



## **An HSI report: The connection between animal agriculture, viral zoonoses, and global pandemics**

### **Introduction**

The 2020 pandemic outbreak of COVID-19 turned the world's attention to the growing global threat of new viral diseases. On December 31, 2019, The World Health Organization (WHO) was alerted by Chinese authorities to an outbreak of a novel strain of coronavirus causing severe pneumonia,<sup>1</sup> subsequently named SARS-CoV-2, a zoonotic disease (transmissible between animals and people). The virus spread from China throughout Asia, to Europe, North America, Latin America and around the world. On March 11, the WHO declared it a pandemic, and noted it is the first to be caused by a coronavirus.<sup>2</sup> At the time of this writing, despite the extraordinary multi-national public health measures to reduce the spread, COVID-19 has caused over 21 million infections with 761,779 deaths<sup>3</sup> and unprecedented economic damage.

During the initial outbreak, most human cases were traced back to a wildlife market in the city of Wuhan, Hubei province, China. SARS-CoV-2 is thought to have originated in bats and may have passed through an intermediate animal host animal before acquiring the ability to infect people.<sup>4,5</sup>

The number of newly emerging infectious disease events (EIDs) is rising<sup>6</sup> and most new human pathogens<sup>7</sup> and recent pandemics have been viral diseases.<sup>8</sup> Examples include acquired immunodeficiency syndrome (AIDS), severe acute respiratory syndrome (SARS), and highly pathogenic avian influenza (HPAI). Consistent with these, the majority of zoonotic EIDs originate in wildlife.<sup>9</sup> Since 1980, on average, over three new human pathogen species have been discovered per year. While a small fraction (less than 14%) of all recognized human pathogen species are viral (others are bacterial, fungal, prions etc.), almost 75% of newly discovered pathogens have been viruses,<sup>10</sup> including the 2020 COVID-19 pandemic. A systematic review published in 2015 found that 91% of zoonotic viruses can originate from wildlife, 34% can originate from domestic animals, and 25% may originate from both wild and domestic species.<sup>11</sup> Transmission goes both ways and people can spread disease to animals as well,<sup>12</sup> for example human influenza A viruses can infect swine.<sup>13,14</sup> Given their close proximity for centuries, humans share more viruses with domesticated animals than wildlife.<sup>15</sup>

Pandemics—diseases that simultaneously affect many people across several countries—have occurred throughout the ages. The sources of pandemics can be as varied as the diseases they represent. This document examines pandemic and potentially pandemic zoonotic viruses directly spread from agricultural settings where animals serve as immediate, intermediate, or amplifier hosts.

The way we interact with both wild and domestic animals has profound implications for public health world-wide. While it is difficult to predict the next zoonotic pandemic,<sup>16,17</sup> there are many known risk factors. The global movement of people and animals through air travel and the trade in domestic and wild animals<sup>18,19</sup> can spread potential pathogens throughout the world, more quickly than ever before. Expanding cities (with large, dense human populations)

#### **WHAT IS A VIRUS?**

Viruses are submicroscopic (~20-250 nm), simple biological structures composed of genetic material surrounded by a protein shell, or capsid. Viruses can only replicate by parasitizing a living cell. They infect all life forms including animals, plants, and microorganisms, such as bacteria. They are ubiquitous, the most abundant biological entities on earth, found in every environment from the deep sea to hot springs and under the ice of polar lakes.

Breitbart M and Rohwer F. 2005. Here a virus, there a virus, everywhere the same virus? Trends in Microbiology 13(6):278-84.

facilitate human-to-human transmission once a pathogen infects people. In many urban centers, live animal markets—where both domestic and exotic species are sold for food and often slaughtered on site—are common and these marketplaces put people and animals (and their blood, bodily fluids, manure and carcasses) into direct proximity. Another driver is the destruction and fragmentation of natural habitat.<sup>20</sup> Anthropogenic activity aimed at meeting the increasing demand for animal protein, including the intensification of production, with high animal density and geographic concentration, is also recognized as an important potential risk factor.<sup>21,22,23,24,25</sup> Intensively farmed animals play a critical role in cross-species transmission of zoonotic viruses, as well as providing amplification of disease transmission to each other and to people.<sup>26</sup>

## VIRAL CHARACTERISTICS

The genome of a virus is not static, but rather exists in a state of perpetual change. Viruses replicate quickly, often imprecisely copying their genetic material with each multiplication. Within a given host, viral populations are genetically diverse, with many different genotypes cocirculating as a “quasispecies.”<sup>27,28</sup> Thus, viral populations are adaptable to new environments, because even if most are not able to propagate, a few survivors can generate whole new viral lines. Those with the ability to infect a diverse host range can lead to the emergence of new human diseases.<sup>29,30</sup> By analyzing the history of viral zoonoses, including all known viral-host relationships and previous patterns of viral emergence, a team of scientists with The Global Virome Project estimated that there are approximately 1.67 million undiscovered viral species in mammal and bird hosts and that between 631,000 and 827,000 of them can reasonably be expected to have zoonotic potential.<sup>31</sup>

## Pandemic risks associated with animal agriculture

### Agricultural expansion

One of the most prominent connections between animal agriculture and new viral pathogens is the interface with wildlife, particularly in previously uncultivated native habitats. Some of the Earth’s most biodiverse regions are the tropics<sup>32</sup> and wetlands.<sup>33</sup> Biodiverse ecosystems are not only rich in animal and plant life, but are also a wild reservoir for coevolved viruses, most of which circulate causing little or no harm to their animal hosts. In undisturbed ecological communities, naturally occurring viral populations are largely contained. However, native biomes, especially forests near equatorial regions including in Asia, Africa, and South America, are being destabilized by human activity.<sup>34,35</sup> Historically, much of the land is being cleared for agriculture.<sup>36</sup>

With urbanization and growing affluence, food production has shifted from primarily cereal staples to a more meat-centered diet,<sup>37,38</sup> although the choice of animal protein differs by culture and geography.<sup>39</sup> Global meat and dairy consumption are projected to rise by 40 million and 20 million tons, respectively by 2028.<sup>40</sup> While many factors drive this dietary shift in urban societies, women’s participation in the workforce, precooked convenience foods, and mass marketing are all thought to play a role,<sup>41</sup> along with social-psychological factors including perceived symbolic links between meat eating and status.<sup>42</sup>

Food production is a major factor leading to widespread land-use change. World-wide, approximately 40% of deforestation in the tropics and subtropics is accounted for by large-scale commercial farming and another 33% is due to local subsistence farming.<sup>43</sup> Far more land is used for animal agriculture than any other human activity.<sup>44</sup> As human activity encroaches into natural habitat, wild species are in greater contact with people and domestic animals, increasing the potential for disease transfer or “spillover.”<sup>45</sup> Although a rare event, viruses, with all their genetic diversity, can develop the

