







# **PREVENTING THE NEXT PANDEMIC**

# Zoonotic diseases and how to break the chain of transmission



A Scientific Assessment with Key Messages for Policy-Makers A Special Volume of UNEP's *Frontiers* Report Series © 2020 United Nations Environment Programme

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Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission



## Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission

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# **Abbreviations and Acronyms**

AIDS	acquired immune deficiency syndrome
BSE	bovine spongiform encephalopathy
CBD	Convention on Biological Diversity
CGIAR	A global partnership for a food secure future
CITES	Convention on International Trade in Endangered Species of Wild Fauna and Flora
CMS	Convention on Migratory Species (Bonn Convention)
COP	Conference of the Parties
COVID-19	coronavirus disease 2019
DNA	deoxyribonucleic acid
EID	emerging infectious disease
FAO	Food and Agriculture Organization of the United Nations
GDP	gross domestic product
HCoV-OC43	human coronavirus subtype OC43
HIV/AIDS	human immunodeficiency virus/acquired immune deficiency syndrome
HPAI	highly pathogenic avian influenza
IBD	inflammatory bowel disease
ILRI	International Livestock Research Institute
MERS	Middle East respiratory syndrome
MERS-CoV	Middle East respiratory syndrome coronavirus
OIE	World Organisation for Animal Health
PED	porcine epidemic diarrhoea
RNA	ribonucleic acid
RVF	Rift Valley fever
SARS	severe acute respiratory syndrome
SARS-CoV	severe acute respiratory syndrome coronavirus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SIV	simian immunodeficiency virus
TGE	transmissible gastroenteritis
UNEP	United Nations Environment Programme
UNESCO	United Nations Educational, Scientific and Cultural Organization
UNICEF	United Nations Children's Fund
WHO	World Health Organization

# **Foreword by the Executive Director of UNEP**

COVID-19 has caused profound damage to human health, societies and economies in every corner of the world. This illness is zoonotic, a type of disease that transmits between animals and humans. It may be the worst, but it is not the first. We already know that 60 per cent of known infectious diseases in humans and 75 per cent of all emerging infectious diseases are zoonotic. Ebola, SARS, the Zika virus and bird flu all came to people by way of animals.

As we seek to build back better after COVID-19, we need to fully understand the transmission of zoonoses, the threats they pose to human health and how to minimize the risk of further devastating outbreaks. This requires an ambitious line of enquiry, in which this report, Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission, is a crucial first step.

The report—produced in partnership with universities, research institutions, UN agencies and the secretariats of several multilateral environmental agreements identifies key anthropogenic drivers for the emergence of zoonoses, from agricultural intensification and increased demand for animal protein to the conversion of land and climate change. These drivers are destroying natural habitats and seeing humanity exploiting more species, which brings people into closer contact with disease vectors. Once established in humans, these diseases quickly spread across our interconnected world, as we have seen with COVID-19.

Understanding these drivers is essential to inform effective strategies and policy responses to prevent future outbreaks. This report makes many recommendations, all based on the One Health approach, which unites experts from multiple disciplines—public health, animal health, plant health and the environment —to deliver outcomes that improve the health of people, wildlife and the planet.

The recommendations include expanding scientific enquiry into zoonoses, regulating and monitoring traditional food markets, incentivizing the legal wildlife trade and animal husbandry to adopt zoonotic control measures, and radically transforming food systems. Above all, governments, citizens and the private sector need to work together. This is a global challenge that nobody can hide from. It crosses every discipline and every border. The drivers of pandemics are often also the drivers of climate change and biodiversity loss—two long-term challenges that have not gone away during the pandemic.



At the heart of our response to zoonoses and the other challenges humanity faces should be the simple idea that the health of humanity depends on the health of the planet and the health of other species. If humanity gives nature a chance to breathe, it will be our greatest ally as we seek to build a fairer, greener and safer world for everyone.

Inger Andersen Executive Director United Nations Environment Programme July 2020



# Foreword by the Director General of ILRI

I am honoured to introduce this collaborative report by scientists of the United Nations Environment Programme (UNEP), the International Livestock Research Institute (ILRI) and the South African Medical Research Council in partnership with other UN and multilateral agencies and leading universities and research institutions. It is altogether fitting that environment, livestock and medical expertise should join up to help understand and stem the rise of human contagions.

This report will deepen the reader's understanding of the virus causing the global COVID-19 pandemic and other pathogens that have similarly jumped species from their animal to human hosts. These 'zoonotic' diseases are increasing as the world's growing human population broadens and deepens interactions among people, animals and environments.

To date, most efforts to control zoonotic diseases have been reactive rather than proactive. COVID-19 has made us all aware that it's time to change that. To prevent future outbreaks of novel zoonotic diseases, we need to address the root causes of their emergence. We need among other things to break down disciplinary and organisational silos, to invest in public health programmes, to farm sustainably, to end the over-exploitation of wildlife, to restore land and ecosystem health and to reduce climate change.

The only way to achieve all of this is to boost collaboration among agencies that work on environment, animal and human health. In the past two decades, 'One Health'—a holistic, inter-sectoral and interdisciplinary approach that focuses on where the health of people, animals and environments converge—has emerged as the most promising way to prevent and manage zoonotic diseases. I have long championed use of 'One Health', but while experts agree that it is the optimal way to ensure a healthier future for all of us, this approach needs to be strengthened and mainstreamed everywhere, particularly the environment aspects of One Health, and it needs to receive vastly greater financial and institutional support. We must work in productive and novel ways across the human, animal and environment sectors and at every level—from village to ministry to global. This collaborative work by leading environment, livestock and human health organisations is an example of such vital crosssector work.

United and proactive in moving a healthy peopleanimal-environment development agenda forward, governments, agencies and communities together can stop future zoonoses from happening. At the same time,



these new coalitions will enable us to 'build back' healthy ecosystems while also meeting the world's Sustainable Development Goals, with historic and enduring returns on investment. This report is an early attempt to outline ways by which institutions of all kinds—in government, business and civil society—might work together to create such a legacy.

Jimmy Smith Director General International Livestock Research Institute July 2020







# **Key messages**

This evidence-based scientific assessment has identified the following ten key messages for decision-makers:

- DE-RISKING FOOD SYSTEMS: Many new sciencebased policy reports continue to focus on the global public health emergency caused by the COVID-19 pandemic, following the fast spread of the infectious SARS-CoV-2 virus of zoonotic origin. We need more evidence-based scientific assessments, such as this one, to examine the environmental and zoonotic context of the current pandemic, as well as the risk of future zoonotic disease outbreaks.
- URGENCY: Diseases are emerging more frequently from animals. Rapid action is necessary to fill the science gap and fast-track the development of knowledge and tools to help national governments, businesses, the health sector, local communities and other stakeholders—especially those with limited resources—to reduce the risk of future pandemics.
- REPORT AUDIENCE: To help fill this gap, a scientific assessment was conducted to explore the role of wild and domesticated animals in emerging zoonotic infectious diseases. This rapid assessment is designed for decision-makers in government, business and civil society at all levels and in all regions.
- 4. SCOPE OF THE PROBLEM: About 60 per cent of human infections are estimated to have an animal origin. Of all new and emerging human infectious diseases, some 75 per cent "jump species" from other animals to people. Most described zoonoses happen indirectly, e.g. via the food system.
- 5. OUTBREAK FREQUENCY AND PREDICTABILITY: The frequency of pathogenic microorganisms jumping from other animals to people is increasing due to unsustainable human activities. Pandemics such as the COVID-19 outbreak are a predictable and predicted outcome of how people source and grow food, trade and consume animals, and alter environments.
- 6. CONNECTIVITY AND COMPLEXITY: The links among the wider environment, biodiversity and emerging infectious diseases are complex. While wildlife is the most common source of emerging human disease, domesticated animals may be original sources, transmission pathways, or amplifiers of zoonotic disease. Such linkages—as well as the interconnectedness with issues such as air and water quality, food security and nutrition, and mental and physical health—should inform policies that address the challenges posed by current and future emerging infectious diseases, including zoonoses.

