Field trial for assessment of avian influenza vaccination effectiveness in Indonesia

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Summary
The aim of this field study was to determine the efficacy of vaccination against highly pathogenic avian influenza (HPAI) virus strain H5N1 in Indonesia. A limited, prototype clinical trial was performed using a standardised treatment group, in which poultry flocks were vaccinated at least twice with a selected H5N1 vaccine, and a control group comprising flocks treated with non-standardised procedures chosen by the farmer. Each group consisted of six flocks comprising either layers or native chickens. Haemagglutination inhibition (HI) antibody levels were determined by regular serum sampling, and outbreak surveillance relied on non-AI-vaccinated sentinel birds. After three vaccinations high antibody titres were produced in the treatment group, and the percentage of layers with an HI titre > 40 was approximately 90%. Although no conclusions can be drawn regarding reduction of virus transmission, this study demonstrated that 11 farms remained free from AI during the observation period, and that a surveillance programme based on differentiating infected from vaccinated animals (DIVA) can be implemented.

Keywords
DIVA – Highly pathogenic avian influenza – Indonesia – Non-AI-vaccinated sentinel – Surveillance – Vaccination.

Introduction

In 1997 an outbreak in Hong Kong of highly pathogenic avian influenza (HPAI) strain H5N1 was reported to the World Organisation for Animal Health (OIE) (22). Since then, the virus has spread to many other countries in Southeast Asia, Africa and Europe (2, 3). Outbreaks are controlled by stamping out infected poultry, sometimes followed by pre-emptive culling of contiguous flocks (11). In Europe, Malaysia, Japan, South Korea and Thailand, this strategy was successful, as the number of poultry outbreaks remained rather limited, and affected countries were

declared free from the virus (3, 22). In some countries, such as China, Vietnam and Indonesia, the virus spread rapidly and many regions have become endemically infected. The fear of a human pandemic (20), but also concern about food security and protection of livelihoods are important drivers for various organisations, such as the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and the United States Agency for International Development (USAID), to participate in the control of HPAI in these affected countries. Control strategies are being developed, and surveillance programmes such as participatory disease surveillance and response (PDS/R) (7) have been implemented. Despite all such efforts, the disease is still present, and human cases of H5N1 infection are still being reported (21).

In endemically affected areas it is not feasible to apply pre-emptive culling or a stamping-out strategy on a large scale because many flocks are affected. Poultry farmers in these areas lose income when their flock is infected, either owing to reduced production or to increased mortality of their poultry. Consequently, the disease in these countries is mainly controlled by vaccination, using various types of vaccines, with the aim of preventing production losses if HPAI occurs within a flock. However, farmers are still confronted with outbreaks, even in birds on vaccinated farms. Explanations that have been given are the use of poor quality vaccines or improper vaccination technique (1).

The question is, therefore, whether it is possible to eradicate the virus by means of a proper vaccination schedule using adequate vaccines, or whether the application of vaccines will induce clinical protection for poultry but will facilitate silent spread of the infection and human exposure to the virus. Experimental studies have shown that various vaccines (either heterologous or homologous) are able to induce good clinical protection against a challenge infection with H5N1 strains of HPAI (5, 8, 14, 15, 18). It is, however, questionable whether experimental data can be extrapolated to the field, because vaccination is often less effective when applied under field conditions. Field data from Vietnam have shown that the number of human cases of AI decreased following the wide-scale application of vaccines (21). However, whether this reduction was attributable to the vaccination campaign, or to increased biosecurity measures or public awareness, has not been established, because no control group was included. It remains, therefore, unclear whether vaccination can be effective with respect to reduction of the number of outbreaks.

In Indonesia, a large number of human cases have been reported and the virus is still circulating despite the wide application of vaccines. The control and surveillance programme for AI in this country should therefore be improved, as also indicated by the Indonesian government. Using current surveillance data, the effectiveness of vaccination in the field has been doubted, as suggested by low coverage and low haemagglutination inhibition (HI) antibody titres. However, the basic question is whether flocks were not vaccinated properly or whether the vaccines were of insufficient quality. Moreover, it has been questioned whether vaccination could reduce horizontal transmission of AI between vaccinated flocks. Finally, a good surveillance system for AI in vaccinated poultry flocks in Indonesia has been lacking.

Therefore, a limited, prototype clinical trial was carried out to measure antibody titres induced by vaccination, the success of immune coverage within flocks, and the reduction in the number of outbreaks of H5N1 in vaccinated flocks. The results should contribute to improving the control strategy and surveillance systems in Indonesia, and may benefit the health status of both poultry and humans. In addition, the difficulties with implementing such a trial, and the use of a surveillance system and vaccination campaign in sectors three and four of the poultry production industry are discussed in this paper. (The FAO has grouped all systems of poultry production into four operational levels – sector one: industrial, integrated farms with a high level of biosecurity; sector two: non-integrated farms with moderate to high biosecurity levels; sector three: small and medium-scale poultry farms with limited biosecurity; and sector four: backyard poultry with no biosecurity measures in place [7]).

