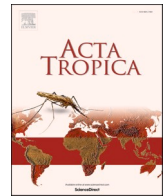




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Tackling zoonoses in a crowded world: Lessons to be learned from the COVID-19 pandemic

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ABSTRACT

The COVID-19 zoonosis is bringing about a number of lessons to humanity. One is that of transforming our links with nature and, particularly, wildlife given the likely COVID-19 origin from illegal wildlife trading. Similar to vector borne diseases (VBD, diseases transmitted by vectors), the COVID-19 pandemic follows related patterns (e.g. no effective or available vaccines, difficult to diagnose, highly localized infection geographical foci, non-human reservoirs) for which we urgently need preventive measures. Towards this aim, governments worldwide must strive to prevent further devastation of natural environments that serve as buffer areas to humans against zoonotic agents (among other health risks), protecting biodiversity and its concomitant causes (e.g. global change), and banning use of wildlife of illegal origin. We herein state that some VBD prevention strategies could also be applied to zoonotic disease prevention, including COVID-19 or any type likely to be related to environmental conditions. The occurrence of future pandemic occurrence will depend on whether governments embrace these aims now.

1. Yet another coronavirus threat

The public health, political, economic, social and natural crisis created by the novel coronavirus disease (COVID-19) has been one of humanity's most jarring historical moments in the last 100 years. With more than 6 million people infected, ca 371,000 dead, and exponential growth in the number of infections (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>, reviewed June 1 2020), the new pandemic is the most pressing immediate problem at a global level (Callaway 2020). While physical distancing is the measure for managing this crisis (e.g. Anderson et al. 2020; Perc et al. 2020), its effect is negative for the world's economies.

While many suggest that this pandemic will be an inflection point in our way of life (for example, providing a glimpse of all possible scenarios for informing and preventing future pandemics; Jandrić 2020), skeptics accept that once the crisis has passed, we will return to the prevailing economic and social models that characterize the western world. A more intermediate posture is to assume that there will be some modifications

(e.g. McKibbin and Fernando 2020). For example, the way we use natural resources will change, since the emergence of zoonotic diseases like COVID-19 are the result of niche invasion, deforestation, illegal animal trafficking, and inadequate regulation of the consumption of wildlife.

The disease COVID-19 is caused by the virus SARS-CoV-2, which is a zoonosis that is likely acquired by the consumption of wild animals for food (Malik et al. 2020) and/or the interaction between residents of rural areas and the wild animals in those areas (e.g. Li et al. 2020a). Markets that sell wildlife illegally and without food handling biosafety measures, are considered high-risk sites for the emergence of zoonotic diseases, since they increase the likelihood that pathogens will jump hosts and infect humans (Bonilla-Aldana et al. 2020; Hui et al. 2020). The Chinese government has indicated some restrictive measures on the use of wildlife as a food source in response to the COVID-19 outbreak, but these measures may only be temporary (Li et al. 2020a). While the main interest of this policy must be the avoidance of risk of this and other epidemic outbreaks of zoonotic origin, it inherently involves a rethinking of our relationship with nature, its administration, and its

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use.

1.1. Pathogens at the wildlife-human interface

This pandemic crisis should remind us of at least two realities of our contemporary lifestyle: (1) we are too close to wildlife due to disruptive patterns of exploitation of nature (e.g. increasing development of natural areas), and (2) international trade and travel spread pathogens quickly at a global level. The fact that our disruptive interaction with nature is so frequent has resulted in the emergence of multiple epidemics worldwide (Jones et al. 2008; Allen et al. 2017; Morens et al. 2020) and has been the main cause of the latest pandemics, which have had animal origins. One of the most well-known pandemics in recent history and which has had a profound impact on societies, is the one caused by the human immunodeficiency virus (HIV hereafter). The two subclades of HIV—HIV-1 and HIV-2—have their origins in African primates such as chimpanzees (*Pan troglodytes troglodytes*) and the sooty mangabey (*Cercocebus torquatus atys*), respectively. While the mechanisms of HIV transmission that led to the first transfer events have not yet been conclusively demonstrated, these species of primates are hunted and eaten frequently in western Africa as bushmeat. In the case of the sooty mangabey, the prevalence of simian immunodeficiency virus (SIV) is above 40%. This could have generated multiple opportunities for the origin of the HIV pandemic (Holmes 2001). It is noteworthy to mention that among zoonotic reservoirs, primates are an over-represented order of animals with epidemic potential (Plourde et al. 2017).

Other pandemics of animal origin are the influenzas, caused by influenza viruses which originated in waterfowl, and belong to the family Orthomyxoviridae. The most important influenza pandemics since the Spanish flu (of 1918-19) have been from influenza group A, which has been isolated in humans as well as in a variety of animals. Other lethal epidemics including Ebola, Marburg and Nipah virus have been associated to bats (Chiroptera), another relevant wildlife group that functions as a reservoir of viruses pathogenic to humans (Guth et al. 2019). In fact, they have also been the reservoirs of the coronaviruses that have caused the most recent high-mortality pandemics of human-to-human virus transmission (i.e. without requiring vectors). The SARS-CoV, Middle East Respiratory Syndrome (MERS) and the current SARS-CoV-2 viruses are responsible for hundreds of thousands of deaths worldwide. However, the origin of these epidemics can be traced spatially to a single location of origin and is generally the product of unforced interactions between animals and humans (for example, in urban wildlife markets or the urbanization of natural areas). In other words, they are the product of avoidable interactions (Li et al. 2020b).

