population migration attracted to areas near dam construction sites are exposed to substantial health risks, as in the case of the Belo Monte Dam (Grisotti 2016). The new settlement areas may be sites of greater vector circulation or habitats of pathogen reservoirs. Also, the specific place where these communities will be relocated may influence the incidence of mosquito-borne diseases as a consequence of wind regimes and

direction, which may facilitate or hinder mosquito bites (Fearnside 1999). Since one of the mechanisms that mosquitoes use to locate humans is by detecting CO₂ in the air, the location of houses with respect to wind directions and dispersion of CO₂ can influence the number of malaria cases (Midega et al. 2012, Endo and Eltahir 2018a, Endo and Eltahir 2018b, Ellwanger and Chies 2018b). Proximity to mosquito-breeding sites can also increase the risk of malaria transmission, an effect that depends on wind direction (Midega et al. 2012). It is likely that wind also impacts the incidence of other mosquito-borne diseases, as this factor influences the behavior of the mosquito itself and does not act directly on the pathogens. A recent study (Huestis et al., 2019) has shown that *Anopheles* mosquitoes can be carried over long distances (up to 300 km) by wind currents. The same study found that many of the wind-transported mosquitoes were female and had fed on blood before migration (Huestis et al. 2019). These findings indicate that modifications in mosquito populations in a given location may influence the dynamics of infectious diseases in very distant regions.

Just as dam construction facilitates the spread of infectious diseases, flooding of areas for irrigation purposes may contribute to the proliferation of disease vectors (Sanchez-Ribas et al. 2012). Although not directly related to the Amazon forest, the case of Panama Canal serves as another example of how water-related construction in a rainforest environment can have profound impacts on the spread of infectious diseases. The percentage of workers hospitalized due to malaria during the construction of the Panama Canal reached 9.6%. Yellow fever was another major problem during the canal construction. The spread of the diseases occurred due to human entry into areas where the mosquito vectors were present, as well as due to the proliferation of vectors with the increase of canal-induced breeding sites. An intense US-led mosquito control program in Panama has been very effective in significantly reducing cases of infection, but not completely eradicating the diseases (Stern and Markel 2004, CDC 2015). Finally, construction of dams, hydroelectric power plants, canals, and irrigation systems in forest areas are activities that enhance close contact of humans with wildlife and its associated pathogens, which is an additional risk factor for infectious disease dissemination.

Road construction and expansion of transportation facilities

Dramatic mortality from vector-borne diseases occurred during construction of the Madeira-Mamoré railway from 1907 to 1912 in what is now the Brazilian state of Rondônia (Katsuragawa et al. 2008). The expansion of transportation facilities has continued in the Amazon region in the 1970s. The construction of the Trans-Amazonian Highway (also known as *BR-230*) represents a milestone in this expansion (Fearnside 1986). Construction began in 1970 and, by 1973, approximately 22,000 individuals had migrated to the highway region. This human flow to a forest region put many workers and migrants in contact with vectors of different diseases, including leptospirosis, leishmaniasis, Chagas disease, bacterial infections, malaria, Mayaro fever, yellow fever, and other arboviral diseases (Pinheiro et al. 1974, Smith 1982, Vasconcelos et al. 2001). Many legal and clandestine highways were and continue to be built in the Amazon region to facilitate transportation of workers and of the products from agriculture, ranching and logging.

Road construction improves infrastructure that is frequently associated with better health outcomes because it facilitates access to healthcare (Bauch et al. 2015, Wood et al. 2017). However, construction of roads and the expansion of transportation also contributes to deforestation, forest fires, hunting, and biodiversity loss, and it significantly increases human mobility in the region (Bonaudo et al. 2005, Laurance et al. 2009, Southworth et al. 2011, Barber et al. 2014), with a direct impact on infectious-disease dynamics.

The extensive transit of people between multiple regions promotes the circulation of pathogens, thus facilitating the spread of infectious diseases. For example, the outflow of human immunodeficiency virus (HIV) from African forests to more populated regions at the beginning of the acquired immune deficiency syndrome (AIDS) epidemic was greatly facilitated by the extension of land transport and human mobility, which remain important factors in the spread of HIV and other pathogens (Lagarde et al. 2003, Eisenberg et al. 2006, Tatem et al. 2006, Barcellos et al. 2010). This is also a concern in the Amazon region, as high mobility connects forest regions with urban areas, creating a “bridge” for infections to enter urban environments. Accordingly, the state of Amazonas has the second highest AIDS mortality rate in Brazil (7.8 deaths per 100,000 inhabitants) (Brazil 2018).

