OFFLU Review paper[1]

Animal intervention strategies under different epidemiological and field conditions that can reduce risk of zoonotic infection

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This paper reviews the combinations of control and preventive measures applied in poultry for avian influenza and the reasons why the measures have been recommended and/or applied, taking into account local epidemiological situations, field observations and other scientific information that provide justification for the measures introduced. It highlights areas where gaps in knowledge exist and the research needed to fill these gaps. It also examines other non-technical factors that are (or in some cases should be) taken into account when developing and recommending control measures. The approach differs from most other reviews because it uses existing recommendations and practices as the starting point and then examines the scientific basis for these recommendations rather than commencing with a review of the scientific literature.

Avian influenza as a zoonotic disease

Although precise pathways for human exposure to avian influenza viruses are rarely determined, most primary cases of Influenza A (H5N1) are likely to be due to direct or indirect contact with infected poultry (i.e. virus from infected poultry in the environment (reviewed by Van Kerkhove et al 2011)).

From first principles, any measure that reduces the incidence of avian influenza virus infection in poultry is expected to reduce the likelihood of direct or indirect contact of humans (and other mammals) with infected birds. This, in turn, would be expected to reduce the probability of cases of infection and disease in humans, adaptation of the virus in mammalian hosts and the potential for emergence of a human pandemic virus. These observations/conclusions provide the scientific basis for introducing

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measures to control and prevent infection at source, in poultry when building measures to protect public health.

The validity of this approach is supported by cessation of human cases of Influenza A(H5N1) after control measures were introduced in poultry, as demonstrated in a number of countries after elimination of virus from poultry, including Hong Kong SAR in 1997. In some places, a reduction or cessation of human cases followed a reduction in the incidence of infection in poultry after a range of measures was introduced (e.g. Vietnam in 2006, Hong Kong from 2001-2003 when viruses were still present in markets) (Sims 2007).

Measures applied for control of avian influenza in poultry are usually designed and implemented by veterinary services but, given the public health aspects of this disease, human health authorities should be involved in decisions on the measures to be applied.

Apart from public health concerns, another important objective is to minimise the damage done to the livelihoods of poultry owners and producers (including millions of poor households) as a result of the control measures introduced (Rich and Perry 2011, Sims 2007). In most countries the adverse effects of control and preventive measures have not been measured, except in a few specific cases (see Rich and Perry 2011 for a general discussion and specific examples in Knight-Jones et al 2011, Kaleta et al 2007, Aral et al 2010).

Application of measures for control of avian influenza and measuring benefits

The measures adopted for control and prevention of avian influenza depend on:

- the subtype and strain of the virus (e.g. H9N2 versus H5N1 subtypes);
- the effects of the virus on poultry production and poultry markets (e.g. export markets for Thailand);
- the perceived or known risk of the particular virus to humans; and
- the country/place concerned (e.g. countries in Western Europe versus South East Asia, commercial sector versus village level poultry), including issues such as the financial resources available, the structure of the poultry sector and veterinary/animal science capacity, which in turn determine the likelihood of success in eradication campaigns (Sims 2010).

Following the spread of H5N1 highly pathogenic avian influenza (HPAI) in Asia in 2003-04, it was recommended that all available measures should be considered when developing programs for control and prevention of avian influenza, and the appropriate mix for each country or place adopted. In other words, a ‘one size fits all’ approach to control and prevention of avian influenza does not exist (see, for example, FAO 2004) and programs based on single measures are rarely successful in preventing infection. As a result, the way measures are used to control and prevent infection of poultry with influenza viruses differs between countries. These recommendations were based on earlier experiences with HPAI and low pathogenicity avian influenza (LPAI), including those from 1997 onwards with disease caused by viruses of the H5N1 subtype in Asia. .

It is also becoming accepted that control and prevention of avian influenza requires a whole of chain approach (FAO 2011a, Rich and Perry 2011). Prevention of avian influenza often requires changes to the way poultry are reared and sold and therefore appropriate policies to facilitate these changes (Sims 2007, Sproul et al 2009).

The use of a multifaceted approach means that the benefits derived from individual interventions for avian influenza have not been determined in most developing countries, in part because limited data are available, but also because measures were usually applied in parallel, often without 'control' populations.

