Influenza control by vaccination

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The increased frequency of highly pathogenic avian influenza (HPAI) outbreaks during the past few years raises questions about the wisdom of current avian influenza (AI) control policies.

In the past when there was an outbreak once every three years somewhere in the world, we could afford to implement a 'stamping out' policy.

However, presently in a number of countries this disease has become more or less endemic. We need to fight AI with all available means, including vaccination. This is to protect our poultry, but of even more importance, to protect human lives.

The expected advantages of vaccination are two fold:

- Vaccination reduces susceptibility to infection. A higher dose of virus is necessary for establishing an infection in vaccinated birds. Reducing the amount of avian virus allowed to multiply in poultry also reduces the likelihood of virus mutation, caused by random errors in transcription.
- A significant reduction in the amount of virus shed by infected birds. A reduction in the amount of virus shed results in less AI contamination of the environment, which in turn reduces the risk of AI spreading to neighbouring poultry flocks or other avian species.

Group	Vaccine	Mortality	AGP serology (No. positive/total)		HI serology (GMT)	
			Pre-chall.	Post-chall.	Pre-chall.	Post-chall.
1	Control	10/10	0/10	NA	0/10 (<8)	NA
2	H5N2 (Mexico 1994)	0/10	10/10	10/10	10/10 (128)	10/10 (776)
3	H5N2 (Europe 1986)	1/10	9/10	9/9	9/10 (120)	9/9 (445)

Table 1. Efficacy of avian influenza vaccines, H5 subtype, administered to three week old SPF White Leghorn chickens, challenged IN with $10^{6.0}$ EID_{50} of a recent Asian isolate at three weeks post vaccination (six weeks of age) (Dr D. Swayne USDA/ARS Georgia).

Intramuscular vaccination in the breast muscle.

Reduced shedding also reduces the risk for humans in close contact with poultry (reducing the incidence of human infections reduces the chance of the AI strain reassortment with the possible emergence of a new human influenza strain).

Available vaccines

Conventional vaccines

These can be divided in two groups–inactivated homologous vaccines and inactivated heterologous vaccines.

The inactivated homologous vaccines are generally autogenous vaccines prepared from the field strain.

Efficacy of homologous vaccines has been proven, however the disadvantage is that no serological distinction can be made between vaccinated and field exposed birds.

Inactivated heterologous vaccines are prepared from a virus with the same H type as the field strain but a different N type (heterologous neuraminidase).

The immune response to the homologous H type ensures protection, while antibodies against neuraminidase of the field virus can be used as a marker for serology testing. It is important to monitor the vaccinated flocks for efficacy of vaccination and for virus circulation.

Assessment of vaccination should be done by HI test one month after the second vaccination. Twenty serum samples per flock should be tested and more than 70% of the tested samples should have a titre greater than 1:16.

The easiest way to test for virus circulation in vaccinated flocks is to regularly monitor clearly identified sentinels (30-60 chickens left unvaccinated in each house) for the presence of AI antibodies. If the sentinels seroconvert the flock is considered AI positive, and must be culled.

Recombinant vaccines

A pox vaccine is available with a H5 insert. The advantage of this vaccine is the absence of antibodies to any N (neuraminidase) in vaccinated birds. This is thus a true marker vaccine. The disadvantage of this vaccine is that it can only be administered to birds with no prior exposure to pox.

Poultry which already have immunity to pox, cannot be vaccinated with this vaccine.

Vaccination trial

The efficacy of AI vaccines should not only be judged on their ability to keep birds alive following challenge. The most important criterion is the reduction of virus shedding after challenge of vaccinated birds in comparison to non-vaccinated birds.

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Group	Virus isolation two days post challenge (titre per ml, log_{10} EID_{50})			
	Oral		Cloacal	
	Animals excreting virus	Average in excreting birds	Animal excreting virus	Average in excreting birds
Unvaccinated controls	10/10	6.16	10/10	5.82
H5N2 (Mexico 1994)	5/10	1.23	3/10	1.00
H5N2 (Europe 1986)	6/10	1.78	3/10	1.53

Table 2. Reduction of virus shedding after challenge in vaccinated and unvaccinated birds (Dr D. Swayne USDA/ARS Georgia).

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To demonstrate vaccine efficacy against the current Asian outbreak of H5N1we can look at the challenge trial conducted by Dr David Swayne, the laboratory director of South East Poultry Research Laboratory in Georgia (USDA/ARS).

Three week old SPF chickens were vaccinated with either an inactivated H5N2 vaccine based on a European isolate from 1986 or with an inactivated H5N2 vaccine based on a Mexican isolate from 1994.

An intranasal challenge with a recent H5N1 HPAI isolate from Asia was done three weeks after a single vaccination.

All the non vaccinated birds died after challenge, while from the 20 vaccinated birds only one died.

This bird was most probably missed during vaccination as it developed no antibodies to AI.

More important was the significant reduction in virus shed from vaccinated birds after challenge (70% of cloaca swabs and 40-50% of oro-pharynx swabs tested negative for virus reisolation).

In addition, the rate of shed from vaccinated birds that did shed virus was 10,000 to 100,000 times less than that of non vaccinated birds (see Tables 1 and 2).

The conclusion of this experiment was that a heterologous vaccine strain (H5N2) isolated more than 10 years ago still gave very good protection with a very significant reduction in virus shedding.

In case of an outbreak in a densely populated poultry area, all poultry in a 5km radius around the outbreak should be culled.

Around this 5km zone, a zone with a radius of 20km should be vaccinated.

All poultry should be vaccinated irrespective of age (0.5ml per bird in birds older than three weeks, 0.25ml per dose in younger birds).

Booster vaccination should be given 4-6 weeks later. If the primary vaccination was given to birds younger than three weeks, then a third vaccination is recommended at 16-18 weeks of age.

Vaccination of replacements

In high risk areas the primary vaccination has to be given at day old. Two booster vaccinations are recommended at 4-6 and at 16-18 weeks of age.

Vaccination half way through lay is advisable. In low risk areas the primary vaccination should be given at four weeks of age and a booster at 16-18 weeks of age.

As pointed out, monitoring of unvaccinated sentinel birds is of utmost importance to check if the field virus is circulating.

In conclusion:

- AI is a big threat to the health of humans and animals.
- To get this disease under control we have to use all the available tools.
- Good biosecurity is the most important tool, but vaccination also has an important role to play. ■