DRIVERS AND CAUSES OF ZOONOTIC DISEASES: AN OVERVIEW

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ABSTRACT
Diseases transmitted between animals and humans are known as zoonotic diseases. The direct and indirect drivers that affect the emergence of zoonotic diseases are numerous and interacting, and their relative impact on the emergence of new diseases differs geographically with natural, cultural, social and economic conditions. In this article, we provide an overview of the concept, status and trends of zoonotic diseases. We focus on the direct drivers with the greatest potential influence on zoonotic disease emergence and which thereby increase the risk of epidemics and pandemics – land-use change, especially resulting from intensified agriculture and livestock production, the trade in wildlife, and wild meat consumption. We also explore evidence accumulated over recent decades that suggests that protected and conserved areas play a measurable and significant role in avoiding land-use change and thus potentially have a role in reducing the exposure to new zoonotic emerging infectious diseases.

Key words: COVID-19, emerging infectious disease (EID), EID drivers, land-use, protected and conserved areas

INTRODUCTION
Zoonotic diseases are those diseases or infections that can be transmitted between humans and wild and domestic animals (Slingerbergh et al., 2004). They have been linked to recent outbreaks that have threatened global health and economies, including Ebola, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and now Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus causing COVID-19 (IPBES, 2020).

For years, scientists and policy actors have been warning about the risk of emerging infectious diseases (EIDs) and recommending how to avoid outbreaks (Dobson & Carper, 1996; Morse et al., 2012). There is evidence of an increasing rate of emergence of novel EIDs. During the last century, on average two new viruses per year spilled from their animal hosts into human populations (Woolhouse et al., 2012). Zoonotic diseases have been receiving increased attention as a research topic, with overall rate of publications increasing from between 1 to 3 per annum in 2006, to more than 18 per annum in 2012, and more than 33 per annum in 2017 (White & Razgour, 2020), contributing to a better understanding of pathogens, their hosts and factors affecting disease emergence.

Zoonotic disease emergence is a complex process. A combination of drivers provides conditions that allow pathogens to expand and adapt to new niches. The drivers are environmental, social, political and economic forces operating at local, national, regional and global levels (Institute of Medicine and National Research Council, 2009). In this article, we focus on direct drivers of zoonotic disease emergence, including land-use change, wildlife trade and wild meat consumption, and intensified livestock production.

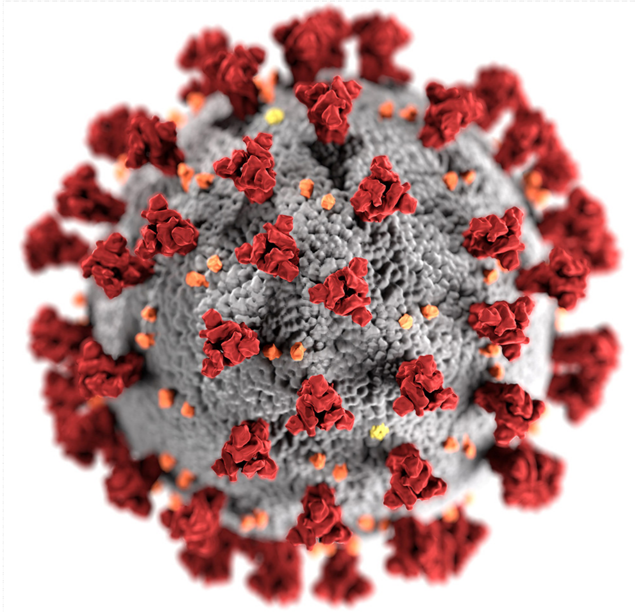
ZOONOTIC DISEASES: STATUS, TRENDS AND CORE CONCEPTS
Zoonotic diseases are particularly important, as 60 per cent of the 1,407 human pathogen species are zoonotic (Woolhouse & Gowtage-Sequeria, 2005), and of these, 72 per cent originated in wildlife (as opposed to domestic animals) (Jones et al., 2008). Moreover, 75 per cent of the 177 emerging or re-emerging pathogens (i.e.,

agents of an infectious disease whose incidence is increasing) are zoonotic (Woolhouse & Dye, 2001; Taylor et al., 2001). These numbers may be underestimates, since new human pathogens are still being discovered at a rate of 3 to 4 species per year, with most of them being viruses (Woolhouse & Antia, 2008). These have caused most recent human pandemics and represent a growing and significant threat to global public health and the economy (Parrish et al., 2008; Jones et al., 2008; Dobson et al., 2020).