- DISEASE DRIVERS: Seven human-mediated factors are most likely driving the emergence of zoonotic diseases: 1) increasing human demand for animal protein; 2) unsustainable agricultural intensification;
  3) increased use and exploitation of wildlife; 4) unsustainable utilization of natural resources accelerated by urbanization, land use change and extractive industries; 5) increased travel and transportation; 6) changes in food supply; and 7) climate change.
- 8. **IMPACT AND COST:** Emerging zoonotic diseases threaten human and animal health, economic development and the environment. The greatest burden of zoonotic disease is borne by poor people, but emerging infectious diseases impact everyone, with monetary losses of emerging infectious disease much greater in high-income countries. Given that a single zoonotic outbreak can incur trillions of US dollars in costs across the globe, prevention is significantly more cost-effective than response.
- 9. **POLICY OPTIONS:** This assessment recommends ten policy response options to reduce the risk of future zoonotic pandemics and to 'build back better': (i) raise awareness of health and environment risks and prevention; (ii) improve health governance, including by engaging environmental stakeholders; (iii) expand scientific inquiry into the environmental dimensions of zoonotic diseases; (iv) ensure fullcost financial accounting of the societal impacts of disease; (v) enhance monitoring and regulation of food systems using risk-based approaches; (vi) phase out unsustainable agricultural practices; (vii) develop and implement stronger biosecurity measures; (viii) strengthen animal health (including wildlife health services); (ix) build capacity among health stakeholders to incorporate environmental dimensions of health; and (x) mainstream and implement One Health approaches. These policy options are discussed in detail in Section Five of this report.
- 10. **ONE HEALTH:** This report confirms and builds on the conclusions of the FAO-OIE-WHO Tripartite Alliance and many other expert groups that a One Health approach is the optimal method for preventing as well as responding to zoonotic disease outbreaks and pandemics. Adopting a One Health approach, which unites medical, veterinary and environmental expertise, will help governments, businesses and civil society achieve enduring health for people, animals and environments alike.



# Introduction

As the UN Framework for the Immediate Socio-economic Response to COVID-19, published in April 2020, says:

"The success of post-pandemic recovery will also be determined by a better understanding of the context and nature of risk.<sup>1</sup> In view of the COVID-19 crisis, this includes developing and maintaining a global mapping of encroachment, illegal trade, wet markets, etc. that are pathways for future pathogen transmission and thus potential future zoonoses identified. It will also mean supporting efforts to arrest ecosystem encroachments and harmful practices, restore degraded ecosystems, close down illegal trade and illegal wet markets, while protecting communities that depend on these for their food supply and livelihoods. This will be delivered in part by adhering to existing guidance by the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) and the Convention on Migratory Species (CMS), as well as by delivering an ambitious agreement at the Fifteenth Conference of the Parties (COP15) of the Convention on Biological Diversity (CBD)."

By mid-2020 though, while the world grapples with the COVID-19 pandemic, most new papers and guidelines focus on the public health responses to the novel SARS-CoV-2 virus and the pandemic it caused. These articles and reports emphasize the prevention and treatment of this contagious disease, or discuss ways to safeguard livelihoods, secure nutrition and re-build national or regional economies that are facing recessions. However, there are almost no scientific assessments that evaluate the issues that may hamper our global efforts to reduce the risk of future zoonotic pandemics in a post-COVID-19 world.

In the spirit of the above-mentioned UN Framework for the Immediate Socio-economic Response to COVID-19, the United Nations Environment Programme (UNEP)—the leading global environmental authority and advocate has teamed up with the renowned International Livestock Research Institute (ILRI) and other key partners to develop an evidence-based assessment report on the risk of future zoonotic outbreaks.

This report is one of the first that specifically focuses on the environmental side of the zoonotic dimension of disease outbreaks during the COVID-19 pandemic. It tries to fill a critical knowledge gap and provide policymakers with a better understanding of the context and nature of potential future zoonotic disease outbreaks. It examines the root causes of the COVID-19 pandemic and other "zoonoses," which the World Health Organization defines as human diseases or infections that are naturally transmissible from vertebrate animals to humans. The report also looks at where zoonoses come from and how we can reduce the likelihood of their occurrence. The report explores the role of animals, and in particular non-domestic animals, in emerging infectious human diseases. This is essential for our global efforts to improve our response preparedness because the frequency of spillover of pathogenic organisms jumping from animals to humans has been increasing considerably, due to the growing magnitude of our unsustainable natural resource use in today's world.

The relationship between the environment, biodiversity, human society and human diseases is complex.<sup>2</sup> While wildlife may be a source of human disease, domesticated animal sources may act as amplifiers of pathogens emerging from the wild. Moreover, as noted in this report, most emerging infectious diseases—whether in wildlife, domestic animals, plants or people—are driven by human activities such as agricultural intensification, wildlife use and mis-use, and human-induced landscape changes, interacting in unpredictable ways that can have negative outcomes.

Against this backdrop, it is important to recognize that disease emergence is not only about the relationship between domestic animals or wildlife and people, but also about the complexity of the system as a whole and the interactions between biotic and abiotic components. Biodiversity, and the complexity of our landscapes and seascapes, is integral to social and ecological resilience.<sup>3</sup> It is also important to take into account the complex relationship between biodiversity and our mental and physical health, including non-communicable diseases as well as infectious diseases. The many linkages here include those related to air, water, food security, and nutrition.<sup>2</sup>

Accordingly, the Convention on Biological Diversity has developed a biodiversity-inclusive One Health Guidance,<sup>3</sup> which looks at the One Health concept as a key ingredient for conservation and sustainable use of biodiversity. The WHO defines One Health as an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes.

This science-for-policy report provides examples of the application of the One Health approach and related policy response options that can be implemented by governments, civil society and the business sector in their efforts to tackle the drivers of zoonotic diseases with the ultimate goal to minimize the risk of future zoonotic disease outbreaks.



# Section One

# **Overview of emerging infectious diseases including zoonoses**

The emergence of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) at the end of 2019 and the vast global public health and economic impacts this novel coronavirus is causing in 2020 are treated as a crisis. While pandemics such as this are sometimes seen as a "black swan"—an extremely rare event—they are actually a widely predicted consequence of how people source food, trade animals, and alter environments.

To manage emerging infectious diseases (EID), including zoonoses, and reduce the risk of them becoming epidemics and pandemics, we need to understand their origins, their various types and importance in different communities, and their drivers. This section introduces the general reader to emerging diseases and zoonoses, before we take a deeper dive into the world of coronaviruses in Section Two.

# What are emerging diseases and what are zoonoses?

People and other animals share many microorganisms and diseases; such co-existence is natural, common and important to health. Only a few of these cause disease. Considering the millions of species of microorganism on Earth, pathogens (microorganisms that harm the host) are extremely unusual. Only about 1,400 microorganisms are known as potential causes of human infections.

New diseases in humans can emerge either as a result of a change in the nature or behaviour of commensal microorganisms that cause disease, or through infection by novel organisms, usually through contact with animals and the environment, where most microorganisms exist.

About 60 per cent of human infections are estimated to have an animal origin,<sup>4</sup> and of all new and emerging human infectious diseases, some 75 per cent "jump species" from (non-human) animals to people.<sup>5</sup> In highincome countries, direct infection with a zoonosis is probably a rare event,<sup>6</sup> with most described zoonoses happening indirectly, e.g. through insect vectors or, more frequently, via the food system.<sup>7</sup> Domesticated animal species share an average of 19 (range of 5–31) zoonotic viruses with people, and wild animal species share an average of 0.23 (range of 0–16) viruses with people.<sup>8</sup> So, unsurprisingly, the vast majority of animals involved in historic zoonotic events or current zoonosis are domestic (livestock, domesticated wildlife and pets), which is logical as the contact rates are high. The emergence of a new wildlife zoonosis is extremely rare, but can be very significant.

