Experiences with vaccination in countries endemically infected with highly pathogenic avian influenza: the Food and Agriculture Organization perspective

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Summary
Vaccination has been used extensively for the control and prevention of highly pathogenic avian influenza (HPAI) caused by viruses of the H5N1 subtype in endemically infected countries. The Food and Agriculture Organization views vaccination as a legitimate aid in the control and prevention of infection and disease caused by HPAI viruses but does not see it as a panacea. Vaccination should be used as just one in a number of measures used together to reduce the effect and risk of infection. It will be required for a considerable time in endemically infected countries. The methods used in Vietnam in implementing blanket vaccination against H5N1 HPAI viruses demonstrate the steps that should be considered when introducing vaccination. So far, it has not been possible to determine the precise effect of vaccination in endemically infected countries because it has been used in combination with other measures. Well managed vaccination campaigns will reduce the incidence of infection in poultry and therefore reduce the risk to humans from these viruses. Vaccination was implemented to protect both poultry and humans, with a major goal being to reduce the risk of emergence of a human influenza pandemic virus. Economic analysis of vaccination should focus on cost-effectiveness of proposed strategies. Ex-ante and ex-post evaluation of vaccination campaigns should take into account the benefits generated in the poultry sector and for human health.

Keywords
Avian influenza – Control – H5N1 – Prevention – Vaccination.

Introduction

When Asian-lineage H5N1 highly pathogenic avian influenza (HPAI) viruses emerged and spread in Asia and later in Africa, Europe and the Middle East, only control measures other than vaccination (which have been referred to as ‘classical’ control measures [32]) were used to combat the disease initially. While these measures were successful in many countries, they did not eliminate infection in others, including the People’s Republic of China (hereafter referred to as China), Vietnam, Egypt and Indonesia (25). This ‘failure’ probably occurred because infection was already widespread before the control measures were implemented, there were weaknesses in disease management systems, in some cases there was limited cooperation from farmers, and reservoirs of infection developed due to the structure of the poultry production and marketing systems (9, 23).

The failure to eliminate H5N1 HPAI viruses resulted in the inclusion of vaccination in strategies to control and prevent
avian influenza, because elimination of virus from these countries would not be achieved in the medium term by classical measures.

Vaccination against H5N1 HPAI viruses was first used officially in the Hong Kong Special Administrative Region (Hong Kong SAR) in 2002 (26). This was followed by official programmes in a number of countries, including Indonesia, China, Vietnam, Russia, India, Pakistan, Egypt and Côte d’Ivoire (22, 28).

This paper reviews experiences with the use of vaccination against H5N1 HPAI in endemically infected countries and includes information on the successes, constraints and issues faced in conducting vaccination from the viewpoint of the Food and Agriculture Organization (FAO).

**Background information on vaccination programmes in endemically infected countries**

In this paper, countries are defined as endemically infected with H5N1 HPAI if disease or infection has been reported in multiple locations each year during the previous two years, and nationwide elimination of infection in poultry has not been reported. This definition includes at least four countries where vaccination is being used widely – China, Vietnam, Indonesia and Egypt.

A full analysis of the reasons leading to endemicity is not possible here, but some of the features that facilitate persistence of H5N1, and which are shared by these countries, are large numbers of small poultry flocks, complex market chains involving live poultry markets and, in some places, large populations of domestic ducks (9, 23) that intermix with gallinaceous poultry. Endemically infected countries do not have the veterinary capacity to closely monitor all poultry flocks.

**Vaccination in the People’s Republic of China**

China first reported outbreaks of avian influenza caused by Asian-lineage H5N1 HPAI viruses in poultry in 2004, but viruses in this lineage had been present in China since 1996 (2, 5, 34). Outbreaks have been contained by a mix of measures including stamping out and vaccination. The H5N1 HPAI viruses are still circulating in the country (16). Vaccination was officially introduced in early 2004, but unsanctioned use of vaccines against H5N1 viruses had occurred prior to this date (26). In 2007, over 13 billion doses of vaccine were used (Guo Fusheng, personal communication). Vaccination is compulsory in most parts of China except in certain disease-free zones, such as parts of Shandong Province. Ring vaccination (5 km radius) is used in a 3 km culling zone surrounding outbreak sites.

All avian influenza vaccines used in China have to be registered through national authorities. Only a small number of modern vaccination plants are licensed to produce vaccines against H5N1 HPAI (3).

In 2007, China used six different vaccines against H5N1 HPAI. Over 90% of vaccines contained killed antigens, produced by reverse genetics, in an oil adjuvant; the remainder were viral vector vaccines, predominantly using Newcastle disease virus as the vector.

