## **Concentrated Animal Feeding Operations (CAFOs): Pandemic Potential**

The next pandemic virus might emerge not in one of China's wet markets but in a CAFO. Some animal and human viruses can swap gene segments (recombination), creating new ("novel" or "variant") potentially dangerous strains. Crowding creates opportunities for viruses to mingle and exchange genetic material and fosters the transmission of infectious diseases in humans and animals alike. Contagion can spread swiftly through military barracks, cruise ships, prisons, and CAFOs.

**Influenza A:** Pigs, birds (wild birds and domestic poultry), and people can share influenza A viruses, setting the stage for genetic mixing and producing novel influenza A viruses that could give rise to a human pandemic. By definition, novel viruses have not been previously identified in humans. Therefore, cross-protective immunity from prior vaccinations or natural infections might be lacking, increasing the risk of severe disease and ease of spread. Widespread immunologic naivety is necessary for a "successful" pandemic from a viral vantage point. Many influenza viruses that infect humans, including past pandemic strains, are animal-human hybrids. The deadly 2009 H1N1 influenza A pandemic strain was a jumble ("triple reassortment") of swine, bird, and human genes.<sup>1, 2</sup> Its genetic roots can be traced to a swine influenza strain (H3N2), also a triple reassortment virus, first detected in the U.S. in a North Carolina hog CAFO in 1998, with which 2009 H1N1 shares six of eight gene segments. The other two gene segments are from Eurasian swine influenza lineages.<sup>3</sup>

Early on, scientists recognized the significance of the appearance of swine H3N2 influenza viruses in the U.S. in 1998. According to a Pfizer Animal Health Technical Bulletin dated August 2008, "The emergence of these H3N2 viruses is widely regarded as a remarkable occurrence, as it was the first time reported that the genome of an influenza virus consisted of gene segments from three different viral lineages." A 2000 article in the Journal of Virology presciently concluded that "Continued surveillance of North American swine herds should be done to ascertain which of the triple-reassortant viruses will remain circulating and to detect the emergence of new and potentially pathogenic virus strains."<sup>4</sup> While the 2009 HIN1 pandemic was ongoing, Garten et al. issued a telling comment in the journal, Science, "The evolutionary distances between the gene segments of this virus and its closest relatives indicate a lack of surveillance in swine populations that may harbor influenza viruses with pandemic potential."<sup>5</sup>

Several well-documented cases of transmission of variant influenza A virus to humans have been traced to contact with pigs at county fairs.<sup>6</sup> CAFOs can help spread influenza A strains circulating in a community. Influenza A viruses can be transmitted between CAFO workers and pigs and between pigs, with the pigs serving as a viral reservoir. There is convincing evidence that such amplification occurred in North Carolina during the 2009 H1N1 influenza A pandemic.<sup>7</sup>

Unfortunately, monitoring for influenza in CAFO pigs is voluntary. Producers are generally reticent, fearing economic losses.<sup>8</sup> Swine influenza, including H1N1, is not a reportable illness (the World Organization for Animal Health need not be notified) because it is considered a

"standard swine flu."<sup>9</sup> The USDA does fund a voluntary surveillance program to look for novel influenza strains in swine.<sup>10</sup>

The United States Department of Agriculture (USDA) confirmed the presence of a highly pathogenic strain of avian influenza A virus (HPAI A H5) in wild birds in the U.S. in January 2022 and an Indiana turkey CAFO in February 2022.<sup>11</sup> The virus has since been detected in several other bird populations (wild, backyard flocks, and commercial poultry operations).<sup>12</sup> While poultry workers have some degree of risk, the threat to the general population is currently low. However, another pandemic could be unleashed if the virus mutates or recombines and adapts to humans.

**Coronaviruses:** There are numerous animal coronaviruses, and they tend to stick to their kind. However, as the COVID-19 pandemic, caused by the coronavirus known as SARS-CoV-2, illustrates all too well, animal coronaviruses can jump species in spillover events, infecting humans with fatal consequences. Other examples in recent history include SARS-CoV and MERS-CoV, less transmissible coronaviruses but ones that carry a much higher mortality rate than SARS-CoV-2. All three coronaviruses originated in bats and spilled over to other intermediate host animals before jumping to humans.\*

Coronaviruses cause severe infections in pigs and cows. Swine coronaviruses (PEDv & PDCo-V)\*\* cause an acute diarrheal illness (Swine Enteric Coronavirus Disease or SECD) in neonatal pigs with a high mortality rate. <sup>13</sup> SECD made its way to the U.S. in 2013.<sup>14</sup> SECD is now well established in the U.S. and considered widespread. Bovine coronaviruses (BCoV) strains can cause severe intestinal inflammation, respiratory disease, and a febrile illness in cattle and is a major cause of morbidity and mortality and economic loss in the beef and dairy cattle industries.<sup>15</sup>

The USDA Animal and Plant Health Inspection Service (APHIS) rescinded federal reporting requirements for SECD in 2018 in response to industry feedback, citing regulatory burden and an ability to manage the disease effectively.<sup>16</sup> Bovine coronavirus disease, likewise, is not reportable.