Regarding arboviral diseases, it is well-known that the Amazon forest harbors an enormous variety of species that may serve as vectors of such diseases; hence, in case a new pathogen is introduced in the region and encounters a suitable host, the infection is installed.

Human migration

Extreme weather events such as prolonged drought, excessive rainfall, and food shortages induce migration of human populations. Agricultural practices and search for land and rural properties can also stimulate migrations to forest areas. Infrastructure projects and price fluctuations on commodity markets can also contribute to the mobility of significant population contingents in the Amazon region. These demographic changes intensify deforestation (Barbieri and Carr 2005, Garcia et al. 2007, Fearnside 2008). Finally, climate-induced migration is a major challenge to health services worldwide (Reuveny 2007, Ridde et al. 2019).

Migratory events result in the exposure of populations to new pathogens since these populations eventually “invade” environments where pathogens or disease vectors circulate. This is most prominent when the environment in question is highly biodiverse, as in the case of the Amazon rainforest. This problem is aggravated when unvaccinated populations enter areas of vaccine-preventable endemic diseases. In addition to directly affecting the health of unvaccinated individuals, this phenomenon may impact the herd immunity of the vaccinated population. Moreover, migrants may introduce new pathogens in populations not originally affected by the disease (Confalonieri 2000, Coura et al. 2002, Aguilar et al. 2007, Castelli and Sulis 2017, Bartlow et al. 2019, Grillet et al. 2019).

Migratory flows can overwhelm the public health system of the migrants’ destination, affecting prevention and treatment policies for infectious disease (Grillet et al. 2019, Paniz-Mondolfi et al. 2019). The recent sociopolitical crisis in Venezuela has caused an increase in non-autochthonous (imported) cases of malaria registered in Brazil, one of the main destinations of Venezuelan immigrants. Although this example is not directly related to deforestation, it illustrates how migratory movements can directly affect migrants’ health and at the same time have impacts on the health system (Grillet et al. 2019). The recent reintroduction of measles in Brazilian Amazonia by refugees from Venezuela is a recent example of how facilitated transportation, poverty and lack of adequate control measures may favor the spread of infectious diseases (Meneses et al. 2019).

It is clear that the triad “deforestation, migration and emerging infectious diseases” is an important issue when assessing the potential consequences of Amazon deforestation. Moreover, the economic impacts resulting from infectious disease-related overload of public health systems adds to the factors that make combating deforestation a major economic issue.

Hunting and consumption of bushmeat

Deforestation puts humans in close contact with wildlife and is linked with hunting in different ways. Hunting is a common practice in Brazil, with significant impacts on biodiversity. Although most forms of wildlife hunting are banned in the country, controlling this activity is extremely difficult, especially considering the vast extent of the Amazon region (Baía Júnior et al. 2010, Pantoja-Lima et al. 2014, Van Vliet et al. 2014, Chagas et al. 2015, Bragagnolo et al. 2019, Souto et al. 2019). It is estimated that just in the triple frontier area of Amazonia shared by Colombia, Peru and Brazil 473 tons of meat from wild animals (“bushmeat”) are sold per year (Van Vliet et al. 2014). Human consumption of bushmeat, including meat from exotic animals, is traditional in the Amazonian countries (Milner-Gulland et al. 2003, Van Vliet et al. 2014). Also, hunting is often associated with logging operations, which bring workers into contact with disease vectors (Eve et al. 2000).

Wild animals host different known and unknown pathogens with a potential of infecting humans. Hunting and handling (butchering) meat of wild animals puts humans in direct contact with biological fluids of these animals and their pathogens. These practices therefore facilitate spillover events and the emergence of new infections in the human population (Wolfe et al. 2004, Wolfe et al. 2005a, Wolfe et al. 2005b, Leroy et al. 2009, Uhart et al. 2013, Aston et al. 2014, Pernet et al. 2014).

Tropical forests such as the Amazon rainforest harbor a wide variety of unknown pathogens. Due to this factor and other social, demographic, and environmental characteristics, Brazil is considered to be a hotspot for the emergence of infectious diseases (Keesing et al. 2010, Allen et al. 2017, Nava et al. 2017). The data mentioned above regarding hunting and bushmeat consumption make hunting-associated spillover events a serious (but still neglected) concern in Brazil.

Prostitution

Deforestation in remote areas such as the Amazon rainforest attracts a diversity of workers from various regions, not only for deforestation, but also for gold-digging and construction of dams and roads.