**Vaccination in Indonesia**

Since it was first recognised in 2003, H5N1 HPAI has become endemic in poultry in parts of Indonesia. The early stages of the epidemic resulted in some 17 million birds being culled or lost due to disease (20).

Soon after H5N1 HPAI was identified, large commercial poultry producers implemented vaccination using a range of vaccines, both imported and locally produced. Vaccination in the commercial sector is not coordinated formally by government.

The Indonesian government introduced vaccination against H5N1 HPAI in early 2004 as one of the measures aimed at controlling the epidemic in small flocks of poultry (21). About 20 different vaccines have been registered. Most of the vaccines used in government programmes contain an Indonesian H5N1 antigen (A/chicken/Legok/2003). Vaccines containing H5N2 viral antigen have also been used. Vaccine and vaccination services were provided free of charge to the backyard poultry sector from mid-2004 onwards, but in 2006 and 2007, due to limited resources, they had to be focused on twelve high risk provinces. Duck and broiler populations are not vaccinated under government sponsored programmes.

**Vaccination in Vietnam**

Vietnam first reported H5N1 HPAI in late 2003 and embarked on a massive stamping out campaign that resulted in the loss of some 45 million poultry (30), with an estimated loss of US$117 million (20). Infection was not eliminated and by mid-2005 Vietnam had reported more human cases of disease (42 cases) associated with H5N1 HPAI virus (HPAIV) than any other country. Most of the human cases studied in 2004 followed exposure to sick or dead household poultry (4).
After receiving recommendations from a joint FAO/World Bank team and others, the Government of Vietnam introduced a number of additional measures, including blanket vaccination in designated high risk provinces/areas, currently conducted twice per year.

Most of the vaccine used in Vietnam contains a killed antigen based on A/Goose/Guangdong/96 in an oil adjuvant and is produced in China.

Vaccination in Egypt

Within weeks of the first official report on 17 February 2006, H5N1 HPAI was registered in most of the country’s governates, indicating that it had not been detected for some time and making viral elimination extremely challenging. On 6 March, Egypt introduced a policy of vaccination against H5N1 allowing the commercial sector to vaccinate. Later in 2006 a vaccination campaign in the backyard and rooftop production systems began. The current Government policy is to provide and deliver vaccine for village/scavenging poultry and to permit commercial companies to vaccinate with a registered vaccine of their choice. Between 1 March 2006 and 27 November 2007, 21 companies imported avian influenza vaccines from a total of six countries. Three vaccines have been registered, one rejected, and ten products are being assessed.

Vaccination in endemically infected countries: the Food and Agriculture Organization position

Use of vaccination for control and prevention of highly pathogenic avian influenza

Ever since H5N1 HPAI emerged as a transboundary disease in 2003 and 2004, FAO has been a strong advocate of the potential value of vaccination in the management of this disease. FAO has consistently recommended consideration of all measures available for control and prevention of this disease and adoption of the mix of measures appropriate to the situation in each country (8).

Consideration of the use of vaccination is particularly relevant to countries where methods other than vaccination have not been or are unlikely to be successful in eliminating infection.

FAO also supports the use of pre-emptive vaccination in uninfected places known to be at high risk of virus incursion, as has been implemented in Hong Kong SAR, in conjunction with other appropriate measures to reduce the risk of infection.

Emergency vaccination following outbreaks of disease has been used successfully in Hong Kong SAR (6) and appears to have contributed to containment of infection around outbreak sites in mainland China, although H5N1 HPAI viruses are still circulating in parts of this country (see below). The risks associated with emergency vaccination also have to be considered, especially in places where infection may already be widespread. Vaccination teams moving from farm to farm can spread virus if appropriate precautions are not taken (21).

FAO does not view vaccination as a panacea for avian influenza control. When used alone, vaccination will not eliminate infection. Nevertheless, it can reduce the levels of infection in poultry, and, consequently, the probability of human exposure to virus. Use of vaccination also provides time for other appropriate changes to be made to husbandry and marketing practices and/or structures that will reduce the long-term risk of infection. This approach was adopted in Vietnam where other measures are being implemented to enhance farm biosecurity and to reduce the risk posed by large live poultry markets (24). These measures will take considerable time, commitment and resources to implement. Poorly managed vaccination campaigns can complicate disease control and may even promote spread of disease.

In countries that include vaccination as a control and preventive measure, FAO supports the approach adopted in Vietnam where the following steps were taken.