Anthropogenic activity heightens the risk of zoonotic EID. According to a 2020 statement from the United Nations, Convention on Biological Diversity:

*“Over the last 60 years, the majority of new zoonotic pathogens have emerged, largely as a result of human activity including changes to land-use (e.g., deforestation) and the way we manage agricultural and food production systems.”*

Maruma Mrema, E. 2020. Statement, April 7. United National Convention on Biological Diversity. [www.cbd.int/doc/speech/2020/sp-2020-04-07-health-en.pdf](http://www.cbd.int/doc/speech/2020/sp-2020-04-07-health-en.pdf). Accessed August 21, 2020.

ability to overcome the adaptive barriers of a new host and jump species.<sup>46</sup> Given the scale of global agriculture, and expansion into nearly every global ecological niche, domesticated animals serve as an important bridge between wild animals and humans. Clear examples, discussed below, are Nipah virus, which jumped from bats to pigs farmed near tropical forests, and avian influenza, which continues to be introduced into domestic poultry flocks farmed within the migratory pathways of wild waterfowl.

## Viral amplification

Industrial agriculture is rooted in western countries' drive to increase production capacity and efficiency to make animal-based foods widely available to the growing human population, and the associated animal housing systems, equipment, feed and genetics have been exported over the world. This industrialization of animal

*“Most of the new diseases that have emerged in humans over recent decades are of animal origin and are related to the human quest for more animal-source food.”*

Food and Agriculture Organization of the United Nations. 2013. World Livestock 2013: Changing disease landscapes, p. 2. [www.fao.org/3/i3440e/i3440e.pdf](http://www.fao.org/3/i3440e/i3440e.pdf). Accessed August 21, 2020.

agriculture is taking hold as traditional farming is being replaced by larger, more concentrated facilities that confine animals indoors. Industrial systems are often more automated (e.g., with temperature and humidity control, feed and water lines, and egg collection belts). For global animal agriculture, pigs, broiler (meat) chickens, egg-laying hens, and ducks are often farmed intensively, while cattle, sheep, and goats are still largely pastoral. Keeping large groups of animals in densely stocked facilities creates “unique ecosystems,”<sup>47</sup> identified as a risk factor facilitating the development of zoonotic pathogens with the potential to infect human populations.<sup>48,49</sup>

Larger farms with more animals have a greater potential virus load, should a farm become infected.<sup>50</sup> In the most intensive systems, laying hens and sometimes broiler chickens are confined to cages; mother pigs (sows) are frequently kept in stalls so narrow they cannot even turn around. Given the severe restriction of movement and prevention of all species-typical natural behavior, the welfare of animals in these intensive confinement systems is poor.<sup>51</sup> These cages and crates are used, in part, to house more animals together in the same building space.

When animals are raised extensively, with little close contact (e.g. in back yard farms), hypothetically any pathogens among them are transmitted at a low rate.<sup>52</sup> However, when thousands of animals are tightly confined together it creates a larger mixing vessel in which viruses (and bacteria) can pass serially through many hosts, potentially generating novel viral strains with the ability to infect people. A 2013 review published in the *Proceedings of the National Academy of Sciences* found “strong evidence that modern farming practices and intensified systems can be linked to disease emergence and amplification.”<sup>53</sup> For example, the transition from low pathogenic avian influenza (LPAI) to highly pathogenic avian influenza (HPAI) can result from a single point mutation. The probability of such a mutation increases in a commercial poultry production site with thousands of confined, susceptible animals.<sup>54</sup>

## Farm Concentration

While high animal density within farms is a risk factor for the amplification of disease, the geographic concentration of farms in the same region is a risk for disease spread.<sup>55</sup> Intensive production is often associated with large numbers of animals on a relatively small area of land.<sup>56</sup> These systems tend to shift to regions where grain is inexpensive and agricultural land is plentiful, growing fastest near densely settled areas and urbanizing environments.<sup>57,58</sup> The result is a progressive increase in animal biomass over limited geographic areas and extensive production systems are gradually being replaced by more large-scale and intensive systems.<sup>59</sup> For example, in Thailand and Vietnam, intensive poultry production is clustered in the areas surrounding Bangkok, Hanoi, and Ho Chi Minh City, close to consumption and exportation centers.<sup>60,61</sup> In Nigeria, medium and large-scale poultry production are spatially concentrated around the demand magnets of the peri-urban and urban south (the number of chicken holdings is 40% near towns, falling to 25% in regions further away).<sup>62</sup> Within highly concentrated areas, the distribution of several species (e.g. pigs, ducks, chickens) may overlap.<sup>63</sup>

Worldwide, pig and poultry populations are concentrated in the midwestern and southeastern regions of the United States,<sup>64,65</sup> eastern China, Europe, southern Brazil, and southeast Asia.<sup>66,67</sup>

When a highly infectious pathogen becomes established in one production site, it can then be transferred to neighboring operations.<sup>68,69</sup> Farm or service personnel moving between locations, such as veterinarians, delivery drivers, or staff can spread disease on fomites<sup>70,71</sup> (objects that can carry infectious agents such as clothes, boots, equipment, and vehicles). Other potential pathways for disease spread include trucks delivering feed, litter, live animals, or those that collect animal waste, even when empty,<sup>72,73</sup> and the rendering of dead animals.<sup>74</sup> Should a virus arise with the ability to transfer among people, staff working in farm animal confinement facilities could subsequently spread it within their communities.<sup>75,76</sup>

Disease transmission between farms depends largely on biosecurity practices. Industrial pig and poultry farms commonly go to great lengths to prevent the entry and spread of disease. This may include using designated equipment, placing disinfectant foot baths at barn entrances, limiting outside visitors, tire washes for incoming vehicles, and “shower-in, shower-out” facilities, among others. While it is often assumed that larger, more integrated production facilities will use more advanced bioexclusion measures, the size of these operations creates inherent risks.<sup>77,78</sup> A farm with just 10,000 broiler chickens uses approximately 42 tons of feed and 100,000 liters of water while generating 20 tons of waste.<sup>79</sup> Each input and output is a potential pathway for disease.<sup>80</sup>

Pathogens can spread in unexpected ways. Ventilation systems in place to regulate air quality, heat, and humidity have been implicated as a major gap in biosecurity<sup>81</sup> and can generate significant quantities of airborne dust with the potential to spread infections agents, as can flies and other insect vectors.<sup>82</sup> Waste management may be an under-recognized driver of microbial leaks.<sup>83</sup> Animal waste disposed of on land or used in aquaculture can contain a large pathogen load and poses an infection risk to wildlife.<sup>84</sup> Depopulation of infected poultry flocks and moving them out of barns can stir up organic materials. Trucking infected poultry on public roadways is a suspected transmission route, generating infected dust and aerosols to susceptible poultry near infected farms.<sup>85</sup>

