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Background Paper

3. 2a i Implementing appropriate OIE/FAO prevention measures in different country contexts

Christianne Bruschke, Alex Thiermann, Bernard Vallat, OIE

Summary

The current highly pathogenic H5N1 strain with its rapid spread over continents and its pandemic potential has led to a global influenza crisis. Although the majority of the countries infected in 2006 succeeded in eradicating the disease, the situation in some endemically infected countries remains very worrisome. Re-emergence of the disease has recently been observed in several countries that had eradicated the disease earlier but these countries seem to be able now to get the virus quickly under control again. In few new countries (Bangladesh, Kuwait and Saudi Arabia) the virus has occurred for the first time in early 2007. Currently this HPAI strain remains primarily an animal disease with only occasional and incidental human infections. Therefore, the OIE and FAO recommend eradication at animal source and implementation of the following principles: early detection and early warning, rapid confirmation of suspects, rapid and transparent notification, and rapid response (increase of biosecurity, containment, culling of infected animals and disinfection and the use of vaccination when appropriate). It has been shown that countries that are able to implement these key control measures have been able to prevent establishment of the disease whereas a delayed or less adequate response may lead to an endemic situation. The main constraint to HPAI control is the weakness of the National Veterinary Services in many developing countries, which are in the frontline of the early detection and rapid response to the disease. Other important constraints are the poor laboratory capacities in many countries, the limited ability to implement biosecurity measures and control livestock movements especially in backyard poultry. Most countries do not have a compensation program implemented and many countries do not have a clear national chain of command and appropriate legislation. However, also in view of the risk of prevention of the development of a pandemic virus all countries should be able to detect and control the virus quickly in animals. Direct technical assistance and support should be given to endemic and newly infected countries where attention must be given to reducing the incidence of the virus. In countries with sporadic outbreaks the goal should be to eliminate the virus with implementation of good surveillance and response measures and countries that are still free from the disease should be supported in the preparation of contingency plans. On the medium and longer term capacity building programs to improve veterinary services including laboratories is essential. The OIE has developed an evaluation tool ("Performance, Vision and Strategy") to evaluate veterinary services and to define programs using national and international resources to help them to achieve the needed quality level as described in the OIE international standards of quality adopted by Member Countries.

Introduction

Avian influenza viruses can be divided into low and highly pathogenic strains. The low pathogenic avian influenza strains are commonly found in wild waterfowl and infection is detected regularly in poultry. Highly pathogenic strains have been globally but infrequently isolated and reported and outbreaks of the disease in poultry can normally be controlled and eradicated by implementing classical control methods.

However, the current highly pathogenic avian influenza (HPAI) strain H5N1 has led to an unprecedented situation spreading over three continents with high economic and social negative consequences. Millions of poultry have been killed or died and many people have lost their livelihoods. Poverty has increased in the affected areas in developing countries. Although financial resources have been targeted to the human health rather than the animal health field under pressure of a possible human pandemic, the main message of the OIE (World Organisation for Animal Health) and the FAO (Food and Agricultural Organisation), supported by the WHO (World Health Organisation), remains that the virus load in the environment and therewith the risk of a pandemic should be diminished by eradication of the virus at animal source. Vaccination is one of the important tools that may be used to achieve this goal (1, 2).

Strategy from the beginning: Eradication at the animal source of the disease

To reduce the virus load and circulation in poultry and spread to unaffected areas or countries, the OIE strategy focuses on the following key actions: early warning, early detection, rapid confirmation of suspects, rapid response and rapid and transparent notification. For all countries it should be made possible to implement these key actions for transboundary animal disease control. Early detection is based on a high awareness of poultry owners and veterinarians but for infections in wildlife it also relies on the awareness of the general public. The disease signs should be known and veterinarians should be able to follow up suspicions and to get a very quick laboratory confirmation of these suspicions. Rapid response includes different aspects like humane culling of infected animals, containment, movement controls and increase of biosecurity.

