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What we know about avian coronavirus infectious bronchitis virus (IBV) in poultry — and how that knowledge relates to the virus causing COVID-19 in humans

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To better understand the challenges associated with the COVID-19 disease in humans, poultry health professionals can draw on their many years of experience attempting to control avian coronavirus infectious bronchitis (IBV) in poultry.

It's important to emphasize that the COVID-19 virus (SARS-CoV-2) is *not* associated with poultry or poultry products. Coronaviruses are divided into Alpha-, Beta-, Gamma- and Delta- coronavirus groups. Coronaviruses are responsible for a wide variety of existing and emerging diseases in humans and other mammals (including food animals) as well as in birds (including poultry). Diseases associated with coronavirus infections cover a wide range including respiratory, enteric, neurological, renal and hepatic.

The coronavirus that affects poultry (IBV) and causes respiratory disease in chickens is in the avian **Gammacoronavirus group**. Avian viruses in the Gammacoronavirus group do *not* infect or cause disease in humans.

The COVID-19 virus is in the **Betacoronavirus group** along with SARS-CoV and MERS-CoV. It was previously shown that SARS-CoV does not infect or cause disease in poultry (Swayne et al. Emerging Infectious Diseases Vol. 10, No 5, May 2004). Because the COVID-19 virus belongs to the same group as SARS-CoV and uses the same ACE-2 host cell receptor, it is highly unlikely that the COVID-19 virus will infect or cause disease in poultry, but it remains to be scientifically proven.

Based on the knowledge at hand, and the current lack of any evidence of bird infections with the COVID-19 virus, poultry and poultry products are not considered to be a source of COVID-19 infection for humans. The COVID-19 virus is primarily spread among people via respiratory droplets that contain the virus, with infections occurring via the nose, eyes and mouth. Although highly infectious, it is an enveloped virus — one that is easily killed by soap and common disinfectants. Below are some frequently asked questions regarding coronaviruses.

Where do coronaviruses come from?

Bats are widely accepted as the reservoir for mammalian (Alpha- and Beta-) coronaviruses. There are about 1,240 different bat species harboring as many or more different coronavirus types. SARS-CoV and MERS-CoV came from a bat reservoir, infected an intermediate host then jumped to humans. It is likely

that the COVID-19 virus originated from bats, Furthermore, preliminary data show some viruses isolated from bats to be close relatives. An intermediate host for the COVID-19 virus has not been identified yet.

The reservoir for avian coronaviruses, including IBV, is not clear. There are some closely related viruses in wild and domestic birds — pheasants, ducks, geese and pigeons, to name a few — but unequivocal evidence of a true reservoir is lacking.

Why is it difficult to produce a vaccine against coronaviruses?

Protective immunity against a respiratory disease like infectious bronchitis (IB) in poultry or COVID-19 in humans requires a strong local immune response.

In poultry, we achieve this by using live attenuated vaccines, but live coronavirus vaccines are difficult to produce because attenuation often renders them unable to produce a strong local immune response. Attenuation is accomplished by passage of the virus in a laboratory host system (embryonating chicken eggs or cell culture), but there is a fine line between attenuation and maintaining the viruses ability to infect and induce an immune response. Over attenuation renders the vaccine safe but not immunogenic, whereas under attenuation will create a vaccine capable of inducing a strong immune response but may cause a severe vaccine reaction. Then there is the problem of back passage of the vaccine in the host leading to a pathogenic virus.

Based on our knowledge of producing vaccines against IBV, production of a live attenuated vaccine against COVID-19 with acceptable safety and efficacy may prove to be very difficult.

What about using killed vaccines against coronaviruses?

There are killed (inactivated) vaccines against IBV for poultry, however they are also difficult to develop. Chemicals such as formalin or beta-Propiolactone used to kill the virus also can destroy the integrity of the spikes, thus yielding a vaccine that does not induce a protective immune response. In addition, for killed vaccines to be effective, they must be given after a live attenuated “priming” vaccine, which, as discussed above, has significant safety issues.

