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Overview Article

Zoonoses in a changing world

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Abstract

Animals are continuously exposed to pathogens but rarely get infected, because pathogens must overcome barriers to establish successful infections. Ongoing planetary changes affect factors relevant for such infections, such as pathogen pressure and pathogen exposure. The replacement of wildlife with domestic animals shrinks the original host reservoirs, whereas expanding agricultural frontiers lead to increased contact between natural and altered ecosystems, increasing pathogen exposure and reducing the area where the original hosts can live. Climate change alters species' distributions and phenology, pathogens included, resulting in exposure to pathogens that have colonized or recolonized new areas. Globalization leads to unwilling movement of and exposure to pathogens. Because people and domestic animals are overdominant planetwide, there is increased selective pressure for pathogens to infect them. Nature conservation measures can slow down but not fully prevent spillovers. Additional and enhanced surveillance methods in potential spillover hotspots should improve early detection and allow swifter responses to emerging outbreaks.

Keywords: zoonoses, spillover, pathogen exposure, pathogen pressure, emergent diseases

Since the initial outbreak of the SARS-CoV-2 pandemic in late 2019 and its subsequent worldwide expansion in 2020, there has been strong attention in the media to zoonoses—particularly viral ones. There is a realization that the recently appeared SARS-CoV-2 will not be the last zoonosis affecting people and that governments need to be prepared to anticipate and respond swiftly next time. There have also been calls from the environmental movement to establish a link between the degradation of nature and the appearance of COVID-19 (e.g., Daszak et al. 2020, Hockings et al. 2020, WWF 2020). In this review, I explore how anthropogenic changes to planetary dynamics influence newly emerging zoonoses, particularly from the perspective of changes to pathogen populations and to the increased risk of exposure to pathogens.

Current understanding suggests that over 60% of human pathogens have an animal origin (Taylor et al. 2001, Woolhouse and Gowtage-Sequeria 2005, Jones et al. 2008), including human diseases such as smallpox (Li et al. 2007) and AIDS (Sharp and Hahn 2010). Ungulates alone support over 250 different human pathogens (Woolhouse and Gowtage-Sequeria 2005). There is a visible acceleration of emerging diseases when human societies shifted from small groups of hunter-gatherers to agriculture-based societies, a process that was accompanied by animal domestication, changes in human diet, and an ever increasing density of people in human communities (Pongsiri et al. 2009). SARS-CoV-2 would be the latest virus that has managed to acquire the ability to infect humans—but not the last.

Three phases to zoonosis

Parasites have evolved in such a way that they need to infect a host in order to complete their life cycles. Infecting the wrong host can result in a dead-end rather than reproduction, and the parasite may not trigger a disease if it infects a target different from the one it has evolved to infect. Following Plowright and colleagues (2017), one can think of three large domains relevant to the acquisition of new diseases—in this case, by humans, but the same principles apply to any new hosts: the outside world, the internal human body (or another host for parasites infecting nonhuman hosts), and the interaction between these two.

The most important factor from the outside world that is relevant for a potential spillover—that is, the spread of a pathogen to a novel host—is pathogen pressure. This refers to the amount of pathogen available at any given place and time. Pathogen pressure is influenced by the distribution and biology of the host, as well as the pervasiveness and severity of the disease—that is, the percentage of the host population that is infected, the amount of pathogen released from the hosts, and the survival and dissemination rate of the pathogen outside its hosts (Plowright et al. 2017).

With regards to the internal human body (or any other or new host), the characteristics of humans and of the pathogen itself determine whether the pathogen will manage to fulfil its reproductive cycle in humans and set a new infectious cycle. This is influenced by physiological, immunological, genetic, and even epigenetic attributes. For example, the bat virus from which the SARS-CoV originated (Lau et al. 2005) and the virus isolated from palm civets (*Paguma larvata*) are unable to bind to human receptors. Nevertheless, selective pressures on the civet's virus allowed for modifications that favor its transmission from human to human, making palm civets an important intermediate in the infection chain leading to a full infective cycle in people (Li et al. 2006, Wang and Eaton 2007). We have now learned that the SARS-CoV and the SARS-CoV-2 viruses use the hACE2 (human angiotensin-converting enzyme 2) receptor as the entry point to infect human cells (Shang et al. 2020).