Zoonosis may be viral, bacterial, parasitic or involve unconventional agents, such as fungi and protozoans (Cleaveland et al., 2001). However, the chance that a zoonotic pathogen is associated with emerging and re-emerging infectious diseases depends on the pathogen group, being greatest for viruses and almost nil for helminths (worm-like parasites) (Woolhouse & Gowtage-Sequeria, 2005). Among viruses, RNA types account for 37 per cent of all emerging and re-emerging pathogens; they are also well represented among emerging pathogens that have apparently entered human populations only in the last few decades. Examples are HIV and the group SARS-Coronavirus. The rates of nucleotide substitution (i.e., the replacement of one nucleotide to another) are much higher for this type of virus, so allowing rapid adaptation and greatly increasing the chances of successfully invading a new host population (Burke, 1998; Woolhouse et al., 2005).

Many of the diseases that exist today, such as influenza, diphtheria or HIV/acquired immune deficiency syndrome (AIDS), have a zoonotic origin (Diamond, 2002). Zoonoses fall into two categories: i) pathogens of animal origin which rarely transmit to humans, but, should it occur, human-to-human transmission will maintain the infection cycle for some time – examples include HIV, SARS-CoV-2, certain influenza A strains, Ebola virus and SARS; and ii) pathogens of animal origin in which direct or vector-mediated animal-to-human transmission is the usual source of human infection – examples include Lyssavirus infections, Zika and Dengue virus, Hantavirus, yellow fever virus, Nipah virus (Bengis et al., 2004).

Zoonotic pathogens exist in many different animal hosts and there are many ways, both direct to indirect, in which transmission to humans occurs (Webster et al., 2017). Although the likelihood of transmission occurring through vector-borne and aerosol droplets is broadly similar (Loh et al., 2015), arboviruses (i.e. viruses transmitted by arthropod vectors, mostly mosquitoes) are less likely to generate pandemics than those transmitted directly as aerosols. Arboviruses are partially constrained by having to pass sequentially through two hosts in their life cycle, their insect vector and then humans, or their reservoir host (Dobson, 2020). The ability of these viruses to expand their geographic range is also limited by climate and their dependence on suitable vectors. If a virus induces strong immunity in humans, its rate of spread will be rapidly curtailed, because uninfected vectors will have a harder time locating infectious hosts (e.g., Ferguson et al., 2016).



Ultrastructural morphology of a coronavirus Image: CDC, Alissa Eckert, MSMI; Dan Higgins, MAMS

Generally, the infection of a human with a zoonotic pathogen represents a dead-end host. This means that most zoonotic pathogens are either not transmissible (directly or indirectly) or only minimally transmissible between humans (e.g., Rabies virus, Rift Valley fever virus, the *Borrelia* bacteria causing Lyme disease). Almost a quarter of all zoonotic pathogens are capable of some person-to-person transmission but do not persist without repeated reintroductions from a non-human reservoir (e.g., *E. coli* O157, *Trypanosoma brucei rhodesiense*). Less than 10 per cent spread exclusively from person to person (e.g., *Mycobacterium tuberculosis* and measles virus) or can do so once successfully introduced from a nonhuman source (e.g., some strains of influenza A, *Yersinia pestis*, or SARS coronavirus) (Woolhouse & Gowtage-Sequeria, 2005).

Therefore, even if a pathogen is capable of infecting and causing disease in humans, most zoonotic pathogens are not highly transmissible within human populations and do not cause major epidemics. However, we currently have no way of predicting whether a pathogen will spillover from one host to another (e.g., species jump). Despite being rare, these events have led to some of the most devastating disease pandemics recorded, including HIV/AIDS and COVID-19.

