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Vaccination against avian influenza

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Vaccination of birds against avian influenza (AI) is a hot topic currently in the poultry industry. While it may be the way forward for control of avian influenza, it is a complex endeavour with many aspects to consider. There are serious risks associated with poorly–implemented AI vaccination programs.

Planning a vaccination program

The aims of a vaccination program should be defined clearly from the start and aligned with the capabilities of vaccine candidates. Few vaccines prevent all infections, and consequently disease and pathogen shedding, and some induce waning, binary or partial immunity. Immunity may not last or may need repeated vaccinations to maintain sufficient levels (waning), and some individuals may never develop immunity while others react fully (binary immunity). A vaccine may achieve only partial immunity by failing to prevent infection or morbidity and mortality and (or) allowing shedding and further pathogen spread. Besides not achieving its purpose, partial immunity could select for increased pathogen virulence. Vaccines that convey only partial protection against infection and shedding may raise the infectious dose required and drive evolution of a raised pathogen reproduction rate. Animals that are protected from death, but are not prevented from shedding, may survive to spread virulent pathogen for longer (Barnett and Civitello, 2020).

Avian influenza vaccines

Swayne and Sims (2021) list the properties of an ideal vaccine for poultry, which include: 1) low cost, 2) effective in multiple species and (3) after a single dose, 4) easily applied to large numbers of birds, 5) ability to distinguish infected from vaccinated birds (DIVA), 6) effective in young birds (ideally day-olds) with residual maternal antibodies and 7) close antigenic match to field virus.

Leslie Sims has compiled a list of twelve aspects of good "Vaccine Stewardship", which were explained by David Swayne at an FAO meeting in April 2023 (Swayne and Sims, 2023) and by Sims at the Global Consultation on Highly Pathogenic Avian Influenza (FAO, 2023). These points include employing other mitigation measures where possible and not just relying on vaccination, using a vaccine that protects against circulating strains, and at the correct dose and time, and monitoring vaccinated birds to ensure immunity is achieved and maintained (with boosters if necessary). Circulating viruses need to be monitored for antigenic changes or new introductions that may require updating of vaccines. It should also be ensured that the process of vaccinating does not spread virus and the vaccination program must be regularly re-assessed to gauge its ongoing necessity and effectiveness.

Avian influenza viruses evolve rapidly through genetic mutation and reassortment of gene segments and vaccines against high pathogenicity strains can lose effectiveness fast. Vaccine seed strains must constantly be compared to circulating field viruses, and updated if necessary, to ensure continued protection and prevent extra evolutionary pressure. Vaccination may have been one cause of the rapid evolution, associated with antigenic variation, of the Goose-Guangdong lineage viruses that emerged in the 1990s. Cattoli et al. (2011) found higher evolutionary rates, and numbers of codons that were likely under positive selective pressure in viruses, from countries that vaccinated against HPAI H5N1, relative to those that did not. These countries had carried out unsuccessful vaccination programs, though other countries' programs had been effective. Possible causes for failure were poor vaccine coverage and poor vaccination monitoring. Vaccination against a low pathogenicity avian influenza H6N2 has been done in South Africa since 2001, with a vaccine derived from one of the two original sub-lineages. Viruses of both lineages, detected in 2012 and 2013, were compared with viruses from 2002 and there was a much higher mutation rate in the vaccine strain sub-lineage (Rauff et al., 2016).

Commercially available vaccines include 1) inactivated, adjuvanted whole virus vaccines, 2) recombinant vaccines with HA and (or) neuraminidase (NA) genes inserted into live virus vectors, such as Herpes and Newcastle disease viruses, 3) haemagglutinin DNA administered in a plasmid, 4) haemagglutinin (HA) antigen or virus-like particles grown in insect cells, and 5) defective-replicating alphavirus (da-H5; equine encephalitis virus) with a H5 AI virus gene insert.

Inactivated whole virus vaccines are most widely used, although introduction of new vaccine antigens can be slow and lag behind the development of antigenic changes in field viruses. Inactivated vaccines can induce a good humoral response but this can be transient and there is poor stimulation of cellular immunity, possibly related to the need to administer them parenterally.

Determinants of vaccine immunogenicity

Antigenic content of an avian influenza vaccine and the adjuvant, as well as antigenic match to the challenge virus, contribute to immunogenicity.

Adjuvants can be added to or built into vaccines to improve their performance in a variety of ways, including increasing the magnitude and duration of immune response. Adjuvants comprise a wide range of chemicals and compounds but a common function is to stimulate the immune system appropriately, to ensure an adequate response to the vaccine's active ingredient. Virus-like particle vaccines can display additional proteins that assist with stimulating the immune cells and ensure a robust response. Mineral oil adjuvants increase antibody production, partly by delaying release if vaccine and prolonging the immune response.

Immune response to a vaccine can also be affected by characteristics or physiological status of the recipient. Examples include sex, age, genetic factors, physiological stress, nutrition and immunosuppression caused by concurrent infection. Environmental factors known to affect immune response in poultry include toxin exposure, water deprivation , excessive heat and cold and overcrowding, and could also affect response to vaccination. Presence of maternally-derived antibodies in young animals can also suppress antibody response to vaccines.

Objectives and associated vaccine specifications (example of California condor vaccination)

The aims of a vaccination program should be defined clearly from the start. Do they include preventing virus transmission, or just disease and deaths? The objectives will then dictate minimum requirements for vaccine candidates, including the magnitude and duration of antibodies elicited in the target species, or closely-related species, and whether these are likely to achieve the desired objective.