But in order for new pathogens to get into the human body, humans need to be exposed to them (and the same goes for any other new hosts). This is ultimately determined by the behaviors

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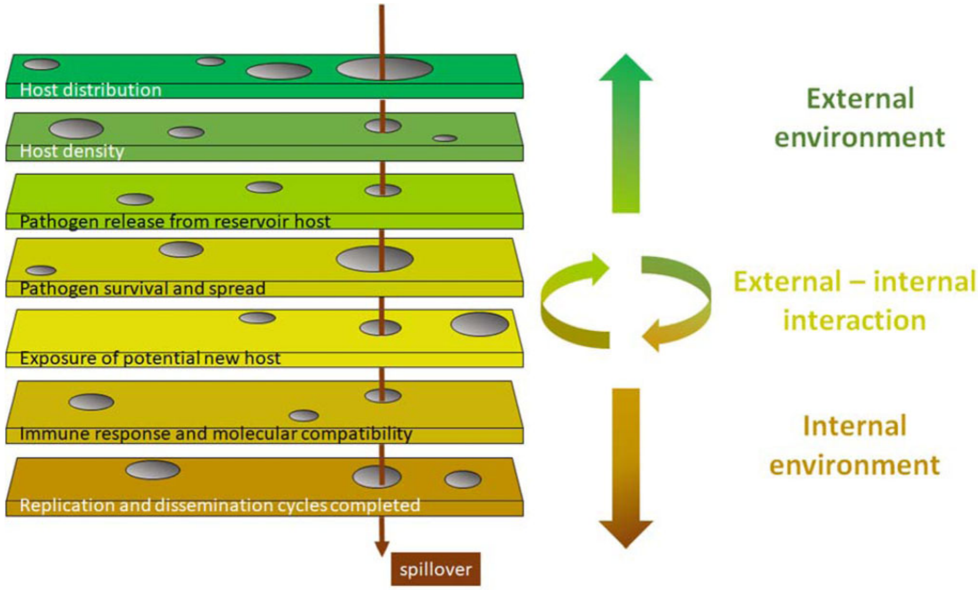

Figure 1. Barriers to spillover. Exposure of a host to a potential pathogen is insufficient to lead to an infectious cycle. There are multiple barriers that the pathogen needs to overcome before a successful infection is established. Some, such as the ecology and natural history of host and pathogen, play out in the outside world (the external environment). But even when a pathogen successfully enters into the internal environment of a potential host, there are still multiple barriers it needs to overcome, such as the host's ability to neutralise the pathogen through its immune response or lack of molecular compatibility, before a successful infection cycle is in place. Source: Modified from Plowright and colleagues (2017).

of humans or of pathogen vectors or both, leading to pathogen exposure and establishing the route and dose of exposure (Cleveland et al. 2007, Plowright et al. 2017). Each of the aforementioned domains presents multiple barriers that break the flow of pathogens and therefore prevent the establishment of new infectious cycles. Successful spillover requires the pathogen to pass through all the obstacles in all the domains (see figure 1).

This is actually quite rare, because pathogens are often confined to one host species (or to a group of related species), and so, in spite of being continually exposed to multiple pathogens that have other species as hosts, most of these cannot and do not infect people; those that manage rarely cause disease in humans and almost always lead to dead-end infection chains (Plowright et al. 2017). Nevertheless, there is a clear recent increase in the incidence of zoonotic outbreaks, in part because of our improved ability to detect them (e.g., through better diagnostic methods and surveillance) and in part because of a true increase of infectious disease outbreaks through zoonotic spillover (Jones et al. 2008).

Impact of biodiversity crisis

Human activities have a strong impact on the environment, leading to changes in the original species composition and their abundance in those places affected. This, in turn, alters the relationship of pathogens and their hosts. Two important aspects are clearly affected by such changes.