Around 80 per cent of pathogens infecting animals are "multi-host," meaning that they move among different animal hosts,<sup>9</sup> including occasionally humans. Domestic animals and peri-domestic wildlife also act as bridges for the emergence of human diseases; this can occur in an evolutionary sense, or the animal could serve as a physical transmitter.

Some of these viruses generated in bio-insecure industrial and intensive agricultural systems result in zoonotic forms of the virus. An example is the highly pathogenic avian influenza (HPAI), an important economic disease of domestic poultry that evolves from low-pathogenic viruses that circulate commensally in the environment in wild bird populations. Another example is Rift Valley fever (RVF), where domestic livestock have served as amplifying hosts for the human- and animal-pathogenic virus that originally circulated between wild animals and mosquitos. The reservoir is the wild animal, while the domestic animal is the bridging host to human infection.

True human pandemic influenza viruses (rather like COVID-19) have a more complex evolution with mixing of viruses in different domestic animal compartments, usually pigs and poultry and interacting with human influenzas to produce highly pathogenic human influenza pandemics.

While we are in the midst of an ongoing pandemic of COVID-19, recent decades have seen other headlinehitting and dramatically destructive novel diseases. Amongst the more prominent examples are: zoonotic influenza (Bird Flu), pandemic human influenza (H1N1), Middle East respiratory syndrome (MERS), and severe acute respiratory syndrome (SARS), most of which have a proven or suspected domestic animal involvement in transmission; only SARS has a suspected peri-domestic wildlife reservoir, though yet unproven.

Other diseases, such as re-emerging West Nile fever, yellow fever and Zika virus diseases are indirect zoonoses. In recent decades, emerging diseases of zoonotic origin have had direct costs of more than USD100 billion; it was earlier estimated that if these outbreaks had become



# The bipartite network of zoonotic viruses sharing among domestic and wild mammalian hosts

Johnson *et al.* (2020)<sup>8</sup> analysed data on wild and domesticated mammalian species that share viruses with humans. The resulting bipartite diagram demonstrates the association between zoonotic viruses and mammalian host species. Host species harbouring the same zoonotic virus are linked by a virus node ( ). Mammalian species nodes are coloured by domestication status and taxonomic order for non-domesticated terrestrial wildlife. Species node size is relative to the zoonotic virus richness calculated in that species. Humans, who are host to all viruses, are not shown in the diagram.

Source: Johnson et al. (2020)<sup>8</sup> published by the Royal Society under the Creative Common license (CC BY 4.0). The diagram legend has been modified for readability.

human pandemics, the losses would have amounted to several trillion dollars.<sup>10</sup> And this is likely to be the case for the current COVID-19 pandemic. Despite the massive real and potential socio-economic impacts of emerging zoonotic diseases, and despite the general consensus that prevention is better than cure, investments and political will to control them at their source have been insufficient to date.

Emerging diseases are of course hugely problematic, with some becoming *epidemic* (affecting a large number of people within a region), others becoming *pandemic* (spread over several countries and continents and affecting large numbers of people around the world). COVID-19 is now a pandemic spread across the planet, sickening and killing people and sending billions into lockdowns of various kinds as health services struggle to cope and killing hundreds of thousands by June 2020.

Also, of great importance to some countries and regions of the world are endemic zoonotic diseases. The so-called "neglected zoonoses" are continuously present in affected (mainly impoverished) populations, yet receive much less international attention and funding than emerging zoonotic diseases.<sup>11</sup> Among the important neglected zoonoses widespread in developing countries are anthrax, bovine tuberculosis, brucellosis, rabies, cysticercosis (pig tapeworm), echinococcosis (hydatid disease), Japanese encephalitis, leptospirosis, Q fever, rabies, Lassa fever virus and trypanosomiasis (sleeping sickness). Most of these are spread by domestic animals, but several have a wildlife interface, or wildlife is of occasional importance (brucellosis, leptospirosis, rabies, alveolar echinococcosis and bat-associated rabies). Only Lassa fever has exclusively a wildlife host (the multi-mammate rat).

Neglected zoonoses persist in communities experiencing complex development problems—typically a mix of poverty, poor sanitation, poor access to water and waste removal services, isolation, socio-political insecurity, political marginalization, low literacy levels, gender inequality and degraded natural resources. These communities often have a high dependence on livestock and high contact with wild or peri-domestic wildlife, which increases their exposure to pathogens. Another often neglected category of diseases with mainly domestic animal origins are those that are foodborne. For poor people, some of the responses made to control outbreaks may inadvertently cause harm, for example by reducing access to animal source food, important for nutrition, as a result of large-scale culling of domestic animals.<sup>12</sup>

Remarkably, a recent study by the World Health Organization (WHO) found the burden of a selection of important food-borne diseases to be comparable to that of "the big three" major infectious diseases: HIV/ AIDS (human immunodeficiency virus-acquired immune deficiency syndrome), malaria and tuberculosis.<sup>13</sup>

Between 2018 and 2019, for example, South Africa experienced the world's largest outbreak of listeriosis, with more than 1,000 laboratory-confirmed cases and more than 200 fatalities of people who got infected after eating contaminated food products.<sup>14</sup>

# When do zoonoses become human disease outbreaks?

Historically, the emergence of new human diseases from animals has been associated with major societal change. For example, during the Neolithic transition from hunter-gathering to agricultural societies, humans lived shorter lives, ate less and poorer-quality foods, were smaller in size and were sicker than their hunter-gatherer ancestors. With the advent of agriculture, the dramatic rise in population and the settlement of people in close proximity to their waste led to increases in human disease; the domestication of animals led to livestock pathogens jumping species into people, where they became the probable cause of diseases such as diphtheria, influenza, measles and smallpox.<sup>15,16</sup>

Subsequent major plagues or outbreaks, associated with major societal stresses and upheavals, were linked with zoonoses or diseases that had originally jumped species from animals to people, but had subsequently become transmitted mainly from person to person. Some of the most dramatic ones are:

1. The true zoonotic bubonic plague or pest (Black Death caused by the bacteria *Yersinia pestis*) of the mid-fourteenth century killed millions in Eurasia and North Africa, wiping out a third of Europe's population.

# Types of zoonotic diseases

### **Emerging zoonotic diseases**

are those that newly appear in human populations or have existed previously but are now rapidly increasing in incidence or geographical range. Fortunately, these diseases are often not highly lethal and most do not spread widely. But some emerging diseases have enormous impacts. Ebola, HIV/AIDS and now COVID-19 are well-known examples of emerging zoonoses particularly harmful to human health and the economy.



#### **Epidemic zoonoses**

typically occur intermittently and are mostly domestic in origin. Examples are anthrax, leishmaniasis and Rift Valley fever. Epidemic zoonoses are often triggered by events such as climate variability, flooding and other extreme weather, and famines. The overall health burden of outbreak/epidemic zoonoses is much less than that of neglected zoonoses, but because epidemic zoonoses cause 'shocks' to food production and other systems, they can significantly reduce the resilience of affected impoverished communities



## **Neglected zoonotic diseases**

are mostly domestic in origin, and continuously present to a greater or lesser degree in certain populations. These common diseases affect mostly poor populations and are commonly neglected by the international donor, standard-setting and research communities alike as well as by national governments. It is likely that poor detection and surveillance of these diseases diminish their recognition and hence prioritization by researchers and policymakers.