The case of the COVID-19 pandemic is a sign of how extremely connected human populations are. The transmission of this virus was declared a pandemic by the World Health Organization (WHO) less than three months after being reported for the first time in the city of Wuhan, China, despite efforts to control its expansion (Daszak et al. 2020). However, based on an exploration of the evolutionary history of SARS-CoV-2, it is likely that the virus was already circulating outside of China within the first 6 weeks of being reported (<https://nextstrain.org/ncov/global>).

Humans also suffered viral pandemics requiring the presence of vectors to disseminate the pathogen. One example is that of the Zika virus (ZIKV, Amarillovirales order, Flaviviridae family), which can illustrate both our intimate relationship with zoonotic pathogens, wildlife and intense human social connections that promote fast pathogen spread.

ZIKV was isolated for the first time in 1947 from serum of a febrile Rhesus monkey (*Macaca mulatta*, family Cercopithecidae), captured in the Zika Forest of Uganda and later isolated from an *Aedes africanus* (Culicidae) mosquito from the same forest (Dick et al. 1952). The first cases in humans were reported in Nigeria a few years later (Macnamara 1954). For 60 years, ZIKV remained confined to a few localities in West-central Africa and Asia, with few infected people and a low

virulence. However, in 2007 the ZIKV emerged suddenly, causing an epidemic outbreak on the island of Yap in the Federated States of Micronesia. By 2014, it had spread among islands in the Pacific, and by early 2015, it was identified for the first time in Brazil. By the end of that year, it had expanded in South America, Central America, the Caribbean Islands, and Mexico (Waggoner and Pinsky 2016). The main mode of transmission of ZIKV is through the bites of competent mosquito vectors (see Benelli and Romano 2017 for a dedicated review), among which a major role has been observed for *Aedes aegypti*, followed by *Aedes albopictus*, which also caused other arbovirus (chikungunya and dengue) pandemics (Benelli and Mehlhorn 2016). The dispersal of *Ae. aegypti* from Africa to the Americas is believed to have occurred during the period of colonial slavery in the 1600s, but the arrival of *Ae. aegypti* in Australia, Europe and Southeast Asia occurred during the XXth century (Lwande et al. 2020). For many decades, the dispersal of this mosquito was confined to tropical and subtropical regions. However, because of climate change, it has now spread to temperate and higher altitude regions, associated with an increase in average temperature in the regions where its distribution had previously been limited (Capinha et al. 2014). While the transmission of the dengue virus and *Ae. aegypti* spread from Sub-Saharan Africa beginning about 500 years ago and now is worldwide, as is dengue virus (Powell et al. 2018). Human migration and global climate change are the reasons for this expansion (e.g. Wilke et al. 2019). In a similar fashion, although on an accelerated temporal scale, human air travel was the factor explaining the swift SARS-CoV-2 worldwide expansion.

2. Lessons learned for vector-borne disease management

Vector-borne diseases (VBD; e.g. malaria, dengue, lymphatic filariasis, schistosomiasis, human African trypanosomiasis, leishmaniasis, Chagas disease, yellow fever, Japanese encephalitis, Lyme disease and onchocerciasis) are some of the most terrible ills currently affecting humankind, and they currently represent 17% of infectious disease cases that cause around 700,000 deaths annually around the world (<https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases> reviewed June 1, 2020). VBDs continue to be a great challenge to governments and health authorities. To our eyes, the links between VBDs and degradation of nature are rather clear:

(i) decrease in natural areas that serve as a buffer between zoonotic agents and humans (Keesing et al. 2010). For example, the reduction of predators or competitors that impact hosts of high vector competency leads to their demographic growth (Ostfeld and Holt 2004; Wild et al. 2011); (ii) the loss of biodiversity, which includes other reservoirs, makes us the most important element in the host choice of many vectors (dilution effect) (Ostfeld 2009; Levine et al. 2017). Of note, when species richness decreases in a locality, the number of infected vectors increases (Liu et al. 2016); (iii) the illegal use of wildlife and degradation of natural habitats has increased the interactions between humans and wild animals, which facilitates our infection by new pathogens (e.g. Chomel et al. 2007). The general endpoints of illegal use include trafficking, consumption, traditional medicine and popular belief, ornamental use and private collections (Broad et al. 2003; t' Sas-Rolfes et al. 2019); (iv) deforestation and climate change increase the planet's temperature, which allows vectors to disperse and colonize new areas (<https://www.ipcc.ch/> reviewed June 1, 2020, see also Wilke et al. 2019). For example, the factors that explain the success of infectious agents transmitted by mosquitoes covary with climate change, land use change, and socio-economic factors (Franklin et al. 2019); (v) the social and economic model does not stop the unregulated or illegal use of forests and jungles (with subsequent land use changes), and even promotes it as a way to perpetuate growth (e.g. Rull 2011; Zhang 2013). In this sense, capitalism and human development with high rates of extraction conflict with nature since ancient (Royal Forestry Society 2020) and medieval (Rhode Island School of Design Museum, 2015) times. Because of this, it is estimated that at a global level more surface area is modified by

humans than in its natural state (Ellis and Ramankutty 2008).