When biosecurity plans fail, government emergency plans go into effect. To prevent the spread to other farms, international guidelines recommend “stamping out” the disease,<sup>86,87</sup> a euphemism for the mass killing of many thousands of animals at a time. Healthy, uninfected animals in the surrounding areas are killed along with infected herds and flocks. One widely used method for destroying whole poultry flocks in the United States is suffocation using water-based, firefighting foam. However, during the 2014–2016 HPAI outbreak, gaps in U.S. emergency response plans,<sup>88</sup> and a significant lack of resources,<sup>89</sup> led to the sporadic use of ventilation shutdown (VSD),<sup>90</sup> a method that slowly kills the animals over several hours by increasing the heat and carbon dioxide levels in the house, causing hyperthermia (extreme heat) and hypoxia (low oxygen).<sup>91</sup> In developing regions of the world, large flocks and herds may also be killed by mass burial, sometimes while the animals are still alive.<sup>92</sup>

## Trade in live animals

The global movement of people, live animals, and animal products is unprecedented, increasing the probability that a novel pathogen could spread around the world. Although there are no binding international regulations on the safe trade of animals and animal products, the World Organisation for Animal Health (OIE) provides recommendations in its *Terrestrial Animal Health Code*, which is recognized by the World Trade

Given that there have been multiple outbreaks of HPAI in large, industrialized facilities, scholars working in public health and rural development concluded:

*“...bioexclusion measures implemented by some large-scale industrial poultry units, including those in industrialized countries, may be insufficient to protect against H5N1 incursion when challenged.”*

Otte J, Roland-Holst D, Pfeiffer D, et al. 2007. Industrial Livestock Production and Global Health Risks. Pro-Poor Livestock Policy Initiative. A Living from Livestock Research Report. [www.fao.org/3/a-bp285e.pdf](http://www.fao.org/3/a-bp285e.pdf). Accessed August 21, 2020.

Organization's Sanitary and Phytosanitary Agreement.<sup>93</sup> OIE member countries report disease outbreaks and the global animal health situation is communicated to trading partners to prevent the spread of reportable animal diseases, those with widespread economic or public health impacts.<sup>94</sup> Following the confirmation of a disease outbreak, movement control areas are established within a country around the affected premises.<sup>95</sup>

While millions of tons of animal *products* are traded world-wide, they do not normally increase the risk of international disease spread.<sup>96</sup> The globalized trade in *live* animals however, can lead to the rapid transmission of pathogens across long distances,<sup>97</sup> despite international safeguards. Animals used for breeding may be shipped intercontinentally or live animals may be transported long distances for slaughter.<sup>98</sup>

The highest volume of live swine exports originates in Europe and North America. In the interest of bringing in "improved" genetics, pigs are commonly transported to Asia.<sup>99</sup> The global swine influenza virus population is geographically separated into two main lineages of Eurasian and North American origin and is endemic in these regions. By examining phylogenetic trees and whole-genome sequence data, it has been demonstrated that the long-distance shipment of live swine into Japan, Thailand, Vietnam, and South Korea brought in both influenza lineages, which now co-circulate in the pig populations of these importing countries.<sup>100</sup>

Regionally, animal movement can spread disease through established production networks, for example from Canada<sup>101</sup> or the Southern United States to the corn-rich Midwest.<sup>102</sup> These established transport networks are so commonly used they have been designated "swine-ways."<sup>103</sup> Both domestic and global transport of swine have been implicated in the movement and mixing of viral influenza strains across large distances.<sup>104,105</sup>

Globally, influenza A viruses established in domestic swine populations present a pandemic risk for humans.<sup>106</sup> As discussed below, in 2009, an outbreak of H1N1 swine influenza in Mexico and the United States with sustained human-to-human transmission spread the virus to 30 countries. This virus, generated by movement of live pigs, may have circulated in the U.S. swine population for years before emergence in humans.<sup>107</sup>

Long-distance transport may be especially risky for the spread of disease also because it is stressful for the animals. The well-established immunosuppressive effects of stress can increase animals' susceptibility.<sup>108</sup> For example, bovine respiratory disease complex or "shipping fever" has long been recognized as a transport-related illness of calves, which is caused by the additive effects of multiple stressors,<sup>109</sup> including those associated with weaning and the subsequent road transport of calves from pastures to feedlots or auction.

### Live animal markets and agricultural fairs

Throughout Asia, semi-outdoor food markets, or "wet markets," are common. Vendors sell vegetables, fruit, fish and live poultry from stalls lined in rows along narrow aisles.<sup>110</sup> Some markets also sell wild animals, such as live bats, marmots, and snakes.<sup>111</sup> Live poultry markets may carry multiple bird species including chickens, ducks, geese, pigeons, and quail, as well as exotic wild-caught and farm-raised fowl.<sup>112</sup> At these markets, consumers purchase meat or select live animals for slaughter on site, at restaurants, or at home.<sup>113,114</sup> Given the historical lack of refrigeration in transport and selling, the cultural preference is to consume freshly slaughtered animals. Despite the growth of supermarket chains, wet markets remain popular.<sup>115</sup>

Live animal markets are hubs in which animals from different sources are put into direct and indirect contact.<sup>116</sup> Emerging and reemerging pathogens are most likely to have the broadest host ranges,<sup>117</sup> and the diversity of closely held animals in live markets facilitates cross-species virus transmission.<sup>118</sup> When animals are gathered tightly together, under high stress, the viral load is amplified.<sup>119</sup>

Millions of live birds are brought to markets in Asian urban centers and slaughtered every day.<sup>120</sup> Infected birds may be sold and slaughtered before showing disease signs or dying of infection. Mathematical modeling has shown that following the introduction of a single infectious bird, the influenza virus could be amplified and

circulate silently in the market, shedding asymptotically.<sup>121</sup> In India for example, HPAI H5N1 outbreaks are highly associated with proximity to cities, improved road networks, and live bird market connectivity.<sup>122</sup>

Not only are live animal markets important initial sources of zoonotic disease, but they also spread pathogens geographically. The movement of animals into and between markets creates networks of potentially contaminating interactions, an “epidemiological interface” between susceptible and infected animal populations, allowing the rapid spread of pathogens across large geographical areas.<sup>123</sup> In China, chickens have been the main poultry species traded and they are transported both within and between provinces.<sup>124</sup>

In Guangdong Province, south China, pig traders collect pigs daily by truck from multiple farms in several counties from as far as 1,417 km away to resell in wholesale markets. At the markets, pigs from several farms may be mixed in a single pen. In some cases, pigs stay in the wholesale markets for multiple days before sent to slaughterhouses. After they are slaughtered, the meat is sold, often in a vegetable and meat market near residential areas.<sup>125</sup>

