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Review

The use of vaccination as an option for the control of avian influenza[1]

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Recent epidemics of highly contagious animal diseases included in list A of the Office International des Épizooties, such as foot-and-mouth disease, classical swine fever and avian influenza (AI), have led to the implementation of stamping-out policies resulting in the depopulation of millions of animals. The enforcement of a control strategy based on culling animals that are infected, suspected of being infected or suspected of being contaminated, which is based only on the application of sanitary restrictions on farms, may not be sufficient to avoid the spread of infection, particularly in areas that have high animal densities, thus resulting in mass depopulation. In the European Union, the directive that imposes the enforcement of a stamping-out policy (92/40/EC) for AI was adopted in 1992 but was drafted in the 1980s. The poultry industry has undergone substantial changes in the past 20 years, mainly resulting in shorter production cycles and in higher animal densities per territorial unit. Due to these organizational changes, infectious diseases are significantly more difficult to control because of the greater number of susceptible animals reared per given unit of time and due to the difficulties in applying adequate biosecurity measures. The slaughter and destruction of great numbers of animals is also questionable from an ethical point of view. For this reason, mass depopulation has raised serious concerns for the general public and has recently led to very high costs and economic losses for national and federal governments, stakeholders and, ultimately, for consumers. In the past, the use of vaccines in such emergencies has been limited by the impossibility of differentiating vaccinated/infected from vaccinated/non-infected animals. The major concern was that through trade or movement of apparently uninfected animals or products, the disease could spread further or might be exported to other countries. For this reason, export bans have been imposed on countries enforcing a vaccination policy. This review considers the possible strategies for the control of avian influenza infections, bearing in mind the new proposed definition of AI, including the advantages and disadvantages of using conventional inactivated (homologous and heterologous) vaccines and recombinant vaccines. Reference is made to the different control strategies, including the restriction measures to be applied in case of the enforcement of a vaccination policy. In addition, the implications of a vaccination policy on trade are discussed. It is concluded that if vaccination is accepted as an option for the control of AI, vaccine banks, including companion diagnostic tests, must be established and made available for immediate use.

Introduction

Recent epidemics of highly contagious animal diseases included in list A of the Office International des Épizooties (OIE), such as foot-and-mouth disease, classical swine fever and avian influenza (AI), have led to the implementation of stamping-out policies resulting in the depopulation of millions of animals. The implementation of a control strategy based on culling of animals that

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are infected, suspected of being infected or suspected of being contaminated, which is based only on the application of sanitary restrictions, may not be sufficient to avoid the spread of infection. This event is particularly foreseeable in areas that have high animal densities, and inevitably results in mass depopulation policies. There is an increased risk of disease spread in these areas and the financial consequences of any occurring epidemic are severe (Dijkhiuzen & Davies, 1995; Meuwissen *et al.*, 1999; Capua & Marangon, 2000; Gibbens *et al*., 2001).

With reference to AI, the European Union (EU) directive that imposes the enforcement of a stamping-out policy (92/40/EC) was adopted in 1992 but was drafted in the 1980s (CEC, 1992). The poultry industry has undergone substantial changes in the past 20 years, mainly resulting in shorter production cycles and in greater animal densities per territorial unit. Due to these organizational changes, infectious diseases are significantly more difficult to control due to the greater number of susceptible animals reared per given unit of time and to the difficulties in applying adequate biosecurity programmes. In order to avoid the destruction of great numbers of animals, the possibility of pursuing different control strategies should be considered.

The slaughter and destruction of great numbers of animals is also questionable from an ethical point of view, particularly when the implications for human health are negligible. For this reason, mass depopulation has raised serious concerns from the general public. The policy has also led to very high costs and economical losses for the Community budget, Member States, stakeholders and, ultimately, for consumers.

In the EU, the use of vaccines in such emergencies has been limited by the inability to differentiate vaccinated/infected from vaccinated/non-infected animals. The major concern was that through trade or movement of vaccinated animals or their products, the disease could spread further or might be exported to other countries, primarily because it was not possible to establish whether the vaccinated animals had been exposed to virus in the field.

This review considers the possible strategies for the control of avian influenza infections, bearing in mind the new definition of AI proposed by the EU (Document Sanco/B3/AH/R17/2000) and by the OIE (*Ad hoc* expert group on Avian Influenza, Animal Health Code Commission meeting of 29 to 30 October 2002), and the possibility of enforcing an emergency vaccination programme with the products currently available. Reference will be made to the type of vaccines available, the efficacy of these vaccines, their limitations, and the possibility of identifying infected animals in a vaccinated population.