Impact on pathogen pressure

The impact of human activities on species often results in demographic changes, with some of them declining in numbers and others increasing. Such changes have an impact on the pathogen pressure and can push a parasite to broaden its spectrum of hosts. In addition to the abundance of the host, there are other parameters affecting pathogen pressure that could be considered, such as the natural history of the infection (duration, intensity, and severity of infection and shedding), the behavior and movements of the hosts, and the efficiency of its spread (density, demographics and health of host). But the impact of the biodiversity crisis affects primarily the density and distribution of hosts, and this is what is highlighted in the following paragraphs.

Several documented examples show that biodiversity loss can release carriers of human disease agents from predation and competition (Civitello et al. 2015, Gascon et al. 2015). In the past decades, human activities have resulted in a substantial reduction and degradation of natural habitats. The IPBES Global Assessment Report estimates that 75% of land surface, 65% of oceans and 85% of wetland areas are significantly altered or lost altogether (Díaz et al. 2019), including the damming of most major rivers (Chao et al. 2008, McCartney 2009) and the degradation of a majority of freshwater habitats (Vörösmarty et al. 2010, García-Moreno et al. 2014). This has affected the population sizes of many species, with many wildlife populations declining and often brought to the brink of extinctions even when the species is not actively hunted, to the point that many are becoming functionally extinct (Maxwell et al. 2016, WWF 2016, Ceballos et al. 2017). Also, common species of low conservation concern show dwindling population sizes and range shrinkages. Rosenberg and colleagues (2019) reported a decrease of almost 3 billion breeding birds in Canada and the United States in comparison with numbers from 1970 (almost one-third of the breeding population), mostly due to habitat loss and degradation; a similar large-scale decrease is presumed for Afro-Palearctic birds (Morrison et al. 2013, Vickery et al. 2014). Across all terrestrial vertebrate orders, the proportion of species with decreasing populations is staggering, with large species, so-called megafauna, particularly badly hit (Ceballos et al. 2017). Amphibians, although they are generally small, are the most threatened terrestrial animal class of vertebrates, with estimates of between 30% and 45% of species on the brink of

Table 1. Examples of pathogens benefiting from perturbations to the original patterns of species distribution and abundance due to anthropogenic causes.

Example	Parasite	Reference
Prevalence of white-footed deer mouse (*Peromyscus leucopus*) over other rodents in the eastern United States results in increased level of tick infection (*Ixodes scapularis*) and Lyme disease transmission.	*Borrelia burdorferi* (Lyme disease)	Ostfeld and Keesing 2000
Lower diversity of hosts (rodents) results in increased human disease risk.	Hantavirus	Suzán et al. 2009
Removal of large vertebrates in Africa can lead to an increase of rodents, a common reservoir of human pathogens, and can, therefore, increase the risk of disease.	Various	Keesing and Young 2014, Young 2014 et al. 2014
Precipitous declines of vultures in India, the key consumers of livestock carcasses, may increase the risk of livestock diseases.	Brucellosis, tuberculosis and anthrax	Markandya et al. 2008
Precipitous declines of vultures in India have led to an increase in rabies infections due to an increase of feral dogs.	Rabies	Frank and Surdarshan 2022.

extinction and many species having recently become extinct in the wild (Collins and Crump 2009, Bishop et al. 2012).

At the same time, the human population and that of domestic animals have exploded, to the point that the biomass of people and livestock combined outweigh that of all terrestrial vertebrates (Bar-On et al. 2018). There are currently roughly 8 billion people, 1.5 billion cows, 1 billion goats, over 1 billion sheep, another 1 billion pigs, 50 million horses, and just short of 25 billion chickens (FAO 2023). The biomass of humans and livestock combined surpasses that of wild mammals by over 20 times, with the present-day biomass of wild mammals seven times lower than that of the period before this accelerated extinction (Barnosky et al. 2011). As a consequence of this dynamic, the original host reservoirs have shrunk, and the pressure for spillovers has increased: From a pathogen's perspective, it has now become very attractive to be able to establish complete infection cycles in humans or domestic animals.