Wholesale markets may be of particular concern, as animals moving through them could first come into contact with infected animals or spread existing infections along the way. Lapses in hygienic measures (inadequate waste removal, disinfection procedures, or proper market closure practices) have been documented at wholesalers.<sup>126</sup> About 90% of live poultry pass through wholesale markets before arriving at retail markets.<sup>127</sup> The 2013 H7N9 virus in China was most likely transmitted from the secondary wholesale market to the retail live-animal market before reaching human patients.<sup>128</sup>

Live animal markets can also be found in developed countries such as the United States, especially in large cities, including New York.<sup>129</sup> In addition, live animal exhibitions and agricultural fairs are potentially important sources of zoonotic viral disease transfer in the United States and other regions.<sup>130</sup> Similar to live animal markets, agricultural fairs bring several species of potentially stressed animals from multiple sources into proximity with other animals and people, where comingling can occur for several days. The presence of pigs at markets and fairs is particularly concerning, as they are “ideal mixing vessels for influenza viruses” since they can be infected with both human and avian influenza.<sup>131,132</sup> In several US States, including Ohio, Indiana, and Michigan, hundreds of human cases of influenza A (H3N2) have been associated with agricultural fairs.<sup>133,134</sup> In a 2012 outbreak, 11 people were hospitalized, including several children, some in strollers, who had been in direct or indirect contact with pigs.<sup>135</sup> Swine exhibitions at agricultural fairs may have played a role in the H1N1 pandemic.<sup>136</sup>

## **Agricultural risks for specific Viruses**

### **Avian Influenza**

Avian influenza has been decimating poultry flocks for more than a hundred years,<sup>137</sup> and there have been three human influenza A pandemics: The 1957 H2N2 Asian flu outbreak, the 1968 H3N2 Hong Kong flu, and the more recent 2009 swine flu caused by H1N1 (discussed below). HPAI outbreaks in Hong Kong,<sup>138</sup> South Africa,<sup>139</sup> the United States, Mexico, Italy, the Netherlands, and Canada since 1983 have resulted in the direct mortality or killing through depopulation of more than a million birds in each instance<sup>140</sup> and there have been hundreds of associated human deaths.<sup>141</sup> H5N1 causes severe disease and is fatal in over 50% of the known human cases.<sup>142,143</sup> Even with a much lower mortality rate, if the virus mutated into a form easily transmissible between people, it could become a much more serious global pandemic than the 2020 outbreak of COVID-19.

### **INFLUENZA VIRUSES**

Influenza viruses are single-stranded RNA, with two surface glycoproteins, hemagglutinin (H) and neuraminidase (N) that are the basis for naming influenza strains. There are 18 H and 11 N subtypes.

Avian Influenza is categorized based on virulence to chickens: low-pathogenicity avian influenza (LPAI) and high-pathogenicity avian influenza (HPAI). LPAI viruses can be any of the hemagglutinin (H1-15) and neuraminidase (N1-9) subtypes, though only H5 and H7 are known evolve into HPAI.

Suarez DL. 2000. Evolution of avian influenza viruses. *Veterinary Microbiology* 74(1-2):15-27.

The current strains of avian influenza have been diversifying and circulating in wild aquatic bird populations over the past century.<sup>144</sup> Anseriformes (primarily ducks and geese) and charadriiforms (gulls and shorebirds) are the primary natural reservoir of low virulence influenza A viruses,<sup>145</sup> and these viruses are carried with little or no harm to the birds.<sup>146,147</sup>

Avian influenza viruses can be transferred from wild waterfowl populations into domestic poultry. In Asian countries such as China,<sup>148</sup> Thailand,<sup>149</sup> and Bangladesh,<sup>150</sup> domesticated ducks raised for commercial production are commonly released into rice paddy fields, which are often situated in natural wetlands. This habitat of wild aquatic birds is under increasing pressure from agricultural intensification.<sup>151</sup> While migratory birds have been traversing the globe in established, overlapping flyways for millennia, domesticated poultry farmed within these ancient routes are very new from an evolutionary perspective.

Introductions of avian influenza in poultry occur commonly but are usually self-limiting or are halted through disease control efforts. When an influenza virus infects a new host species it rarely transmits well enough to cause an epidemic, however the transmission of a pathogen tends to increase with host density. The growth in poultry production over the past thirty years has created an enormous ecological niche for avian influenza viruses.<sup>152,153</sup> After being transferred in to domestic poultry, and after circulating in these populations, there have been several cases where the virus acquired a limited ability to infect humans.<sup>154</sup>

The outbreak of avian influenza in Hong Kong at the end of 20<sup>th</sup> century ignited the global spread of several H5N1 genotypes<sup>155</sup> and marked the first time a purely avian influenza virus caused human respiratory disease and death.<sup>156</sup> In the years preceding the 1997 outbreak, the local chicken industry on the outskirts of Hong Kong had been transforming from backyard and subsistence-based production to more intensive systems. The concentration of farms increased, reaching 20 farms per square kilometer with over 400,000 total birds. The surrounding farms and others importing from southern China sold chickens, ducks, geese, quail, and pigeons to approximately 1000 retail shops and stalls in the city. The birds were slaughtered and butchered at the markets, where approximately 120,000 live poultry were sold every day.<sup>157</sup>

The Goose/Guangdong (Gs/Gd) lineage strain which gave rise to the outbreak is thought to have originated in migratory waterfowl passed to commercial flocks in the area surrounding Hong Kong.<sup>158</sup> The outbreak started with the death of 2,000 birds in a breeding flock (100% mortality), and was followed by infection in two nearby flocks, where it killed 75% of the birds. The first known human infection associated with the outbreak was identified in May 1997, a three-year old boy who did not survive. Human cases continued to be documented in November and December, at the same time dying poultry in market stalls were tested and confirmed for H5N1 infection. Another local farm outbreak occurred on December 21, where it was reported to have progressed slowly along a row of caged birds. Following this, the decision was made to depopulate all poultry from Hong Kong markets and farms. As many as 1.5 million birds were destroyed. In all, there were eighteen reported human cases associated with the outbreak, six of which were fatal.<sup>159</sup>

Since HPAI H5N1 first infected poultry in Hong Kong in March 1997, a diverse array of sub lineages have spread across the globe, carried intercontinentally by migrating birds.<sup>160</sup> Since 1996, at least 21 reassortants have emerged,<sup>161</sup> with more than 40 genotypes of H5N1 viruses identified in China alone,<sup>162</sup> and the virus is now firmly established (endemic) to poultry in Asia.<sup>163,164</sup> New H5 and H7 subtypes infecting humans have emerged. In total, 2644 laboratory confirmed avian influenza cases in people have now been reported in more than 20 countries.<sup>165</sup>