Setting clear objectives for the programme

The objectives of vaccination in Vietnam were to reduce the levels of infection in poultry and the number of human cases. It was identified before the programme commenced that elimination of infection would not be achieved in the medium term given the many high risk production and marketing practices in place that needed to be addressed concurrently.

Obtaining high-level political support

Support for vaccination was obtained from the highest level of government through the provincial system down to the commune level. Without this support the initial campaign would not have been successful.

Obtaining and controlling sources of appropriately priced, quality-assured vaccine capable of protecting against circulating strains of virus

A limited number of vaccines were selected for use, including vaccines containing killed virus antigens and a
fowlpox vector vaccine (Trovac® Merial). These vaccines were all subjected to tests in Vietnam before being registered for use.

**Determining the extent and timing of the programme**

A decision was made to vaccinate all long-lived poultry in high risk locations using a blanket campaign centred mainly on and near the Red River and Mekong River deltas but also including other areas deemed to be at risk. The programme was based on two blanket campaigns per annum with one campaign designed to provide protection to poultry during the lunar New Year (Tết) festival, a period when considerable trade in poultry occurs. In the initial campaign two doses of vaccine were provided one month apart.

Small village flocks were included based on the epidemiology of human cases. Large commercial farms were permitted to use vaccine following the recommendations provided for administration by the vaccine manufacturer.

The timing of vaccination is a matter for individual countries to decide based on the objectives of the campaign and available resources. FAO generally prefers vaccination at the recommended age because the immune response to vaccination is usually better and there are fewer adverse effects on production. However, there are some situations where an intensive campaign involving poultry of all ages can be beneficial, such as the pre-Têt campaign in Vietnam.

**Testing vaccination logistics**

The blanket vaccination programme was tested in two trial provinces to assess logistical problems likely to be encountered when the programme was expanded. The trials demonstrated a number of issues, including training and payment of vaccinators, quality of vaccine guns, the time required to vaccinate small flocks, the need to improve information and awareness about vaccination, and issues with the cold chain and withholding periods. All of these issues were subsequently addressed.

**Regularly reviewing the control programmes**

Vietnamese authorities, with support from FAO, continuously review the control and preventive measures in place, including the vaccination campaign. A formal review is held each year to which local and international experts are invited. Several research studies have been conducted specifically on vaccination, including studies on the costs of vaccination and its efficacy against newly isolated viruses. These research studies are supported by regular post-vaccination monitoring. Vaccines are subject to further scrutiny and testing if field results suggest protection is less than optimal.

The vaccination campaign is evolving towards targeted vaccination. Some provinces already use vaccination at the recommended age as an adjunct to blanket campaigns. The programme will be modified as new information on the disease becomes available through research and surveillance.

Endemically infected countries that intend implementing vaccination should examine the experiences in Vietnam and elsewhere when developing their programmes and should seek support from international agencies and specialised institutes, such as the World Organisation for Animal Health (OIE)/FAO Network of Expertise on Avian Influenza (OFFLU), that are familiar with the strengths and weaknesses of existing programmes. The national strategy should be adapted according to the local situation, as is being done in Vietnam, which is making the switch from blanket application to more targeted vaccination.

Vaccination is clearly not necessary for control of HPAI in all countries, especially where surveillance systems allow early detection of all cases of infection and veterinary capacity allows control measures to be applied quickly. Control measures work best if applied before infection has a chance to spread widely or become established in populations of poultry that do not necessarily develop signs of disease such as domestic ducks, or lead to reports of disease, such as poultry held in infected live bird markets or traders’ yards. Areas with a high poultry density with birds reared under conditions of poor biosecurity coupled with complex market chains also appear to promote spread, and for control to be effective vaccination will probably be required together with appropriate changes to management.

When newly infected with HPAI viruses most countries will adopt control programmes without vaccination. However, FAO strongly recommends that disease contingency plans for avian influenza include an early review point to examine the probability of success (and adverse effects) associated with the initial control methods used (9). At this point the benefits of using vaccination as an adjunct to other measures should be considered. The review should assess the extent of infection and the capacity of veterinary authorities to determine where infection is occurring. By including this process in contingency plans any shift in policy from control programmes without vaccination to those that include vaccination can be readily justified without being considered a policy reversal.

It has been argued that the way forward for the poultry industry is the introduction of highly biosecure industrialised farms (reviewed in 10). While industrial production systems have their place, it is also important to protect small-scale producers who rely on poultry for
income and income diversity but are limited in their ability to implement or enhance measures to increase the biosecurity of their flocks. One of the ways of preventing disease and limiting infection in these flocks is vaccination, and this should be supported as long as the threat of HPAI persists, provided it is practical and cost-effective.