Definition of AI

AI viruses all belong to the *Influenzavirus A* genus of the *Orthomyxoviridae* family and are negative-stranded, segmented RNA viruses. The influenza A viruses can be divided into 15 subtypes on the basis of the haemagglutinin (H) antigens. In addition to the H antigen, influenza viruses possess one of nine neuraminidase (N) antigens. Virtually all H and N combinations have been isolated from birds, thus indicating the extreme antigenic variability that is a hallmark of these viruses. Changes in the H and N composition of a virus may be brought about by genetic reassortment in host cells. One of the consequences of genomic segmentation is that if co-infection by different viruses occurs in the same cell, progeny viruses may originate from the reassortment of parental genes originating from different viruses. Thus, since the influenza A virus genome consists of eight segments, 256 different combinations of progeny viruses may theoretically arise from two parental viruses.

Current EU legislation (CEC, 1992) defines avian influenza as 'an infection of poultry caused by any influenza A virus which has an intravenous pathogenicity index in six-week-old chickens greater than 1.2 or any infection with influenza A viruses of H5 or H7 subtype for which nucleotide sequencing has demonstrated the presence of multiple basic amino acids at the cleavage site of the haemagglutinin'. However, it has been proven that highly pathogenic avian influenza (HPAI) viruses emerge in domestic poultry from low pathogenicity (LPAI) progenitors of the H5 and H7 subtypes. It therefore seems logical that not only HPAI viruses, but also their LPAI progenitors must be controlled when they are introduced in domestic poultry populations (Anonymous, 2000). The new proposed definition of AI for the OIE and the EU (Anonymous, 2000) is 'an infection of poultry caused by either any influenza A virus which has an IVPI (intravenous pathogenicity index) in 6-week-old chickens greater than 1.2 or any influenza A virus of H5 or H7 subtype'. With reference to the present paper, the term avian influenza applies to all avian influenza viruses of the H5 and H7 subtype, regardless of their virulence and of their pathogenicity for domestic poultry.

Rationale Behind the Use of Vaccines

When an outbreak of avian influenza occurs in an area with a high population density in which the application of rigorous biosecurity measures is incompatible with the modern rearing systems, vaccination should be considered as a first option to control the spread of infection. The expected results of the implementation of a vaccination policy on the dynamics of infection are primarily those of reducing the susceptibility to infection (i.e.

a higher dose of virus is necessary for establishing productive infection) and reducing the amount of virus shed into the environment. The association between a higher infective dose necessary to establish infection and less virus contaminating the environment represents a valuable support to the eradication of infection.

Clearly, the efficacy of an emergency vaccination programme is inversely correlated to the time span between the diagnosis in the index case and the implementation of mass vaccination. For this reason, it is imperative that if emergency vaccination is considered as a possible option in a given country, vaccine banks must be available in the framework of national contingency plans.

Conventional Vaccines

Inactivated homologous vaccines

These vaccines were originally prepared as 'autogenous' vaccines (i.e. vaccines that contain the same AI virus strain as the one causing the problems in the field). They have been used extensively in Mexico and Pakistan during AI epidemics (Swayne & Suarez, 2000).

The efficacy of these vaccines in preventing clinical disease and in reducing the amount of virus shed in the environment has been proven through field evidence and experimental trials (Swayne & Suarez, 2000). The disadvantage of this system is the impossibility of differentiating vaccinated from field-exposed birds unless unvaccinated sentinels are kept in the shed. However, the management (identification, bleeding and swabbing) of sentinel birds during a vaccination campaign is time consuming and rather complicated since they are difficult to identify, and they may be substituted with seronegative birds in the attempt to escape restrictions imposed by public health officials.

Inactivated heterologous vaccines

These vaccines are manufactured in a similar way to the inactivated homologous vaccines. They differ in the fact that the virus strain used in the vaccine is of the same H type as the field virus but has a heterologous neuraminidase. Following field exposure, clinical protection and reduction of viral shedding are ensured by the immune reaction induced by the homologous H group, while antibodies against the neuraminidase induced by the field virus can be used as a marker of field infection (Capua *et al*., 2000).

For both homologous and heterologous vaccines, the degree of clinical protection and the reduction of shedding are improved by a higher antigen mass in the vaccine (Swayne *et al*., 1999). For heterologous vaccines the degree of protection is not strictly correlated to the degree of homology between the haemagglutinin genes of the vaccine and challenge strains (Swayne & Suarez, 2000). This is definitely a great advantage because it enables the establishment of vaccine banks since the master seed does not contain the virus that is present in the field, and may contain an isolate (preferably of the same lineage) available before the epidemic.