Better information is also needed on the manner in which measures are applied (with a number of studies conducted on this aspect but yet to be published). Poor implementation of any measure will not be successful. Examples abound where stamping out, vaccination, cleaning and disinfection, movement controls and supposed improvements in biosecurity (measures that are known to be effective elsewhere at reducing the risk of infection and discussed in more detail below) did not achieve the desired goals because of the way they were applied. The manner in which measures are implemented depends on a number of factors including, but not limited to, the quality and standards of veterinary services, the support for the measures by poultry owners, and also political and economic decisions that take into account matters beyond technical advice on disease control (see, for example, Pongcharoensuk et al 2011).

Specific measures for control and prevention of avian influenza

Approaches to control of H5N1 HPAI have been developed through observations and experiences gained over the past 15 years with control and prevention of this disease, many of which remain unpublished in peer reviewed journals. However, further studies have been conducted on key factors such as the importance of domestic ducks and live poultry markets in the transmission and persistence of influenza A (H5N1) that were identified at an early stage through isolation of virus from healthy ducks and from poultry or poultry faeces in poorly regulated markets (Chen et al (2004), Sims et al 2005) providing additional evidence for their importance in countries where these two potential 'reservoirs' exist (for example, Gilbert et al 2006, Martin et al 2011b, Wan et al 2011). It is evident from these and other studies that there are many complex factors at play in determining where H5N1 HPAI virus occurs and persists (Hogerwerf et al 2010), and that anthropogenic factors play an important role in disease transmission (Paul et al 2010), as can wild birds (for example, Ottaviani et al 2010). Most of these issues were considered when devising control and preventive measures for this disease when it emerged as a regional problem in 2003-04 and as a global problem from 2005 onwards (FAO 2004, FAO 2008, FAO 2011, OIE 2011a) given that similar observations have been made since the earliest known (and successful) attempts to control outbreaks of HPAI (Halvorson 2009).

Observations from the field (high number of human exposures, small number of human cases) indicate that Influenza A (H5N1) is a low attack rate zoonotic disease, a feature of the disease that has been exploited when implementing control measures aimed at minimising the effects of influenza A (H5N1) viruses on public health in countries where the virus is endemic in poultry. The introduction of vaccination in poultry in Vietnam is one example in which the over-riding goal was to reduce the risk of human exposure (Domenech et al 2009). It was recognised when this measure was introduced that it would only reduce the incidence of infection in poultry, not eliminate the virus, but would, potentially, provide time for other measures to be adopted.

Clearly, the risk of human infection remains wherever infection persists in poultry and contact occurs between poultry and humans. Therefore it has been recommended that all countries with infection in poultry should work towards virus elimination (FAO 2008).

When countries report disease outbreaks to OIE for the World Animal Health Information Database (WAHID) they provide information on the measures used to control and prevent the disease. Most lists of measures appear to be similar but the outbreak duration and eradication time of the disease varied from country to country (OIE, 2011b), with several countries indicating that the disease remained endemic. The fact that similar measures have been applied successfully in most countries but in others the disease persisted demonstrates the need to understand the differences between countries that have been successful in eliminating virus from poultry and those where infection remains endemic.

Appropriate measures for these countries have been discussed in a publication on countries with endemic infection (FAO 2011b). This publication describes modifications made to control and preventive measures that reflect the realities of the epidemiological situation in these countries, the production systems in place, existing veterinary capacity, and the level of commitment (from producers to central government) to country-wide elimination of virus. These factors were believed to have favoured persistence of virus. The conclusions were based mainly on observations of the affected countries rather than purposive scientific studies. However a number of the conclusions are supported by other studies aimed at identifying risk factors for infection across a number of countries (see, for example, Hogerwerf et al 2010, Martin et al 2011a).