Vaccination can be a valuable additional tool in the response when necessary and appropriate. Experiences since the onset of the current AI crisis in 2003, has indicated that HPAI H5N1 is difficult to control especially in those countries that are not able to rapidly detect and immediately respond to the outbreaks. High quality veterinary services are the basis of animal disease control and eradication. Important constraints to the effective control of HPAI can be found in developing or in-transition countries since many of these countries have weak or nonexistent veterinary services. Often the veterinary services are understaffed and have insufficient financial resources. Proper legislation and a clear national chain of command are essential for a good animal disease control. This is often more difficult to achieve in countries with a highly decentralized political structure. A good compensation policy that is known to the animal owners is a good incentive for disease reporting. Animal owners that know that they will not be compensated for the losses when their animals are culled will probably choose a financially better option than reporting the disease like selling the diseased animals or using them for consumption. It should be recognized that for countries with weak veterinary services where it is difficult to implement the classical control methods, it will also be difficult to implement a good vaccination program including monitoring of the vaccinated animals for field virus circulation.

These countries often also do not have very good laboratory capacities with insufficient personnel and financial resources. Since HPAI is a global problem, international solidarity in combating the disease is essential.

International standards and guidelines on HPAI

As the international standard setting body for animal health, the OIE has defined standards on the notification, trade aspects and surveillance of the listed diseases. The Terrestrial Animal Health Code (referred to hereafter as the Code) (3) aims to assure sanitary safe international trade in terrestrial animals and their products. This is achieved through the detailing of health measures to be used by the veterinary services of the importing and exporting countries to guarantee the safe international trade of animals and animal products. Such measures aim to avoid the transfer of pathogenic and/or zoonotic agents without the imposition of unjustified trade restrictions.

The Avian Influenza chapter of the Code has been updated in 2004 taking into account the latest scientific information on the disease. The new chapter of the Code differentiates between low and high pathogenic avian influenza, defines HPAI as an infection of poultry and gives trade recommendations on poultry and poultry products like fresh meat, meat products, eggs but also feathers and down. The Code also provides guidelines for surveillance of the disease. The Code in several related chapters and appendices, also defines standards applicable to Avian Influenza such as the difference between an infected or non-infected country, zone or compartment; standards for declaring disease freedom; standards for trade; standards on conducting risk assessments; humane killing methods of animals in the event of the need for stamping out of infected populations; disposal methods for dead animals; biosecurity standards for poultry establishments and standards for the inactivation of viruses.
The accompanying manual of the Code is the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (referred to hereafter as the Manual) (4) which provides a harmonised approach to disease diagnosis by describing internationally agreed laboratory diagnostic techniques. To be able to compare the results of different laboratories in different countries the Manual should be followed and quality systems should be implemented in the laboratories. The Manual also gives general guidelines on the quality principles of veterinary vaccine production and guidelines for the development, production and use of disease specific vaccines.

During the current HPAI H5N1 outbreak the OIE has received many requests from member countries for guidance in the decision-making process whether to vaccinate or not and also for guidance in the design of vaccination programs. The OIE regarded these questions as very relevant and convened an *ad hoc* group on "Development of Guidelines for Avian Influenza Vaccination". This *ad hoc* group met twice and the outcomes were a general information document on avian influenza vaccination and a document with guidelines on the decision making process including a checklist on the essential needs for the establishment of a vaccination program.

The FAO and OIE have a new and updated global strategy for HPAI control that is based on the above mentioned principles.

Assessing the need for vaccination
Vaccination against avian influenza can be a very valuable tool in the control of the disease but it is also a logistically demanding and costly exercise. Therefore it is recommended to carry out a careful assessment of the advantages and disadvantages of implementing a vaccination program and the capacity and capability in the country or region to implement a vaccination program.