At a local scale, there are many man-made perturbations that alter the original patterns of species distribution and abundance. This can result in situations with relatively few but very abundant species: the reduction or removal of predators or competitors, habitat fragmentation limiting host species dispersal, invasive species, pollution or enrichment of nutrients, etc. (Dobson and May 1986). When the species that benefits from these alterations is also an efficient human–pathogen host, the pathogen pressure increases proportionally. Examples of such species and the parasites they host are listed in table 1.

Impact on pathogen exposure

Human activities are having a huge impact in terms of homogenizing the planet. Homogenization (fewer species, less ecological trait diversity; see, e.g., Daru et al. 2021, Hughes et al. 2022) leads to the replacement of natural ecosystems with less complex human-made ones, which leads to a reduction in biodiversity and, ultimately, fewer ecosystem functions. The process also leads to the expansion of the contact areas between cultural ecosystems and wild ones. This is likely to have an impact in the relationship between humans (and their animals) and pathogens, increasing the pathogen exposure and sometimes leading to zoonotic spillovers.

Human settlement and agricultural activities result in habitat fragmentation, deforestation, and the replacement of natural vegetation by crops (Patz et al. 2004, Jones et al. 2013, UNCCD 2017, Rohr et al. 2019). Agriculture has already led to clearing or conversion of 70% of the grasslands and 50% of the savannas, 45% of the temperate deciduous forests, and 27% of the tropical forest biome (which is where 80% of the new croplands come to be; Foley et al. 2011). All in all, agriculture occupies roughly 40% of the world's terrestrial surface and uses more than two-thirds of the world's fresh water (Foley et al. 2011, Rohr et al. 2019). Whereas crop and grazing lands occupied 27% of land surface in 1900, they had expanded to 46.5% 100 years later (UNCCD 2017). Current estimates are that agricultural production will need to increase to keep pace with global population growth, which would require transforming an additional 10 million square kilometers of natural ecosystems, an area roughly the size of Canada (Foley et al. 2011, Rohr et al. 2019). The expansion of agriculture and human settlements fragments habitats and results in the expansion of ecotones, facilitating the coexistence of species from different habitats (Despommier et al. 2006). This can lead to increased pathogen exposure, which, in turn, can result in pathogen spillover. Not only does this process affect humans, but it can affect other animals too. For instance, deforestation has resulted in new zoonotic diseases involving primates, such as monkey malarias (Fornace et al. 2016), some of which can infect humans and vice versa (Ramasamy 2014). Encroachment into natural areas not only leads to biodiversity loss but can introduce diseases to wildlife that can devastate wild populations and create reservoirs for the disease to be transmitted back to domesticated animals (Rohr et al. 2019) and also increases the risk of zoonotic infections of humans (Berazneva and Byker 2017, Pienkowski et al. 2017). An example of this is the avian flu, first detected in domestic animals before spreading to wild birds (WHO 2014) and now infecting a wide variety of species in the wild that reinfect domestic animals. The 2022 bird flu epidemic resulted in 40 million culled animals at a cost of more than US$2.5 billion just in the United States (Fahrarat et al. 2023), and it resulted in 868 reported human infections worldwide, of which 457 were deadly (Parums 2023). Some examples of increased exposure to pathogens as a result of human encroachment of natural habitats are shown in table 2.

Table 2. Examples of pathogens that benefit from human encroachment into natural areas.

Example	Parasite	References
Increased contact between human populations and wildlife due to deforestation in West Africa	HIV and Ebola	Del Río and Guarner 2015, McMahon et al. 2018
Habitat alteration affecting mosquito density and expansion of their distribution.	Malaria	Yasuoka and Levins 2007
Deforestation leading to an upsurge of vector exposure in Africa, Asia, and Latin America	Malaria	Coluzzi 1984, 1994, Bunnag et al. 1979, Tadei et al. 1998
Encroachment of domesticated animals into natural areas brings them in contact with wildlife in Africa	Rinderpest	Sunseri 2018
Increased contact between domestic animals (e.g., dogs) and wildlife increase risk of infections in Brazil	Leishmaniasis	Courtenay et al. 2002.