For countries with endemic infection in poultry it has been recommended that control and prevention (and eventual elimination) should be approached progressively using a measured and rational approach with a clearly defined strategy, objectives and an appropriate adaptively managed work plan (FAO 2008). This recommendation was based on a review of the information on control measures available at the time. Three country types were identified in which slightly different approaches were required – those free from infection in poultry, those that are recently infected and those where virus is endemic. For those places free from virus in poultry the focus is on appropriate preventive measures and development of systems for rapid case detection. For countries that are recently infected the objective is rapid elimination of the virus from poultry. Field evidence suggests that this approach has been successful in most places given that most countries that reported disease caused by Influenza A (H5N1) viruses in the past 7 years have eliminated the virus. Only a small number of countries remain endemically infected but these are places with large complex poultry production and marketing systems and other constraints to virus elimination described above.

An important aspect of all control and preventive measures is that those affected by the measures have to see valid reasons for their introduction (Rich and Perry 2010, Wiegers and Curry, 2009)) and that 'top down' approaches to control and prevention that do not consider the various actors involved are not always effective (Bett et al 2010).

Stamping out

The 'classical' approach to HPAI control and elimination based on early detection and stamping out has proved to be effective in most cases for elimination of HPAI and some LPAI viruses from poultry. It can result in large scale destruction of poultry in affected areas with high concentrations of poultry as occurred in Canada (Bowes et al 2007) and the Netherlands (Stegeman et al 2004). However, the persistence of H5N1 HPAI in Egypt, Indonesia, China, Vietnam and Bangladesh resulted in modifications to the approach to control and prevention of this disease because the viruses remained entrenched in these countries even after application of 'classical' approaches to control based around stamping out when the disease was first reported.

Limited culling of known infected flocks and direct contacts has replaced wide area culling in most countries with endemic infection in poultry, including Vietnam and China. Some other countries have also adopted this approach. Evidence for the benefits of limited culling includes successful programs in Thailand and Hong Kong SAR (in outbreaks in 2001, 2002, 2003 and 2008).

For HPAI, for which there is no known long term carrier state (on an individual bird basis) and limited duration of survival of the virus outside the host, especially in tropical and sub-tropical areas, it is highly likely that outbreaks in areas with low concentrations of poultry and limited poultry movement will be self limiting – a factor that should be considered when planning responses to outbreaks especially if wide area culling is being considered.

A number of modelling studies on stamping out for avian influenza have been conducted and the results have been summarised (Stegeman et al 2011). The value of any model depends on the quality of the data on which it is constructed and this has been a limiting factor for many of the models developed for avian influenza in Asia. Spatial models for outbreaks in the Netherlands, where good experimental and field data are available, suggest that only through mass culling can disease be brought under control in areas with very high poultry farm density and that focusing of stamping out on farms likely to generate high numbers of secondary cases is, potentially, a more effective strategy than other methods of culling (Te Beest et al 2011). Models of transmission in Great Britain suggest that most outbreaks of HPAI would probably not proceed beyond the initial infected farm (Sharkey et al 2008) but if a large outbreak occurred wide area culling would be the most appropriate strategy from a control perspective provided the high economic and social costs of this approach were also considered (Truscott et al 2007). What these studies and field experiences show is that even with stamping out there are various options to consider and that the method used depends on the nature of the poultry sector in the infected area and the extent of spread of the virus.

Further studies are needed to determine the most appropriate and cost effective strategies for disease control and prevention especially in places at high risk of disease outbreaks, bordering infected countries, where disease has recurred over several years as a result of re-incursion of viruses (e.g. West Bengal). At present wide area culling is the method of choice in India (see, for example, Kapur 2008).

Some of the potential negative effects of wide area stamping out that have been observed include resistance from farmers and movement/sale of poultry ahead of culling operations; animal welfare issues when culling poultry in remote locations or poor countries; and the cost (both direct costs and indirect costs to those affected) as was the case in the early response in Vietnam where some 40 million poultry were culled, especially if the culling program does not result in sustained freedom from infection because not all infected flocks are detected (FAO 2011b).