The first aim of vaccination is to induce a protective immunity in a flock and, thus, increase the resistance to infection, decrease the viral shedding of the birds and decrease the transmission of the virus. To be an effective tool, vaccination should not be used as a stand-alone measure but it should always be combined with other control measures like movement controls and increase of biosecurity and should provide for an exit strategy.

Current disease situation
Several steps need to be taken before a vaccination program for a particular country or region can be designed and implemented. First of all the current disease situation in the country should be analysed. This includes an assessment of the prevailing epidemiological situation and an assessment of the logistical requirements to conduct an effective campaign. The epidemiological assessment should focus on the risk of primary introduction as well as on the risk of secondary spread thereafter. All results of avian influenza surveillance in poultry and in wildlife should be included in the risk assessment. The status of neighbouring countries or trade partners should also be taken into account. Local trade, e.g. live bird markets, are seen as risk factors for the spread of the disease whereas pet birds and fighting cocks may also play a role.

Countries still free from HPAI should be aware of the risk of primary introductions of the virus into poultry populations from the previously mentioned sources. The risk of secondary spread is determined by the implementation of the necessary eradication measures when a first outbreak occurs. If the virus is already present in poultry, it is important to focus on the reduction of secondary spread to such a level that the virus can be eliminated locally. The response capacity with the classical control measures in case of an outbreak is an important factor in the decision whether to vaccinate or not.

Biosecurity
Low biosecurity levels increase the risk of a primary introduction on farms. In general, the risk of introduction of the virus increases with decreasing biosecurity levels. Some important biosecurity measures are: 1) poultry to be kept indoors ; if not possible, contacts with wild birds should be avoided or management practices should be instituted to mitigate the risk of contact, 2) to keep only one species of poultry on the premises, 3) to exclude pet birds from premises where commercial poultry is kept, 4) to use an all in – all out production system, 5) to avoid having ponds that attract wild birds to the premises, 6) to ensure that feed and drinking water for poultry is not accessible for wild birds, 7) to ensure that poultry workers do not have access to other birds, 8) to have a fence around the poultry house 9) that only those persons that really need to be there are admitted to the poultry house, 10) that persons change clothes and boots before entering the poultry house. In countries with many backyard poultry it is difficult to implement these biosecurity measures.

Poultry species
The poultry species reared is an important factor in the decision-making process since little is known of protective titres post vaccination other than in chickens and turkeys. It has been repeatedly documented that immunity in ducks and domestic geese wanes quicker than in chickens and these species would therefore require more frequent vaccinations. (5,6) Suboptimally vaccinated flocks might permit virus circulation to occur in a clandestine manner for some weeks. Human cases can be seen as a reason to start a vaccination program. Where poultry, such as ostriches for example, are reared under extensive farming systems and where it is often difficult to fully mitigate the risk of virus introduction from migratory wild birds, vaccination should be considered as a complementary disease control measure (7) If the risk of primary introduction or secondary spread is considered as being high, and/or if the virus spreads quickly and the classical response measures can not be implemented quickly, vaccination may be considered as an alternative option.

Implementation of vaccination
When, based on the above mentioned factors, a decision has been taken to implement vaccination in a country or region, a good vaccination plan should be designed.

Vaccine choice
First of all the choice for a vaccine strain to be used should be made. A vaccine should always be of high quality, produced according to OIE quality standards and licensed by

the national licensing authorities. Vaccines should be selected on the basis of evidence that the vaccine significantly reduces virus excretion from the vaccinated birds if they are subsequently infected and that the product is able to prevent virus circulation in the target species.

Before a proper decision on the vaccine strain to be used can be made, the haemagglutinin (H) type of the currently circulating field strain or the virus that is expected to be introduced into the country should be known. The haemagglutinin should be homologous between field and vaccine strain since this is considered the most immunogenic part of the virus (8). If only one H-type is circulating, a monovalent vaccine may be used. In such circumstances it is not necessary to use vaccines containing more than one virus strain. Bivalent vaccines containing H5 and H7 strains will protect against both circulating H-types. If there is a risk of AI incursions of either or both subtypes H5 and/or H7 it is advisable to use a bivalent vaccine. The neuraminidase (N) of the vaccine can be either homologous or heterologous to the circulating virus strain. A heterologous N- type vaccine strain can facilitate the detection of circulating field virus in the vaccinated flock using serology.