DRIVERS OF ZOONOTIC DISEASE EXPOSURE

Land-use change

Because land-use change increases peoples' contact with wildlife and their potential pathogens that may be new to humans, it is believed to be the leading driver of emerging zoonosis (Loh et al., 2015), and has been linked to more than 30 per cent of new diseases reported since 1960 (IPBES, 2020). There are many direct and indirect drivers of land-use change, but very often this sequence occurs: roads are first driven into previously inaccessible natural areas, often to serve extractive activities like logging or mining; these facilitate more human incursions; and so lead to the conversion of further natural areas for settlements and subsistence and commercial agriculture. Land-use change and fragmentation processes increase the amount of natural edge habitat and the interface between wildlife and human-dominated areas. Edge length shows a positive correlation with the rate of contact between humans and wildlife, and consequent pathogen sharing (see Faust et al., 2018). Models of pathogen spillover from wildlife to domestic animals and humans predict that the highest spillover rates occur at intermediate levels of habitat conversion while the spillovers that lead to the largest epidemics are projected to occur less frequently at the extremes of either intact ecosystems or complete loss of ecosystems (Faust et al., 2018).

There are several well-documented examples of pathogen transmission between wildlife and humans linked with land-use change. An association has been shown between Ebola virus outbreaks and deforestation in Central and West Africa (e.g. ERM, 2015; Leendertz et al., 2016; Rulli et al., 2017), with an estimated time lag of two years between deforestation and outbreak occurrence (Olivero et al., 2017). The fragmentation process can stimulate the movement of wildlife into human-modified landscapes, especially when food for wild animals is no longer sufficient within the remaining

Deforestation in the Brazilian Amazon © Araquem Alcântara, WWF-Brasil natural habitat. In disturbed forest habitats, for example, fruit bats are more likely to feed near human settlements, an important factor in a number of spillover events (Dobson et al., 2020). In Australia, Hendra virus spillover from flying fox fruit bats to domestic horses, and then to humans, has been associated with diminished nectar flows due to habitat loss or climate change; bats then switch to anthropogenic food sources, including fruiting trees planted in horse paddocks (Plowright et al., 2015). Similarly, Nipah virus spillover in Malaysia from bats to pigs, and eventually to humans, has been associated with reduced forest habitat, which - together with fruiting failure of forest trees during an El Niño-related drought - pushed flying foxes from natural habitats to cultivated orchards and pig farms (Looi & Chua, 2007). Similar mechanisms have been suggested for Ebola outbreaks in Africa (Olivero et al., 2017). Although the vast majority of emerging infectious diseases come from wildlife, it is important to note that land-use change does not affect only the dynamics of wild animals. Land encroachment encourages the presence of domestic pets, which can be potential hosts of infectious diseases, within natural habitats. Dogs and cats, for example, share major vector-borne infectious diseases with man, such as rabies, leishmaniasis, Lyme disease and rickettsiosis (Day, 2011).

Transmission of pathogens driven by land-use change depends not only on increased contact between wildlife and humans (and their livestock), but also on the abundance of potentially infected wild hosts (Faust et al., 2018; Dobson et al., 2020). When natural habitat is transformed into agriculture, the available habitat is reduced for many wild species, creating less diverse wildlife communities. However, it can also increase the abundance of vectors and hosts, which are able to adapt to altered environments (Patz et al., 2004; Prist et al., 2016; Gibb et al., 2020), potentially intensifying transmission rates and the chance of spillover to humans.

While birds are an important source of zoonotic diseases (Boroomand & Faryabi, 2020), the majority arise from mammals, with a particularly high proportion reported for rodents, bats and primates (Han et al., 2016; Olival et al., 2017; Johnson et al., 2020): indeed, bats and primates are likely to share many viruses with humans (Johnson et al., 2020). The impact made by zoonoses from these mammal groups is all the greater because they contain many different species (Han et al., 2016; Johnson et al., 2020; Mollentze & Streicker, 2020). Bats have been implicated in many deadly emerging infectious viruses, including Ebola virus, SARS-CoV, MERS-CoV, Nipah virus, Hendra viruses (Han et al., 2015), and now probably SARS-CoV-2 (Platto et al., 2020; Zhou et al., 2020). Bats have been shown to have a higher proportion of zoonotic virus (Olival et al., 2017) than any other mammals, possibly due to their intrinsic social, biological and immunological features (Han et al., 2015). The close evolutionary links between humans and non-human primates may also contribute to a greater risk of pathogen spillover from this group (Han et al., 2016; Olival et al., 2017).