The types of poultry vaccinated will differ from place to place depending on the role they are seen to play in the transmission of infection and the availability of suitable vaccines for the target species. Vaccination of breeders, among other targeted populations, is essential if biosecurity measures cannot prevent infection of these valuable birds, and provides some protection via maternal antibody to newly hatched chicks.

**Vaccine selection**

Any vaccines used in control and prevention of avian influenza must comply with current OIE standards (33) and, most importantly, should afford protection against the viruses found in the country. Ideally, the vaccine antigen should be a close match to field strains, although the choice of vaccine is determined by a number of factors, including the cost, availability and quality of the vaccines.

FAO has supported and will continue supporting vaccination trials aimed at demonstrating the efficacy of vaccines in endemically infected countries. The Organization recognises that existing vaccines are imperfect and strongly supports the need for research into new vaccines suitable for cost-effective mass administration. The current method of vaccination using killed antigens, requiring individual injection of poultry followed by a booster injection, is an impediment to large-scale vaccination programmes, especially given the rapid turnover of poultry and the potential adverse effects on production of vaccination of poultry in lay. Where possible, FAO recommends priming vaccination in hatcheries, but this recommendation is contingent on availability of suitable registered vaccines that offer appropriate levels of protection and/or priming of the immune system for subsequent doses of vaccine.

**Stopping vaccination: exit strategies**

The ultimate goal of all control programmes for HPAI is elimination of the virus. However, FAO sees no prospect of global eradication of Asian-lineage H5N1 HPAI viruses in the medium term and possibly not in the long term. Given this prospect, vaccination may become a necessary measure for the long-term prevention and control of this disease in endemically infected countries even though this is not the desired outcome. Above all, long-term government sponsored vaccination programmes face problems of sustainability.

At present, the endemically infected countries using vaccination do not have a formal exit strategy from vaccination but, in most cases, still review the need for and extent of vaccination programmes regularly. Cessation of vaccination in these places will only occur once the risk of infection falls to levels that will allow a push towards elimination and sustained freedom from infection. The HPAI situation in neighbouring countries must also be taken into consideration before stopping vaccination. Nevertheless, within countries it is possible to stop vaccination within certain compartments and perhaps even zones depending on the nature of production systems. This has already been achieved in some parts of China and is the first step in reducing reliance on vaccination. China has achieved this by establishing systems of modern intensive poultry production in a number of provinces that reduce or even eliminate the need for vaccination (as has been done also in parts of Thailand). However, in other husbandry systems, such as free grazing systems, changes to the way that poultry are reared will take considerable time to implement (and may never be introduced), and therefore vaccination will be needed as one of the measures for control of infection until appropriate changes are made.

**Post-vaccination monitoring and surveillance**

Regardless of whether vaccination is used, appropriate surveillance systems and full disease investigations are required in all countries infected with H5N1 HPAI viruses (32). As the use of vaccination changes the context of surveillance, methods used for monitoring and surveillance will differ in places where vaccination is employed.

FAO is concerned about the possibility of so-called silent infection that can occur in vaccinated chickens, but is equally concerned about infected unvaccinated flocks that are sent to market as a coping mechanism by farmers in infected places (24). To increase the probability of detection of HPAIV infection in vaccinated flocks, the threshold for investigations should be modified so that less severe outbreaks, as can occur in infected vaccinated flocks, are investigated. This enhanced passive surveillance needs to be supported by extensive use of active surveillance measures to detect virus circulation, particularly in live bird markets.

Unless systematic post-vaccination monitoring and surveillance are conducted it is not possible to clearly establish the weaknesses and benefits of the vaccination campaign or to identify new strains of virus when they emerge.

Strategies that differentiate infected from vaccinated animals (DIVA strategies), in which a negative marker vaccine (1) is used as the sole vaccine, provide one method
of assessing whether infection has occurred in vaccinated poultry. However, interpretation of tests is complicated, in part due to the circulation of other avian influenza viruses (3, 33). The cost and technical issues relating to some DIVA tests also inhibit acceptance and, as a result, they have not been applied widely in Asia (17, 24).

Unvaccinated sentinel birds can also be used but have not been used widely in endemically infected countries because most farmers are reluctant to include unvaccinated poultry in their flocks and their management/identification is difficult. In endemically infected countries, it is not possible to have unvaccinated sentinels in all flocks. However, if certain populations of poultry are not vaccinated (such as Muscovy ducks in Vietnam) these birds can be used as sentinels. Other methods for monitoring flocks of vaccinated poultry, such as routine dead bird monitoring (33), should also be used.