# Global hotspot map of estimated risk in zoonotic disease emergence

Allen *et al.* (2017)<sup>23</sup> analysed emerging infectious diseases (EID) of wildlife origin based on a broad set of predictors, such as the distribution of tropical forested regions, human population density, mammal species richness, agricultural land use, and others. The resulting heat map shows the global spatial patterns of estimated risk of zoonotic EID events after factoring out reporting bias.

- 2. Epidemics of European diseases in the Americas shortly after the arrival of Europeans in the sixteenth century were responsible for the deaths of up to 95 per cent of the indigenous populations and accelerated the destruction of their ancient civilizations.<sup>17</sup> It is thought that more infectious diseases of the temperate zone emerged in the Old World, compared to the New World, because diverse species of animals capable of harbouring ancestral pathogens were domesticated in the Old World.<sup>16</sup>
- The tuberculosis outbreak of the nineteenth century, associated with the industrialization in Western Europe and over-crowding, killing up to one in four people. Unlike the current situation, where most illness is caused by non-zoonotic tuberculosis, a substantial proportion of the nineteenth-century outbreak was thought to be caused by zoonotic tuberculosis.<sup>18</sup>
- 4. The expansion of colonial rule in Africa facilitated outbreaks of zoonotic sleeping sickness that killed one third of the population in Uganda and up to one fifth of the people living in the Congo River Basin in the first decade of the twentieth century.<sup>19</sup>
- 5. The 1918 influenza pandemic killed some 40 million people in the last months of World War I and the following years (1918–1921).

The global human population has increased from about 1.6 billion in 1900 to about 7.8 billion today. The population of the domesticated animals that provide people with food, and of pests or "peri-domestic animals" (such as rats) that thrive in new environments created by people, increased in parallel. In general, these exploding human, livestock and pest populations have reduced the size of wildlife populations while paradoxically increasing contacts among people, livestock and wildlife (with more people hunting fewer wild animals in diminished and degraded ecosystems, and an increasing number of human-wildlife conflicts worldwide).

However, this broad-brush picture conceals some great regional and local differences. Some countries have declining rather than expanding human populations. And over the last century, "natural environments" have returned to depopulated rural areas (e.g., parts of the northeastern United States) as small farms proved unviable and farmlands reverted to forested lands. Despite these exceptions, overall there have been significant increases in human populations, encroachment of humans and livestock into wildlife habitats, and concurrent massive decreases in natural environments. These changes have important implications for ecosystem, animal and human health alike. One of these consequences is an increase in emerging zoonoses. Many of these diseases are emerging in high-income settings, but there is an increasing trend for these diseases to emerge in low- and middle-income countries.<sup>20-22</sup>

While still imperfect, our understanding of the factors favouring emerging diseases is growing. For example, one study makes the case that the risk of zoonotic emerging infectious diseases is elevated in forested tropical regions where land use is changing and wildlife diversity, in terms of mammalian species richness, is high.<sup>23</sup>

# Seven major anthropogenic drivers of zoonotic disease emergence

A broad range of studies on zoonotic disease emergence implicates the following seven main drivers of their emergence.<sup>20,24-26</sup> Many of these drivers are now occurring in the same places, amplifying their impact. A description of each of these drivers is provided below.

# 1. Increasing demand for animal protein

High-income countries have experienced little change in consumption of animal source foods during the last four decades. In contrast, Southeast Asia has seen a rapid increase: Since the 1960s, the share of the region's daily food supply of proteins from animal products has doubled to 21 per cent; from fish, it has increased by half to 15 per cent. The share of total calories from both fish and animal products doubled to total of 12 per cent of the supply. Meanwhile, South Asia has also seen an increase in animal protein consumption, but not as strong. Sub-Saharan Africa has also followed the pattern seen in Southeast Asia, although it has been less marked. This per capita increase in animal protein consumption in many lowand middle-income countries has been accompanied by significant growths in population. Together, these factors have driven a strong growth in meat production (+260 per cent), milk (+90 per cent), and eggs (+340 per cent) over the last 50 years. This trend is predicted to continue in the coming decades, with most growth in animal-source food consumption occurring in low- and middle-income countries. Compared with other protein sources, livestock product consumption is rising rapidly, whereas the longterm trend for pulses is of sustained consumption levels.

# 2. Unsustainable agricultural intensification

Increasing demand for animal-source foods stimulates the intensification and industrialization of animal production. The intensification of agriculture, and in particular of domestic livestock farming (animal husbandry), results in large numbers of genetically similar animals. These are often bred for higher production levels; more recently, they have also been bred for disease resistance. As a result, domestic animals are being kept in close proximity to each other and often in less than ideal conditions. Such genetically homogenous host populations are more vulnerable to infection than genetically diverse populations, because the latter are more likely to include some individuals that better resist disease. Factory farming of pigs, for example, promoted transmission of swine flu due to a lack of physical distancing between the animals.<sup>27</sup> In poorer countries, there are additional risk factors in that livestock production often occurs close to cities, while biosecurity and basic husbandry practices are often inadequate, animal waste is often poorly managed, and antimicrobial drugs are used to mask poor conditions or practices. Since 1940, agricultural intensification measures such as dams, irrigation projects and factory farms have

# Pathogen flow at the wildlife-livestock-human interface



Source: Adapted from Jones et al. (2013)<sup>25</sup>

been associated with more than 25 per cent of all—and more than 50 per cent of zoonotic—infectious diseases that have emerged in humans.<sup>28</sup> Moreover, around one third of croplands are used for animal feed. In some countries, this is driving deforestation.<sup>29</sup>

# 3. Increased use and exploitation of wildlife

There are many ways in which wildlife are used and traded. Section three provides more detail on the complexities. However, in general, an increasing use and exploitation of wildlife includes the following:

- Harvesting wild animals (wild meat, sometimes called "bushmeat") as a source of protein, micronutrients and money for the poor;
- Recreational hunting and consumption of wildlife as a status symbol;
- 3. Consumption of wildlife in the belief that wild meat is fresh, natural, traditional and safe;
- 4. Trade in live animals for recreational use (pets, zoos) and for research and medical testing; and
- 5. Use of animal parts for decorative, medicinal and other commercial products.

In general, use and trade in live and dead animals can lead to increased close contact between animals and people throughout the supply chain, which increases the risk of zoonotic disease emergence. In some regions, as human populations and wealth have increased, there has also been an increased demand for wild animals and their products. In West Africa, for example, exploitation of wildlife for food has increased over the last 10 years.<sup>30</sup>

Infrastructural development can often facilitate wildlife exploitation: new roads in remote areas can increase

Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission

human access to wildlife and help spread diseases within and between countries more rapidly. As animals in the wild become scarcer, attention has turned to the farming of some species of wild animals.<sup>31</sup> While this might have the potential to reduce the pressure on wildlife, farming wildlife or "ranching" is often more costly than harvesting or hunting animals from the wild, and less preferred by local communities; it also may create cover for the "laundering" of wild animals.<sup>32</sup> In addition, any significant increase in the farming of wild animals risks "recapitulating" the increases in zoonoses that likely accompanied the first domestication of animals in the Neolithic era, some 12,000 years ago.<sup>16</sup>

## 4. Unsustainable utilization of natural resources accelerated by urbanization, land use change and extractive industries

Rapid urbanization, especially when unplanned and with poor infrastructure, creates novel and diverse contacts among wildlife, livestock and people. The greater movement of people, animals, food and trade that is associated with accelerated urbanization often provides favourable grounds for the emergence of infectious diseases, including zoonoses. For example, irrigation systems encourage some vector-borne zoonoses to spread; deforestation and fragmentation of ecosystems and wildlife habitats encourage contacts at the humanlivestock-wildlife ecosystem interface;<sup>32</sup> and increased human settlements and fencing constrain herding and migratory movements of both domesticated and wild animals. Ecological tourism and human settlements near caves and forested areas, particularly those with poor housing conditions, can increase human-wildlife contacts and human exposure to insects, ticks and other vectors of wildlife pathogens.