In humans, killed vaccines against respiratory viruses are used, for example against influenza virus, but this requires growing the virus to high titers, inactivating it and using safe adjuvants. This has proved difficult to achieve for human coronaviruses.

Why don’t we have recombinant vaccines against IBV in poultry? And could a recombinant vaccine be developed for the COVID-19 virus?

The coronavirus surface-spike glycoproteins are embedded in a lipid envelope and have conformationally dependent epitopes that induce neutralizing antibodies in the host. When the spike protein is removed from the virus envelope or when it is expressed in a laboratory system, those conformationally dependent

epitopes are not faithfully reproduced. Thus, vectors such as fowl pox and herpesvirus of turkeys have not been suitable vaccine platforms for expressing coronavirus spikes.

Spike protein production by the virus in a natural infection is very specific and difficult to mimic, thus other recombinant vaccines, such as DNA vaccines, RNA vaccines and subunit vaccines, do not accurately reproduce spike. Additionally, these vaccines usually do not stimulate adequate local immunity and have to be given many times to provide any protection.

Then there are genetically altered coronavirus vaccines derived from infectious clones. Making changes to the genome of the pathogenic virus to create a safe, attenuated live coronavirus vaccine that is still capable of inducing an effective immune response is complex and often results in non-viable viruses or insufficient protection. It can be a fast track to finding a vaccine candidate, but the safety of these live vaccines must be rigorously tested.

Fortunately, it is not all bad news. The immune system of a bird is very different from that of a human. What doesn't work in poultry may actually work well in humans. In addition, financially we can do a lot more in development and delivery of vaccines in humans than in poultry, where tight margins make it necessary for vaccines to improve the welfare of the flock while still yielding a satisfactory return on investment. The goals and performance parameters for human vaccines are obviously much different than production agriculture. Currently, there are many different coronavirus vaccines and platforms being developed or optimized for human use.

How do different serotypes/genetic types of coronavirus complicate vaccine development?

In poultry, there are many types (serotypes/genetic types) of IBV that do not cross protect. Consequently, recovery from one type does not immunize the bird against another type. For this reason, we have had to develop a number of different IBV vaccines (Ark, Mass, Conn, DE, etc.) to control the disease.

Fortunately, there appears to be only one type of COVID-19 virus circulating in humans. However, full genome sequencing has shown that the virus is changing. A number of mutations have been observed, but none appear to be maintained at this time, which suggests they are not important for transmission or virulence. From a vaccine standpoint, only one type of COVID-19 virus circulating in humans means that only one vaccine type should be needed to protect against this disease.

Are there treatments for coronaviruses?

For humans, we have antiviral drugs like oseltamivir (Tamiflu) for Influenza, but there have not been any successful drugs developed specifically for coronaviruses. Drugs against the viral-encoded proteases have been tried, as well as drugs that interfere with entry and egress of the virus from the host cell. These and many other potential antivirals are presently being tested by several companies.

Two drugs currently in the news, chloroquine and hydroxychloroquine are being examined for their ability to ameliorate COVID-19 infections. These drugs have been used against malaria, lupus and

rheumatoid arthritis for many years. Preliminary data out of China indicate that the drugs stop the spread of the COVID-19 virus in cell culture and are somewhat effective in treating humans. But, until controlled clinical trials are conducted, their effectiveness against COVID-19 remains a question.

It is likely that this pandemic will not be over anytime soon. In the meantime, follow the Centers for Disease Control and World Health Organization recommendations to protect yourself and your family. Poultry flocks do not appear to be at risk.

Web sites for additional information on COVID-19:

https://www.cdc.gov/coronavirus/2019-ncov/index.html

https://www.who.int/emergencies/diseases/novel-coronavirus-2019

Note: This statement was developed on behalf of the American Association of Avian Pathologists, an international association whose mission is to promote scientific knowledge to enhance the health, well-being, and productivity of poultry to provide safe and abundant food for the world. For more information, visit aaap.info.