Recombinant vaccines

Several recombinant fowlpoxviruses expressing the H5 antigen have been developed (Beard *et al.,* 1991, 1992; Webster *et al*., 1996; Swayne *et al*., 1997, 2000b), and one has been licensed and is being used currently in Mexico (Swayne & Suarez, 2000). Experimental data have also been obtained for fowlpoxvirus recombinants expressing the H7 antigen (Boyle *et al*., 2000). Other vectors have been used to successfully deliver the H5 or H7 antigens, such as constructs using infectious laryngotracheitis virus (Lüschow *et al*., 2001).

The only field experience with a recombinant virus to control AI has been obtained in Mexico (Villareal-Chavez & Rivera Cruz, 2002), where it has been used in the vaccination campaign against a LPAI H5N2 virus. No such product has been licensed in the EU to date.

Trade Implications

Until recent times, vaccination against avian influenza viruses of the H5 and H7 subtypes was not considered or practised in developed countries since it implied export bans on live poultry and on poultry products (CEC, 1994). Export bans have also been imposed in cases of infection with an H5 or H7 virus, regardless of the virulence of the isolate. Export bans frequently represent the major cause of economic loss due to OIE List A diseases.

While the severe clinical signs caused by HPAI ensure a prompt diagnosis and facilitate the implementation of a stamping-out policy, the inconspicuous nature of the disease caused by viruses of low pathogenicity make this infection difficult to diagnose. Detection of infection is only possible with the implementation of appropriate surveillance programmes. Bearing in mind the new proposed definition of AI, and the potential mutation of LPAI of the H5 and H7 subtypes to HPAI, it is easy to understand why these bans have been imposed. For the sake of trade, freedom from AI should be demonstrated in a given country or compartment by ongoing surveillance programmes. This approach is supported by the fact that, in several recent outbreaks, infection with a virus of low pathogenicity was only detected once infection was widespread, and often out of control.

In the absence of vaccination, trade bans imposed on a given area last until freedom from infection can be demonstrated in the affected population. Prolonged trade bans are also imposed when a vaccination policy is adopted that does not enable the application of a 'Differentiating Infected from Vaccinated Animals' ('DIVA') strategy (either for the type of vaccine used or because the monitoring system in place does not guarantee that infection is no longer circulating). On the contrary, if it is possible to demonstrate that the infection is not circulating in the vaccinated population, the trade bans may be lifted.

Such 'marker' vaccination strategies offer attractive control options for OIE List A diseases. In case of an outbreak of AI in a densely populated poultry area, the option of vaccination should be pursued. In order to safeguard international trade, a control strategy that enables the differentiation of vaccinated/infected from vaccinated/non-infected animals should be implemented. The possibility of using vaccines would support restriction-based control measures, thus reducing the risk of a major epidemic and the subsequent mass stamping-out policy.

Options for Control

It is extremely difficult to establish fixed rules for the control of infectious diseases in animal populations due to the unpredictable number of variables involved. However, with reference to AI, some basic scenarios may be hypothesized, and on the basis of the considerations already made some guidelines may be drawn (Table 1).

There are several crucial steps that must be planned for if AI represents a risk. First, the index case must be promptly identified. This does not represent a problem if the virus is of high pathogenicity, but it can be a serious concern if the virus is of low pathogenicity. For this reason, countries or areas at risk of infection should implement specific surveillance systems to detect infection with LPAI as soon as it appears.

Second, a timely assessment of whether there has been spread to the industrial poultry population of that area must be performed. This is a crucial evaluation that must be made available for decision-makers.

Once an AI outbreak has been identified, eradication measures based on the stamping-out or controlled marketing of slaughterbirds on infected farms must be enforced. The choice between these two options must be taken bearing in mind the pathogenicity and transmissibility of the virus, the density of poultry farms around the affected premises, the economic value of the affected birds, the logistics for slaughter/stamping out and the collaborative approach of farmers/producers. With reference to the Italian experience, a stamping-out policy was generally applied to LPAI-infected young meat-birds, breeders and layers, while controlled marketing was applied for older meat-birds approaching slaughter age. This strategy enables the reduction of the restriction periods (i.e. if infected young turkeys, breeders or layers were kept on the farms, the restriction period could be of several months) and hence facilitates faster restocking. In addition, restriction measures on the movement of live poultry, vehicles and staff must be imposed in the areas at risk.

Finally, if vaccination is the proposed strategy, vaccine banks should be available for immediate use and a contingency plan must be enforced. A territorial strategy must also be implemented. It must include restriction measures (Table 2 and Table 3) and an ongoing set of adequate controls (Figure 1) that enable public authorities to establish whether the virus is circulating in the vaccinated population and to assess the efficacy of the vaccination programme.