These issues are compounded if compensation for affected poultry farmers is not available or does not cover a significant portion of the value of culled birds. In all cases where stamping out is applied as a control measure current recommendations state that compensation should be paid to affected farmers to minimise the losses following reporting of disease (World Bank 2006). Availability of compensation does not guarantee all cases will be reported as was demonstrated in outbreaks in Hong Kong in 2002 and Japan in 2004. Surveys of farmers and traders in developing countries also demonstrate this effect (Bett et al 2010) but field observations suggest that availability of adequate levels of compensation probably results in better reporting than in places where no or poor compensation is given. Some countries claim they do not have the resources to pay compensation or pay at levels that are too low to stimulate disease reports, which mean other methods, need to be found to encourage reports, including training and support of community-based animal health workers to detect and report disease. Adverse effects of compensation (including corrupt practices) observed in other programs have also influenced some countries in their decision not to pay compensation for avian influenza. Most observations on compensation, including suggestions regarding appropriate levels of compensation have not been subjected to scientific studies quantifying the effectiveness of compensation as a driver of reporting or the adverse effects of a lack of or too little compensation on disease reporting. Experiences with compensation from Nigeria, where (eventually) high level compensation was apparently paid and virus was eliminated, warrant closer examination to assess whether the link was causative. In Turkey, contract farmers working for integrated companies were not covered by compensation programs and suffered considerable losses (Aral et al 2010) demonstrating that even when compensation is available it may not be paid to those who grow the poultry, reducing its effectiveness as a tool for encouraging disease reporting.

Ultimately the success of stamping out depends on early detection and elimination of infected animals. It will not be successful if disease reporting and surveillance systems are not sufficiently robust to detect all cases when they first occur, as is the case in most of the countries where influenza A(H5N1) viruses are endemic in poultry. The key factors are the incentives/disincentives for reporting by farmers, the quality of animal health services (Hamilton and Bruckner 2010) and also the nature of the disease (in particular, whether or not it is apparent to farmers or animal health workers that their poultry may have avian influenza – which is not necessarily the case with LPNAI). Unless active surveillance programs are in place most outbreaks of LPNAI will not be detected (see, for example, European Union Reference Laboratory for Avian Influenza 2011, OFFLU 2011). Even H5N1 HPAI viruses may not be detected without active surveillance in markets and domestic water fowl populations as is the case in China where no outbreaks of disease in poultry due to H5N1 HPAI virus have been recorded up to end October 2011 but virus is still being detected in markets. Vaccination can also complicate surveillance and therefore it is necessary to build appropriate surveillance programs to detect virus circulation in places where vaccines are used. In places with mass vaccination programs involving millions of poultry, such as the ones that have been used in China and Vietnam, resources are not available to test every flock for evidence of infection but sufficient samples should be collected (often through targeted surveillance) to ensure viruses circulating in vaccinated poultry are detected and characterised (Sims 2010).

As with control measures for H5N1 HPAI, surveillance systems vary from place to place. Recommendations on influenza surveillance for poultry have been made (OFFLU 2011) with the design of surveillance programs depending on the objectives and the resources available (Cameron 2011). Much emphasis has been placed on participatory surveillance and response in Indonesia for H5N1 HPAI (Azhar et al 2010) whereas more traditional methods of disease reporting and surveillance are used in China and Vietnam. The Indonesian system appears to have provided better information on disease prevalence at the village level than the systems in China and Vietnam but it is not yet clear whether the overall benefits outweigh the cost of obtaining the information about this disease, which, despite the regular detection and response, is proving difficult to eliminate.

Stamping out can be used for LPAI as it is with HPAI but is usually confined to outbreaks caused by viruses defined as low pathogenicity notifiable avian influenza (LPNAI) – that is, viruses of the H5 and H7 subtype that have not acquired (but have the potential to acquire) characteristics of high pathogenicity viruses. Alternatives to whole farm depopulation out have been used in the United States for some outbreaks of LPNAI, including the use of vaccination and controlled marketing. Significant cost savings occurred as a result of implementation of modified approaches with a 10:1 cost benefit calculated for a program incorporating vaccination and controlled marketing over total depopulation for one large layer farm complex infected with an LPNAI virus (Halvorson 2009). This is but one example of cases where alternative approaches to classical stamping out have been used to eliminate LPAI from poultry flocks. Vaccination has also been used in Italy for similar purposes for elimination of LPNAI (Capua et al 2009).

At present, few farms are depopulated following infection with influenza viruses of the H9N2 subtype, which is endemic in poultry across much of Asia and the Middle East.