Tropical rainforests host a high diversity of rodents, primates and bats, with a particularly impressive bat richness in the Amazon (Jenkins et al., 2013). This explains, in part, why tropical forests are among the areas with the highest EID risk (once reporting effort is taken into account) (Allen et al., 2017). Other reasons include the current high rates of deforestation and fragmentation, the resulting simplification of ecosystems and proximity to expanding livestock production. Tropical forest loss and fragmentation is on the rise: approximately 70 per cent of remaining forest is within 1 km of the forest's edge, subject to the degrading effects of fragmentation (Haddad et al., 2015). It is no surprise, therefore, that land-use change in the tropical forest is expected to drive more pandemic emergence in the future (Loh et al., 2015; Murray & Daszak, 2013; Faust et al., 2018).

Wildlife trade and wild meat consumption

Recent studies have found human–animal contact is a key risk factor for zoonotic disease emergence. Human–animal contact occurs in natural settings, live animal markets, wildlife farms and within the wildlife trade (Daszak et al., 2020; Li et al., 2020). The danger of spillover varies widely in such situations, though as yet there is a lack of data on the scale of these risks.

The wildlife trade has expanded dramatically recently. Although data are not fully available for domestic trade, the international legal wildlife trade has increased 500 per cent in value since 2005, and 2,000 per cent since the 1980s (UN Comtrade Database, 2020). It has been estimated that one in five terrestrial vertebrates is traded (Scheffers et al., 2019).

Wild meat complements and supports local diets and livelihoods in many regions (Fa et al., 2009), especially in some parts of the developing world. Wild meat often provides income in regions where few alternatives exist (Coad et al., 2019). Wild meat consumption in urban areas may be less due to the ready availability of alternative protein sources and more influenced by cultural influences, such as people's beliefs and social norms (Morsello et al., 2015). The legal and illegal wild meat trade feeds food markets and wider market networks beyond national boundaries.

Wildlife farming is the captive breeding of traditionally undomesticated animals to produce pets, food resources, traditional medicine and materials like leather, fur and fibre (Damania & Bulte, 2007; Tensen, 2016). It too has grown rapidly in recent decades (Nijman, 2010). While wildlife farming in some instances can reduce consumption of wild individuals, alleviate poverty and improve welfare for farmers[1], it can have negative impacts on wild populations[2] and farms may function as spillover hotspots due to the intense human–wildlife interactions (Koopmans et al., 2004; Koopmans, 2020).

There is an urgent need to tackle live animal markets and any wildlife trade that is poorly regulated, particularly high risk trade. However, calls for complete bans on all wildlife trade risk exacerbating poverty, undermining human rights, damaging conservation incentives and harming sustainable development (Roe et al., 2020). A more nuanced call, endorsed by 380 experts from 63 countries, focused on the need to shut down high-risk wildlife markets (with priority given to those in high-density urban areas), scale up efforts to combat wildlife trafficking and trade in high-risk taxa, and strengthen efforts to reduce consumer demand for high-risk wildlife products[3].

Regulations are required for disease surveillance, veterinary care, sanitary transport, hygienic market conditions and control of the source of traded animals (Bell, 2004; Daszak et al., 2020; Li et al., 2020). Contact between humans and high-risk species, in particular, should be more strictly regulated, and accompanied by intensive disease surveillance (Betsem et al., 2011). Village-based alternatives that prevent communities from exposing themselves to potential risks should be encouraged.

Intensification of livestock production

By concentrating large numbers of animals in very small areas, livestock production intensifies human–animal and human–wildlife–livestock interaction (Chomel et al., 2007; Jones et al., 2013). This facilitates pathogen spillover from wildlife to livestock and has increased the likelihood that livestock become intermediate hosts in which pathogens are transmissible to humans (Jones et al., 2013).