Commercial transactions are a clear route for local and regional disease transmission.<sup>166</sup> Both live bird markets and the trade in legal and illegal live poultry have been just as likely to spread the disease as wild birds.<sup>167</sup> Transmission patterns of avian influenza show that it can infect flocks of all types, even in areas of the world where high biosecurity is standard.<sup>168</sup>

Avian influenza viruses can evolve into more virulent forms after becoming established in large groups of closely confined animals.<sup>169</sup> As flocks with LPAI may show only mild clinical signs, indistinguishable from other common illness, the viruses can circulate indefinitely, gradually mutating into more highly pathogenic forms. Both H5 and H7 viruses have this capacity.<sup>170</sup> There are several documented cases of HPAI emerging after LPAI circulated in domestic flocks, for instance in Mexico in 1994, Italy in 1999,<sup>171</sup> in the Netherlands in 2003,<sup>172</sup> and in British Columbia in 2004.<sup>173</sup> In a 2018 review of 39 cases in domestic birds, all but two instances of conversion from LPAI to the highly pathogenic form were reported in commercial poultry production systems.<sup>174</sup> While these findings could be explained by better detection and documentation by large, commercial facilities,<sup>175</sup> present understanding is that HPAI usually emerges in intensive poultry rearing conditions,<sup>176,177,178</sup> including commercial free-range facilities.<sup>179</sup> Most detected conversions events have taken place in high-income countries, in poultry farms located within high poultry density areas (only 2 have been detected in rural backyard flocks, and even then, these occurred in Italy and France in regions of intensive poultry production).<sup>180</sup> When new strains arise, they can then be spread by both wild birds and via the trade in domestic poultry.<sup>181</sup>

Even when the initial signs of infection are mild, the presence of an H5 or H7 virus in poultry is always cause for concern because of the potential for mutation. For this reason, the World Organisation for Animal Health requires reporting all instances of H5 or H7 avian influenza,<sup>182</sup> even when these are not yet highly pathogenic forms.

Given the vast global networks of commercial industrial, small-holder, and backyard poultry presenting opportunities for animal to human exposure, the number of human H5N1 avian influenza cases remains relatively small.<sup>183</sup> However, if avian and human influenza viruses infect the same individual, or if a virus gradually mutates into a novel, more infective form, a human pandemic could emerge.<sup>184,185</sup> Persistent H5N1 virus in Southern China repeatedly introduces the virus into nearby countries, such as Vietnam and Indonesia.<sup>186</sup> The avian influenza virus has “an entrenched ecological niche”<sup>187</sup> and more HPAI strains are expected to arise.<sup>188</sup> It may be just a question of time before an avian influenza virus becomes capable of human-to-human transmission, with the potential for a global pandemic.<sup>189,190</sup>

Should a pandemic emerge, history suggests that the stockpiles of vaccines and antivirals would have a limited impact on preventing the associated morbidity and mortality.<sup>191</sup> Because viruses mutate and are genetically diverse, the choice of candidate viruses for development of human vaccines would be difficult and would have to be continually updated.<sup>192</sup> The world is unprepared for an outbreak of the scale and deadliness that avian influenza could cause.

## Nipah virus

Pig farming was an important factor in the initial human infection and spread of Nipah virus (NiV). The Nipah virus was named after the village Sungei Nipah in Malaysia.<sup>193</sup> The natural reservoir for NiV is the *Pteropus spp.* fruit bat, commonly known as the flying fox. In humans, NiV causes headache, fever, and seizures that can result in unconsciousness.<sup>194</sup> The case fatality rate is as high as 75%.<sup>195</sup> As of 2019, there are no specific antiviral drugs or vaccines for animals or people.<sup>196</sup>

The catalyst for the emergence of NiV is uncertain, but the close proximity of fruit bats foraging in orchards next to intensive pig production facilities is thought to have facilitated the transmission of the novel paramyxovirus from its reservoir.<sup>197</sup> The index farm, where the outbreak originated, housed approximately 30,000 pigs. This farm supplied gilts (young female pigs that have not yet given birth) and piglets to smaller operations in the vicinity.<sup>198</sup>

Human infections were first detected in 1997,<sup>199</sup> with ultimately 265 cases of viral encephalitis in Malaysia and 105 deaths.<sup>200</sup> The commonality among cases was primarily a history of close contact with swine.<sup>201</sup>

The disease caused illness in pigs as well, which showed a variety of symptoms including labored respiration, harsh coughing, trembling, and neurological twitches, although some cases were mild. The death rate for growing pigs was 1-5%, but much higher (approximately 40%) in piglets, which may have been due to the inability of sows to nurse their young.<sup>202</sup>

The virus spread among pigs kept in close confinement, possibly through oral-nasal contact, artificial insemination, unsterilized needles, or equipment. Farm dogs and cats may also have played a role in spreading the virus.<sup>203</sup> It was also transmitted between farms in the high-density pig production areas of adjacent states.<sup>204</sup> At the time of the outbreak, peninsular Malaysia had a pig population of 2.4 million animals, which were being actively traded. Infected pigs, such as replacement breeding sows, were moved both between and within states, and from farm to farm.<sup>205</sup>

The virus also spread to other countries. In March of 1999, 11 cases of febrile encephalitis or pneumonia were treated at Singapore hospitals, with one death. All were men who worked together in the same abattoir and handled swine.<sup>206</sup> It was determined they were infected by live pigs imported from Malaysia for slaughter.<sup>207</sup> In an effort to stamp out the disease, 901,228 pigs from 896 farms were killed from the end of February into April of 1999.<sup>208</sup>

The outbreak caused panic and grief among pig farm workers, many of whom had family members who became ill or died. Some pig farms were abandoned, leaving the animals without feed or water. The movement of pigs to market was halted and pigs were culled by shooting them, either in a pit before being buried or in their pens.<sup>209</sup>

Further outbreaks in Bangladesh and India in 2001 were traced to the consumption of raw date palm sap contaminated by fruit bats.<sup>210</sup> Outbreaks continued to occur regularly in these areas.<sup>211</sup> In 2014 seventeen people were infected by a henipavirus, most likely NiV or a closely related virus, which caused severe illness among humans and horses in southern Philippines with high fatality rate. Horses were most likely infected by fruit bats, but humans are thought to have been exposed while slaughtering infected horses, and/or through the consumption of undercooked meat from infected horses. Infected humans then likely transmitted it to other people.<sup>212</sup>

NiV is spreading in various parts of world and has the potential to cause severe outbreaks.<sup>213</sup> It causes severe disease in most cases. In Bangladesh and India, the death rate of infected persons is 70%. While human-to-human transmission has so far been limited, it has been suggested that if a novel strain develops with a sustained person-to-person transmission, it could become humanity's "most devastating pandemic."<sup>214</sup>