Some LPAI viruses are poorly transmissible between poultry (Gonzales et al 2011); others such as H9N2 viruses are readily transmitted with some strains capable of spread via the airborne route (Shi et al 2010), a factor that should influence the design of control and preventive measures for this disease.

Vaccination

Many of the issues related to vaccination for control and prevention of avian influenza have been reviewed previously (CAST 2007). This review highlighted many of the gaps in knowledge on vaccination programs and discussed the ‘science’ and ‘art’ of vaccination, both of which need to be considered when planning and implementing vaccination programs.

Well managed vaccination of poultry can reduce the risk to humans by reducing the quantity of circulating virus. Used alone, vaccination will not normally eliminate HPAI but it can be used as one of the tools for doing so, as was the case in Mexico (H5N2 HPAI) and Hong Kong in 2002 (H5N1 HPAI) (Sims et al 2005).

In most outbreaks in newly infected countries, vaccination against HPAI probably has a limited role to play except to protect valuable birds or those at high risk of infection such as poultry reared outdoors. Implementing emergency vaccination requires plans and resources (including suitable vaccines, which could be made available from vaccine banks (OIE 2011c)) to be in place well before an outbreak occurs. Modelling conducted in Australia on simulated outbreaks in the intensive poultry sector suggest that emergency vaccination would have limited benefits compared with other strategies at least for moderate sized outbreaks (Hamilton 2011). Modelling of simulated outbreaks in the UK also suggests emergency vaccination would not be required to control outbreaks of HPAI (Truscott et al 2007).

If countries with endemic infection in poultry see few prospects of virus elimination in the short term it has been proposed that they should assess whether and how vaccination can play a role in minimising the damage done by the virus, including reducing the probability of human infections, while other measures to control and prevent the disease are gradually introduced (FAO 2011). This process involves questions regarding the logistics of vaccination delivery such as the capacity to deliver vaccine of appropriate quality to the places where it is needed and when it is needed, the cost of the program and issues related to rates of turnover of poultry and effects on population immunity (Hinrichs et al 2010).

A number of countries with endemic infection in poultry have concluded that vaccination has a role to play and it has been used as one of the measures for disease control and prevention in, China (Chen 2009) and Vietnam (where large scale government sponsored programs have been implemented) and also Indonesia and Egypt (where much of the vaccination has been done by the private sector) (Domenech et al 2009). Not all countries where H5N1 virus is endemic have opted to use vaccination even in parts of the poultry sector where vaccination could potentially be delivered effectively, such as the large scale commercial layer sector, for which supply chains for other poultry vaccines are already in place. It is important to understand the basis for decisions not to use vaccines.

Not all vaccination programs have been implemented well and the lessons from these programs need to be assessed when considering vaccination as part of a control or preventive program (Peyre et al 2009). Targeting of vaccination is recommended (Hinrichs et al 2010) and has already been used in Vietnam where vaccination has been focused on areas perceived to be at higher risk including the Mekong and Red River deltas, and in China where export farms implementing high level biosecurity measures do not use vaccination against H5N1 HPAI viruses. Studies on alternate vaccination strategies for Vietnam in which comparisons were made between different methods to improve targeting of vaccination have been completed but results are not yet available (USAID).

Many factors influence the quality of the immune response generated by vaccines, including the timing of vaccination (affected by pre-existing maternally derived antibodies) (Abdelwhab et al 2011, Poetri et al 2011), the quality of vaccines (antigen content and the quality of the adjuvant, vaccine storage)

(Kumar et al 2007, Eggert and Swayne 2010), the number of doses (Ellis et al 2006), concurrent diseases, the species or strain of bird being vaccinated (see, for example, van der Goot et al 2007), and, perhaps most important of all, whether or not poultry are actually vaccinated (failure to vaccinate rather than vaccine failure) (FAO 2011b) .

