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Vaccinating Wild Birds and Mammals to Prevent Suffering and Death from Avian H5N1

My policy efforts until recently have usually focused on supporting or criticizing published research by scientists or policy people. These efforts were focused mainly on the past. Changing my focus to studying the deadly and highly contagious avian H5N1 sweeping the globe necessitates suggesting research yet to be carried out to attempt to put this tragedy under control. Consequently, my efforts are focused on the recent present and the future. One prominent example is the recent discovery of the numbers of dairy cow and poultry workers catching only mild infections from avian H5N1.

BTN3A3 protein protects humans but not birds and mammals from avian H5N1 virus

At present, avian H5N1 virus is responsible for the death of hundreds of millions of poultry birds, of millions of wild birds, and of thousands of mammals, many of whom would otherwise be alive. The tragedy of these deaths is echoed by University of Washington experts Peter Rabinowitz, a professor of environmental and occupational health sciences and of family medicine, and Julianne Meisner, an assistant professor of epidemiology and of global health. Unfortunately, birds and mammals in the wild are not easily located to immunize them. the two UW experts just referenced and I share the concern for wild animals.

There is a reason that humans have avoided death. An accident of genome evolution that occurred millions of years ago, an extraordinary bit of luck, protects us from the avian H5N1 flu virus, at least for now. A June 28 2023 study published in Nature by several mainly Scottish authors identifies a single protein called BTN3A3 that protects humans and some other primates from the deadly and highly transmissible avian H5N1 flu virus.

Vaccines for the deadly and highly contagious avian H5N1 virus

Millions of doses of vaccine are being developed and held in reserve to be used in humans if an avian H5N1 pandemic is beginning. Vaccines are under development independently by two U.S. government agencies: an mRNA vaccine by the Biomedical Advanced Research and Development Authority, BARDA, and a non-mRNA vaccine by the U.S. Department of Health and Human Services, DHHS. For low- and middle-income countries an mRNA vaccine is being developed by the World Health Organization, WHO , which is expected to be completed in two years. There are likely other vaccine candidates in development as well. Presumably, these vaccines are directed at the clade 2.3.4.4b of avian H5N1 virus.

Pandemic or not, we should vaccinate targeted wild bird and mammal populations to develop immunity in them against the deadly and highly contagious avian H5N1. The first populations targeted should be

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animals that tend to congregate in large groups--for instance seals resting on sand at the water's edge, and Antarctic penguins. By vaccinating these large groups, we will at least rescue large numbers of birds and mammals from death. This won't solve the problem of deadly and highly contagious avian H5N1 sweeping the globe but would be valuable and straightforward to do. It could slow down avian H5N1 transmission.

There are proven methods for vaccinating wild animals. The Cornell University Wildlife Health Lab provides a method used successfully for a rabies vaccine.

> "Because giving shots to large populations of wild animals is difficult, an oral rabies vaccine was developed in the 1970s. The vaccine is contained inside a plastic pouch that is either inserted into a block of fish- or bone-meal or is coated with fish-meal crumbles.
>
> The fish scent attracts the target animals: raccoons, foxes, and coyotes. As they bite into the bait, the plastic sachet is broken, releasing the vaccine into their mouths where the vaccine can activate the [mucosal] immune system."

The vaccine delivery method can be employed for animals not in groups as well. The vaccine would be valuable to provide at least temporary protection to birds and mammals; and if we are lucky, it could provide longer-term protection.

Professor Massimo Palmarini's and colleagues recent work focuses on how avian H5N1 virus can bypass BTN3A3 protection. As quoted in a message to me:

> "It is also important to realise that barriers to cross-species transmission are multifactorial. There are many barriers blocking avian IAV replication in human cells (eg. receptor affinity in the HA, polymerase activity, restriction factors such as BTN3A3 and MX1 and others). Hence a single block by itself can be bypassed easily by the virus…. While it's far harder for the virus to bypass all these blocks. So, there are many avian viruses circulating that have an NP-resistant mutation bypassing BTN3A3…they are not immediately a risk…but if they also get a more 'mammalian polymerase'…and their HA can bring both mammal and avian receptor etc etc…it becomes a real issue."

This work warns us that BTN3A3 protection in humans may be bypassed; but it does not provide information on the opposite issue, how protection can be readily transferred to wild birds and mammals using CRISPR or by some other means.

Using CRISPR to insert a functioning BTN3A3 gene into targeted birds and mammals

The clade 2.3.4.4b of avian H5N1 virus will indeed kill wild birds and mammals as they are not protected by BTN3A3. This is the reason for exploring genetic engineering a functioning BTN3A3 gene into a targeted bird or mammal. Once delivered, that animal should be protected by the BTN3A3 protein.

Using CRISPR, "Fixing the break might disable a gene (the easiest thing to do). Alternatively, this repair might fix a mistake or even insert a new gene (a much more difficult process)." The obvious way to protect a population of animals is through mating, a painfully slow process; therefore, the prospects are dim for introducing the BTN3A3 protein into a population. Perhaps an expert in CRISPR has ideas on how to do this.

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Enlisting veterinarians to prevent pandemics

In the New Yorker, an August 14, 2024 article titled "The Veterinarians Preventing the Next Pandemic," the writer Rivka Galchen said

> "…infectious diseases that can move from an animal to a human. Diseases cross over very rarely, with less than a tenth of one per cent of animal viruses ever successfully making the leap. And yet from another perspective the crossovers are common: more than two-thirds of emerging diseases in humans have animal origins… Canine rabies was eliminated from the United States in 2004, but the disease persists in other animals. [Sally Slavinski, a veterinarian at New York City's Department of Health and Mental Hygiene] recalled the 2009 outbreak of raccoon rabies in Central Park, in which some five hundred raccoons needed to be trapped, vaccinated, and released."

This demonstrates the need for a vaccine for veterinarians for avian H5N1. A concern about vaccines under development for humans is that the developers may not want it to be released for animal use. The developers may even be under contract by the funders to not provide the vaccine for animal use.

In conclusion, vaccination of animals against avian H5N1 may have several benefits, the most important of which is slowing the spread of this deadly and contagious virus. And if it can be carried out successfully, providing populations of animals with BTN3A3 protection.