Materials and methods

Study area

The trial was carried out in three sub-districts within the district of Sukabumi in the province of West Java on Java, Indonesia. Selection criteria for these sub-districts included: recent outbreaks of H5N1 HPAI in the area, the presence of commercial layer flocks of sector three, adequate veterinary infrastructure, and access to laboratory facilities.

A survey was carried out by the Centre for Indonesian Veterinary Analytical Studies (CIVAS), an Indonesian non-governmental organisation, to locate poultry flocks, and to provide technical data on these farms. The minimum number of flocks to be included in this clinical trial to provide sufficient power to demonstrate a difference in effectiveness between a treatment and a control group was calculated to be approximately 200, with 100 flocks per group. As expected, the number of flocks in the selected sub-districts was not sufficient to meet this requirement. Therefore, the trial was initiated with a lower number of

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flocks. It was considered a demonstration project to gain insight into the adequacy of laboratory procedures, to improve vaccination coverage and surveillance programmes, to build experience in the design and implementation of vaccination and surveillance programmes, to extend the ability to conduct field research, and to contribute to capacity building in Indonesia.

Criteria for inclusion of farms

The farms to be included in the trial were those producing commercial layers and native-breed broilers, as the production cycles of these two types would last long enough for the chickens to develop a vaccine-induced immune response. The production period of the layer flocks was approximately 1 year and that of the native broiler chickens was 3 months. Farms of sectors one and two were not included because government veterinarians generally do not have access to these farms.

Two groups were formed: a treatment group and a control group. These two groups differed in the vaccination programme for AI, as described in the next paragraph. In the treatment group there were more flocks than there were farms: either there were more sheds on the farm or the production period of native chickens was shorter than the duration of the trial, so when a flock was slaughtered it was replaced by a new flock. The owners might have been more interested in participating a second time than owners of the control native farms.

Vaccine and vaccination scheme

Treatment group

The vaccine used for the treatment group was a locally produced commercially available vaccine based on the HPAI H5N1 seed strain A/chicken/Legok/03. The vaccine, Medivac AI vaccine, was produced by PT Medion (Bandung, Indonesia) according to OIE guidelines (22). Medivac AI contains field isolated avian influenza virus of H5 subtype. The inactivated viruses are emulsified in mineral oil adjuvant to enhance and prolong the efficacy of the vaccine. Each dose contains at least 50 times the 50% protective dose (PD_{50}) (5).

The vaccine was injected intramuscularly into the leg according to the recommendation of the manufacturer. The vaccination was carried out by farm staff or by para-veterinarians of the Dinas Peternakan (Government Livestock Services) supervised by veterinarians from CIVAS.

The aim was to vaccinate layers in the treatment group three times, at 4, 10 and 17 weeks of age. Native chicken

Table I

Vaccination and sampling scheme for flocks in the treatment group

Farm type	Vaccination at age	Sampling at age
Layer	4, 10, 17 weeks	8, 14, 21 weeks
Native chicken	10, 30 days	28, 70 days

broilers were vaccinated twice, at 10 and 30 days old (Table I).

Backyard (sector four) poultry within a radius of 1 km around each flock in the treatment group were vaccinated every four months by Dinas Peternakan and CIVAS staff using the same vaccine batches as for flocks of the treatment group. This area is referred to as 'the ring'. The aim of vaccination in this area was to reduce the chance of infection occurring in chickens near to a flock in the treatment group, which could increase the risk of introduction of virus into the study flock. This is not unlikely, because the biosecurity level of these flocks is not very high.

Control group

It was considered unethical to include a group of intentionally unvaccinated flocks in this trial, as the area was endemically infected. Any introduction of virus would probably result in high mortality, and a high virus load, resulting in loss of income for the owner, and increased risk of exposure for humans. The control group consisted of flocks that were vaccinated by the farmers according to their own vaccination scheme. Vaccines were purchased by the farmers and applied by farm staff. Vaccination schedules on control farms differed. Layer flocks were generally vaccinated twice, at 4 and at 16 to 18 weeks of age; native chicken flocks were vaccinated once at 10 days of age. Information about the vaccines used was either not provided by the farmers or was incomplete. The vaccines could include any vaccine available, either legally or illegally, including Medivac AI. No ring vaccination around farms in this group was applied by Dinas Peternakan or CIVAS.

Surveillance

Two variables were determined:

– antibody responses after vaccination

– the number of H5N1 outbreaks in each flock.

In a vaccinated population, the surveillance strategy should be based on virological and/or serological methods and clinical surveillance (22). In flocks where homologous

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AI vaccines are used, the OIE (22) suggests a surveillance system based on the DIVA principle. A DIVA strategy is defined as one that differentiates vaccinated from infected animals (12, 19), and it involves the use of accompanying serological tests, or sentinel birds that are not vaccinated against AI (hereafter referred to as 'sentinels') (22). Such a surveillance system is, however, currently lacking in Indonesia.