Infrastructure development, including new roads and railways, transformation of natural areas to commercial and retail use, and other drivers of land-use change can also contribute to the destruction and fragmentation of wildlife habitats and increase human-wildlife contact and conflict.



Encroachment into wildlife habitats that are altered for the purpose of extracting their natural resources e.g., mining, oil and gas extraction, logging but also harvesting bat *guano*—also encourages new or expanded interactions between people and wildlife. These activities often come with other changes, such as new human settlements, road building and movements of people and products, which further increase human access to wilderness areas and often provoke changes in how local communities acquire and store their food (e.g., via wildlife hunting, introduction of livestock rearing, and keeping food stocks that attract pest animals).

# 5. Travel and transportation

Diseases can now move around the world in periods shorter than their incubation periods (the time between exposure to a pathogen and the first clinical sign of illness). The increasing amounts of human travel and trade, including the increasing handling, transport and (legal and illegal) trade of animals and animal products, increases the risk of zoonotic diseases emerging and spreading.

# 6. Changes in food supply chains

Food supply chains are lengthening and diversifying, especially in low- and middle-income countries. This trend—which is being driven by increased demand for animal source food, new markets for wildlife food, and poorly regulated agricultural intensification—is creating additional opportunities for disease transmission. These include the following:

- 1. There are increased opportunities for crosscontamination.
- 2. It can be more difficult to identify where a given food comes from. Traceability challenges make it harder for officials to follow up quickly on any potential problems.
- Changes in processing can encourage the proliferation of zoonotic diseases (e.g., the formation of biofilms—microbial ecosystems—in food processing plants).
- 4. Rapidly expanding and poorly managed informal wildlife and fresh produce markets (including so-called "wet" markets) bring products along poorly regulated supply chains to supply rapidly growing cities. While traditional markets provide many benefits, especially for poor people—including their convenience, lower costs, sales of traditional foods, and support of livelihoods (especially women)—their levels of hygiene are often low, and biosecurity is poor, increasing the risks of disease. The same is often true along the supply chains from rural areas to the markets in the cities.
- 5. Industrial meat processing plants can also be sites of disease transmission. Food from modern retail outlets is not always safer than that from informal markets.<sup>33</sup> For example, there have been many

## Impacts of climate change on zoonoses



Caster bean tick, deer tick or sheep tick (*Ixodes ricinus*) is a well-known vector of Lyme disease in Europe Photo credit: Dagmara\_K/Shutterstock.com

Climate change is a major factor in disease emergence. The survival, reproduction, abundance and distribution of pathogens, vectors and hosts can be influenced by climatic parameters affected by climate change. For example, climate variability tends to affect the many diseases transmitted by insects, ticks and other arthropod vectors. Warmer temperatures could also increase the incidence of disease both by increasing the vector population size and distribution and by increasing the duration of the season in which infectious vector species are present in the environment. Many newly emerging infectious diseases arise in tropical regions where the warm temperatures suit the lifecycles of both pathogen and vector.<sup>16</sup> The impacts of climate change on zoonotic diseases as well as on food and economic insecurity and other problems are predicted to be harshest in low- and middle-income countries, where disease surveillance and data are particularly scarce.<sup>37</sup>

Climate change is a force of growing importance that influences the future geographic distribution and abundance of species such as bats, monkeys and rodents, including those in which zoonotic pathogens often originate; and of mosquitos and other vectors that transmit viruses such as the chikungunya virus and West Nile virus. Climate change can increase or decrease the incidence of the insect-transmitted Chagas disease, sand-fly transmitted leishmaniasis, and other vector-borne and zoonotic diseases, generally with greater illness occurring at higher degrees of warming.<sup>38</sup> In 2010 in Africa, an outbreak of Rift Valley fever, a mosquito-borne zoonotic disease, occurred with higher than average seasonal rainfall; other outbreaks have occurred even with short periods of heavy rainfall.<sup>16</sup>

An extensive literature review of emerging diseases in Brazil revealed relationships between infectious diseases outbreaks and (1) extreme climate events (El Niño, La Niña, heatwaves, droughts, floods, increased temperature, higher rainfall), the frequency of which might be affected by climate change; and (2) environmental changes (habitat fragmentation, deforestation, urbanization, wild meat consumption).<sup>39</sup>

Arctic and subarctic regions are especially vulnerable to climate change due to the thawing of the permafrost, which significantly transforms soil structures, vegetation and habitats. Degradation of the permafrost can expose historic burial grounds, enabling the revival of deadly infections from the past.<sup>40</sup> Rising temperatures are raising the risk of zoonotic diseases in the vast Republic of Sakha (Yakutia) which makes up one fifth of Russia's territories. Extended growing periods and expanded habitats are providing some zoonotic pathogens and their vectors with more favourable living conditions.

outbreaks of COVID-19 from the massive, crowded, artificially chilled industrial meat plants in Europe and America, but much fewer from smaller, naturally ventilated meat plants in many low- and middleincome countries. Thus, it cannot always be assumed that the modernization of food value chains will reduce risk. Moreover, especially in low- and middleincome countries, people are consuming more animal-source foods than in the past, which results in potential exposure to pathogens, including zoonotic pathogens.<sup>34</sup>

## 7. Climate change

Many zoonoses are climate sensitive and a number of them will thrive in a warmer, wetter, more disasterprone world foreseen in future scenarios.<sup>35</sup> Some pathogens, vectors and host animals probably fare more poorly under changing environmental conditions, disappearing in places and resulting in the loss of their population-moderating effects or the establishment of other species in the new ecological niches created by their departure. There is some speculation that the SARS-CoV-2 may survive better in cooler, drier conditions when outside the body.<sup>36</sup> Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission

## Immunodeficiency disorders in primates



Chimpanzees in Uganda Photo credit: CherylRamalho / Shutterstock.com

Two of the most significant zoonotic disease transmissions in recent history are the human immunodeficiency viruses, HIV-1 and HIV-2, the etiologic agents for acquired immune deficiency syndrome (AIDS) in humans.<sup>41,42</sup>

The closest relatives of HIV-1 are simian immunodeficiency viruses (SIVs) that infect wild-living chimpanzees (*Pan troglodytes troglodytes*) and gorillas (*Gorilla gorilla gorilla*) in Western Equatorial Africa. Chimpanzees were the original hosts of this clade of viruses. Four lineages of HIV-1 have arisen by independent cross-species transmissions to humans and one or two of those transmissions may have been via gorillas.<sup>43</sup>

On the other hand, the closest relatives of HIV-2 are simian immunodeficiency viruses in a monkey, the sooty mangabey (*Cercocebus atys*), whose natural range is in west Africa.<sup>44</sup> SIV-HIV species crossing seem to have occurred originally at least six times between sooty mangabeys (primate) and humans.<sup>45</sup> Sooty mangabeys and chimpanzees are both often kept as pets and used for food, thus resulting in their frequent direct contact with humans.<sup>46,47</sup>

More than 40 species of African monkeys are infected with their own, species-specific SIV.<sup>47-49</sup> These viruses are of relatively low pathogenicity and they do not induce an AIDS-like disease in their natural hosts, suggesting that they have associated and evolved with their hosts over an extended period of time. However, recent evidence shows that SIVcpz can cause AIDS-like disease and reduced fertility in Eastern Chimpanzees.<sup>50</sup>