Applications in the Field

Inactivated homologous vaccines

These products have recently been used in the attempt to control AI infections in Pakistan and in Mexico (Swayne & Suarez, 2000), but under those specific conditions they have not have been successful in eradicating the infection. Conversely, in one instance, in Utah (Frame *et al*., 1996), the use of this vaccination strategy has been successful. The reason for the discrepancy of the results probably lies in the efficacy of the direct control measures,

Table 1. *Guidelines for the application of control policies for AI*

H5/H7 virus pathogenicity	Index case flock	Evidence of spread to industrial circuit	Population density in area	Policy
HPAI/LPAI	Backyard	No	High/low	Stamping-out
HPAI/LPAI	Backyard	Yes	Low	Stamping-out
			High	Vaccination
HPAI/LPAI	Industrial	No	High/low	Stamping-out
HPAI/LPAI	Industrial	Yes	Low	Stamping-out
			High	Vaccination

Table 2. *Basic restriction and monitoring measures to be enforced on the movements of live poultry and poultry products originating from and/or destined for farms or plants located in the vaccination area (VA)*

Commodity	Restrictions to movements towards the VA	Restrictions to movements inside the VA	Restrictions to movements outwards the VA
Hatching eggs	– shall be transported directly to the hatchery of destination – (and their packaging) must be disinfected before dispatch – tracing-back of egg lots in the hatchery shall be guaranteed	– must originate from a vaccinated or unvaccinated breeding flock that has been tested, with negative results, according to Figure 1 – shall be transported directly to the hatchery of destination – (and their packaging) must be disinfected before dispatch – tracing-back of egg lots in the hatchery shall be guaranteed	– must originate from a vaccinated or unvaccinated breeding flock that has been tested, with negative results, according to Figure 1 – shall be transported directly to the hatchery of destination – (and their packaging) must be disinfected before dispatch – tracing-back of egg lots in the hatchery shall be guaranteed
Day-old chicks	– must be destined for a poultry-house where: – no poultry is kept – cleansing and disinfection operations have been carried out	– must originate from hatching eggs satisfying the conditions already mentioned – must be destined for a poultry-house where no poultry is kept and where cleansing and disinfection operations have been carried out	– must originate from hatching eggs satisfying the conditions already mentioned – must be destined for a poultry-house where no poultry is kept and where cleansing and disinfection operations have been carried out
Ready-to-lay pullets	– must be housed in a poultry-house where no poultry has been kept for at least 3 weeks, and cleansing/disinfection operations have been carried out – must be vaccinated at the farm of destination	– must have been regularly vaccinated against AI – must have been tested, with negative results, according to Figure 1 – must be destined for a farm located in the VA and housed in a poultry-house where no poultry has been kept for at least 3 weeks, and cleansing/disinfection operations have been carried out – must be officially inspected within 24 h before loading – must be virologically and serologically tested with negative results before loading (sentinel birds)	– must not have been vaccinated – must have been tested, with negative results, according to Figure 1 – must be destined for a poultry-house where no poultry has been kept for at least 3 weeks, and cleansing/disinfection operations have been carried out – must be officially inspected within 24 h before loading – must be virologically and serologically tested with negative results before loading
Poultry for slaughter	– must be sent directly to the abattoir for immediate slaughter – must be transported by lorries that operate, on the same day, only on farms located outside the VA – lorries must be washed and disinfected under official control before and after each transport	– shall undergo a clinical inspection within 48 h before loading – must be directly sent to the abattoir for immediate slaughter – must be serologically tested before loading – the abattoir must guarantee that accurate washing and disinfection operations are carried out under official supervision – shall be transported by lorries that operate, on the same day, only on farms located inside the VA – lorries must be washed and disinfected before and after each transport	– shall undergo a clinical inspection within 48 h before loading – must be sent directly to an abattoir designated by the competent veterinary authority for immediate slaughter – must be serologically tested before loading – the abattoir must guarantee that accurate washing and disinfection operations are carried out under official supervision – shall be transported by lorries that operate, on the same day, only on farms located inside the VA – lorries must be washed and disinfected before and after each transport
Table eggs	– must be sent directly to a packaging centre or a thermal-treatment plant designated by the competent authority – must be transported using disposable packaging materials, which can be effectively washed and disinfected	– must originate from a flock that has been tested, with negative results, as laid down in Figure 1 – must be sent directly to a packaging centre or a thermal-treatment plant designated by the competent authority – must be transported using disposable packaging material or packaging material that can be effectively washed and disinfected	– must originate from a flock that has been tested, with negative results, as laid down in Figure 1 – must be sent directly to a packaging centre or a thermal-treatment plant designated by the competent authorities – must be transported using disposable packaging material or packaging material, which can be effectively washed and disinfected