As an example, the United States Department of Agriculture's Animal and Plant Health Inspection Service approved vaccination of critically endangered California condors (*Gymnogyps californianus*) (Fig. 1) after twenty-one out of 561 died from high pathogenicity avian influenza in March and April 2023. Approval was granted on the grounds that they are critically endangered, carefully managed and the small population allows monitoring and control of the vaccine. An inactivated vaccine was approved and trials in black vultures, as a less vulnerable species and relatively close relative of condors, were carried out to assess the safety and immunogenicity of the vaccine and the required dosing regimen. Since safety and satisfactory antibody levels were established, trials in a small number of captive condors started in July 2023. However, two doses were required to achieve antibody levels consistent with protection in 9/10 vultures and only 7/10 of the single-dose group had protective antibody levels (U.S. Fish and Wildlife Service, 2023). In such an endangered population and with probable outside sources of HPAI virus, 70% protection is probably unacceptable and even 90% may be too low. However, the risk that the vaccine will not be completely effective needs to be weighed against the resources required to carry out the vaccine program and the associated risks to the condors (injury, disrupted breeding etc.).

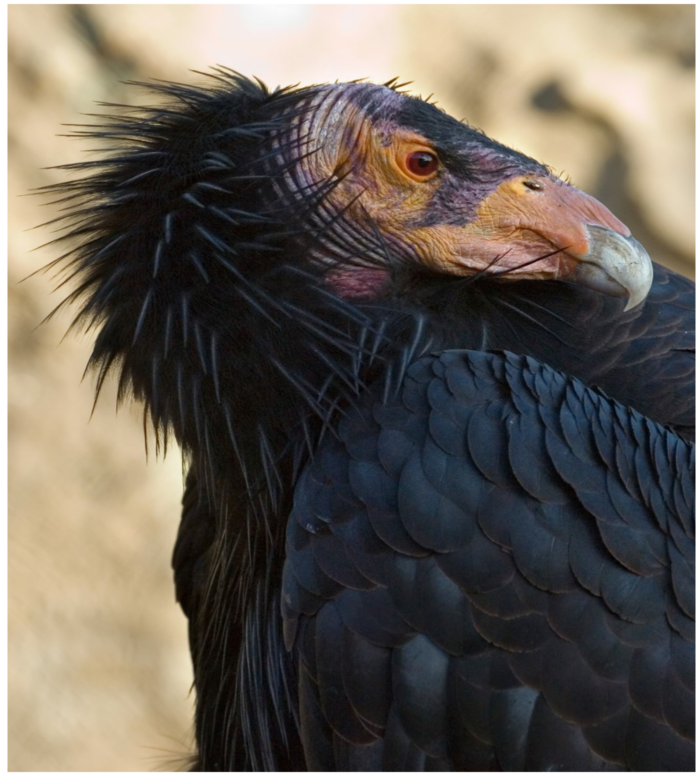

Figure 1: The California condor is a critically endangered species vulnerable to avian influenza. (Photo: C. Szmurlo)

Selected references

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New publication

Dr Laura Roberts et al. investigated the feasibility of vaccinating African penguins (Fig. 2) against avian influenza by doing a vaccination trial using two different types of vaccines. The study found evidence that vaccination using a tobacco leaf-produced H5 haemagglutinin-based virus-like particle could be a more practical and effective option than vaccination with inactivated whole viruses. The logistical challenges of wildlife vaccination require that the number of doses be minimized and further research should explore mass application methods.

The work was published this month as a short communication in the Veterinary Record. Read the full paper at: https://doi.org/10.1002/vetr.3616 .

Figure 2: African penguin parent and chick (Photo: D.G. Roberts)

Outbreak events

A **Cape fox** came into the town of **Velddrif** on the West Coast and attempted to enter houses. It appeared extremely aggressive, biting inanimate objects in its path, and had saliva and blood dripping from its mouth. The fox was killed and subsequently tested positive for **rabies**. A vaccination campaign was held in Velddrif in response to the case and approximately 120 dogs and cats were vaccinated against rabies.

Six **rock pebblers** (Fig. 3) kept as pets in **Swellendam** died over a two-week period. Samples taken from one of the parrots tested positive for *Chlamydia*, indicating an outbreak of **psittacosis**. The property was placed under quarantine and all remaining birds were treated with doxycycline. The owner was also advised of the zoonotic potential of psittacosis and precautions to take to avoid infection.

***Salmonella* Enteritidis** was cultured from chick box liners on four broiler **chicken** properties around **Worcester** and **Cape Town**. The parent flock is the likely source of infection.

A **horse** died near **Loxton** after showing clinical signs suspicious for **African horse sickness**, including swelling of the head and eyes and frothy fluid coming out of the nostrils.

Eight pet **rabbits** at a school in **Langebaan** died suddenly. The school reported that the rabbits had bloody discharges, so **rabbit haemorrhagic disease** is suspected to be the cause of the deaths.

Figure 3: Rock pebbler or regent parrot (Photo: J.J. Harrison)

Serological evidence of a previous infection with an **H6 low pathogenicity avian influenza virus** was seen after routine testing on an **ostrich** farm near **De Rust**.

A **pig** carcass from a farm near **Paarl** was condemned at the abattoir after lesions characteristic of **erysipelas** were seen on the skin after slaughter.

Two **cows** were treated for **mastitis** in **Genadendal** after clinical signs were seen during routine disease surveillance.

A **ram** recently brought onto a farm near **Vanrhynsdorp** developed dyspnoea and lack of appetite. **Pasteurellosis,** triggered by the stress of transport, was suspected and the ram was treated with antibiotics and anti-inflammatories.

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