**COVID-19:** Evidence suggests that SARS-CoV-2, the coronavirus responsible for the COVID-19 pandemic, jumped from a bat to a wild mammal prized for its fur, and spillover to humans occurred in a wet market in Wuhan, China. The raccoon dog is a leading candidate, but a mink or another animal might have been the original intermediate host.<sup>17, 18, 19</sup> China is the global fur industry hub. Many of the animals processed for their fur are raised in captivity, in what essentially constitutes wildlife CAFOs.<sup>20</sup> Of note, minks are highly susceptible to COVID-19. COVID-19 raged through mink CAFOs worldwide in 2020, including in the U.S., necessitating massive culling.<sup>21</sup> Two-way transmission between minks and humans was well documented.<sup>22</sup>

SARS-CoV-2 seems to be adopting an influenza virus-like survival strategy. It readily mutates and recombines, allowing it to evade the human immune system repeatedly.<sup>23</sup> The virus has infected numerous animal species, establishing a stable and sizable reservoir of virus in wildlife populations.<sup>24, 25</sup> These factors ensure its indefinite survival and portend the emergence of novel strains capable of inciting a future pandemic.<sup>26</sup>

Although there are reports of limited SARS-CoV-2 seroconversion in cows and domestic pigs, common food animals are not particularly susceptible to SARS-CoV-2.<sup>27</sup> The available evidence does not implicate CAFO livestock in the COVID-19 pandemic. However, that could change given the virus' behavior to date and its ample wildlife reservoir. Conceivably, pig and cow coronaviruses might evolve (mutate or recombine with SARS-CoV-2) to produce variant strains capable of causing another coronavirus pandemic. A spillover is more likely to occur in a CAFO because they densely confine large numbers of livestock.

Some experts postulate that the deadly 1889-1890 "Russian flu" was due to a coronavirus that jumped from bats to cows to humans.<sup>28</sup> HCoV-OC43, a human coronavirus that typically causes self-limited common cold symptoms, likely evolved from an ancestral BCoV strain based on genetic analysis, and could be the weakened progeny of a past human pandemic strain.<sup>29, 30</sup>

\*SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus): Bats  $\rightarrow$  (unknown intermediate host)  $\rightarrow$  humans SARS-Co-V-1 (Severe Acute Respiratory Syndrome Coronavirus): 2003: Bats  $\rightarrow$  palm civets  $\rightarrow$  humans MERS-CoV (Middle Eastern Respiratory Syndrome Coronavirus): 2012: Bats  $\rightarrow$  dromedary camels  $\rightarrow$  humans

\*\*PEDv (porcine epidemic diarrhea virus) & PDCoV (porcine deltacoronavirus)<sup>19</sup>

**Climate change and deforestation:** The worldwide adoption of the CAFO-style animal food production system contributes substantially to climate change and deforestation. The clearing of land, including vital rainforests, to accommodate cattle feedlots and grow livestock feed crops could play a role in the next pandemic. Wild animals are forced to disperse to find new habitats and food sources, increasing the risk of close encounters with other animals and humans, thus facilitating the exchange of viral genetic information and spillover events.<sup>31</sup> Global warming-induced changes in animal habitats further increases the risk of cross-species transmission of viruses.<sup>32</sup>

The agricultural industry is not required to publicize CAFO animal disease sampling data. The lack of transparency hinders the ability of public health professionals and agencies to detect and respond to new and emerging zoonotic threats.

CAFO biosecurity measures, surveillance, and compulsory reporting of some animal viruses (e.g., HPAI, but not swine influenza or bovine coronavirus disease) by agencies such as the USDA APHIS, and mass culling to manage animal disease outbreaks reduce but do not eliminate the chances that the next pandemic virus will escape from a CAFO.<sup>33</sup> Vigilance, even if it entails "regulatory burden," coupled with industry transparency is in order.

Prevention. https://www.cdc.gov/flu/about/viruses/change.htm

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