Table 3. *Basic restrictions applied during the Italian 1999–2000 vaccination programme to the trade of fresh meat produced from poultry originating from the vaccination area (VA)*

Commodity	Unrestricted to international trade	Restricted to national trade
Fresh poultry meat	Originating from birds vaccinated against AI with a heterologous subtype vaccine, can be dispatched to other countries, provided that the meat comes from slaughter turkey flocks that: i) have been regularly inspected and tested with negative results for AI as laid down in Figure 1: ● for the testing of vaccinated animals, the anti-N discriminatory test shall be used ● for the testing of sentinel animals, either the haemagglutination-inhibition test, the AGID[a] test or the ELISA[b] test shall be used; however, the anti-N discriminatory test shall also be used if necessary ii) have been clinically inspected by an official veterinarian within 48 h before loading. Sentinel animals shall be inspected with particular attention iii) have been serologically tested with negative results with the anti-N discriminatory test iv) must be sent directly to a slaughterhouse designated by the competent authority and be slaughtered immediately on arrival Produced from poultry not vaccinated against AI and originating from the VA	Originating from holdings located in the VA, cannot be dispatched to other countries if produced from poultry: i) vaccinated against AI with a homologous subtype vaccine ii) vaccinated against AI with a heterologous subtype vaccine and not tested, with negative results, using the anti-N discriminatory test iii) originating from seropositive poultry flocks subjected to controlled marketing iv) coming from poultry holdings located in the restriction zone (minimum 3 km radius) that must be established around any LPAI infected farms for at least 2 weeks

[a]AGID, Agar Gel Immunodiffusion.
[b]ELISA, enzyme-linked immunosorbent assay.

which must be implemented to support a vaccination campaign.

Inactivated heterologous vaccines

This vaccination strategy has been used successfully over the years in Minnesota (Halvorson, 2002). However, in these instances vaccination was never implemented to control infections caused by viruses of the H5 or H7 subtypes. In addition, the heterologous neuraminidase was not used as a marker of infection.

Conversely, in Italy during 2000 to 2002 this strategy was used to supplement control measures for the eradication of the H7N1 LPAI virus (CEC, 2000). In order to control the re-emergence of

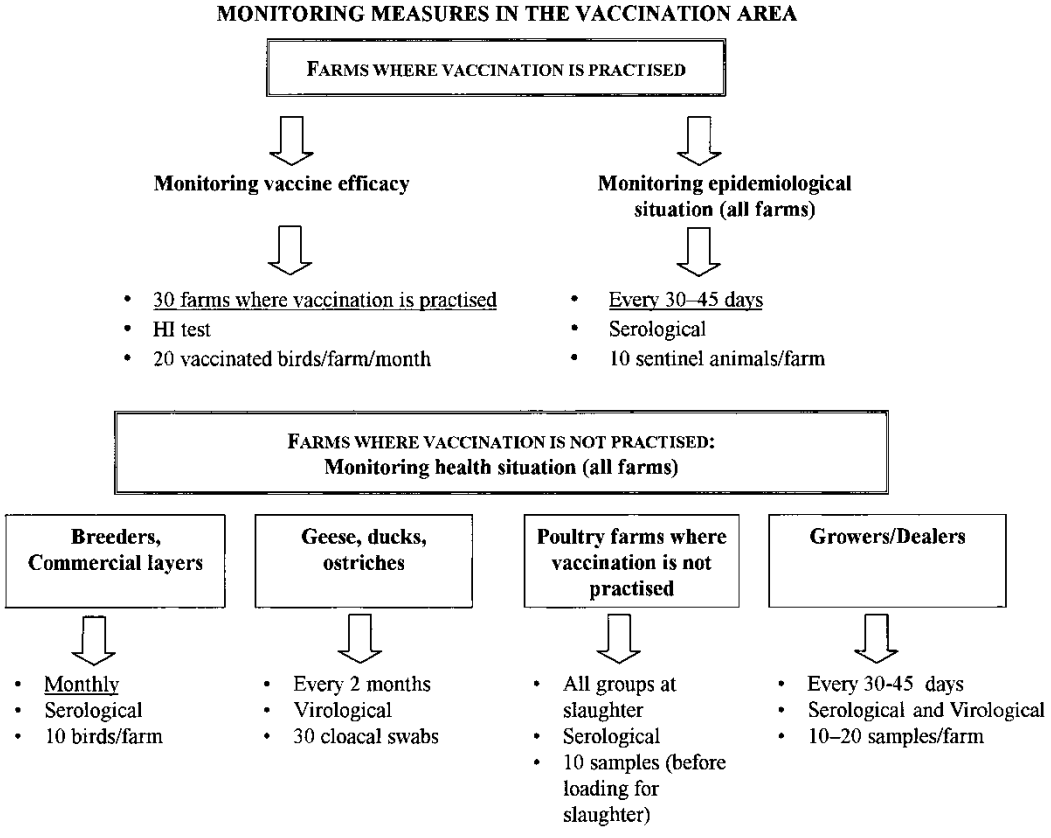

Figure 1. *Monitoring measures to be applied in the vaccination area.*

LPAI virus and to develop a novel control strategy, a co-ordinated set of measures, including strict biosecurity, a serologic monitoring programme and a 'DIVA' strategy were enforced.