Potentially, partial immunity in vaccinated populations could help to drive the emergence of viruses that can evade vaccinal immunity (escape mutants) and therefore every effort should be made to stimulate a strong immune response in at-risk vaccinated poultry populations using vaccine antigens that are well matched to field strains (even though considerable cross protection to antigenically distant strains is provided by avian vaccines). Antigenically variant avian influenza strains have emerged (Tian et al 2010) and it is possible that vaccination is playing a role in driving evolution of some antigenic variants (Lee et al 2004, Cattolli et al 2011). Vaccination programs should be designed to stimulate a strong immune response. However, if vaccines are used widely it is expected that antigenic variants will emerge (as they do with human influenza viruses) given the difficulty in developing and maintaining high level immunity in all vaccinated poultry. Antigenic variation in avian viruses has implications for human pandemic preparedness in selecting strains for candidate human pandemic vaccines (WHO 2011), a process that is already in place and supported by provision of data by OFFLU on avian isolates derived from disease investigations and surveillance programs.

There are merits in developing improved vaccines and vaccination programs, including programs that stimulate both arms (humoral and cell mediated) of the immune system to broaden protection, as is the case with many other avian vaccination programs. New vectored vaccines for H5N1 HPAI viruses under development potentially offer advantages over existing vaccines containing killed antigen or can be used in combination with them (Liu et al 2011, Rauw et al 2011) but their benefits need to be assessed under field conditions.

Maintaining mass vaccination campaigns is expensive but the cost has to be weighed up against that of other control and prevention options as well as the extent of reduction of risk to the human population of a human influenza pandemic (brought about because of transmission of virus from poultry to humans and subsequent adaptation in humans). The economics of large scale vaccination have been reviewed (Hinrichs et al 2010).

In China and Vietnam it has not been possible to determine the precise role of vaccination in reducing the threat to humans although it is appears that the risk has fallen over time given the reduction in the number of reported human cases. Again, a causal link has not been firmly established. In Vietnam, the introduction of vaccination in 2005, along with other measures, was followed by a period in which no new poultry outbreaks were reported, no peak of cases occurred during the Tet festival in 2006 and no human cases were reported for over 12 months. At least one modelling study (based on reported cases) suggests some positive effects in Vietnam on reduction of transmission of virus in poultry between communes (Walker et al 2010), providing indirect evidence of the benefit for humans.

The absence of virus-positive poultry in Hong Kong markets after full implementation of vaccination of poultry destined for these markets (other than one antigenic variant strain in 2008) also provides support for the benefits of a well managed vaccination program in reducing exposure of humans to influenza A(H5N1) viruses. The introduction of other measures to markets including a single rest day had not prevented reinfection of these markets (Sims 2007).

The nature of vaccination programs also needs to be considered when assessing effectiveness of vaccination. Maintaining high level flock immunity is difficult in places with high rates of turnover of poultry. However, it may be possible to aim for high levels of immunity at certain times of the year just prior to high risk periods (which was the basis for the initial mass campaign in Vietnam in 2005 given the seasonal peaks of occurrence in the period around the Tet festival in 2004 and 2005). More work is needed to understand the effectiveness and risks of such targeted strategies especially the effect of waning immunity on selection for antigenic variants if the program leads to infection occurring in sub-optimally immune birds as their immunity wanes.

As HPAI (regardless of the subtype involved) is still regarded as an eradicable disease (and has been eliminated from poultry in most countries when it occurred), long term vaccination without an exit strategy is not recommended by FAO and OIE. Nevertheless, it is evident that vaccination against H5N1 HPAI will be used as part of the preventive program for this particular disease for some time in some countries with endemic infection in poultry and those where the risk of infection remains high. Such long term use of vaccines does not necessarily signal acceptance of endemic infection. Rather, it is a reflection of the time required and difficulties encountered in making the necessary changes to production and marketing systems and improvements to animal health and production services needed for further progress towards elimination of the virus. These other factors probably contributed to the disease becoming endemic in the first place; on-going vaccination as the main conrol measure in the face of endemic infection, without other changes and measures will not result in virus elimination.