The conclusion that HIV-1 was derived from a virus infecting chimpanzees is of particular interest, because chimpanzees and humans are so closely related. This raises a number of interesting questions: 1) as to the origin of the chimpanzee virus; 2) whether adaptation of SIVcpz to infecting chimpanzees made the virus more capable of infecting humans; and 3) whether SIVcpz infection of chimpanzees is of low pathogenicity or not.<sup>43</sup> Based on the analysis of strains found in four species of monkeys from Bioko Island in Equatorial Guinea, which was isolated from the mainland by rising sea level about 11,000 years ago, it has been concluded that SIV has been present in monkeys and apes for at least 30,000 years, and probably much longer. Therefore, it is thought that SIV may have previously crossed the species barrier into human hosts multiple times throughout history, but it was not until relatively recently at the advent of modern transportation and global travel that HIV spread regionally and globally beyond decimations in local populations.<sup>51</sup>

# Other factors playing a role in zoonotic disease emergence

The seven main drivers of zoonoses emergence, described above, are all anthropogenic, that is, the result of human action. Other factors, of course, also affect disease emergence, particularly the agent type, virulence and modes of transmission of the pathogen; the susceptibility of the pathogen's host; and the longevity and range of the pathogen's animal reservoir. Pathogens that are widely distributed, mutate rapidly and are multi-host are considered most likely to jump species. RNA viruses mostly lack the "proofreading" mechanisms of DNA viruses and hence develop many more mutations as they evolve, some of which may make the virus better able to infect a new host. Pathogens that spread using the respiratory functions of the host (which are over-represented among emerging diseases) have fewer barriers to moving from one host to another than pathogens spread via other routes.

Certain people are more susceptible than others to infection with pathogens. Age, health, sex, physiology, nutritional status, exposure history, simultaneous infection with more than one pathogen, immunocompetence, genetics and underlying diseases all influence an individual's susceptibility to infection. Certain animals, in their turn, are more likely to harbour zoonotic or potentially zoonotic pathogens based on their physiological characteristics, ecosystem niche, social behaviour and relatedness to humans. Some studies detected higher numbers of zoonotic viruses in animal species that have become abundant and have expanded their range by adapting to human-dominated landscapes.8 Livestock, rodents, bats, carnivores and non-human primates have been identified as of special concern in several studies. However, as with all animals, they are not risks in and of themselves, and it is only when there is close contact with people that there is the potential for this risk to be realized.



Baby owls in a cage sold in an animal market in Yogyakarta, Indonesia Photo credit: Ibenk\_88 / Shutterstock.com



# Section Two

# **Coronaviruses in a One Health context**

In this second section, we move from zoonoses in general to the specific alarming and ongoing pandemic of COVID-19, a disease caused by a zoonotic coronavirus. The section starts with some background on coronaviruses and continues from the One Health perspective, reflecting both veterinary and medical experiences and commonalities between important coronavirus diseases and pandemics.

# What are coronaviruses?

Coronaviruses are a large group of viruses that infect many animals and humans and are responsible for numerous diseases. They are named "corona" for the crown-like arrangement of the spike-shaped proteins on the surface of their membranes. Some human coronaviruses usually cause mild upper respiratory illness like the common cold. They can also cause serious diseases such as infectious peritonitis in cats and respiratory and enteric infections in cattle. The only known serious human coronavirus diseases are SARS, MERS, COVID-19, and possibly the Asian Flu from the late 19th century; all are likely to have zoonotic origins. In addition to these well-known, sporadic, locally important and long-established diseases, there have been at least six major outbreaks of novel coronaviruses in the last century, all of which imposed high costs across several continents:

- 1. Infectious bronchitis virus (IBV) causes infectious bronchitis in poultry. It emerged in the 1930s and is still one of the main causes of economic losses in the poultry industry, with repeated waves of disease caused by different strains.<sup>52</sup>
- Transmissible gastroenteritis (TGE) virus was first reported in the United States in 1946 and subsequently spread to Europe, Africa, South America and China.<sup>53</sup>
- Porcine epidemic diarrhoea (PED) virus emerged in 1971 as a pig disease causing a global pandemic of enormous cost and is still a major problem in piglets. Since then different strains have caused waves of disease in Asia, Europe and the Americas.<sup>54</sup>
- 4. SARS-CoV, the coronavirus that causes severe acute respiratory syndrome, or SARS, was first reported in China in February 2003 and likely originated from bats, probably then spreading to other animals (likely civet cats) and then to humans. The illness then spread to more than two dozen countries in North

America, South America, Europe and Asia before it was contained. Over 8,000 cases were reported and nearly 800 people died of the disease. Since 2004 there have not been any reported cases.<sup>55</sup>

- 5. MERS-CoV, the coronavirus that causes Middle East respiratory syndrome, or MERS, was first reported in Saudi Arabia in 2012 and has a higher mortality rate than SARS. MERS-CoV can occur zoonotically from human contact with camels but has secondary cycles of spread from ill people to other people through close contact. To date, there have been around 2,500 laboratory confirmed cases mostly human to human, of which more than one third proved fatal. Sporadic cases continue to occur as the infection remains present in dromedary camels.<sup>56</sup>
- 6. SARS-CoV-2, the coronavirus that causes a severe acute respiratory syndrome known as COVID-19, already has had its genome compared to the genetic sequences of more than 200 other coronaviruses from around the world that infect various animals. SARS-CoV-2 appears to be a recent mix, or genetic recombination, of coronaviruses.<sup>57</sup> As a result of this recombination, one of the proteins of SARS-CoV-2 enables the virus to enter the cells of humans. Other research has shown the virus to be 96 per cent identical to a previously identified bat coronavirus, with a common ancestor about 50 years ago. It is hypothesized that this is the origin of the unknown pathway that resulted in the transmission of SARS-CoV-2 to humans in 2019.58

# Fai Cor

# Family of Coronaviruses

Coronaviruses are diverse. They belong to the Coronavirinae subfamily in the Coronaviridae family. The Coronavirinae subfamily comprises four genera:

#### Alphacoronavirus Alphacoronaviruses cause

respiratory tract illnesses and common colds in humans, and gastroenteritis in animals.

#### Gammacoronavirus

They infect mainly avian species and sometimes mammals including cetaceans. IBV is a gammacoronavirus that causes avian infectious bronchitis.

For references see page 60.

Betacoronavirus Betacoronaviruses affect mainly mammals, and include those that cause MERS, SARS and COVID-19.

## Deltacoronavirus

They are found primarily in birds and some mammals. Porcine deltacoronavirus (PDCov) recently emerged, causing severe diarrhoea in newborn piglets.

# Emergence of significant diseases caused by coronaviruses and other pathogens



# Avian infectious bronchitis

Pathogen: Infectious bronchitis virus (IBV) Genus: Gammacoronavirus Host: Chickens Place of emergence: North Dakota, USA

IBV causes an acute, highly contagious respiratory disease in chickens. It can also damage the reproductive tract, causing decreased egg quality and production. First documented in USA, the disease is now prevalent in all countries with an intensive poultry industry.

# 1971

## Porcine epidemic diarrhoea (PED)

Pathogen: Porcine epidemic diarrhoea virus (PEDV) Genus: *Alphacoronavirus* Host: Pigs Place of emergence: United Kingdom

Following the first appearance in the UK, it spread to other European countries and Asia. A highly virulent PEDV strain emerged in 2013 and caused nationwide outbreaks in the US, and rapidly spread to North, Central and South American countries. The virus is not zoonotic and poses no risk to humans, or food safety.

1940



# Severe acute respiratory syndrome (SARS)

Pathogen: SARS coronavirus (SARS-CoV) Genus: Betacoronavirus Natural reservoir: Horseshoe bats Intermediate host: Masked civet cats Place of emergence: Guangdong, China

This pneumonia-like infection spread from Guangdong, China, to more than 26 countries in Asia, Europe, North America and South America before it was contained. SARS-like coronavirus has been found in horseshoe bats, suggesting that bats are natural reservoirs.