VBDs have ecological and epidemiological patterns that render them difficult to control once infection has taken place (Hollingsworth et al. 2015; Rizzoli et al. 2019): the causal infectious agents of these zoonoses have complex life cycles, are difficult to diagnose, vaccines are not at all effective or nonexistent, there is a low regional prevalence with highly localized infection foci, non-human reservoirs and low apparent pathogenicity. SARS-CoV-2 and other viruses that originate in wildlife are not exempt from the rules that operate for VBDs. As such, the most cost-effective and least traumatic methods (to reduce the number of deaths) is to base the control of these pathogens and their vectors on preventative methods, which requires completely rethinking humans' relationship with natural systems.

3. Future prospects

Starting from the above-described scenario, herein we want to highlight two major points. First, this crisis offers a unique opportunity for the international community to reflect about what is best for humans and nature. In this regard, the governments of the world could work in a coordinated way to keep conditions (*i*)-(v) from continuing to prevail around the world with clear and strict regulations. Desirably, this approach must be coherent with the measures proposed according to Ecosystem Health, Conservation Medicine, EcoHealth, Planetary Health and/or One Health (Benelli and Duggan 2018; Alonso Aguirre et al. 2019). While there are certain conflicts with respect to the performance of these practices at a country level (e.g. Chien 2013), these proposals attempt to achieve health beyond human health alone, integrating multiple dimensions, such as environmental, social and economic, in addition to promoting interdisciplinary approaches.

Secondly, if governments follow this action, the same strategies that would protect us from viral diseases (for example, coronaviruses) should also include VBDs. Our proposal is not new in the sense of needing a better relationship with nature to achieve global health (e.g. Kelly et al. 2017). What is new is that plans for prevention of zoonotic diseases like COVID-19 should be similar to plans for prevention of vector borne diseases, particularly considering environmental conditions modified by humans that favor emergence of pathogens. One example is the implementation of zoonotic vigilance (species monitoring) networks, which are early alert systems that allow the prevention of outbreaks in both humans and animals. This strategy can be focused on those areas where we have detected illegal wildlife markets and where laboratory tests to identify zoonotic viruses can take place (Buheji 2020; Tiwari et al. 2020). The creation of these systems would allow us to avoid the risk of VBDs and therefore their social, human, and economic impacts (Rahimi and Abadi 2020).

The discussion of strategies to prevent VBD and COVID-19 implies a deeper analysis of the world we are living in rather than only outlining the causes of such diseases. For example, for improving the human relationship with nature, governments must consider not just spaces set aside for wildlife and wildlife commerce, but also rethink the current economic model. In this respect, it is paradoxical that many governments are abandoning social distancing practices for fear of the economic crisis that will surge after the pandemic. What these governments are failing to see is that whether they abandon physical distancing practices or not, either scenario will lead to an economic crisis. Perhaps this lack of vision based on emphasizing economic growth also fails to think about and plan preventive measures. For example, for several countries current political discussions are biased toward the clinical treatment of COVID-19 rather than its prevention. This is partially explained by rapid transmission of virus to large numbers of people and rapid clinical deterioration to severe disease which in combination overwhelm the capacities of medical institutions (Kandel et al. 2020). In no way do we wish to devalue research focused on vaccines or antiviral medications, but there must be a healthy balance between prevention and treatment to also resolve the problem of emerging diseases and new

disease origins. Biasing all efforts toward the immediate response does not allow the prevention of new pandemics (Daszak et al. 2020), which will surely appear if the current conditions of use of natural systems persists. Other claims are also heavily biased towards protection of current economic models as the source of human welfare which terribly dismisses our relationship with nature and wildlife (e.g. McKee and Stuckler 2020). These views ignore the scale of human-induced modification of our planet which really requires a total shift in our way of facing our future. Moreover, cooperation among governments and scientists should follow a strategy where nature and human welfare must always be in a win-win scenario. This collaboration must be more multidisciplinary, multi-sector and multinational than ever. In this sense, the COVID-19 and other VBD must be taken as an opportunity by the international community to start such collaboration.

4. Conclusions

As has occurred for vector borne diseases, human interference in natural environments is the fundamental cause of the non-vector borne zoonotic disease COVID-19. Governments ought to safeguard natural areas that serve as buffer zones against zoonotic diseases affecting humans, which would at the same time preserve biodiversity. Specifically, countries and international organizations ought to prevent illegal use of wildlife, towards a healthy future.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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