The 'DIVA' strategy was based on the use of an inactivated oil emulsion heterologous vaccine containing the same H subtype as the field virus, but a different N suntype, in this case an H7N3 strain. The possibility of using the diverse N group, to differentiate between vaccinated and naturally infected birds, was achieved through the development of an '*ad hoc*' serological test to detect the specific anti-N1 antibodies (Capua *et al*., 2003).

Control of the field situation was achieved through an intensive sero-surveillance programme aimed at the detection of the LPAI virus through the regular testing of sentinel birds in vaccinated flocks and through the application of the anti-N1 antibody detection test. Serological monitoring was also enforced in unvaccinated flocks, located both inside and outside the vaccination area. In addition, the efficacy of the vaccination schemes was evaluated in the field through regular serological testing of selected flocks.

After the first year of vaccination, the epidemiological data collected indicated that the H7N1 virus was not circulating. This was considered sufficient by the EU Commission to lift the marketing restrictions on fresh meat obtained from vaccinated poultry provided that animals had been tested with negative results using the discriminatory test (CEC, 2001).

It is clear that, due to the unpredictable nature of the epidemiology of this disease, which could result in the introduction of other AI subtypes, this solution is to be considered 'tailored' for a given epidemic.

Recombinant vaccines

The only field experience with these vaccines has been carried out in Mexico, where a fowlpox recombinant has been used in the vaccination campaign against the H5N2 virus. Avian influenza has not been eradicated in Mexico, probably because an eradication programme based on a territorial strategy and including monitoring and restriction was not established.

Recombinant live vectored vaccines also enable the differentiation between infected and vaccinated birds, since they do not induce the production of antibodies against the nucleoprotein antigen, which is common to all AI viruses. Therefore, only field infected birds will exhibit antibodies to the agar gel precipitin test or the enzyme-linked immunosorbent assay directed towards the detection of group A (nucleoprotein) antibodies.

Since these vaccines have encountered some difficulties in licensing, their use is restricted to countries in which they are legally available. In addition, these vaccines will not replicate, and induce protective immunity, in birds that have had field exposure to the vector (i.e. fowlpoxvirus or infectious laryngotracheitis viruses) (Swayne *et al*., 2000a; Lüschow *et al*., 2001). Since serological positivity to these viruses is widespread (due to field exposure and vaccination) in the poultry population, and can be in some instances unpredictable, the use of these vaccines is limited to a population that is seronegative to the vector virus. In addition, the use of these vaccines is restricted to species in which the vector virus will replicate. For example, infectious laryngotracheitis virus will not replicate in turkeys and, since these birds are particularly important in the epidemiology of AI, the use of this vaccine is limited to areas in which turkeys are not present.

Discussion

From the data presented, it appears that emergency vaccination is a sensible option if there is evidence of the introduction of a highly transmissible AI virus in a densely populated poultry area, or whenever the epidemiological situation indicates that there could be massive and rapid spread of infection. In addition, emergency vaccination should be considered where applicable, when birds of high economic value (e.g. pedigree flocks) or rare (endangered) birds are at risk of infection. It is clear that vaccination represents a tool to support eradication, and will be a successful tool only if coupled with restriction and increased biosecurity.

Considering the advantages and disadvantages of the products and diagnostic tools that are available currently, if no recombinant products are licensed in that country, heterologous vaccination rather than homologous vaccination should be practiced in case of an emergency. The main reason for this would be that it would enable the differentiation of vaccinated birds from naturally exposed birds, through the development/application of an appropriate test. At present only the anti-neuraminidase-based test is available and has been validated. In our opinion, however, this test represents a starting point on which future developments of the 'DIVA' strategy can be based. The development of novel candidate vaccines and of additional tests that enable the detection of field infection in vaccinated populations should be a priority for pharmaceutical industries and for research institutions since, for all the reasons already listed, vaccination is already an option for the control of AI.

If the country has access to licensed recombinant products, the use of these vaccines is acceptable taking into consideration the immune status of the population against the vector since seropositivity impedes the replication of the vector virus, and therefore the establishment of immunity. The issue

of the replicating capacity of the vector in different species must also be addressed.