This attraction of people to remote forest areas commonly occurs in socially vulnerable conditions and is associated with increased prostitution and unprotected sex (Parriault et al. 2015, Freire et al. 2018, Lopes et al. 2019, Maciel et al. 2019). As a consequence, in multiple Amazonian regions there are increases in sexually transmitted infections, particularly syphilis and HIV (Zavaleta et al. 2007, Bartlett et al. 2008, Parriault et al. 2015, Benzaken et al. 2017, Mosnier et al. 2018, Costa et al. 2019, Maciel et al. 2019, Neto et al. 2019, Cavalcante et al. 2019).

One of the main factors contributing to the faster spread of HIV in the early 1920s in what is now the Democratic Republic of Congo was the increased number of sex workers in the region, especially in areas of forests that were being cleared for railroad construction (Faria et al. 2014). However, prostitution is often overlooked in studies evaluating the connections between deforestation and infectious diseases. This problem must receive more attention in programs of health promotion for Amazonian populations, with a special focus on sex workers, men who have sex with other men, and other vulnerable groups. The introduction and spread of sexually transmitted infections in indigenous populations in the Amazon region is of particular concern (Bartlett et al. 2008, Orellana et al. 2013, Benzaken et al. 2017).

Loss of animal and plant biodiversity

Environments with high biodiversity harbor many potential new pathogens. At the same time, preserving these environments and their rich biodiversity is, to a certain extent, a way to prevent emerging infectious diseases (Keesing et al. 2010). The relationship between biodiversity and infectious diseases is complex and may seem paradoxical at first, but some precepts are clear: preserved ecosystems act as health promoters, maintaining pathogens in the forest environment. From another perspective, disturbances in highly biodiverse ecosystems facilitate the emergence and spread of new human infections. These basic precepts need to be taken into account in future studies, development projects and political decision-making focused on the Amazon region.

Currently, the loss of animal biodiversity is a serious problem in the Amazon region. The disappearance of predators can favor increases in the populations of species that act as reservoirs for pathogens. An increase in the population of a given animal species may favor the proliferation of blood-feeding vectors that feed on these animals. In addition, loss of plant biodiversity is linked to the fragmentation of habitats occupied by different animal species. Deforestation and habitat fragmentation threaten animal species and may even cause extinction. Together, the loss of animal and plant biodiversity diminishes and even extinguishes ecological niches occupied by predators, disease vectors, and pathogens. On the other hand, biodiversity loss creates new niches that may be occupied by alternative reservoir species, vectors, hosts, and pathogens (Morens et al. 2004, Pignatti 2004, Aguirre and Tabor 2008, Pongsiri et al. 2009, Ometto et al. 2011, Altizer et al. 2013). In brief, the loss of biodiversity profoundly alters the dynamics of the infections.

Deforestation and habitat loss decrease the quality of life of the human population, since environmental degradation is often accompanied by stress, malnutrition and increased contact with pollutants. These physiological aggressions can affect the immune system, causing immunosuppression and making both humans and other species more susceptible to pathogens, which facilitate the spread of infections between wildlife and humans (Aguirre and Tabor 2008, Becker et al. 2019). The combination of biodiversity loss, habitat fragmentation, and human contact with forest areas creates ideal conditions for the introduction of known and unknown pathogens into the human population.

HOW TO MITIGATE THE IMPACTS OF DEFORESTATION

Problems and activities associated with Amazon deforestation and impacts on infectious diseases are summarized in Figure 1. Brazil and other Amazonian countries have all of the main drivers for the emergence of infectious diseases: rich biodiversity and multiple social and ecological challenges. For these reasons, the emergence of infectious diseases in these countries cannot be completely prevented. However, there are many actions that should be implemented to prevent infectious diseases.

Vulnerability of human health to climate change can be evaluated and measured through different methods (Kovats et al. 2003, Ebi et al. 2006, Confalonieri et al. 2009). Various ways to identify climatic drivers of infectious disease also exist (Metcalf et al. 2017). Identifying the factors that stimulate the emergence of these diseases is therefore essential. Different regions present different challenges in addressing infectious diseases, thus requiring specific solutions.

Inequality-related issues are at the core of several concerns discussed in this article. For example, inadequate patterns of land use and poor sanitation are directly related to deforestation, facilitating the spread of infectious diseases in multiple ways. Reducing social inequality is therefore essential to realistically addressing infectious diseases in Amazonian countries. To achieve this goal, investment in education, environmental sanitation, health facilities, and income generation are fundamental priorities, especially for the most vulnerable populations.