Another potential negative effect of vaccination against HPAI is that it removes the signal of clinical disease in poultry for detection of infection in chickens (less so in ducks where, for some strains and older birds, infection can already be subclinical without vaccination) (Sims 2010). This is counterbalanced by the likely reduction in virus excretion if well vaccinated poultry are subsequently infected, which reduces the risk to humans. In most recent human cases (in 2011) in rural areas, disease in humans has been preceded by deaths of poultry in the village (e.g. all cases in Cambodia which on a per capita basis has had the most human cases in 2011) suggesting it is not the absence of the signal of poultry mortality that is the main issue but rather failure to report disease in poultry when it occurs. Nevertheless if vaccination removes the signal of clinical disease but does not reduce virus shedding in poultry subsequently exposed to the virus there are public health disadvantages in using vaccines. Experimental evidence suggests that this can occur in ducks given a single dose of vaccine (Eggert and Swayne 2010)

Vaccines are used widely to reduce the effects of H9N2 avian influenza in poultry flocks in many parts of Asia and the Middle East. Few governments in affected regions control access by farmers to these vaccines, other than through drug registration procedures. Vaccines are also used for LPNAI in Mexico and have been used successfully to control LPNAI outbreaks in Italy (Capua et al 2009). Vaccines were also used successfully as part of the control programs in large farms in the US that were not fully depopulated as described in the previous section (Halvorson 2009).

Alternative methods for raising resistance of poultry to influenza viruses are also being explored with development of transgenic chickens. While the initial results were interesting (did not prevent disease in experimentally infected birds onward transmission was prevented) (Lyall et al 2011) much more work and societal support for such measures are needed if they are to be adopted in the future

Biosecurity measures

Biosecurity measures introduced to farms or in markets to reduce the likelihood of introduction of HPAI viruses can markedly reduce the risk of infection of poultry and provide a return on investment (Fasino et al 2011). A key constraint is that the measures must be cost effective for the production system and producer (Sims 2008). Most small village flocks in Asia are not confined, despite some advice to the contrary, because once the birds are confined it costs more to house and feed them. The appeal of scavenging poultry to villagers is that they can be reared with virtually no financial input. This demonstrates that the measures proposed for small scale poultry producers must be practical and affordable, focusing in particular on behavioural change and simple cost effective measures. Egypt represents a special case because most smallholder poultry are reared in buildings or on rooftops (Fasino et al 2011) rather than as scavenging flocks.

Some production systems cannot be made ‘biosecure’ such as free grazing of ducks but this does not mean that these systems should be banned. Instead, other ways to protect these poultry must be found such as better controls on movement (not always easy to implement) and vaccination, especially if high level immunity can be generated at an early age.

Markets and traders’ yards are considered important points in market chains for virus transmission and persistence (Abdelwhab et al 2010) and for human infections (Wan et al 2011). Improvements in hygiene and changes in management practices such as market rest days or bans on overnight keeping can help to reduce the likelihood of infection occurring and persisting but unless strict controls are placed on sources of poultry, reinfection will occur. The appropriate number of rest days depends in part on attitude to risk. In one study in Hong Kong, using H9N2 virus as the marker, two rest days were shown to offer little or no improvement to a single rest day (Lau et al 2007). From first principles the banning of overnight keeping would be effective at preventing markets becoming permanently infected given the duration of stay will be less than the incubation period of the virus. However this requires all birds in stalls to be sold on a daily basis and increases the financial risk for traders (who are paid substantially more for live than dressed poultry) especially if fluctuations in demand are difficult to predict). The experiences from Hong Kong SAR are noteworthy here with most stall holders opting out of the live poultry trade when this measure was introduced albeit after being provided with ex gratia payment.

Biosecurity measures should be based on examination of each of the potential pathways for virus introduction at each point along production and marketing chains and to ensure that appropriate, cost effective measures are in place to minimise the risk posed for each pathway. The main pathways for introduction of influenza viruses are live poultry, wild birds, feed, water, rodents and other pests, people, vehicles and other fomites and possibly local airborne spread (Sims 2008). A number of case-control studies have identified specific risk factors for virus entry to farms. The mode of entry of virus differs from place to place but broadly speaking these studies have shown that anthropogenic spread is an important means of transmission for HPAI (Halvorson 2009). However, measures also need to be introduced to prevent contact with wild birds to prevent infection with influenza viruses.