FAO supports the use of proven surveillance technologies that help increase understanding of the epidemiology of avian influenza and prevent infected poultry from going to market. However, due to the large number of poultry flocks and the limited veterinary capacity in endemically infected countries it is not feasible to test all vaccinated flocks before sale. Potentially, surveillance could be focused on flocks deemed to represent a high risk of spreading disease. Even if such testing could be implemented it only provides information at one point in time (usually several days prior to sale) and would not guarantee that infected poultry did not enter market chains.

The surveillance system implemented should match the capacity of the country and the stage of the control programme. Poorly resourced countries invariably need to strengthen their veterinary surveillance capacity in order to ensure that appropriate surveillance measures are in place. A good surveillance system should involve the people who see the birds on a daily basis, but reporting is unlikely to occur unless they also see benefits in reporting potential cases of disease. The surveillance programme in a country approaching disease elimination will differ markedly from one where the goal is to reduce levels of infection.

Post-vaccination monitoring is conducted regularly in China and is reported every month in the Ministry of Agriculture's Official Veterinary Bulletin. The monitoring includes serological testing of vaccinated poultry in breeding farms, commercial farms, markets, slaughterhouses and small dispersed flocks. Results of the surveillance suggest high levels of seroconversion post-vaccination in the poultry tested, especially in chickens, with slightly lower levels of seroconversion in vaccinated ducks; this could be explained by differences in the magnitude of the serological response to vaccination in ducks compared with gallinaceous poultry. Each month, more than 300,000 serum samples are tested. Virological surveillance is also conducted and, through this testing, circulating H5N1 HPAI viruses continue to be detected.

Vietnam has also conducted considerable post-vaccination monitoring and surveillance. H5N1 HPAI viruses continue to circulate at low levels, as demonstrated by detection of infection in unvaccinated Muscovy ducks, occasional outbreaks of disease, positive results from market surveillance and detection of virus in smuggled poultry. Seromonitoring has shown that the level of protection in flocks decreases rapidly after about four months, which is probably due to a combination of declining antibody levels and introduction of unvaccinated poultry to previously vaccinated flocks.

Post-vaccination monitoring of village-based poultry flocks in sixteen districts in Indonesia, vaccinated under an operational research programme, is currently underway. At the time of writing results were not available.

**Antigenic variation and vaccination failure**

The possibility of emergence of antigenic variants poses a threat to vaccination campaigns. Potentially, an antigenic variant could arise when vaccination is used (13), particularly if vaccination campaigns are not implemented appropriately. This possibility has to be considered when planning vaccination programmes. Endemically infected countries should use vaccines in a way that minimises the risk of emergence of antigenic variants, as this has implications for the risk of infection for other countries and for preparation of potential human influenza pandemic vaccines. Given the low fidelity of replication of the influenza genome, the likelihood of emergence of genetic variants is probably highest in places where infection is widespread and poorly controlled. Therefore, vaccination is not the only driver of antigenic change and, in fact, can help to reduce the rate of mutation by reducing the amount of viral reproduction.

To minimise the risk of selection of antigenic variants, vaccination should produce a strong immune response in vaccinated populations (i.e. wherever possible avoiding partial immunity, especially at times of high risk of exposure to virus, which can potentially result in increased selection pressure for escape mutants). The reality in any blanket or ring vaccination campaign is that a proportion of the vaccinated poultry will have titres that do not provide protection. There are many reasons for partial post-vaccine immunity: prime vaccination without boosters, vaccines of low potency, immunosuppressive diseases, antigenic mismatching, an inappropriate vaccination schedule, an insufficient vaccine dose, exposure to virus before post-vaccinal immunity develops or an inadequate antigenic payload. Governments implementing large-scale vaccination should aim to reduce
the likelihood of partial immune responses by promoting best vaccination practices. Properly vaccinating all birds in all production systems is a highly challenging task.

The potential for emergence of antigenic variants is not sufficient reason for rejecting the use of vaccination, but efficient and sustained systems need to be developed that allow rapid detection of new strains of virus, the sharing of these viruses and the incorporation of suitable new antigens into vaccines when required. Efficient national monitoring of emergence of potential virus variants requires full collaboration between the poultry industry and veterinary authorities.

At present, in many countries a new set of safety and efficacy data has to be presented to registration authorities before a new antigen can be incorporated into an avian influenza vaccine. This contrasts with human influenza vaccines, for which it is expected that new antigens will be incorporated regularly and registration systems are designed to allow this to occur. Institutional bodies, such as OFFLU, should adopt systems for assessing antigens for avian influenza vaccines. Individual countries should examine the possibility of modifying registration procedures to allow changes in antigens without full re-registration.

