

## **Avian H5N1 Flu Deaths are Marching Forward (The Beat Goes On)**

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*This April 2024 version is an update of the November 2023 version. Much has occurred since November 2023, so an update is needed. This update also covers some of the material from the previous November 2023 version, which is included to make the update flow better. The November 2023 version will be preserved on the Center for Arms Control and Non-Proliferation website. The new version will be posted too on the CACNP website.*

### **Introduction**

Before the year 2015, avian H5N1 [killed nearly 60% of poultry workers](#) and others who became infected through close contact with infected poultry. Fortunately, the virus was [rarely transmissible among humans](#). From 2015 to 2020 [avian H5N1 fatalities in humans had almost disappeared](#), since the strains from nature that appeared in poultry markets were no longer deadly to humans. They were, so to speak, “defanged.” We thought we were finished with H5N1 avian flu virus. We thought we were in a good place. (All three of the above links open the same document.)

The June 8, 2023 Bulletin of the Atomic Scientists article “[Once ‘defanged,’ H5N1 bird flu is gaining teeth again](#)” reported a new threat to birds and mammals, a deadly and highly transmissible avian H5N1 flu virus (highly pathogenic H5N1 avian influenza). This article covers 2021, 2022, and early-2023. We are now in the spring of 2024, so this June 2023 published article is out of date.

Worldwide, this virus is likely responsible for the death of and purposeful culling of billions of poultry birds and the deaths of tens of millions of wild birds. Recent deaths of large numbers of birds and mammals who otherwise would be alive is alarming and sad.

### **Could birds become extinct?**

[As reported in the Guardian](#) in a March 2023 article, Peru scientists have “counted the deaths of at least 63,000 sea birds...many more can be seen strewn along the country’s coastline...Scientists estimate the true number of bird flu deaths is probably much higher.” Most wild birds will die unobserved and uncounted; so worldwide, the number of bird deaths is thought to be very large.

The calculation that follows yields very crude numbers based on somewhat shaky data but nonetheless yields numbers of bird deaths that might be compared to the world’s total bird population to estimate whether birds could become extinct. Perhaps most importantly, the calculation provides an outline for the data that we would need to make a more meaningful estimate.

One very interesting analysis of wild-bird deaths from the Netherlands is reported in [another Guardian article](#) where scientists attempt to take underestimates into account.

“[O]f the approximate 8,000 sandwich terns that died in the Netherlands, only a handful are included in the official numbers – in this case a more than 200x difference between reported numbers and observed. The lack of appreciation for the scale of wild bird mortality is concerning as there may be species/population level ramifications.”

One quantitative estimate of bird deaths is reported in [a Nature article](#):

“The semiannual estimate of confirmed highly pathogenic H5N1 avian influenza cases in wild birds (predominantly dead birds) peaked at 34,000 during the second half of 2021, although in many instances the number of wild-bird cases reported to WOA/FAO includes only birds tested and positive for HPAI and is therefore a substantial underestimate.”

This Nature article reports 34,000 (underestimated) deaths for the second half of 2021. Assuming the same number of deaths in each half-year from the beginning of the year 2000 until the spring of 2024 yields  $4.25 \text{ half-years} \times 34,000 \text{ deaths/half-year}$  is around 145,000 deaths of wild birds.

To estimate the actual numbers of deaths, use the “200x difference between reported numbers and observed.” Actual deaths are then estimated to be  $200 \times 145,000$  about 29 million dead birds.

The number is uncertain and likely too small, but nevertheless carrying out the calculation illustrates that very many birds have died. And more will die in the future as “the beat goes on.” Another uncertainty: Some birds and animals become infected but do not die, so may become immune to further infection.

[According to the National Geographic](#), there are between 50 billion and 430 billion birds on Earth. For a calculation using the least favorable denominator number, 50 billion, the probability of extinction of all wild birds is  $29 \times 10^6 / 50 \times 10^9 = 5.8 \times 10^{-4}$ . Despite how crude the calculation is, this probability is low enough to make it unlikely that all birds would become extinct, especially since some infected birds don't die.