## H1N1 Swine Flu

For nearly the entire 20<sup>th</sup> century, pigs in North America had primarily been infected by one influenza subtype, the classical swine flu, a strain likely related to the 1918 pandemic,<sup>215,216</sup> which killed approximately 50 million people.<sup>217,218</sup> However, starting in the late 1990s, new influenza lineages began to infect North American pigs.<sup>219</sup> One proposed hypothesis for the relatively recent rise in variants is the increase in herd sizes as farms have become progressively larger.<sup>220</sup> A review and meta-analysis published in 2017 found swine influenza viruses to be more prevalent with both higher pig stocking densities and greater numbers of pigs per farm.<sup>221</sup> A Brazilian study comparing prevalence of influenza in extensive and intensive pig farms found about a quarter of samples from intensive farms were positive, with no positive results from extensive herds.<sup>222</sup>

Pigs have receptors for both mammalian and avian influenza A in their respiratory tract,<sup>223</sup> an ongoing concern for a 'triple reassortant virus,' with human/avian/swine lineage.<sup>224</sup> In early 2009, a review article coauthored by scholars working in the College of Veterinary Medicine at Kansas State University and Avian Flu Action in Cheshire, United Kingdom detailed the idea of pigs as mixing vessels with the ability to host influenza strains from humans and birds, suggesting they could be germinating a future pandemic strain.<sup>225</sup> The authors were cautious and prescient: "the creation of novel reassortant swine influenza viruses with zoonotic and pandemic

potential could also happen in modern swine facilities in the backyard of a highly industrialized country in North America or Western Europe.”<sup>226</sup>

Within a few months of this review publication the world faced an influenza pandemic for the first time in 40 years.<sup>227</sup> In March and April of 2009, there was an outbreak of respiratory illness in La Gloria, Veracruz, Mexico with subsequent testing indicating at least one patient was infected with a novel H1N1 influenza virus.<sup>228</sup> Early speculation faulted a near-by intensive pig farm, though a corporate partner in the farm indicated no pigs at their facilities were infected.<sup>229</sup> By April, the U.S. Centers for Disease Control and Prevention (CDC) reported two cases in southern California,<sup>230</sup> and a week later indicated that six additional individuals in California and Texas also tested positive for H1N1. In all of these cases there was no known contact with pigs, indicating they were likely exposed to other infected people.<sup>231</sup> The last week of April, the WHO convened an Emergency Committee to assess the emergence of this novel influenza virus in North America.<sup>232,233</sup>

While the first pig to human transmission event remains uncertain, early investigation estimated the first infection in the La Gloria cluster may have occurred around February 15, 2009.<sup>234</sup> Separate work examining H1N1 genetic data indicates a high likelihood that human infection started in Mexico,<sup>235</sup> leading to the suggestion that the virus traveled from there into the United States. While the precursor event for pandemic H1N1 is not precisely known, earlier investigations of sporadic infections with triple-assortant swine influenza in humans between 2005-2009 indicated that in most cases patients were exposed to pigs at fairs, farms or live animal markets.<sup>236</sup>

By June, just two months after identification of H1N1, the WHO indicated this novel strain of influenza met the criteria to be called a pandemic.<sup>237</sup> At the time of that June announcement almost 30,000 people had contracted the virus<sup>238</sup> and by December 2010, an estimated 11-18% of the world’s population may have been infected.<sup>239</sup> During the first year the virus was circulating, the CDC estimated that deaths worldwide may have ranged from approximately 150,000 to 575,000 people.<sup>240</sup>

As previously warned by the scholars working at Kansas State University and Avian Flu, the novel reassortant swine influenza virus with pandemic potential had emerged from pigs, the “viral mixing vessels.” However, their published work did not just predict one pandemic, further warnings were more apropos to 2020:

*“Even though pigs can generate novel influenza viruses capable of infecting humans, at present it is difficult to predict which particular virus will cause the next human influenza pandemic. The index case (“patient zero”) probably linking a wild bird, chicken or domestic duck with a pig and/or a person could be anywhere in the world, but a Southeast Asian “wet market” is most likely to be the locale in which the next pandemic virus is generated.”*

Ma W, Kahn RE, and Richt JA. 2009. The pig as a mixing vessel for influenza viruses: Human and veterinary implications. *Journal of Molecular and Genetic Medicine* 3(1):158-66. [www.ncbi.nlm.nih.gov/pmc/articles/PMC2702078/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2702078/). Accessed August 21, 2020.

Surveillance of swine influenza in Mexico found evidence of extensive gene flow between humans and pigs in Mexico and between Mexican pigs and pigs in other countries. Imports of live swine in the 1990s likely introduced new swine influenza strains from the United States and Europe.<sup>241,242</sup> The emergence of this pandemic strain was closely linked to the increase in Mexico’s imports of live swine.<sup>243</sup>

Analysis of viral precursors of pandemic H1N1 confirmed they were of swine origin but they also had genes from avian, human, and other swine influenza strains,<sup>244,245</sup> which may have been circulating in pigs for years. One predecessor to pandemic H1N1 was a 1998 outbreak of respiratory disease in Midwest pig populations.<sup>246</sup> Investigating the cause of these viral outbreaks, scholars noted “...genetic analysis of the influenza viruses isolated from pigs in 1998 provides compelling evidence of interspecies transmission of human and avian

viruses to pigs and of genetic reassortment among the human, swine, and avian influenza A viruses.” This was the first known triple-reassortant swine/avian/human influenza,<sup>247</sup> the viral predecessor to pandemic H1N1. Serious concern was sparked again in June of 2020 when a newly published study of provinces in China with high pig population densities reported that since 2016 there have been increasingly frequent infections with a new reassortant H1N1 virus termed G4. The new virus arose out of the complex viral ecosystem in the region, which includes the avian European and Asian lineages, the H1N1 strain associated with the 2009 pandemic, and a North American H1N1 strain (with genetic material from pig, human, and avian influenza viruses). The authors concluded that this virus has “all the essential hallmarks of a candidate pandemic virus.”<sup>248</sup>

## Ebola

In 1976, acute viral hemorrhagic fever was described from 318 human cases in Zaire.<sup>249</sup> Symptoms of Ebola virus in people include fever, muscle pain, and headache followed by vomiting, diarrhea, rash, and internal and external bleeding.<sup>250</sup> Ebola viruses, enveloped RNA filoviruses, are infamous for being highly contagious and causing death rates as high as 90% in some human outbreaks.<sup>251</sup> Person-to-person spread is through direct contact with blood, secretions, and semen of infected individuals.<sup>252</sup> There are four strains that cause disease in humans<sup>253</sup> and pigs are also susceptible.<sup>254</sup> When infected with Zaire Ebola, pigs develop respiratory tract infection, shedding virus from oro-nasal mucosa for up to 14 days after infection and are able to transmit the virus to other pigs.<sup>255</sup> In contrast to the severe systemic disease often leading to death in people, pigs develop a respiratory syndrome that can easily be mistaken for other porcine respiratory diseases and pigs may be a host for Zaire Ebola virus.<sup>256</sup> Pigs have been infected with Zaire Ebola virus in the laboratory and although the risk of them infecting people is very low, the Food and Agriculture Organization of the United Nations advises limiting exposure as a precaution, and that pigs be kept in enclosures where they cannot mix with other species<sup>257</sup> as the consequences of even rare spillovers are disastrous. While the probability is very low, concerns have also arisen that Zaire Ebola virus could get into the pork supply and become a foodborne pathogen.<sup>258</sup>