The experiences in China and Indonesia are pertinent in this regard. China identified an antigenic variant H5N1 virus in 2006 and rapidly incorporated a new antigen (produced by reverse genetics) into vaccines for use in areas where this particular strain was present. Antigenic variants were detected in Indonesia in 2007 and although work is proceeding on development of a new vaccine seed strain for incorporation into vaccines, a new vaccine is not yet available and information on the extent of infection with antigenic variants is still being obtained.

Provision of information by China on antigenic variants when they were detected in 2006 (2) was welcomed by the international community and it is expected that variant strains will always be reported promptly, wherever they emerge.

Antigenic variants in Indonesia were detected through a collaborative project designed to evaluate the protection conferred by currently available vaccines against selected Indonesian H5N1 field viruses. To shed new light on circulating H5N1 field viruses as well as the efficacy of currently used vaccines, OFFLU has developed a project, implemented by FAO, to monitor avian influenza virus variants in Indonesian poultry, assess vaccine efficacy and design an effective and sustainable vaccination strategy.

Studies on vaccine efficacy are also being conducted in Vietnam to assess the effectiveness of different vaccines against local virus isolates in chickens, ducks and minor poultry species. Most H5N1 HPAI viruses in Vietnam fall within one of two main clades (Clade 1 and Clade 2.3.4). Occasionally, viruses from other clades (including Clades 3 and 7) have been detected (14). So far none of these appear to be significant antigenic variants based on preliminary results from challenge trials (K. Inui, personal communication). Several outbreaks of H5N1 HPAI have been reported in poultry vaccinated with fowlpox vector vaccine but it is not clear whether these were due to faulty vaccination or failure of the vaccine to protect against infection. Trials are continuing on the use of this vaccine under field conditions in chickens with pre-existing maternal antibody to H5 avian influenza viruses.

Antigenic variants have been detected recently in Egypt (31). Further information on their distribution and prevalence is being collected through a project similar to that in place in Indonesia, implemented by FAO.

Social and economic considerations of vaccination in endemically infected countries

A formal economic analysis was not conducted before vaccination was implemented in endemically infected countries. Nevertheless, it was evident in countries adopting vaccination that the control measures implemented previously had not succeeded in containing infection and the rise in the number of human cases demanded a different response.

Some studies have been carried out on the costs of vaccination (12, 15). These studies suggest that birds could be vaccinated at a cost per dose of between US$0.04 to US$0.14 depending on the production systems and the veterinary services (15). Cost-effectiveness analyses have begun to depart from using as the denominator the cost of vaccinated birds to using the cost of vaccinated birds at risk.

At farm-level, incentives to vaccinate will vary according to the production system, the producers' perceptions of disease risks and perceptions of the risk of prosecution if vaccination is compulsory but avoided.

Once a vaccination campaign is in place the incentives to vaccinate can change. A partially vaccinated population is likely to dampen the impact of disease and hence the need for individual producers to adopt actions such as vaccination to avoid the disease. This has been more clearly understood with vaccination against foot and mouth disease, but patterns of HPAI epidemics within countries currently vaccinating would suggest that current vaccination strategies may continuously change farm-level incentives to vaccinate.
A vaccination policy requires investments in veterinary capacity, covering both human and physical infrastructure. These fixed or investment costs are well recognised and without them the success of vaccination is not assured. Fixed costs can include costs for establishing facilities for monitoring viruses and the serological response to vaccination; for testing and certifying vaccines; for development and maintenance of an efficient cold chain; and for campaign management, including communications. The importance of having these fixed cost investments in place for general disease campaigns, including vaccination, has been detailed elsewhere (11).

In addition, the variable or recurrent costs relate to vaccine procurement/production, distribution and delivery to the birds, and post-vaccination monitoring and surveillance. The variable costs are the main costs used in assessing vaccination cost-effectiveness.

During vaccination campaigns, achieving high levels of efficiency will be the key to success and it is recommended that implementation should initially take priority over estimating the benefits.

All economic and social analyses must take account of the objectives of the campaign. The potential for H5N1 viruses to convert to a human pandemic influenza virus should be a major consideration. Although H5N1 HPAI is primarily an important animal disease and only rarely is transmitted to humans (resulting, however, in serious disease), the potential or projected costs associated with a human influenza pandemic dwarf these other losses and complicate cost-benefit analyses of vaccination.

In endemically infected countries where vaccination is used, the overall goal should be to adjust the amount of vaccine required to meet the objectives of the control programme. At present, the objectives are to reduce virus circulation so as to minimise the number of poultry outbreaks and to reduce the risk of human infection.