To summarize, the steps used to estimate the probability that birds could become extinct are

- (1) Find the number of observed deaths for many locations (e.g., from local public health reports)
- (2) Estimate the actual deaths for each location (e.g., the Netherland scientists 200x calculation)
- (3) Sum the number of estimated deaths for each location

If enough locations to cover much of the world are used, we will have an estimate of the probability that birds could become extinct. Let's take two cases:

- (a) The number of estimated deaths is close to or exceeds the number of birds on earth. Then we can say with reasonable confidence that birds could become extinct.
- (b) The number of estimated deaths falls significantly short of the number of birds on earth. Then we can say with some confidence that birds will not become extinct. This was the result of our example calculation where we found that the probability of extinction of all wild birds is  $5.8 \times 10^{-4}$ .

You may think that the probability of extinction is not worth calculating. Why not leave it qualitative: “Scientists estimate the true number of bird flu deaths is probably much higher?” That is, trying to calculate the number of H5N1 flu deaths is not worth the effort as it cannot be determined with any precision. I would argue the opposite. The imprecise calculation at least gives me a better understanding

of the problem, so is worthwhile for that reason; and besides, the calculation may yield believable conclusions.

### **Bird species at the risk of extinction**

We should think instead about what species of birds might be at risk of extinction.

Meat- and fish-eating birds such as condors, eagles, hawks, and vultures are at greater risk of contracting the new avian flu virus, and some species may be at risk of extinction. For example, there is now an effort to vaccinate California condors to protect them from extinction. The vaccine was first tested successfully in black vultures; a species related to California condors. In October 2023, a report from UNDARK magazine described the status of [the efforts of testing the vaccine in condors](#).

“Condors are social creatures. They roost in groups and gather in hungry hoards to devour decaying animal corpses, sharing saliva and pooping everywhere — ideal conditions for the disease to spread... While vaccines for HPAI [highly pathogenic avian influenza] are used in some other nations, U.S. health officials have never authorized vaccination for any animal in the country — not even poultry — for reasons ranging from practical to political. But in the face of a deadly threat to one of the country’s most endangered species, condor advocates hoped they could convince the USDA to make an unprecedented exception...H5N1 is different because it appears to kill birds slower, giving them time to transport the disease within a wide radius.

Hopefully, condors will receive a strong immune boost from the vaccines.

There is considerable recent progress [vaccinating condors](#). A February 2, 2024 document from the U.S. Fish and Wildlife Service discusses the progress.

“Based on the results of the vaccine trial, the Service determined it is appropriate to move forward with HPAI vaccinations of captively managed and free-flying condors... As of this report, 94 birds have received at least the initial dose of the vaccine.... Based on the results of the vaccine trial, the Service determined it is appropriate to move forward with HPAI vaccinations of captively managed and free-flying condors...The Incident Command continues to collaborate with condor recovery partners to support release of vaccinated condors. Thus far, six vaccinated birds have been released across the range. In Arizona, The Peregrine Fund released the last rescued condor that survived an exposure to HPAI in the spring. Condor 757 had natural antibodies from the exposure but was provided a booster vaccination prior to being released earlier this week. Additionally, the Northern California Condor Restoration Program and the Service’s Hopper Mountain National Wildlife Refuge Complex in southern California have released a total of five vaccinated birds.”

[Wikipedia](#) quotes two sources for the number of condors in the U.S. In 2023, there were an estimated 558 condors and 94 of them have been vaccinated. So, now in 2024, vaccination has been carried out on more than 17% of the condor population.

Wildlife Service will determine how long the antibodies last. It is possible the condors might need to be re-vaccinated every year or so, a daunting task.

### **Deaths of Seals in New England**

A few years ago, more than 300 seals along the coast of Maine died from eating infected birds or as Jonathan Runstadler at The Cummings School of Veterinary Medicine at Tufts University in the Department of Infectious Disease and Global Health suggests in [an interview](#) with the Journal of the

American Medical Association “It’s certainly plausible that [seals] are spreading virus by droplet or aerosol to each other...They’re having interactions at close range, and a lot of vocalizations.”

“In June 2022, more than 330 harbor and gray seals had died from the virus — enough that the National Marine Fisheries Service immediately declared an “unusual mortality event.

In May 4, 2023 article by Andrew S. Lewis published by the Yale School of the Environment titled [Avian Flu Outbreaks in Marine Mammals Mark New Era for Deadly Virus](#) discusses the Maine seal deaths.