Prevention of infectious diseases also requires a robust monitoring system focused on the circulation of pathogens in the environment, humans, and non-human animals. In the environment, monitoring of pathogens in water, soil and sediments is needed for detection of health risks and for planning sanitation programs, especially in the Amazon region, where public health issues are very common (Staggemeier et al. 2011, Prado and Miagostovich 2014, Spilki 2015). For monitoring in humans and animals, it is necessary to invest in low-cost diagnostic methods that are easy to apply in remote places. Genome-based technologies are emerging for diagnosis and surveillance of infectious diseases and for the study of emerging pathogens (Ellwanger et al. 2017, Gardy and Loman 2018, Gu et al. 2019, Gwinn et al. 2019). Selection of specific sentinel human and animal populations (blood donors, livestock, vectors, among others) helps to detect the emergence of new infectious diseases and of disease outbreaks, enabling actions to mitigate the spread of such events (Ellwanger et al. 2019).

It is also important to invest in laboratory facilities and in training personnel to identify new pathogens quickly, safely, and effectively. Regarding arboviruses, development of techniques with low cross-reactivity is essential. Outbreak-response networks need to be strengthened and expanded through national and regional surveillance systems. Two actions should be highlighted: vaccine development and vector control. Together with environmental sanitation, these two factors could bring robust advances in the control of infectious diseases in the Amazon forest and in other tropical regions (Barata 1997, Waldman 2001, Lima-Camara 2016, Cardoso and Navarro 2007, Donalisio et al. 2017).

Brazil already has basic infrastructure and technical capacity for prevention and mitigation of infectious diseases. However, for these actions to be effectively applied, the government needs to supply resources to the agencies and to the professionals who are committed to these goals. Civil society should support the work of scientists and health professionals, and demand that the government appropriately allocate resources to agencies responsible for health promotion and environmental surveillance throughout the country, including the training of community health agents (Luna 2002). The vast territorial extent of Brazil is a challenge for epidemiological surveillance. Many activities of great social and environmental impact occur in conditions of geographical isolation or informal processes. Similarly, many public health emergencies occur in hard-to-reach places with little installed capacity for monitoring, prophylaxis, and treatment of diseases resulting from ecological disturbances. Investing in technologies for remote monitoring of environmental impacts and for remote health care can help overcome the challenges of epidemiological surveillance in Brazil.

The civil society needs to be more engaged with environmental issues, and it is the role of scientists and educators to encourage the population to be involved in actions focused on biodiversity preservation. Therefore, scientists must work to popularize science and raise awareness of the importance of preserving Amazon ecosystems from a broad perspective, including human health. Several new ways to promote this approach exist, including the use of mobile apps focused on environmental education, science podcasts, and platforms for promoting individuals' engagement in science tasks (Palumbo et al. 2012, Bagnolini et al. 2017, von Konrat et al. 2018).

In addition to reducing deforestation, it is necessary to recuperate degraded areas. Reforestation, afforestation, and restoration of forest environments help mitigate climate change through carbon sequestration, and social, ecological and economic benefits are obtained through the recovery of degraded forest areas (Bonan 2008, Brancalion et al. 2019, Bustamante et al. 2019, Prevedello et al. 2019). However, the carbon and biodiversity benefits of preventing Amazonian deforestation are much greater than those of forest recovery, both per hectare and per unit cost, making avoiding deforestation the current priority in the Amazon region (Fearnside 2017b).

Any interference in nature has consequences. Increasing forestation and biodiversity may increase the burden of some infectious diseases since this can facilitate the contact of humans with pathogens. In addition, urbanization can have a favorable effect on the control of such diseases, as it provides the population greater access to health services and better sanitation (Bauch et al. 2015, Wood et al. 2017). Therefore, reforestation and actions to preserve biodiversity could have undesirable effects on human health if these actions are not coupled with the implementation of public health infrastructure, especially in cities and new settlements located in forest areas.

Beyond maintaining vegetation cover, it is necessary to limit and regulate human activity in the Amazon forest. Policies and inspection actions focused on the control of deforestation must be strengthened and expanded, limiting artisanal gold digging, industrial mining, agriculture, livestock and logging operations in Amazonia. Forest fires must be controlled more actively. Protected areas and indigenous lands (*terras indígenas*) must be respected. Besides preserving indigenous culture of ethnic groups, demarcation of indigenous lands contributes to the maintenance of forest areas with their original characteristics. Non-governmental organizations need to be recognized as important actors in the control of Amazon deforestation (Barlow et al. 2016, Nogueira et al. 2018, Artaxo 2019, Brito et al. 2019, Carvalho et al. 2019).