In July of 2008, there was an outbreak of the Reston strain of Ebola virus in domestic swine in the Philippines, causing severe respiratory disease in pigs and causing many pigs to abort.<sup>259</sup> People can become infected with Reston Ebola virus and although it has not yet shown to cause illness in humans, it causes severe illness in non-human primates.<sup>260</sup> Contact with pigs may increase the risk of the virus adapting and becoming infectious to people, potentially causing another epidemic of an Ebola virus.<sup>261,262</sup>

## Menangle virus

Menangle virus was newly described in 1997 when the pregnancy rate and litter size at a large pig farm in New South Wales, Australia decreased markedly, with stillborn and deformed piglets.<sup>263</sup> The virus, an RNA rubula virus, was not eradicated from the farm until 1999.<sup>264</sup> Fruit bats roosting near the pig farm are considered the likely source as bats in Queensland were later found to be carriers.<sup>265</sup> Two workers associated with the large pig farm outbreak in 1997 developed fever, headache, rash, and weight loss; subsequent serology determined that the virus from handling pigs was the most likely cause.<sup>266</sup> Direct contact and indirect exposure to infectious virus in secretions, feces, and urine are likely modes of transmission between pigs and to humans.<sup>267</sup> Menangle virus does not appear to be easily transmitted to people, but pigs can be efficient and susceptible hosts, potentially capable of infecting other pigs and humans, if exposed through cuts or abrasions.<sup>268</sup>

## Picobirna viruses

Picobirna viruses are small RNA viruses first described in people in 1988, which have subsequently been found in humans across the world and in a number of different types of farmed animals.<sup>269,270</sup> Picobirna viruses may cause or be a co-factor in chronic diarrhea with prolonged shedding of the virus in both people<sup>271</sup> and pigs; they may also circulate in shared human and pig environments.<sup>272,273</sup> Picobirna viruses in pigs are genetically related to those in people<sup>274</sup> and it is suggested that the strains could be transmitted from people to pigs.<sup>275</sup> Infected pigs could be persistently infected asymptomatic carriers and serve as reservoirs of infection.<sup>276</sup> In addition,

picobirna viruses have been detected in 100% of raw human sewage and in 33% of final effluent samples from metropolitan areas in the US.<sup>277</sup> Because the viruses in people and pigs are so related, the potential exists for human picobirna viruses to enter swine populations via treated, yet still contaminated waters.

## SARS and other coronaviruses

Coronaviruses, from the Latin *corona* (“crown,” because spikes of these viruses created an image similar to a solar corona) are large RNA viruses with a very broad host spectrum and significant genetic diversity.<sup>278,279</sup> The first coronavirus, avian infectious bronchitis virus, was discovered in 1937 and in 1967 electron microscopy on specimens from colds in humans identified particles that strongly resembled the avian infectious bronchitis virus.<sup>280</sup> Strains that infect humans generally cause mild symptoms and until Severe Acute Respiratory Syndrome (SARS) emerged were associated only with the common cold.<sup>281</sup> There are four main sub-groupings of coronaviruses, although only two are known to infect people.<sup>282</sup> However, coronaviruses are notorious for their ability to jump species and cause disastrous outbreaks to emerge.<sup>283</sup> In the past 20 years, this has resulted in outbreaks of severe respiratory disease in humans including SARS, Middle East respiratory syndrome (MERS), and COVID-19, with case fatality rates up to 36% for MERS.<sup>284,285</sup> Before SARS was discovered in people, coronaviruses were a veterinary concern, as they can cause serious disease in poultry and pigs.<sup>286,287</sup>

An alarming outbreak of contagious atypical viral pneumonia was first described in China in 2002; by March 2003, WHO named the disease Severe Acute respiratory Syndrome (SARS) and issued a global alert for the virus.<sup>288</sup> SARS was identified in live animals at the Shenzhen market in Guangdong Province, which sold a number of wild and domestic species confined to wire cages (including beaver, Chinese hare, Chinese muntjac, domestic cats, ferret badgers, Himalayan palm civets, and racoon dogs).<sup>289</sup> After SARS-CoV emerged in Hong Kong in mid-February of 2003, it subsequently spread to 29 countries, causing disease in more than 8,000 patients, and had killed at least 774 people.<sup>290</sup> SARS-CoV, the first coronavirus known to cause severe disease in humans,<sup>291</sup> was not closely related to any previously known coronaviruses, and the potential origins of the pathogen were not then obvious.<sup>292</sup> Luckily, SARS-CoV-2 is milder than its cousin, or the 2020 COVID-19 pandemic could have been even more catastrophic. The current prevailing theory is that SARS-CoV originated in horseshoe bats with masked palm civets acquiring and then spreading the virus to people through the wildlife trade.<sup>293</sup> Although surveillance of farm animals following the SARS outbreak indicated that pigs could become infected with the virus,<sup>294</sup> neither pigs nor poultry are amplifiers of the virus and apparently unable to spread it to people.<sup>295</sup>

In 2016, a novel coronavirus, Swine Acute Diarrhea Syndrome (SADS-CoV) was discovered in Guangdong province, only 100 km from the origin of the SARS pandemic.<sup>296</sup> The disease caused a large-scale outbreak of fatal disease in pigs in China, resulting in the destruction of nearly 25,000 pigs to contain the 2016 outbreak<sup>297</sup> and another outbreak in 2019 in China that killed 2,000 pigs.<sup>298</sup> SADS-CoV is also known as swine enteric alphacoronavirus (SeACoV) and porcine enteric alphacoronavirus (PEAV).<sup>299,300</sup> Unlike SARS-CoV, SADS-CoV is an alpha coronavirus and although it has not been reported to cause illness in people, it is still not entirely known whether it has the ability to infect humans.<sup>301,302</sup> SADS-CoV likely originated in bats, with rodents as a potential intermediate host, and there is a risk that it could species jump again from pigs to people.<sup>303,304</sup>