Whereas the coevolution of hosts and pathogens in intact ecosystems favours low pathogenicity microorganisms, it is the opposite in intensive production systems where low genetic diversity and intense livestock management creates higher rates of contact and a greater number of opportunities for pathogens to transmit and amplify (Jones et al., 2013). Increasingly extensive transportation networks, the sale and transport of live animals, and the juxtaposition of agriculture and recreation with wildlife also contribute to the emergence and increasing virulence of zoonotic pathogens. Many wildlife species have thrived in this transitional landscape and have become reservoirs for disease in livestock and humans (Jones et al., 2013).

The expansion of livestock and poultry production, the greater size of farms and the increased number of individual animals at each farm create greater potential for transmission of pathogens to people (IPBES, 2020). Examples of zoonotic pathogens that circulate in livestock populations include the avian influenza viruses H7N9 and H5N1, both of which are highly lethal although with low transmission rates to humans; numerous bacterial, viral and parasitic pathogens in cattle, including the human coronavirus HCoV-OC43 (Cui et al., 2019); and several variants of swine flu including H1N1, H1N2 and H3N2 (Maldonado et al., 2006). The emergence of Middle Eastern Respiratory Syndrome (MERS) in people may have been due to transmission of a coronavirus of at origin (Yang et al., 2014), but which recently became endemic in domesticated camels (Elfadi et al., 2018), allowing repeated transmission to people (Azhar et al., 2014).

Other drivers of spillover risk include recreation which places people and high risk taxa in close proximity such as recreational caving (in caves with bat roosts) and some wildlife watching where humans come in relatively close proximity to wildlife (e.g., Gorilla viewing). In addition, actions that create unnatural concentrations of wildlife such as supplemental feeding of cervids also could potentially increase disease spread.

THE ROLE OF PROTECTED AND CONSERVED AREAS

The approach to EIDs has been largely reactive, focusing on pathogen control once it has already emerged from wildlife (Childs & Gordon, 2009; Loh et al., 2015). A more proactive approach is needed to prevent disease emergencies (Dobson et al., 2020). Protected and conserved areas (PCAs) can play an important role in preventing future disease outbreaks by maintaining ecosystem integrity (Dobson et al., 2020).

PCAs are diverse and are managed through a range of governance types. PCAs include national parks and other protected areas, as well as other area-based conservation systems, including Other Effective area-based Conservation Measures, and Indigenous and Community Conserved Areas. All have the potential to play a measurable and significant role in avoiding land-use change (Ricketts et al., 2010; Jusys, 2018; Soares-Filho et al., 2010). In a global analysis, Joppa and Pfaff (2010) found that protection reduces conversion of natural land cover for 75 per cent of the countries assessed. Even though there are important research gaps that need to be addressed in order to fully understand the overall health effects of PCAs (Terraube et al., 2017), it is clear that PCAs can buffer against the emergence of novel infectious diseases by reducing rapid changes in host/reservoir abundance and distribution, and limiting contact between humans, livestock and wildlife (Kilpatrick et al., 2017; Terraube et al., 2017; Terraube, 2019). Furthermore, PCAs offer significant opportunities for EID monitoring and surveillance: for example, in the Virunga National Park, monthly health checks are performed on habituated Mountain Gorillas[4]. In addition, PCAs can greatly reduce poaching and thus reduce one aspect of high-risk wildlife trade.

The main drivers of zoonotic diseases – rapid land-use change, high-risk wildlife trade and encroachment into natural areas – also threaten the ecological integrity of many PCAs (Gibb et al., 2020; Guo et al., 2019). With a rapidly accelerating human footprint and biodiversity in fast decline (WWF, 2020), we can no longer take for granted the role that PCAs have historically played in regulating the dynamics of zoonotic diseases (Lafferty & Wood, 2013).

The cost of preventing future spillover pandemics by avoiding deforestation and regulating wildlife trafficking (which can at least partially be done through PCA establishment and implementation) is a minor fraction of the vast economic and societal costs of coping with a pandemic (Dobson et al., 2020).