Observations and assessments of biosecurity measures on farms demonstrate that there is still considerable work to be done to reach standards that would prevent virus from entering all farms. While the main objective for most poultry owners is to prevent virus from gaining entry to farms, cost effective measures should also be introduced to limit onward transmission of virus within and beyond infected farms once disease occurs. This covers items such as procedures for handling dead poultry, manure and waste water that have been identified as important for transmission to other farms. Many of the measures require changes to management procedures rather than physical facilities. Any changes must be acceptable to farmers otherwise they will not be implemented (Sims 2008).

Other measures

Communication campaigns have been used to modify behaviour and to reduce high risk practices such as dressing, preparing and eating sick or dead poultry for food. The campaigns have increased awareness and resulted in some behavioural change (van Kerkhove et al 2009) but they have not always been successful in having long term effects on behaviour, as seen with human cases in Cambodia in 2011, many of which were associated with preparation of sick or dead poultry for food and subsequent consumption. Many factors influence the willingness to report disease in poultry (Elbers et al 2010) and to change behaviour, including poverty.

Many countries have implemented routine disinfection programs for control and prevention of avian influenza and the use of these chemicals forms part of outbreak management. It is evident from field observations that there has been considerable misuse of these chemicals (FAO 2011c). Cleaning is not always used as a preliminary step to disinfection and many disinfectants are applied to areas with high loads of organic matter that reduces the efficacy of the disinfectants or contact times are too short for virus inactivation. Formal studies have not been conducted to evaluate the cost effectiveness of disinfection programs applied in and around villages for prevention of avian influenza.

Movement management has been applied around outbreak sites and at key points within and between countries, with variable effects. Movement management is an essential component of all avian influenza control and preventive programs but traditional cross border trade routes and poultry smuggling reduce their effectiveness. Again few of the movement controls in place have been assessed for the benefits they provide. Those recommended in the OIE terrestrial code, if implemented correctly would be expected to prevent incursions of virus through legal trade. Thailand's movement controls for grazing ducks within the country may provide lessons for other countries looking at improving controls but the numbers of ducks involved is far lower than in some other countries in the region.

Major changes have been introduced to the methods of sale of poultry in a number of places. A number of large cities have banned the sale of live poultry in markets (e.g. Beijing, Ho Chi Minh City) or placed very strict controls on the manner in which live poultry can be sold (e.g. Hong Kong SAR). These measures reduce the likelihood of contact between infected poultry and humans and it is pertinent that no new locally acquired human cases have been detected in Ho Chi Minh City and Hong Kong since these were implemented. The main risk associated with changes to the way poultry are sold is that unmet demand for live poultry will result in illegal sales of live birds in uncontrolled premises, requiring additional enforcement.

Trends in research on control measures

Several trends are apparent with research in avian influenza including more studies examining the benefits and identifying potential side effects of mass vaccination of poultry and work on new vaccines. This work includes trials of different vaccination protocols in the field. Greater use of modeling to assess control measures and risk factors is occurring with the results of some studies confirming what has been assumed from years of experience with AI control. Studies examining how and why measures were (or were not) implemented in the field to identify their likely effectiveness/weaknesses and additional studies on market chains have also been conducted.

A key guiding principle for all these studies should be to ensure that the information provided from the studies will assist in the management of the disease. For example, case control studies that conclude improvements in farm biosecurity are beneficial in assisting in control of avian influenza do not provide value to disease managers unless backed up with information on how this can be achieved. A trend towards greater involvement and empowerment of stakeholders in the development and implementation of control and preventive measures is also occurring. It should be strongly encouraged and studied to assess the benefits of such programs.

Conclusions

The current recommendations for control and prevention of avian influenza are based on first principles of avian influenza control, field observations and some specific studies. The recommendations have been refined over time taking into consideration the epidemiological situation in different countries, including the structure of the poultry sector and resources available. There are many gaps in knowledge, particularly on the effectiveness of individual measures and how the measures are applied but in many countries the combination of measures used has been followed by elimination of virus. Any measures applied incorrectly will not have the desired effect – be they stamping out, vaccination, farm biosecurity measures or movement controls. The quality of implementation depends to a large degree on the quality and standards of animal health services, providing sound justification for improving animal health and production services in countries affected or at risk of this disease to achieve better control and prevention of avian influenza in poultry.

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