Porcine epidemic diarrhea coronavirus (PEDV) is a highly pathogenic and lethal pig coronavirus, causing severe diarrhea, vomiting, and dehydration that kills 80 to 100% of piglets.<sup>305</sup> Severe outbreaks occurred in Asia and Europe, before it explosively emerged in early 2013 in the United States and caused the death of over eight million piglets.<sup>306</sup> PEDV is spread principally via fecal-oral transmission, but can also contaminate surfaces and be spread by pigs that do not appear ill.<sup>307</sup> Although it has not yet jumped species, it is a potential threat since it can infect human cells and it is similar to other genetically diverse and adaptable coronaviruses.<sup>308,309</sup>

## Disease “X”

Since 2018, the WHO has maintained and updated a list of priority diseases with epidemic potential for which there are insufficient, or no known, interventions. WHO points out that it is not an exhaustive list, nor does it try to predict the most likely causes of the next epidemic. The list currently includes COVID-19, Ebola virus, SARS, and Nipah viruses, which have been detailed herein. In addition to these specific diseases, WHO also includes “Disease X,” which “represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease.”<sup>310</sup>

## Conclusions

The apt “One Health” concept recognizes that the health of people is closely connected to the health of animals and our shared environment.<sup>311</sup> The way society interacts with animals has serious implications for global human health. Zoonotic diseases are emerging in situations where the welfare of animals is poor, either through their confinement in intensive production facilities or live animal markets, as they are transported locally or internationally, or where farming encroaches on the habitat of wild animals. The virus that will cause the next global pandemic could already be circulating among farmed animals. While we cannot eliminate epidemics, we can decrease the chances that the next one will result from risky agricultural practices. Sweeping changes are already starting to take hold; in July of 2020, China announced it would gradually phase out the slaughter and sale of poultry in live bird markets.<sup>312</sup>

Elizabeth Maruma Mrema, the Acting Executive Secretary of the Convention on Biological Diversity states that:

*“... the lessons learned from COVID 19 and other epidemics also point to the need for concerted action supported by a long-term vision; one that enables us to fundamentally transform our collective understanding of, and relationship with, the natural world, to prevent, insofar as possible, future pandemic outbreaks.”*

Maruma Mrema, E. 2020. Statement, April 7. United Nations Convention on Biological Diversity. [www.cbd.int/doc/speech/2020/sp-2020-04-07-health-en.pdf](http://www.cbd.int/doc/speech/2020/sp-2020-04-07-health-en.pdf). Accessed August 21, 2020.

*“The 20th century was a period of unprecedented ecological change, with dramatic reductions in natural ecosystems and biodiversity and equally dramatic increases in people and domestic animals. Never before have so many animals been kept by so many people—and never before have so many opportunities existed for pathogens to pass from wild and domestic animals through the biophysical environment to affect people causing zoonotic diseases or zoonoses.”*

United Nations Environment Programme. 2016. UNEP Frontiers 2016 Report, Emerging Issues of Environmental Concern, p.18. [wedocs.unep.org/bitstream/handle/20.500.11822/7664/Frontiers\\_2016.pdf?sequence=1&isAllowed=y](http://wedocs.unep.org/bitstream/handle/20.500.11822/7664/Frontiers_2016.pdf?sequence=1&isAllowed=y). Accessed August 21, 2020.

A 2020 scientific assessment published by the United Nations Environment Programme recognized the increasing demand for animal protein and unsustainable intensification as “major anthropogenic driver[s] of zoonotic disease emergence.”<sup>313</sup> A well-structured, carefully considered food production system would encompass a whole ecosystems approach, valuing animal welfare, and planetary health along with the growing global human populations’ food requirements.

The growth in farmed animal populations is staggering. Nearly 3 billion ducks, over 7 billion hens, almost 1.5 billion pigs and over 68 billion broiler chickens were slaughtered world-wide in 2018.<sup>314</sup> Higher income in transitioning economies is driving a change in dietary preferences and per capita consumption of animal-source food is increasing in low to middle-income countries.<sup>315</sup> The growing demand for animal-based protein and milk are often asserted without question. However, the emerging disease risks associated with the unprecedented

growth of animal agriculture, along with environmental and animal welfare concerns call into question the wisdom of continuing along the current path. The common “solutions” advanced to address the disease threat posed by expanding and intensifying animal agriculture are band-aid fixes, including increasing farm and market surveillance,<sup>316</sup> improving biosecurity,<sup>317,318</sup> and providing more communication and training to agricultural workers<sup>319,320</sup> but these fail to address the root of the problem. A much more effective and sweeping option is to reduce our reliance on animal sourced foods altogether. Such a shift would reduce animal population density and the transportation networks that move animals, and diseases, into new regions. It could also reduce

the stocking density and number of animals confined in the remaining intensive systems, permitting a higher level of welfare in cage- and crate-free alternative housing.

A viable alternative to meeting the growing protein demand is to curb expanding meat production with a shift toward more plant-based options. Reducing meat consumption, through efforts such as the Meatless Monday campaign,<sup>321</sup> or partial substitution of plant protein in ground and processed meats<sup>322</sup> are viable options. In the future, another potential alternative is cultured meat, produced using in vitro tissue engineering techniques.<sup>323,324</sup> Meat analogs are now widely available and supportive policies promoting these options could fundamentally change our reliance on industrialized farming and reduce concomitant disease risks.

While COVID-19 was not explicitly predicted, pandemics are expected, albeit with an undefined timeline and place of origin. The intensification and industrialization of animal agriculture creates a large, susceptible antigenically naive population, which nature will exploit. Meeting the demand for animal protein by ramping up intensive production around the world alters viral host dynamics, generating new pathways for the dissemination of viruses and the evolution of new viral strains. Industrialized farming is just one of many risk factors for the emergence and spread of disease, however intensively farmed animals play a critical role as intermediate hosts by bringing animal viruses, which would normally have little contact with alternative hosts, into close contact with people.<sup>325,326</sup> While SARS-CoV-2 apparently emerged at a wildlife market, the next outbreak could just as easily be associated with intensive farming, as medical doctors and scholars have warned.<sup>327,328,329</sup>

COVID-19 has had a major impact on public health, but a more virulent virus with the same rate of infectivity could be much more devastating. The global response to COVID-19 has demonstrated that a concerted effort among countries can reduce the impact of a public health emergency. A much greater and more urgent emphasis should be focused on the prevention of future pandemics by fundamentally restructuring our food system to reduce reliance on animal-based protein.

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<sup>6</sup> Jones KE, Patel NG, Levy MA, et al. 2008. Global trends in emerging infectious diseases. *Nature* 451:990–3. [www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960580/). Accessed August 21, 2020.

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<sup>8</sup> Morse SS, Mazet JA, Woolhouse M, et al. 2012. Prediction and prevention of the next pandemic zoonosis. *Lancet* 380:1956–65. [www.thelancet.com/journals/lancet/article/PIIS0140-6736\(12\)61684-5/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61684-5/fulltext). Accessed August 21, 2020.

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