In an opinion differing from Runstadler, Deborah Fauquier, a veterinary medical officer with the National Marine Mammal Health and Stranding Response Program, says that “as of now, it appears that last summer’s outbreak of H5N1 in Maine resulted from bird-to-seal transmission.”

Importantly, Fauquier observes “that there have not been any positive H5N1 infections in Maine seals so far this year.” The last new avian flu virus infections of seals were seen in July 2022.

The fact that no seal deaths had occurred was an extremely positive development. Unfortunately, large numbers of [seal deaths have now returned](#) to locations in New England.

“When Dr. Jonathan Runstadler was called to the scene at Nahant Beach in March [of 2024], he found more than 70 dead birds littering the shoreline, including sea ducks, loons, and sea gulls...But of greater concern to scientists is this strain’s ability to infect mammals...Last month, a sick goat in Minnesota became the first livestock animal in the United States to contract H5N1, and within the last two weeks, the US Department of Agriculture announced that cows had been infected for the first time on farms in Texas, Kansas, New Mexico, Idaho, and Michigan...Most of the infected birds in Massachusetts live along the coastline, according to Andrew Vitz, MassWildlife’s state ornithologist. Data provided by the Department of Agriculture show an uptick in the state’s cases starting in mid-January, particularly in Canada geese...In addition to the dead birds in Nahant Beach, sick flocks have recently been reported in other parts of the North Shore, including Salisbury, Newbury, Plum Island, and Manchester-by-the-Sea...“It’s really not the time to let your dog off-leash on a beach and get a seabird between its jaws that may or may not be infected,” Hill said.

On Monday, the CDC said that existing bird flu vaccine candidates for humans could be manufactured quickly and that preliminary testing showed they could provide “reasonable protection” against H5N1 viruses.

“This is not like we’re starting from ground zero,” said Syra Madad, an infectious disease epidemiologist at NYC Health + Hospitals. “We’ve known about this [virus] for many, many years, and we luckily have effective therapeutics and candidate vaccines that can certainly be scaled up. From that standpoint, we’re at an advantage.””

### **Avian flu has spread to distant locations**

Erik Karlsson, a virologist at the Pasteur Institute in Cambodia said that Infected birds are “dead birds flying,” a phrase likely borrowed from “dead men walking,” which was used by prisoners to describe someone on their way to execution. The complete phrase “dead birds flying spreading the disease before succumbing to it” explains how birds can spread avian H5N1 infections to distant locations; and in particular explains why birds and seashore mammals in places such as the [Galapagos Islands](#) and [Antarctica](#), now have been infected with avian H5 N1 influenza. Also, it can explain that mammals far inland in the U.S. and inland elsewhere have become infected.

### **Do U.S dog and cat owners need to worry about picking up avian H5N1 infections from their food?**

Twenty-eight [domestic cats in Poland](#) have tested positive for highly pathogenic H5N1 avian influenza.

“Since 19 June 2023 the General Veterinary Inspectorate has begun to receive the first unofficial information from different parts of the country about cat infections with an agent of unknown aetiology. The infections had a high mortality rate.”

Since these were domestic cats living in “different parts of the country,” it is likely they were infected from eating highly pathogenic H5N1 avian influenza infected food purchased by the cat owners.

Do U.S. dog and cat owners need to worry about feeding their pets canned or dried dog and cat food? From the article titled [An Inside Look at How Canned Dog Food is Made](#) by Nancy Kerns in Whole Foods Journal, the ingredients and the final canned food is heat sterilized several times, which would kill the viruses and bacteria. Kerns visited three cat and dog food canning facilities in the U.S. Furthermore, it is unlikely that dried food can contain live virus since it is baked and dried, and likely sterilized previously as well.

Uncooked foods that are becoming popular to feed dogs in the U. S. is another story. There needs to be very careful selection of food sources to ensure that they are free of avian H5N1 avian flu.

### **What is the danger to humans?**

Will this avian flu virus kill us as well? So far, there have been very few human fatalities. [A June 28 2023 study published in Nature](#) by several authors identifies a single protein called BTN3A3 that protects humans and some other primates from the deadly and highly transmissible avian H5N1 flu virus. The study is authored by more than a dozen scientists mostly from Scotland. (BTN3A3 was [discovered originally](#) as a potential therapeutic target for breast cancer.)