1970

# 1920



# 1920s

#### Human Immunodeficiency Virus (HIV) infection Pathogen: HIV

Genus: Lentivirus Natural reservoir: Chimpanzee for HIV type 1, and Sooty Mangabey for HIV type 2 Place of emergence: Kinshasa, Democratic Republic of Congo

Based on genetic sequencing and historical records, the emergence of HIV is traced back to 1920s in Kinshasa, DRC. It is thought that simian immunodeficiency viruses (SIVs) in primates crossed over to humans at the time, presumably as a result of hunting and meat consumption. SIVs then adapted to the new human host to become HIV.

For references see page 61.



# West Nile fever Pathogen: West Nile virus

1930

Genus: Flavivirus Host: Birds Place of emergence: West Nile district, Uganda

Mosquitoes serve as disease vectors carrying the virus from infected birds to people and some mammals. Humans are usually incidental and dead-end hosts for the virus. The first recognized outbreak occurred in Israel in 1951, then Egypt. The virus re-emerged in Romania in 1996, and has established itself in the US since 1999. West Nile virus belongs to the same genus as dengue virus and yellow fever virus.



1950

## Zika virus disease Pathogen: Zika virus (ZIKV)

Genus: Flavivirus Natural reservoir: Primates including humans Place of emergence: The Zika forest, Uganda

ZIKV was first discovered in a febrile sentinel rhesus monkey from the Zika forest, and in the *Aedes africanus* mosquito from the same forest a year later. The first human cases were detected in Uganda and Tanzania in 1952. An outbreak occurred in the Yap Islands, Federated State of Micronesia in 2007, followed by a major epidemic in the Americas in 2015-16.



# Ebola virus disease

Pathogen: Ebola virus Genus: Ebolavirus Natural reservoir: Unconfirmed but likely to be African fruit bats of the Pteropodidae family Intermediate host: Apes and monkeys Place of emergence: Two simultaneous outbreaks in Democratic Republic of Congo (DRC) and South Sudan

The largest outbreak in history occurred primarily in Guinea, Liberia and Sierra Leone from 2014 to 2016, killing 11,323 people. The virus also recently re-emerged in eastern DRC from 2018 to 2019. Case fatality ratio of Ebola varied from 25% to 90%.



# Middle East respiratory syndrome (MERS)

Pathogen: MERS coronavirus (MERS-CoV) Genus: *Betacoronavirus* Natural reservoir: Probably bats Intermediate host: Dromedary camels Place of emergence: Saudi Arabia

First reported in Saudi Arabia, MERS has spread to 27 countries with a large outbreak in Korea in 2015. A study in 2018 shows high prevalence of MERS-CoV strains in local camels in Saudi Arabia, compared to imported camels from Africa.



# Swine acute diarrhoea syndrome (SADS)

Pathogen: SADS coronavirus (SADS-CoV) Genus: Alphacoronavirus Natural reservoir: Probably bats Host: Pigs Place of emergence: Guangdong, China

SADS-CoV caused severe and acute diarrhoea and vomiting in newborn piglets. The outbreak killed nearly 25,000 piglets in Guangdong. Case fatality ratio: 90% in piglets less than five days old. This coronavirus did not appear to jump to humans.

2000



# Coronavirus disease 2019 (COVID-19)

Pathogen: SARS-CoV-2 Genus: *Betacoronavirus* Natural reservoir: Probably bats Intermediate host: Unknown Place of emergence: Wuhan, China

SARS-CoV-2 appears to be a recent mix, or genetic recombination, of two coronaviruses. Genome sequencing suggests that SARS-CoV-2 is 96% identical to a coronavirus in horseshoe bats.

2010

# 1980



# **1986** Bovine spongiform encephalopathy or

mad cow disease Agent: Pathogenic prions Host: Cattle Place of emergence: United Kingdom

Mad cow disease is a progressive, fatal neurological disorder in cattle. The human form of the mad cow disease known as variant Creutzfeldt-Jakob disease is linked to consumption of beef from cattle infected with the disease.



1990

# Hendra virus infection

Pathogen: Hendra virus Genus: Henipavirus Natural reservoir: Large fruit bats (Pteropus spp.) or flying fox Host: Horses Place of emergence: Hendra, Australia

Sporadic outbreaks have occurred in Australia over the years since its initial appearance in 1994. So far, no cases have been reported outside Australia. Case fatality ratio is 75% in horses, and 50% in humans. Hendra virus belongs to the same genus as Nipah virus.



### Highly pathogenic avian influenza (HPAI) or bird flu

Pathogen: HPAI virus subtype H5N1

Genus: Alphainfluenzavirus Natural reservoir: Wild waterfowl Host: Poultry Place of emergence: Guangdong, China

First human cases found in Hong Kong in 1997 were traced back to wild and domestic waterfowl in Guangdong in 1996. Re-emerging in Hong Kong in 2002, the virus spread rapidly to South East Asian countries. Over 100 million domesticated chickens and ducks either died of the disease or were culled to stop the outbreak in Asia.



2020

# **Nipah virus infection**

Pathogen: Paramyxovirus Genus: Henipavirus Natural reservoir: Large fruit bats (Pteropus spp.) or flying fox Host: Pigs Place of emergence: Guangdong, China

Nipah virus emerged as a respiratory and neurologic disease in pigs, and then spread to humans. A large outbreak in Malaysia from 1998 to 1999 was followed by five outbreaks in Bangladesh from 2001 to 2005. To control the outbreak in Malaysia, at least one million pigs were culled.



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SARS-CoV-2 is an enveloped virus, meaning that its RNA is packaged within an outer **lipid** (fatty) **membrane**. The lipid membrane is stable enough to protect the RNA from the surrounding environment, but also able to break open inside the host cell to release the RNA. This balance means the membrane is susceptible to being destroyed by detergent.

The membrane contains several virus proteins. The large **spike** (**S**) **proteins** allows the virus to bind to and enter host cells. The distinctive 'corona' of spikes gives the virus its name.

Seven human coronaviruses have been identified so far, of which three are capable of invading deep into the lungs and causing more severe disease. One possible reason is that the S protein of SARS-CoV-2, like SARS-CoV (the virus responsible for SARS), binds to ACE-2 receptors on human cells. ACE-2 receptors are found throughout the body but are particularly concentrated in the upper and lower airways of the lungs.

SARS-CoV-2 also binds to ACE2 particularly well. It is 10–20 times more likely to bind ACE2 than SARS-CoV. The **membrane (M) proteins** give shape and integrity to the virus particle. They are also thought to help assemble new virus particles inside the host cell.

The **envelope** (E) proteins are thought to assist virus growth and ability to cause disease. They may form small pores that alter the properties of the host membranes, prevent M protein from clumping together, and assist in assembly of new viral particles inside the host cell.

Inside the viral envelope is the viral RNA, which is bound to the nucleoprotein (N). N proteins form a tight spiral that wraps and coils the RNA, protecting it from damage. When the RNA is first released into the host cell, the N protein also reduces the host cell's natural defences against the virus.

The coronavirus **RNA** molecule is 30,000 'letters' long, making it one of the largest RNA viruses discovered. While RNA viruses have a high mutation rate, coronaviruses also possess a genomic proofreading mechanism. This can keep them from accumulating negative mutations that would weaken them. Coronaviruses can also swap blocks of RNA with each other, potentially trading useful mutations.

While the new coronavirus likely originated from bats, it is not yet known whether or which mutations allowed this jump from animals to humans. The RNA of SARS-CoV-2 is 96% similar to a virus found in a bat in China. However, the bat virus contains key differences in its S protein, and is not able to infect humans. It is also likely that SARS-CoV-2 viruses will contain **host cell proteins** from previous host cells. The virus also makes additional proteins following host cell entry that allow it to multiply and make new virus particles. In addition to vaccine efforts targeting the S-protein on the virus particle, these intra-cellular proteins are potential targets for intervention.