In addition to the impact on habitats, there is a direct impact of encroachment on many species that are hunted for bushmeat or for traditional or religious and superstitious uses or that simply fall victim to the latest fashions (Mbotiji 2002, Wolfe et al. 2005, Maxwell et al. 2016). Consumption of wild animals for food is widespread across the world, but commercial logging—and the logging roads that come with it—and armed conflicts have turned wildlife hunting into a commercial activity in some regions (e.g., West and Central Africa), bringing people in close contact with animals and their pathogens (Wolfe et al. 2005, Karesh and Noble 2009). The bushmeat trade encompasses several activities that involve exposure to and contact with potential vectors, such as capturing and handling the animals and butchering and transporting the carcasses. Hunters are often unaware of the risks of zoonotic infections and transmission to humans (Ozioko et al. 2018). For instance, bushmeat seized at a French airport was shown to contain viral particles of three bacteriophage families with the potential to cause transmission to humans (Temmam et al. 2017). In fact, hunters are probably infected with some regularity by pathogens that are then not able to transmit further from human to human (Wolfe et al. 2004), something that we now know happened in the years before the SARS epidemic (Wang and Eaton 2007).

The trade itself can also increase the risk of spillovers, as was seen above with the bushmeat. The wet markets that are prevalent in Southeast Asia (but not exclusively) do not always have adequate storage facilities and end up bringing together species that otherwise would not come into contact (Woo et al. 2006, Naguib et al. 2021). This provides opportunities for pathogens to overcome natural barriers that prevent them from infecting other potential new hosts, as was mentioned above for SARS (Li et al. 2006, Wang and Eaton 2007). Market animals have been implicated in outbreaks of more traditional diseases such as *Salmonella* (Ribas et al. 2016) but also of recent novel zoonotic outbreaks: The epidemic caused by SARS-CoV was linked to palm civets (*P. larvata*) being sold in markets in China's Guangdong province; this virus of bat origin, which can persist in civets for weeks, was isolated from most marketplace civets (Li et al. 2006). In addition, markets are a place where infection can take off because of the concentration of people that are part of those market dynamics. The early SARS cases were associated with people that had close contact with wildlife—handling, killing, or selling animals or preparing and serving wild animal meat in restaurants (Xu et al. 2004, Wang and Eaton 2007)—and although SARS-CoV-2 did not originate at the notorious Wuhan wet market (Huang et al. 2020), the market certainly helped to propagate the infection to epidemic proportions (Huang et al. 2020, Rodríguez-Morales et al. 2020).

Impact of climate crisis

One of the most visible impacts of human activities on nature is the alteration of the climate, an issue that is prominent nowadays in society. It is unlikely that the climate trajectory that humans have set the planet on will be drastically adjusted, and even if we could magically return to the preindustrial warming climate situation, this would not lead to the preindustrial ecological situation. Climate is a key parameter influencing the natural history of organisms, and the ongoing changes have an impact on the distribution and abundance of organisms, favoring the expansion of some organisms and reducing the possibilities of others.

That being said, predicting the impact of climate change on disease is extremely hard, because it requires understanding of the complexities of the host, its parasites, and their interactions with the multiple factors that can covary with climate change, some in opposite directions (Rohr et al. 2011). This caveat notwithstanding, a recent computer modeling exercise suggests that, in the coming 50 years, the changes in the climate and land use could expose many wild mammals to new viruses and may, therefore, promote zoonotic spillovers (Carlson et al. 2022).

Many pathogens are indeed climate sensitive—particularly to rainfall or temperature or both (Wilson et al. 2010, Altizer et al. 2013, McIntyre et al. 2017, McMahon et al. 2018). Human activities are estimated to have already caused roughly a 1.0 degree Celsius of warming of the planet above preindustrial levels, and that number is rising. The impacts of this development on natural systems are being observed across the globe (Masson-Delmotte et al. 2018, Pörtner et al. 2022). Scientists are seeing measurable changes in the distribution and phenology of many species (Parmesan 2006, Sheldon 2019), including infectious diseases (Mills et al. 2010, Altizer et al. 2013). Some of these shifts result in people becoming exposed to pathogens that have successfully expanded their range and colonized new areas or that have recolonized areas from which they had been already eradicated (Gortazar et al. 2014). Several examples of ongoing changes in the distribution of disease vectors likely due to climate change are listed in table 3.