Below is a shortened highly redacted version from the Nature article of the DISCUSSION section that outlines the protective properties of the BTN3A3 protein.

“Our study reveals that human BTN3A3 is a powerful barrier for the replication of avian IAVs [influenza A viruses] but not human IAVs...The anti-avian IAV properties of BTN3A3 arose in primates...We showed that BTN3A3 interferes mostly with avian IAV viral RNA replication, at the early stages of the virus life cycle.

Transmission of these viruses within farmed animal populations provide them with the opportunity to further adapt to the mammalian host, in addition to provide further opportunities for onwards transmission [spillover] to humans. Hence, H5N1 viruses with a BTN3A3-resistant genotype may be better posed in the future to adapt to humans.

Global efforts during the SARS-CoV-2 pandemic and over the years for IAV infections have shown that surveillance based on virus genomic sequences can be a useful tool not only to provide insight into disease spread and epidemiology, but also for the early identification of viruses with undesirable phenotypic traits from a public health perspective.”

The following more technical quote from the Nature article in the BTN3A3 evolution section illustrates the effort by the authors who carried out the study to find the origin of the BTN3A3 gene in various primate species.

“We then examined the origin of anti-avian IAV activity in the BTN3 gene family. Phylogenetic analysis of the BTN3A genes of the Haplorrhini suborder (tarsier, monkeys, apes and humans) indicated that BTN3A1–3 originated through two successive duplications after the split between the new world monkey lineage (Platyrrhini) and the old world monkey and ape lineage (Catarrhini) around 40–44 million years ago...Humans, chimpanzees (*Pan troglodytes*), gorillas (*Gorilla gorilla gorilla*), orangutans (*Pongo abelii*), macaques (*Macaca mulatta*) and green monkeys (*Chlorocebus sabaeus*) all have at least one BTN3A1 or BTN3A3 gene capable of inhibiting Mallard viral replication...The other

primate group does not make the protein. The evolutionary history of these genes could explain the many gains and/or losses of antiviral function.”

So, an accident of genome evolution that occurred millions of years ago, an extraordinary bit of luck, protects us from the new avian flu virus, at least for now.

There is concern, however, that the avian H5N1 virus might evade BTN3A3 to infect humans from a so-called “spillover” event. Spillover is the word used to indicate that an avian flu virus has mutated to now infect humans. Spillover events are what we must prevent.

[In a June 2023 article published online](#) by Laura Graf and Peter Staeheli largely confirms the study by the Scottish group and identifies a second protein, MX1. Both BTN3A3 and MX1 interfere with an early step of the viral replication cycle. The Graf and Staeheli article argues why we must be alert to identifying in advance potential spillover events, “Only by understanding the diversity of adaptive mutations that viruses must acquire for successful transmission into the human population will we be able to identify, in a timely manner, zoonotic IAVs that have pandemic potential.”

A recent study identifies [deaths from avian H5N1](#). “Globally, from 1 January 2003 to 26 February 2024, 887 cases of human infection with avian influenza A(H5N1) virus were reported from 23 countries. Of these 887 cases, 462 were fatal (CFR of 52%).” If we eliminate the deaths from 2003 through 2018 that were due to poultry workers being infected directly by birds with avian H5N1, the 23 deaths from 2019 onward (1+2+1+7+4+6+2) are much fewer, more in line with humans being protected by BTN3A3.

Clearly, the pandemic in birds and mammals is not over. Especially if you live near the seashore, observe shore birds to see if they are behaving normally going about their daily business. More than one dead bird or strangely behaving birds should be reported to local health authorities.

If COVID-19 virus can serve as an example, current versions of COVID-19 are much less deadly with generally mild symptoms compared to the deadly versions at the pandemic’s beginning. Also, avian H5N1 in cattle results in a mild infection that disappears. Most likely, the cattle have resistance to deadly infection. While less likely, the strain of avian H5N1 in cattle could be less deadly. It seems that some cattle avian H5N1 has spread to poultry. If this less deadly virus strain establishes itself throughout the virus population, a situation similar to COVID-19 might result.