There are many calls for PCAs to be better funded, more equitably managed, protected, scaled up and strengthened as part of post-COVID recovery plans (Hockings et al., 2020). Not only would this reduce the loss of biodiversity, help sequester carbon and support livelihoods, but it would also diminish the risk of future zoonotic diseases emerging. It would be an affordable and sensible insurance policy against future pandemics.

CONCLUSION

The COVID-19 pandemic was not the first, nor will it be the last, zoonotic disease to undermine economies and take human lives. Indeed, scientists warn that this may just be the beginning of a new cycle of emerging infectious diseases capable of gaining worldwide traction. A growing body of scientific evidence is helping us understand the complex interconnections between the health of people, wildlife and our shared environment. The most important drivers of emerging infectious diseases, such as land-use change, high risk wildlife trade and the intensification of livestock production, are also among the most significant causes of the destruction of nature.

There are many policy interventions we can take to avoid the occurrence and spread of new zoonotic diseases. Effectively and equitably managed PCAs will be a crucial element. Put them in place and manage them effectively, and we can reduce land-use change and fragmentation of natural habitats, and thereby reduce risks of EID spillovers, better control poaching, and minimise the worst impacts of the unregulated wildlife trade. Many of the priority actions that are needed in respect of PCAs are set out in greater detail in another paper in this special issue (Reaser et al., 2021).

Beyond that, PCAs will also protect us from the dangers of climate change and support livelihoods and enhanced well-being, income, clean water, clean air and green spaces for everyone's physical and mental health (Hockings et al., 2020). The benefits of PCAs have never been more clear, and the COVID-19 pandemic reminds us of yet another reason to invest in their protection for now and in the long term.

ENDNOTES

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RESUMEN

Las enfermedades que se transmiten entre animales y humanos se conocen como enfermedades zoonóticas. Los generadores directos e indirectos que afectan la aparición de las enfermedades zoonóticas son numerosos e interactúan entre sí, y su impacto relativo en la aparición de nuevas enfermedades difiere geográficamente en función de las condiciones naturales, culturales, sociales y económicas. En el presente artículo se ofrece un vistazo general del concepto, la situación y las tendencias de las enfermedades zoonóticas. Nos centramos en los generadores directos con el mayor potencial de influencia en la aparición de enfermedades zoonóticas y que, por lo tanto, aumentan el riesgo de epidemias y pandemias: los cambios en el uso de la tierra, especialmente como resultado de la intensificación de la agricultura y la ganadería, el comercio de animales salvajes y el consumo de carne silvestre. También exploramos las pruebas acumuladas en los últimos decenios que sugieren que las áreas protegidas y conservadas desempeñan una función importante y cuantificable para evitar el cambio en el uso de la tierra y, por lo tanto, pueden contribuir a reducir la exposición a nuevas enfermedades infecciosas zoonóticas.

RÉSUMÉ

Les maladies transmises entre animaux et humains sont connues sous le nom de maladies zoonotiques. Les facteurs directs et indirects qui affectent l'émergence des maladies zoonotiques sont nombreux et interagissent les uns avec les autres. Leur impact relatif sur l'émergence de nouvelles maladies diffère géographiquement selon les conditions naturelles, culturelles, sociales et économiques. Dans cet article, nous présentons un récapitulatif du concept, de l'état actuel et des tendances des maladies zoonotiques. Nous visons les facteurs directs ayant la plus grande influence potentielle sur l'émergence des maladies zoonotiques et qui augmentent ainsi le risque d'épidémies et de pandémies, c'est-à-dire le changement d'affectation des terres résultant en particulier de l'intensification de l'agriculture et de la production animale, le commerce des espèces sauvages, et la consommation de viande sauvage. Nous explorons également les données accumulées au cours des dernières décennies qui suggèrent que les aires protégées et conservées jouent un rôle mesurable et significatif pour éviter les changements d'utilisation des terres. De cette manière elles ont potentiellement un rôle à jouer dans la réduction de l'exposition aux nouvelles maladies infectieuses émergentes zoonotiques.