There are also instances in which the pathogens themselves are presented with suitable environmental conditions in areas that previously were not. An example of this is the cholera infections by *Vibrio* bacteria, which are estimated to double in the Baltic region for every degree centigrade increase in annual maximum water temperature (Altizer et al. 2013). The impact of climate on ecosystems can alter their carrying capacity for some species, resulting in alterations in the populations of hosts or vectors and, therefore, in pathogen pressure (Mills et al. 2010). For instance, all three recorded pandemics of the bubonic plague

Table 3. Examples of pathogens whose distribution and phenology are likely being affected by climate change.

Example	Parasite	References
Hispid cotton rat (*Sigmodon hispidus*), a hantavirus host, expanding its range northward in the United States	Hantavirus	Mills et al. 2010
White-footed deer mouse (*Peromyscus leucopus*) expanding northward in the United States	*Borrelia burdorferi* (Lyme disease)	Mills et al. 2010
Asian tiger mosquito (*Aedes albopictus*) expanding into Europe and the Americas	Chikungunya virus	Ruiz-Moreno et al. 2012
Ticks (*Ixodes* sp.) expanding in northern Europe and North America, and heat tolerant ones (e.g., *Rhiphicephalus microplus*) increasing in Africa.	Tick-borne encephalitis, Lyme disease	Ogden et al. 2021, Nutall 2022

can apparently be linked to climate-driven rodent population dynamics in Central Asia, first driving up rodent numbers and then causing them to crash down, forcing fleas to look for other hosts—including humans (Stenseth et al. 2006). Similarly, climatic factors can play an important role in outbreaks of hantavirus and other pathogens that rely on rodents as hosts (Jonsson et al. 2010).

Impact of trade and globalization

Land-use changes provoked by human activities, such as deforestation, agricultural expansion, dam building and wetland modification, and road construction and urbanization, are important drivers of global change leading to increased pathogen pressure or pathogen exposure, which, in turn, can result in infectious disease outbreaks (Patz et al. 2004).

Increased exposure because of agricultural expansion

Expanding agriculture transforms the original natural ecosystems into homogeneous agricultural ones and brings natural and man-made ecosystems into contact. It is in these contact zones that people and their animals are exposed to new pathogens, offering opportunities to the pathogens to expand their host range.

Agriculture already occupies nearly half of the world's land (see above) and, if projected human population growth, behavior, or technology do not change dramatically, it will continue expanding in the coming years. Millions of square kilometers of natural habitats will have to be converted to agriculture in order to fulfil food demand by 2100 (Crist et al. 2017, Rohr et al. 2019). Most of this change is expected to take place in tropical developing countries, which already suffer large mortalities because of infectious diseases (Lozano et al. 2013).

Agricultural drivers appear to be associated with roughly 25% of diseases and 50% of zoonotic diseases that have emerged in humans since 1940 (Rohr et al. 2019). As the agricultural frontier expands, people and their domestic animals are often brought into contact with wildlife, and the risk of pathogen exposure can increase. This increases opportunities for spillovers, given that nearly 80% of livestock pathogens can infect multiple host species, humans included (Wiethoelter et al. 2015; see also the abovementioned example about bird flu). China, Java in Indonesia, east Nepal, northern Bangladesh, Kerala, and northeast India have been identified as hotspots in Asia where high forest fragmentation takes place in areas with high human and livestock densities (Rulli et al. 2021). In addition, intensive livestock production leads to higher pathogen pressure through the increase of both the population size and the density of potential hosts (particularly pigs and poultry), which, in turn, leads to increased risk of disease transmission (Jones et al. 2013). When the interaction between livestock and wildlife is reduced, the possibility of spillover is also reduced. For example, Alexander (2000) showed that the frequency of primary avian influenza infections in domestic birds is directly related to the degree of contact they have with feral birds. Research also showed that, in Malaysia, the Nipah virus epidemic took off when flying foxes (hosts) entered into contact with pigs in intensive farms set up close to mango plantations (Pulliam et al. 2011), and awareness of this situation led to restrictions on planting fruit trees near pigsties in the country.