Vaccine strategies

Different vaccine strategies such as emergency, preventive and routine vaccination can be applied in different field situations. The term emergency vaccination is mostly used when vaccination is performed to create a buffer zone in the area most at risk in an epidemic situation. Emergency vaccination is often implemented as a ring vaccination in a defined area around an outbreak to prevent the virus spreading further and to protect the environment around the outbreak. However, even when implementing emergency vaccination it remains essential that infected flocks are culled and other measures like movement controls, disinfection and increase of biosecurity are implemented.

Preventive vaccination can be applied when a country or region faces a significant risk of AI introduction, and the risk assessment shows that other prevention tools will not be efficient enough and that it will probably not be possible to implement response measures quickly enough to prevent further spread. A DIVA strategy, which means a strategy in which vaccinated animals can be distinguished from (vaccinated and subsequently) infected animals should be part of such a vaccination program.

Routine vaccination can be an appropriate method in countries and regions where the disease is endemic and where the classical control cannot be effectively implemented to eliminate the virus. The primary goal of vaccination can be to protect smallholder livelihoods and reduce economic losses due to mortality and morbidity, but the final goal should be to reduce spread and eradicate the virus. Generally, in endemic areas it is difficult to control the disease without vaccination. Nevertheless, it is strongly advised to also implement classical disease control measures whenever possible in addition to vaccination. From a financial and livelihood viewpoint, the cost of maintenance of an effective vaccination program is a significant factor. Used properly, routine vaccination can be valuable in reducing mortality and production losses. In the longer term, it could also decrease the prevalence of infection to a level where stamping out and surveillance could be applied and the disease could be finally eradicated.

All three strategies can be applied in a mass or targeted manner. Mass vaccination is applied to all susceptible birds in a country or part of a country. All poultry are to be vaccinated. The choice for this option can be made when it is unlikely that an outbreak (present or at risk) can be controlled in any other way. With targeted vaccination only defined categories of birds are vaccinated. When there is insufficient vaccine available immediately for mass vaccination, or when insufficient financial or personnel resources are available, a choice of categories to be vaccinated can be made based on the risk

analysis. It may be decided to vaccinate only certain species, certain compartments or only one or more of the sectors 1-4 or it may be decided to vaccinate only valuable parent flocks. A risk analysis addresses the bio-security levels of the holdings, the value of the flocks and the extent of the threat of the infection. The compensation mechanism in the case of an outbreak will influence willingness to notify disease outbreaks and therefore also the decision whether to practice targeted vaccination.

Vaccination plan

Each country should have a control strategy and contingency plan for avian influenza and be prepared to deal with any outbreaks. A vaccination plan should be an integrated part of the overall contingency plan and should be made in advance to identify those logistical, personnel and financial aspects that influence the campaign. It should thus be clear in advance to all people involved which actions need to be taken if an outbreak occurs and how the necessary control measures, such as culling and movement restrictions will be implemented. The chain of command should also be clear. A very important and often difficult aspect is the cold chain needed in the vaccine storage and distribution. Currently there are no vaccines available that are thermostable and would not need these cold chain facilities. Each country needs to have the facilities to maintain the quality of the vaccine according to the instructions of the manufacturer.

Arrangements should also be made to ensure that imported vaccines do not remain for a long period at customs at the airport. The number of vaccine doses to be ordered is dependent on the number of poultry to be vaccinated and on the capacity of the veterinary services to implement the vaccination program. A factor often not taken into consideration and which is essential in calculating the number of doses needed and the logistics of a vaccination campaign, is that to ensure effective immunity levels, follow-up vaccinations will be necessary. The vaccination schedule, the number of birds, the personnel resources to apply the vaccines and the required equipment should thus be taken into account to provide for both initial and follow-up vaccinations. All steps in the vaccination plan should be communicated to the stakeholders, e.g. farmers, veterinarians, laboratory personnel, consumers, public, decision makers, authorities, donors, etc.. Vaccination of free-range village poultry presents special logisrtical and technical problems which need to be carefully assessed.

