What are the prospects that we might soon face another coronavirus-like viral pandemic?

here are signs of a <u>mid-summer surge</u> in COVID-19 cases, particularly in the Midwest and West, that have som a concerned. But even the very risk-averse expect it to be small relative to past years.

The bigger issue: Are we prematurely letting down our defenses against other viruses as the SARS-CoV-2 pandemic fades from the headlines? Although the more than <u>1.1 million deaths</u> and hundreds of thousands of cases of Americans with <u>lingering long COVID</u> remain a grim reminder of what we have endured, most people have neglected to get the most recent vaccine booster, stopped masking and instead have turned their attention to sun and fun.

However, those of us who study viruses are acutely aware that coronaviruses, one of which is SARS-CoV-2, the etiologic agent of COVID-19, are zoonotic agents – that is, they can spread infection between people and animals. These infections can be caused by viruses, bacteria, parasites, and fungi. Some infections can be severe and life-threatening, such as rabies, MERS, anthrax, bubonic plague, and SARS-CoV-2, while others are milder.

The zoonotic nature of COVID transmissibility has been particularly unsettling, as we initially found the virus in <u>bats</u> and <u>minks</u>, and then in <u>pets</u> and later, in local <u>deer populations</u>. Thus, not only do we have to be concerned about the human population, but our animals as well.

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We remain vulnerable to outbreaks, and even pandemics, of zoonotic diseases, and epidemiologists and infectious disease experts are concerned that the next serious one could be caused by a new strain of an old foe, a variant of the <u>N5H1 strain of avian influenza virus</u>. Recently, the Food and Agriculture Organization (FAO) of the United Nations, the World Health Organization (WHO), and the World Organization for Animal Health (WOAH) strongly urged that nations collaborate to prepare for this latest threat to our lives and livelihoods.

<u>Avian influenza</u>, or "bird flu," traditionally spreads among both wild and domestic bird populations. Influenza virus strains such as bird flu and <u>swine flu</u> are able to co-infect animals so that they can mix and match segments of genetic material (RNA) to create new and more infectious and/or more virulent virus strains. Both avian and swine flu have been the source of nasty pandemics, with the 1918-19 <u>Spanish flu</u> (H1N1) perhaps being the most notorious.

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Influenza strains are designated by the unique epitopes found on the <u>hemagglutinin (HA) and</u> <u>neuraminidase (NA)</u> proteins, which are found on their surface and assist with their entry and exit into and from cells, analogous to the <u>spike protein of SARS-CoV-2</u>. A new H5N1 strain might then have an enhanced ability to jump from birds to mammals, raising concerns that it might be just a matter of time before the virus jumps to humans. The greatest concern is that the virus would then become capable of human-to-human transmission.

How does this happen? There are two ways that flu viruses commonly evolve. One is called "antigenic *drift*," which consists of small genetic mutations that give rise to changes in the surface proteins of the virus, hemagglutinin (HA) and neuraminidase (NA). Those mutations usually produce viruses that are closely related to one another, which means that antibodies elicited by exposure to one flu virus will likely recognize other viruses that arose from antigenic drift.

Another type of change is called "antigenic *shift*," a major genetic change that gives rise to new, significantly different HA and/or NA proteins in flu viruses capable of infecting humans. This is more likely to occur when there is co-infection by different viruses — say, human and avian flu viruses simultaneously infecting an animal host — and there is reassortment of RNAs such that new viruses result that are different enough that most people do not have immunity to them.

Such a "shift" occurred in the spring of 2009, when an H1N1 virus with genes from viruses originating from North American swine, Eurasian swine, humans, and birds emerged to infect people and spread quickly, causing a pandemic.

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Based on reports from across the world, there is reason to be concerned that we could be in store for a shift event. In 2022, 67 different countries reported H5N1 flu in both domestic and wild bird populations , with over 130 million poultry lost from virus infection or from culling performed to stop virus spread. The 2022 outbreak was the deadliest on record in the U.S., affecting nearly every state and forcing culls of more than 50 million birds. (That's the main reason that poultry and egg prices spiked last year.)

Equally if not more disturbing are <u>recent reports of H5N1 among mammals</u> in 10 different countries since 2022. This is certainly an underestimate, as outbreaks of avian flu in mammals would be unexpected and, therefore, underreported. Over two dozen species of mammals are known to harbor the virus, including cats and dogs. The extent of this spread makes it inevitable that the virus will reach humans.

Avian flu kills almost all the birds it infects, and globally, from <u>January 2003 to May 2023, 876 cases of</u> <u>human infection with avian influenza A(H5N1) virus were reported from 23 countries</u>. Of those cases, 458 were fatal (case fatality rate of 52%). During the past 18 months, a handful of human cases — but, as yet no human-to-human transmission — have been reported. Infection has been associated with severe symptoms and some deaths.

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Like our initial encounter with COVID-19, we are ill-prepared for this "pandemic-in-waiting." If a new H5N1 variant were highly transmissible from human-to-human, once again we could quickly get behind the curves of infections, hospitalizations, and deaths.

The U.S. response to the COVID pandemic was hindered by a deluge of misinformation and disinformation that emanated from <u>Russia's propaganda apparatus and its U.S.-based "useful idiots</u>," including a handful of healthcare professionals and even one presidential wannabe (Robert F. Kennedy, Jr.). It has made communication about the benefits of vaccines, masks, and other interventions extremely

challenging, and the numbers of vaccinations against <u>other preventable diseases</u>, <u>such as measles</u>, <u>are</u> <u>down</u> since the emergence of SARS-CoV-2.

There is plenty to be done to prepare. Our immunity against H5N1 is likely to be minimal, so new vaccines are urgently needed. Public health leaders, animal health scientists, and vaccine manufacturers should already be communicating with each other about the risk. Exposure to sick animals needs to be reported. An infrastructure for animal surveillance must be set in place, and we are still underperforming on this, even after all that we have learned from COVID-19. Emerging variants of H5N1 need to be identified and their sequences uploaded onto easily accessible databases.

The Biden Administration has just created an Office of Pandemic Preparedness and Response Policy (OPPR) in the Executive Office of the President, "charged with leading, coordinating, and implementing actions related to preparedness for, and response to, known and unknown biological threats or pathogens that could lead to a pandemic or to significant public health-related disruptions in the United States." It will "take over the duties of the current COVID-19 Response Team and Mpox Team at the White House and will continue to coordinate and develop policies and priorities related to pandemic preparedness and response." President Biden's past public health appointments have been barely mediocre on their best days, so we are skeptical.

We need to be vigilant about the threat of new influenza viruses. Our population and livestock, and even our pets, might soon be in jeopardy.

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