Another important resource syphoned by agriculture is fresh water. Roughly 80% of freshwater resources used by humans are for agricultural purposes (Foley et al. 2005), and these often require infrastructure to redistribute fresh water, such as dams and reservoirs or irrigation networks. All of these infrastructures increase exposure to and the risk of infection with waterborne vectors, such as schistosomiasis or mosquito-borne diseases such as malaria and filariasis (Harb et al. 1993, Amerashinghe and Indrajith 1994, Steinmann et al. 2006, Sokolow et al. 2017). For schistosomiasis, Sokolow and colleagues (2017) suggest that dams in sub-Saharan Africa may block the natural dynamics of river prawns that feed on the snail hosts (Sokolow et al. 2017), which may result in an increased local pathogen pressure. If this is the case, it provides the possibility of fighting the disease locally by reintroducing prawns where they have dwindled (Hoover et al. 2019).

Impact of globalization

In a globalized world, the interdependence of the world's economies requires the continuous movement of goods and people across international borders. This results in the unwilling movement of pathogens and the resulting exposure of people and domestic animals to them. Nearly one quarter of food produced for human consumption is traded across international borders (D'Odorico et al. 2014), and trade is expected to continue rising as developing countries continue to grow. Trade and international travel, which, up to the COVID pandemic, had been growing for years, have resulted in the introduction of multiple invasive alien species and pathogens all around the world (Daszak et al. 2020). Imported fresh products have resulted in several food-borne outbreaks in the United States (Patz et al. 2004) and elsewhere too. Travel is thought to be a factor in the spread of diseases such as norovirus (de Graaf et al. 2016) or influenza virus, which can spill over from poultry and swine (Hosseini et al. 2010), and travelers are not only at risk of exposure to diseases at their destinations, but they can also take along diseases to another region. This is well documented in historical times (e.g., diseases brought by Spaniards to the America's and vice versa), but in a hyperconnected world, travelers are an important potential vector to spread pathogens. (Hosseini et al. 2010). This was seen both during the SARS epidemic and, more recently, during the COVID epidemic. In both instances, the role of travelers in spreading the disease is well documented (e.g., Hung 2003, Murphy et al. 2020, Rudan 2020, Farzanegan et al. 2021). In addition to travelers, 270 million people are migrants—that is, they relocate from one country to another—and the rate seems to be increasing (Baker et al. 2022). Another group of people on the move are refugees, often without access to adequate medical care and carrying diseases such as tuberculosis, hepatitis B, and intestinal parasites, sometimes asymptomatically and therefore difficult to detect in a timely manner (Loutan et al. 1997).

The global pet trade is also a potential source of infections that results from the movement of animals through many countries, with the risk of introducing novel pathogens to a given region. For example, the global amphibian trade is suspected to have brought several species to the brink of extinction (Auliya et al. 2016) and has led to the spread of amphibian pathogens *Batrachochytridium dendrobatidis* and *Batrachochytridium salamandrivorans*, which have been detected in animals imported through the pet trade (Wombwell et al. 2016). In addition to the pet trade, the illegal wildlife trade (see above) is another source of exotic pathogens that facilitates pathogen exposure by putting animals and people in contact with parasites "imported" from other geographical regions (Bezerra-Santos et al. 2021).

Conclusions

I have used the concepts of pathogen pressure and pathogen exposure, as was used by Plowright and colleagues (2017), to explore the impact that the changes the world is undergoing may have with regards to the appearance of zoonoses, particularly those affecting humans.

It is clear that the mere appearance of a new pathogen is insufficient to cause a new disease, because there are many factors that end up determining whether a pathogen can infect a potential host and whether the infection can become self-propagating—host distribution, pathogen release from the host and survival, human (or other new host) exposure, or immune response to name just a few. We are exposed daily to multiple viruses, but only very few have evolved the mechanisms to cause a successful infection cycle in human beings.