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For references see page 62.



Colourized scanning electron micrograph of a cell (blue) infected with SARS-COV-2 virus particles (red) Photo credit: US National Institute of Allergy and Infectious Diseases

# Common elements and origins of coronavirus pandemics

The six coronavirus pandemics named above share some of the following common elements.

# Bats

Bats are natural reservoir hosts as well as vectors of many microbes that can affect animals and people. Contact between bats and other animals, including humans, allows for inter-species transmission of the pathogens they harbour, potentially resulting in disease outbreaks. Most of the recent coronavirus pandemics have been hypothesized to have an initial origin in bats. More than 200 novel coronaviruses have been found in bats and they are likely the source and natural hosts for all coronavirus lineages.<sup>59</sup> Bats are also associated with many other important zoonoses such as Ebola, Nipah (via bridging with pigs or indirectly through contamination of domesticated plants) and very rarely rabies. Bat species harbour at least 61 potential zoonotic viruses.<sup>60</sup> They can resist, provide opportunities for recombination, and spread many serious zoonoses as a result of their unique physiological features (bats are the only mammals able to fly), ecology and immunology. At the same time, bats provide many ecosystem services such as flower pollination and seed dispersal for hundreds of species of plants, and aid in controlling insect populations; they also maintain ecosystems by providing food for predators such as owls, hawks and snakes.<sup>61</sup>

# Agricultural intensification and increased demand for animal protein

These coronavirus disease outbreaks followed rapid intensification of agricultural practices and systems, and dramatic changes in the ways animals were kept or farmed, many of which were made without proper precautionary measures being taken. As mentioned previously, this was a demand driven process, associated with increasing wealth, allowing people to consume more animal source food. For instance, the emergence of infectious bronchitis virus in the United States was associated with post-World War I intensification of poultry systems based on bird confinement (resulting in greater stress and more frequent contacts) and new breeding techniques (resulting in less genetic variation and disease resistance). In addition, the transmissible gastroenteritis (TGE) virus and porcine epidemic diarrhoea (PED) virus were associated with post-World War II increases in intensive pig production systems and a related decline in pig health, similar to the case of industrialization of poultry production.

SARS-CoV and SARS-CoV-2 may be associated with wildlife harvest, trade practices and the intensification of wildlife farming in East Asia. The latter has been actively encouraged in some countries; by 2006, nearly 20,000 wildlife breeding and farming ventures were established in China.<sup>62</sup> As wealthy consumers tend to prefer wild-caught animals, the meat from these farms is often consumed by China's rapidly growing middle class.<sup>63</sup>

There is concern that many wildlife farms are prone to low biosecurity and that they also enable illegally poached wildlife to be "laundered"—presented and sold as legally farmed animals.<sup>31</sup> Both factors would increase the risk of zoonotic disease outbreaks.







Video Link: https://www.youtube.com/watch?v=mOV1aBVYKGA © WHO



SARS-CoV-2 virus particles Photo credit: US National Institute of Allergy and Infectious Diseases



Flying foxes or fruit bats (Pteropus sp.) Photo credit: nutsiam / Shutterstock.com

MERS-CoV was associated with increases in dromedary camel numbers and a shift from extensive to intensive camel production systems. An analysis of potential drivers of MERS-CoV emergence in Qatar suggests that the socio-economic transformation in the last three decades and the growing popularity of camel racing triggered major changes in camel farming practices.<sup>64</sup> Camels were raised in designated camel complexes in a high-density environment alongside the workers who fed and took care of them. Races and contests in the Gulf region also required camels to travel frequently and extensively, both across borders and within the country. These factors played an important role in the transmission of MERS-CoV from camels to humans.

# **Traditional markets**

Both SARS-CoV and SARS-CoV-2 have been associated with traditional informal markets or fresh produce markets (sometimes called wet markets). These markets sell fresh meat, fish and other perishable agricultural produce. Some of these informal markets sell live poultry and other domesticated animals; many sell live aquatic products (fish and shellfish); and some sell live or dead wild animals. The products can be sourced from many different places, including from distant parts of the world.

SARS-CoV was associated with civet cats sold in informal markets. SARS-CoV-2 has been associated with a traditional food market where wildlife was purported to be sold. Other studies, however, have cast doubt on the

initial emergence event leading to human infection.<sup>65,66</sup> There is general consensus that informal markets can be epidemiologically risky, especially those selling live domesticated animals or live or dead wild animals and those with poor hygiene.<sup>67,68</sup> However, expert opinions differ as to whether live animal markets should be regulated more strictly, gradually upgraded with buy-in from vendors, or banned completely in order to reduce disease transmission risk. It should be noted that strict regulation of food has proven difficult in governancepoor contexts and banning desired products often







Electron microscope image of the novel coronavirus, SARS-CoV-2 (round blue spheres) in cell culture.

Photo credit: US National Institute of Allergy and Infectious Diseases

shifts the market underground.<sup>69</sup> As mentioned earlier, informal, traditional or fresh produce markets have many benefits for people, including low prices, ease of access, the availability of preferred fresh and traditional foods, income-earning opportunities for women, worker independence, and attractions for tourists. However, these need to be weighed against the wider benefits to humanity (including local people) of preventing disease outbreaks and global pandemics. Ideally, solutions would be found that preserve the benefits while mitigating the risks of traditional markets.

## **High economic costs**

The three recent human coronavirus outbreaks (MERS, SARS and COVID-19) have shown a relatively low human population mortality rate compared to historic plagues (some of which killed up to 90 per cent of the populations affected); relatively high lethality in comparison to colds or seasonal influenza; and intense social disruptions. All six coronavirus pandemics (IBD, PED, TGE, SARS, MERS, COVID-19) have had high economic costs and, for some diseases, very high animal mortality rates.

As of 29 June 2020, there were more than 10 million confirmed cases of COVID-19, including more than 500,000 reported deaths. These figures are likely to be great underestimations of the true numbers of infections and deaths. With medical staff and facilities in frontline disease regions in or near overwhelm, COVID-19 may also be responsible for many more indirect deaths due to sick people choosing not to seek medical care because of their concerns about contracting COVID-19 in hospitals or not wanting to overwhelm health services. Reported to occur in 216 countries and territories (as of mid-June 2020) and on every continent other than Antarctica, the disease initially concentrated in "disease hotspots" experiencing especially high disease burdens. These included, among others, Wuhan in China, Lombardy in northeast Italy, New York City in the United States, Madrid in Spain, London in the United Kingdom, and Rio de Janeiro and São Paulo in Brazil.

The huge health impacts of this new coronavirus necessarily imply enormous economic impacts. The International Monetary Fund predicts that the global economy will shrink by 3 per cent in 2020, a downgrade of 6.3 percentage points from estimates in January 2020. The Fund also estimates that over the next two years, cumulative output losses from the COVID-19 pandemic could reach USD9 trillion.

The International Labour Organization estimates that COVID-19 will wipe out 6.7 per cent of working hours globally in the second quarter of 2020—equivalent to 195 million full-time workers. The Chinese economy shrank 6.8 per cent in the first three months of 2020, the country's first such contraction on record. With the modern global economy so closely interconnected, much up- and downstream damage is anticipated. Among the more serious harms are the potential impacts on food systems, which could lead to more than a quarter of a billion people suffering acute hunger by the end of 2020, according to the World Food Programme. Countries highly reliant on food imports, such as Somalia, and those highly reliant on food exports, such as Nigeria, are equally vulnerable. The impacts of this disease are already being felt across many sectors. According to UNESCO, for example, more than one billion students worldwide missed attending school or university in April 2020.



A market in Guangzhou, China Photo credit: tostphoto / Shutterstock.com