The Brazilian National System of Conservation Units (*Sistema Nacional de Unidades de Conservação da Natureza* - SNUC), which was created by law in 2000, establishes the criteria for the creation, implementation and management of protected areas (PAs). The SNUC classifies PAs into two main categories: “strictly protected areas,” which have as their primary objective the preservation of biodiversity and therefore can be used only for a few purposes (such as research), and “sustainable-use” PAs, which allow people to live within their borders and harvest forest products sustainably (Brazil 2000, Bauch et al. 2015). Besides contributing to biodiversity preservation, implementation of strictly protected areas has been associated with decreases in the incidence of diseases such as malaria, diarrhea and respiratory infection; sustainable-use PAs, on the other hand, have shown a positive correlation with malaria, probably due to greater exposure of people to mosquitoes (Bauch et al. 2015).

Historically, Brazil has a prominent role in the field of tropical medicine. The country should therefore be a protagonist in controlling deforestation and climate change and their impacts on infectious diseases. Since the country has the largest portion of the Amazon rainforest, Brazil should keep its leading role in health research in Latin America (Lacerda et al. 2019).

FINAL CONSIDERATIONS

Human pathogens represent only a tiny fraction of the world’s parasite diversity (Balloux and van Dorp 2017). It is naive to imagine that infectious diseases can be totally controlled. The human population needs to learn how to live in a balance with pathogens, controlling and managing disease dissemination and taking measures to hinder the emergence of new infections (Bañuls et al. 2013). For example, many infectious diseases are endemic to the Amazon region as a result of the region’s natural landscape (Confalonieri 2005). Almost all cases of malaria in Brazil occur in the Amazon region (Lacerda et al. 2019). A huge decrease in the human cases of these diseases would only be feasible through the absence of human contact with the forest, which is unrealistic and not beneficial for humans. Therefore, it is necessary to identify the regions with the highest risk for emerging infections, to invest in diagnostic technologies, and to develop better therapeutics.

Climate change and anthropogenic changes in forest environments can have varied effects on infectious diseases, including decreasing either vector populations or the number of disease cases in some situations, especially regarding malaria (Sanches-Ribas et al. 2012, Gottdenker et al. 2014, Laporta 2019). However, these cases in no way justify neglecting the impacts of deforestation on human health and biodiversity. The few potential “benefits” from climate change will be outweighed by a plethora of hazardous collateral effects. Based on the studies discussed in this article, it is evident that the decrease in the spread of some infectious diseases as a result of deforestation is very small and context-dependent compared to the large effect that deforestation has in promoting the spread of disease vectors and pathogens. Moreover, the Amazon region and other forest areas play multiple essential functions for the balance of life on Earth in ways that are not directly related to infectious diseases.

CONCLUSIONS

The influence of Amazon deforestation on the emergence of infectious diseases is supported by a large amount of consistent data. Deforestation and related human disturbances provide the link between a variety of factors involved in the emergence and spread of the infections. The complex interactions between proposed development projects and the respective burden of diseases in the Amazon region need to be considered.

Prevention and control of infectious diseases in the Amazon region are complex tasks and involve actions to mitigate all of the problems discussed in this article. Therefore, participation of different professionals and institutions is needed, including government agencies, universities, research institutions, non-governmental organizations, schools, and local communities. A One Health perspective should be

applied, primarily to identify the factors contributing to the emergence and transmission of infectious diseases. Specific measures can be taken to address each specific problem, but these measures require integrated actions involving different spheres of the society. For example, the government may act with the help of non-governmental organizations to monitor deforestation in the Amazon region. Similarly, public health agencies, schools and scientists should work together to stimulate vaccination and other preventive and health promotion strategies.

Controlling deforestation means preserving biodiversity and protecting human health. Brazil has a great responsibility in this regard as the holder of the largest Amazon territory and must, therefore, actively and constantly ensure its preservation. From a broader perspective, the extent of Brazil's commitment to the preservation of the Amazon region will be reflected in planetary health.

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AUTHOR CONTRIBUTIONS

JHE wrote the initial version of the article. BKL revised the content of the initial version of the article. JHE, BKL, VLK, JMVV, ABGV, FRS, PMF, LC, LLG, GLW, SEMA, MRB, VPH and JABC contributed with opinions on the content of the article and writing the text. JHE and JABC coordinated the work, revised and edited the text. All authors approved the final version of the article.

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FIGURE LEGEND

Figure 1. Problems and activities associated with Amazon deforestation and impacts on infectious diseases. The problems and activities associated with the emergence of infectious diseases can result from Amazon deforestation (e.g., floods and water pollution). In other situations, they act as promoters of deforestation (e.g., road construction and mining). Some factors are both consequences and causes of deforestation, as in the case of human migrations and urbanization, as represented by bidirectional arrows. This figure was created using *Mind the Graph* illustrations (available at www.mindthegraph.com).