Analyses restricted to the costs and benefits to poultry farmers of alternative control measures are complicated because none of the control measures used in isolation guarantee protection from infection, the extent to which they do so is poorly defined, and the potentiating effects of measures used in combination may be greater than the sum of the benefits from the measures used alone.

The cost and effort required to manage and implement a large-scale vaccination campaign in endemically infected countries can be a disincentive for governments to engage in vaccination and should be estimated. Long-term, government-sponsored vaccination can also be difficult to sustain due to requirement for huge resources, negative perceptions of vaccination from earlier experiences affecting smallholder attitudes, and ‘vaccination fatigue’ at the field level (large-scale campaigns are extremely labour intensive). The potential for fatigue was recognised when vaccination campaigns were first implemented in Vietnam and forms the basis for targeting vaccination to selected high risk populations, with regular reassessment of the target population based on new information on the epidemiology of the disease from post-vaccination surveillance and disease investigations.

In countries with very large populations of smallholder and village poultry the cost and logistics of vaccinating are prohibitive, unless government sponsored vaccination campaigns are targeted at high risk areas, as has been done in Indonesia (21).

In Vietnam, vaccination is not used in some remote communities where the risk of introduction of virus is considered to be low due to the limited contacts with poultry traders outside of the local community (i.e. traders are the group considered most likely to introduce virus from elsewhere). Already in China, vaccination is not used in some highly biosecure farms in areas where the risk of infection is deemed to be low. These examples demonstrate that targeting of vaccination can reduce the overall cost of control programmes while not necessarily increasing the risk of disease.

Support from the private sector (especially the commercial sector) for vaccine campaigns should be encouraged and cost-sharing options elaborated. From commercial producers who see vaccination as a form of insurance this support is readily obtained. However, support is potentially more difficult to obtain from those producers who only see vaccination as a cost because disease occurs rarely in the birds they farm (e.g. duck farmers) or from those with minimal resources who do not normally invest scarce resources in their poultry (e.g. cash poor households that raise scavenging poultry).

In places where vaccine is required to contain or prevent H5N1 HPAI the aim should be to make vaccination a ‘mainstream’ activity, forming part of normal production practices, but it must still be controlled by government authorities so as to ensure that only approved vaccines are used, that supply of vaccine is regulated, that producers obtain approval to use vaccination, and that surveillance and monitoring systems are in place. Options that might encourage use of and payment for vaccines in endemically infected countries, such as preventing entry of poultry to live bird markets unless the birds are vaccinated (with audit checks on compliance), should be considered so that at least some of the cost of vaccination is met by farmers. The adverse effects of such a move (e.g. shifts to ‘black market’ sales of unvaccinated poultry) need to be considered.
Control programmes for avian influenza based on stamping out involve the destruction of infected poultry and sometimes surrounding flocks of poultry. This usually requires payment of compensation to affected farmers. Vaccination can help to reduce the number of poultry destroyed, therefore reducing the number of farms depopulated and the amount of compensation that has to be paid. This has significant social benefits.

FAO supports a public–private mix for funding of vaccination programmes to reflect both the public and private good components of vaccination campaigns. Cost sharing has to be tempered by the willingness of farmers to pay for vaccination, which, if not assured, will undermine compliance with vaccination programmes.

Communication with farmers, rural communities and veterinary paraprofessionals on the need for and benefits of vaccination, using tightly targeted campaigns, is essential if vaccination is to be successful.

Assessing the benefits of vaccination in endemically infected countries

None of the endemically infected countries have implemented vaccination alone – it has been coupled with other measures, making assessment of the benefits directly due to vaccination difficult to determine. For this reason it is not recommended that resources should be invested in calculating the benefits of HPAI vaccination in isolation, but rather that once HPAI has been brought under control and ideally eradicated a cost-benefit analysis of the overall strategy should be performed. This follows the models for the use of cost-benefit analyses for other major contagious disease control campaigns (6, 18, 19, 29).

In Vietnam, although vaccination in late 2005 was followed by a marked fall in avian cases and no human cases for a 12-month-period, it was not possible to ascribe all of these gains to vaccination. Nevertheless, investigations have revealed that the vast majority of subsequent outbreaks from late 2006 occurred in unvaccinated or improperly vaccinated poultry. In the first waves of outbreaks before vaccination was conducted approximately 45 million birds died or were culled. Subsequently, no more than a few thousand deaths in birds per wave have been reported and human cases have been reduced.