Vaccination monitoring

Since AI vaccination does not always protect fully against infection and transmission of field virus there is a possibility of virus circulation in a vaccinated population. (9) It is therefore strongly advised to implement a post vaccination monitoring or surveillance system to provide data about circulation of field virus including analysis of possible antigenic drift. Moreover, monitoring systems can also help to determine if and when vaccination has been applied, and the extent of vaccination compliance. However, although it is not a preferred situation, if monitoring cannot be implemented, vaccination campaigns can still be carried out. The disadvantage in that case is that it will be unknown whether there is still virus circulation in an area and it will be difficult to plan and implement an exit strategy. Furthermore when field viruses are not isolated, mutations will not be detected. Therefore, surveillance and monitoring system is highly recommended.

To implement a monitoring system several factors have to be considered. First of all the infrastructure to conduct laboratory tests should be available. This includes laboratory equipment and necessary reagents, qualified technical personnel and implemented quality control systems. Another prerequisite is that sufficient qualified field staff should be available to visit farms and take samples. The samples should be transferred to the laboratory preferably under cold conditions. Telephone, fax, data transfer systems, record keeping and identification systems should be working

properly. It should be recorded which farms have been visited when, the location of the farms should be known, as well as the type of holding, the species involved, the dates of vaccination, batch used, etc. To monitor vaccination compliance, serum samples should be taken regularly to determine the level of vaccine-induced antibodies. The main purpose of monitoring is normally to detect virus circulation in a vaccinated population. This can be done by implementing the DIVA principle. In the case of avian influenza the DIVA principle can be achieved by the following ways. Firstly serological tests based on detection of antibodies against the neuraminidase of the heterologous vaccine can be used. For example when an H5N2 or H5N9 vaccine was used in the current H5N1 outbreak a serological test detecting antibodies against N2 or N9 can be used. If these specific serological tests against a different N-type are not available sentinel birds that are not vaccinated against AI and that are properly identified can be placed randomly in the vaccinated population. These birds should be monitored clinically and serum samples should be taken regularly for serology to detect antibodies against AI. An infection with low pathogenic AI may also lead to positive serology and each positive serology should be carefully followed up. When the animals show clinical signs of AI, tracheal and cloacal samples should be tested immediately for the presence of field virus and all mortality should be tested for AI as well. When rapid tests are used in the field as follow up a confirmation in the laboratory should be performed. Only tests as described in the Manual and approved by the OIE should be used.

To detect virus circulation in an area or region, targeted surveillance in high risk places, for example live bird markets, can be considered. Since antigenic drift may occur after implementation of vaccination strategy if virus is isolated, AI typing should be carried out in Reference Laboratories.

Legal framework

Some countries do not have an effective legal framework to implement the control measures against HPAI and it is not always clear which regulations apply to the control of HPAI. The decision makers should supervise and support the vaccination campaign and should facilitate the implementation of these measures. In poor countries a first round of vaccination could be paid by public resources but for the longer term, a cost sharing policy should be made available and farmers should be informed well in advance about the costs of the vaccination.

Exit strategy

Each vaccination program should also contain an exit strategy. Vaccination is an expensive measure and is a logistically demanding exercise for the Veterinary Services. When it is possible to further control the virus with the classical control methods, vaccination should be stopped. The epidemiological situation has to be monitored carefully before an exit strategy can be applied. Although it cannot be determined in advance whether the campaign will be successful, an exit strategy should be developed. In addition to this, measures that can reduce the risk of new introductions should be developed and implemented.

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