In conclusion, recent events including devastating epidemics in densely populated poultry areas, public health concern on animal welfare issues and the introduction of novel technology into vaccinology have encouraged consideration of alternative control strategies for OIE List A diseases that were unthinkable of only a few years ago. This has also been supported by the development of reliable, sensitive and specific diagnostic companion tests. Countries, areas and enterprises at risk of infection should imperatively enforce surveillance programmes and have contingency plans in case of a disease outbreak, which may include vaccination. If the latter is considered as an option, among other issues the contingency plan must foresee the establishment of licensed vaccine banks that enable the 'DIVA' strategy, thus safeguarding animal health, animal welfare and international trade.

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RÉSUMÉ

Utilisation de la vaccination comme une option pour le contrôle de l'influenza aviaire

Les récentes épidémies correspondant aux maladies animales très contagieuses incluses dans la liste A de l'Office International des Epizooties (OIE) telles la fièvre aphteuse, la peste porcine classique et l'influenza aviaire (AI) ont conduit à l'application des mesures de police sanitaire entraînant l'abattage de millions d'animaux. L'application d'une stratégie de contrôle basée sur l'abattage des animaux qui sont infectés, suspectés d'être infectés ou suspectés d'être contaminés, qui est basée uniquement sur la mise en place de mesures de restrictions sanitaires au niveau des élevages, n'est pas suffisante pour éviter la diffusion de l'infection, particulièrement dans les régions à forte densité animale entraînant ainsi une dépopulation (vide sanitaire) de nombreux élevages. En Europe, la directive qui impose l'application des mesures de police sanitaire (92/40/EC) pour l'AI a été adoptée en 1992 mais a été rédigée dans les années 1980. L'industrie avicole a subi des changements substantiels dans les vingt dernières années, résultant principalement en

des cycles de production plus courts et des densités animales plus élevées sur un territoire donné. Ces changements organisationnels font que les maladies infectieuses sont de plus en plus difficiles à contrôler de par la présence d'un plus grand nombre d'animaux sensibles élevés par unité de temps donnée et par les difficultés à appliquer les mesures adéquates de biosécurité. Les actions d'abattage et de destruction d'un grand nombre d'animaux doivent conduire à une réflexion particulièrement quand les implications en santé humaine sont négligeables. Pour cette raison, la dépopulation à grande échelle a soulevé beaucoup d'inquiétude de la part du grand public et a récemment entraîné des coûts très élevés et des pertes économiques pour les gouvernements fédéraux et nationaux, les professionnels et finalement le consommateur. Autrefois, l'utilisation de vaccins dans de telles situations d'urgence a été limitée du fait de l'impossibilité de différencier les animaux vaccinés/infectés des vaccinés/non infectés. Le souci majeur était qu'à travers le commerce ou le mouvement d'animaux apparemment non infectés ou de leurs produits la maladie pouvait diffuser ou pouvait être exportée dans d'autres pays. Pour cette raison, l'interdiction d'exportation a été imposée au pays mettant en place une politique de vaccination. Cette synthèse considère les stratégies possibles du contrôle des infections à influenza aviaire, en s'appuyant sur la nouvelle proposition de la définition de l'AI, en incluant les avantages et désavantages de l'utilisation des vaccins inactivés conventionnels (homologues ou hétérologues) et des vaccins recombinants. Des comparaisons sont faites avec les différentes stratégies de contrôle, incluant les mesures de restriction à appliquer dans les cas de mise en place d'une politique de vaccination. De plus, les implications d'une politique de vaccination sur le commerce sont discutées. Il est conclu que si la vaccination est acceptée comme une option pour le contrôle de l'AI, des banques de vaccin, incluant des tests de diagnostic correspondants, doivent être constituées et disponibles pour un usage immédiat.