Results from Hong Kong SAR, the destination of a considerable quantity of live poultry from mainland China, provide one indicator of the success of China’s vaccination programme. Hong Kong SAR detected H5N1 HPAI viruses regularly in markets from 2001 to 2003. It was not until vaccination was introduced for all poultry destined for Hong Kong’s live poultry markets that no further cases of disease in commercial poultry and no positive swab samples from intensive virus surveillance in markets were recorded. This lasted from late in 2003 until June 2008 when a strain of H5N1 HPAI virus was detected in multiple markets during routine market surveillance. Preliminary studies suggest that this strain may be an antigenic variant (31) against which current vaccines may not provide adequate protection. If this proves to be the case and the variant strain of virus is widespread in southern China, new antigens will have to be incorporated into vaccines. This example also clearly highlights the essential need for concomitant intensive surveillance to accompany any vaccination programme since syndrome surveillance without laboratory analysis on appropriate collected samples becomes less sensitive in populations of vaccinated birds.

The large commercial sector in Indonesia uses considerable quantities of vaccine and the information available shows that vaccination has reduced the levels of disease and commercial losses in this sector, but outbreaks of disease still occur.

Overall, the government vaccination campaign in Indonesia appears to have had little impact on disease incidence, particularly at the smallholder and village levels. Although the number of reported human cases in Indonesia in 2008 has fallen slightly, the role of vaccination in this reduction is not clear.

As in Indonesia, the large commercial sector in Egypt has used vaccination as a tool to reduce the impact of the disease but successes with government-sponsored vaccination campaigns are still difficult to define and are insufficient.

Conclusion

Vaccination will play an integral role in the control and prevention of H5N1 HPAI in the foreseeable future, especially in countries with endemic infection. Ultimately, these countries are still aiming to eliminate infection and the use of vaccination can help to bring down the levels of infection until other preventive and control measures can be fully implemented, potentially allowing a push towards elimination of infection. Although it has been difficult to pinpoint the precise contribution of vaccines in achieving successes in control of HPAI in endemically infected countries, the combination of measures used in China and Vietnam (which included vaccination) appears to have drastically reduced the levels of infection. FAO will continue to support countries that choose to use vaccines to do so in the manner that minimises the costs of control programmes while reducing the likelihood of infection in poultry and humans.
L'expérience de la vaccination contre l'influenza aviaire hautement pathogène dans les pays à infection endémique : le point de vue de l’Organisation pour l’alimentation et l’agriculture


Résumé
La vaccination est largement pratiquée en tant que moyen de lutte et de prévention de l'infection due aux virus de sous-type H5N1 dans les pays où l'influenza aviaire hautement pathogène (IAHP) est endémique. Sans y voir une panacée, l'Organisation pour l'alimentation et l’agriculture (FAO) considère que la vaccination constitue un outil d’aide légitime en matière de lutte et de prévention de l’IAHP. Il convient néanmoins d’appliquer la vaccination en association avec d’autres mesures visant à réduire les risques et les conséquences de l’infection. Cette stratégie devra être appliquée durablement dans les pays où l’infection est endémique. Les méthodes appliquées au Vietnam pour assurer une couverture vaccinale complète contre les virus de l’IAHP H5N1 montrent les étapes à suivre dans le cadre d’une campagne de vaccination. Étant donné que les pays à infection endémique recourent à la vaccination en complément d’autres mesures de lutte, il est impossible d’établir avec précision l’efficacité de la vaccination pratiquée seule. Si elles sont correctement gérées, les campagnes de vaccination permettront de réduire l’incidence de l’infection chez les volailles ainsi que la menace que ces virus font peser sur la santé humaine. La vaccination a été introduite pour protéger les populations de volailles ainsi que l’homme, avec l’objectif majeur de réduire le risque d’émergence d’un virus pandémique de grippe humaine. L’analyse économique de la vaccination doit porter principalement sur le rapport coût-bénéfice des stratégies envisagées. Quant aux évaluations ex-ante et ex-post des campagnes de vaccination, elles doivent prendre en compte les retombées positives pour le secteur avicole et pour la santé publique.

Mots-clés
Influenza aviaire – Prévention – Prophylaxie – Sous-type H5N1 – Vaccination.

Experiencias de vacunación contra la influenza aviar altamente patógena en países endémicamente infectados, desde la perspectiva de la Organización para la Agricultura y la Alimentación


Resumen
En países endémicamente infectados, la vacunación ha sido un medio muy utilizado para controlar y prevenir la influenza aviar altamente patógena (IAAP) causada por virus del subtipo H5N1. Desde el punto de vista de la Organización...
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