That being said, humans have become a major force shaping the planet. People and their domestic animals are now so dominant that, in some instances, they have altered the original dynamic that existed between pathogens and their hosts. The impact of human-caused disturbance on ecosystems and the climate and the interconnectedness of the economy affect the distribution of both parasites and (potential) hosts. This, in turn, can alter the pathogen exposure to which human communities or domestic animals are subject, with some managing to establish successful infectious cycles. As human and domestic animal populations continue to increase, the possibility of pathogen spillovers resulting in new infectious diseases also increases. Reverting this trend looks unlikely in the foreseeable future, with human population expected to stabilize at around 10 billion by 2050 (according to UN projections). In the current planetary circumstances, any pathogen that manages to overcome all the hoops and loops needed to set an infectious cycle in humans or their animals will be handsomely rewarded. As a species, we are probably more exposed to pathogens now than we once were when we were scarcer and lived in much smaller groups, a condition that led to many infectious cycles petering out and dying off by themselves.

In spite of loud calls and struggles to conserve and restore nature, for decades now, there have been no indications to believe that the planet's homogenization process will slow down or that agricultural practices will change radically worldwide in the coming years. Human population growth has understandably resulted in global efforts to reduce hunger. In addition, as people's livelihoods improve and they progress along the economic ladder, their dietary habits also change. The ever expanding food production is accompanied by an ever expanding agricultural frontier, which is an important driver of both the ongoing extinction crisis and the homogenization and simplification of ecosystems worldwide. The agricultural frontier brings humans and livestock into contact with wildlife and its parasites, increasing the pathogen exposure and the likelihood of spillover events. The risk is even higher when the original host and domestic animals or people share some of the internal factors, as was shown by Fischhoff and colleagues (2021), who found that a multitude of mammals share the ACE2 (angiotensin-converting enzyme 2) receptor that the SARS-CoV2 virus binds to and are therefore potential reservoirs for it. Zoonoses are not a new phenomenon and the SARS-COV-2 one will not be the last one.

Although it is not realistic to think new spillovers can be completely avoided, we are getting a better understanding of where the higher risks could be located (e.g., Rulli et al. 2021). Together with improved monitoring methods, this should make early detection at potential hotspots a real possibility. We saw the potential and flexibility of large-scale monitoring using molecular techniques during the COVID-19 pandemic, although other simpler techniques that are easy to interpret and, therefore, practical for local stakeholders to use, will be necessary (Cunningham et al. 2017). All in all, increased surveillance activities—monitoring for pathogens and wildlife trade—in high risk locations, as well as in the buffer zones between protected areas and inhabited areas seem a realistic proposition (Aguirre et al. 2021), particularly areas with intensive animal husbandry practices at the edge of the agricultural frontier, where wildlife and domestic animals overlap most. And it is better still if the monitoring is accompanied by a strong enforcement of the nature of protected areas, with an eye to minimizing the exchanges between wildlife and domestic animals or humans—yet another reason to expand and strengthen nature conservation.

Additional pathogen surveillance fits squarely with the One Health approach, which postulates that human, animal, and ecosystem health are interrelated and interdependent and that successful responses to threats to humans require holistic and transdisciplinary approaches that bring together these three components (Cunningham et al. 2017, Ogden et al. 2019).

The trends that we currently see in our changing world—the replacement of wild animals and plants with domestic ones, the simplification of ecosystems (with the associated species declines and extinctions), climate change and global warming, agricultural expansion, the movement of goods and people—are very entrenched, and it will take time and huge efforts to revert them. These trends, fed by human activities, have an impact on both pathogen pressure and exposure and push microorganisms and viruses to adapt to new hosts previously not infected by them. Efforts to conserve and restore nature and to promote an ecologically sustainable use of Earth's resources are more important than ever to change the planet's current depleting trajectory, but even in the most optimistic scenarios, they will not yield results soon enough to reduce the number of spillover events. It is impossible to stop pathogens from jumping into humans and domestic animals, but with improved surveillance methods, it should be possible to detect such episodes early and improve our response whenever an outbreak is detected.

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