ZUSAMMENFASSUNG

Vakzination als eine Option zur Bekämpfung der aviären Influenza

Die in den letzten Jahren aufgetretenen Epidemien der in der Liste A der internationalen Epizootie-Behörde (OIE) aufgeführten hoch kontagiösen Tierkrankheiten wie Maul- und Klauenseuche, klasssische Schweinepest und aviäre Influenza (AI) haben zur Durchführung der Ausrottungspolitik geführt, was die Tötung von Millionen von Tieren zur Folge hatte. Die Durchsetzung einer Bekämpfungsstrategie, die auf der Merzung von Tieren beruht, die entweder infiziert sind oder verdächtig sind, infiziert oder kontaminiert zu sein, d.h. einer Strategie, die nur auf der Anwendung hygienischer Maßnahmen auf den Farmen beruht, mag nicht ausreichend sein, die Ausbreitung der Infektion zu verhindern, insbesondere in Gebieten mit hoher Tierbesatzdichte, was dort die Tötung sehr großer Tierpopulationen bedeutet. In der Europäischen Union wurde die Direktive, die die Durchführung der Ausrottungspolitik für die AI (92/40/EC) festlegte, im Jahr 1992 erlassen, jedoch bereits in den 80iger Jahren entworfen. Die Geflügelindustrie hat sich jedoch in den letzten 20 Jahren entscheidend geändert, was vor allem zu kürzeren Produktionszyklen und zu höherem Tierbesatz je Gebietseinheit geführt hat. Diese organisatorischen Veränderungen bedingen eine wesentlich schlechtere Kontrollierbarkeit von Infektionskrankheiten aufgrund der größeren Zahl von empfänglichen Tieren pro gegebener Zeiteinheit und der Schwierigkeiten der Einhaltung adäquater Sicherheitsmaßnahmen. Ebenso ist die Schlachtung und Vernichtung großer Tierzahlen aus ethischer Sicht fraglich, insbesondere wenn die Bedeutung der Infektion für die menschliche Gesundheit unerheblich ist. Aus diesem Grund hat die Massentötung von Tieren in der allgemeinen Öffentlichkeit eine erhebliche Beunruhigung ausgelöst. Außerdem hat sie in letzter Zeit sehr hohe Kosten und finanzielle Verluste für Bundes- und Länderregierungen, Tierhalter und letztlich auch für die Verbraucher verursacht. In der Vergangenheit war der Einsatz von Vakzinen in solchen Notfällen limitiert durch die Unmöglichkeit der Differenzierung von geimpften/infizierten von geimpften/nicht infizierten Tieren. Die Hauptsorge war, dass durch Handel oder Transport von scheinbar nicht infizierten Tieren oder Produkten die Krankheit weiterverbreitet werden und in andere Länder exportiert werden könnte. Aus diesem Grund wurde gegen Länder, die eine Impfpolitik betreiben, Exportsperren verhängt. Unter Berücksichtigung der neu vorgeschlagenen Definition der AI werden in diesem Übersichtsreferat die möglichen Strategien zur Bekämpfung aviärer Influenzainfektionen einschließlich der Vor- und Nachteile der Anwendung konventioneller inaktivierter (homologer und heterologer) Impfstoffe sowie rekombinanter Vakzinen dargestellt. Die verschiedenen Bekämpfungsstrategien werden erwähnt ebenso wie die Beschränkungsmaßnahmen, die im Falle der Durchsetzung der Impfpolitik angewendet werden. Außerdem werden die Auswirkungen der Impfpolitik auf den Handel diskutiert. Es wird gefolgert, dass im Falle der Annahme der Vakzination als eine Option für die Bekämpfung der AI Banken für Impfstoffe und der dazugehörenden diagnostischen Tests eingerichtet werden und für den sofortigen Gebrauch verfügbar gemacht werden müssen.

RESUMEN

La vacunación como una opción para el control de la influenza aviar

Las epidemias recientes de enfermedades animales muy contagiosas incluídas en la lista A de la Oficina Internacional de Epizootias (OIE) como la fiebre aftosa, la pesta porcina clásica o la influenza aviar (AI) han conllevado la implementación de políticas de sacrificio masivo que han resultado en la eliminación de millones de animales. El hecho de forzar una estrategia de control basada en la selección de animales infectados, sospechosos de estar infectados o sospechosos de estar contaminados, que se basa únicamente en la aplicación de restricciones sanitarias en granjas, puede no ser suficiente para evitar la diseminación de la infección, particularmente en áreas con una elevada densidad de animales, dando como resultado una despoblación en masa. En la Unión Europea, la directiva que impone la política de sacrificio masivo (92/40/EC) para la AI fue adoptada en 1992 pero el borrador fue escrito durante los años ochenta. La industria avícola ha sufrido cambios substanciales en los últimos veinte años, resultando mayoritariamente en ciclos de producción más cortos y en densidades animales más elevadas por unidad territorial. Debido a estos cambios de organización, las enfermedades infecciosas son significativamente más difíciles de controlar debido al gran número de animales susceptibles por una unidad de tiempo dada y debido a las dificultades en aplicar las medidas de bioseguridad adecuadas. El sacrificio y destrucción de gran número de animales es también cuestionable desde un punto de vista ético, teniendo además en cuenta que las implicaciones en la salud humana son negligibles. Por esta razón, la despoblación en masa ha provocado preocupación en el público en general, además de provocar grandes pérdidas económicas y un alto coste a los gobiernos nacional y federal, a las empresas relacionadas y en definitiva al consumidor.