As a homologous vaccine was used, at least in the treatment group, the surveillance had to be based on sentinels, according to the DIVA principle as described by the OIE (22). This excludes the possible contribution of infection to antibody titres and allows detection of incursions and subsequent outbreaks of H5N1 virus strains.

Sentinels were placed in each flock in both the treatment and control groups. The sentinels originated from the same farm as the one on which they were placed. The sentinel birds in the native chicken flocks were labelled with a metal ring around one leg, and were easily identifiable in the flock; the birds in the layer flocks were housed in cages, as were the other birds in the flock. The sentinels received equivalent treatment with respect to vaccinations against all diseases except AI. Within each shed, 10 to 50 sentinels were maintained, depending on the number of birds in each shed. The sentinels were housed in the same way as the other birds: either they could mingle freely within the group (native chickens) or were put in individual cages (layers). Serum samples were taken from the sentinels at the time of first vaccination of the flock, in order to demonstrate the absence of antibodies against H5 at the start of the trial. It was assumed that birds were not infected with H5N1 if clinical signs were absent.

Sampling

The farms included in the trial were visited regularly by CIVAS staff members for sampling and clinical inspection. Dead sentinels were reported immediately by the owners to CIVAS, and swab samples were collected from the trachea and cloaca of every dead sentinel bird. If sentinels were found dead by CIVAS, or if these birds or other birds in the flock showed signs of AI, the same procedure was followed. Swabs were placed in a tube containing transport medium and were stored at 4ºC during transport to the laboratory, which took place within 24 h after collection.

Serum samples were collected regularly to monitor vaccine-induced antibodies and introduction of H5N1 virus. Serum samples from 20 randomly selected vaccinated birds were collected on the days on which flocks of the treatment group were vaccinated; samples were collected from flocks of the control group at similar times. Layers were also sampled one month after the last

vaccination; native chickens were sampled at the end of the production period (at the age of 2 to 3 months). Serum samples from ten randomly selected sentinels were collected at the same sampling points to demonstrate that they were still seronegative for H5, and to monitor subclinical infections with low pathogenic avian influenza (LPAI) H5 strains. At the end of the production period, sentinels were swabbed and serum samples were taken to demonstrate the absence of infection with AI virus.

Two months after each vaccination of backyard chickens in the ring around the flocks in the treatment group, serum samples were taken from 20 randomly selected birds per ring to monitor antibody titres.

Laboratory tests

The swabs were transported in medium to the Bbalitvet reference laboratory in Bogor, Indonesia. The samples were stored at −70ºC until they were tested for the presence of H5 AI antigen. A polymerase chain reaction (PCR) kit (Invitrogen™) (9) was used to detect H5 RNA in each sample according to the manufacturer's instructions. Positive samples were cultured in embryonated specific pathogen free (SPF) eggs according to the standard procedures of Bbalitvet, which follow the method described in chapter 2.1.14 of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*) (22).

The serum samples were tested in the provincial animal health laboratory of West Java in Cikole. Blood samples were centrifuged and serum was stored at 4ºC until tested. Tests were carried out shortly after arrival of the samples in the laboratory. The sera were tested by an HI test using twofold dilutions according to the procedures described in the *Terrestrial Manual* (22), using 4 haemagglutination units (HAU) of H5N1 strain A/ch/Legok/03 as the antigen. Erythrocytes from SPF chickens were provided by PT Medion, Bandung. A positive and a negative serum sample were included in each test, and tests were carried out in duplicate. Titres were expressed as 2^x of the serum dilution that caused complete inhibition of agglutination (22).

Results

Farms

A total of twelve farms were included in the trial. The treatment group consisted of two layer and four native chicken farms, and the control group contained four layer and two native chicken farms. In the treatment group, for reasons already discussed, more flocks than farms were included and used for the calculation of the average titre

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(Table II). The treatment was not allocated randomly, as some farmers were willing to cooperate only when they could apply their own vaccination programme. These farms became part of the control group.

Table II
Technical data from the flocks in the treatment and control groups

Group	Farm type	Number of farms	Total number of flocks*
Treatment	Layer	2	5
	Native chicken	4	9
Control	Layer	4	4
	Native chicken	2	2

* In the treatment group there were more flocks than there were farms: one layer farm had more sheds that were included. With respect to the native chicken farms, the production period of poultry was shorter than the duration of the trial, so when a flock was slaughtered it was replaced by a new flock

Serology

The average titre was based on samples with a titre $>2^1$. So-called non-responders were not included in this calculation. The vaccination coverage (percentage of birds with a predefined titre) was calculated for a cut-off of 2^4 and for a cut-off of 2^5 (10).

Treatment group

In the layer farms, the average geometric titre of serum after two vaccinations was $2^{5.9}$ (standard deviation [SD] $2^{1.7}$), and after the third vaccination it was $2^{7.2}$ (SD $2^{2.0}$). The mean was based on samples from a total of five flocks from two layer farms, collected in 2007. None of the samples had a titre of 2^1, indicating that in these flocks no non-responders were present after the second and third vaccinations. The distribution of titres was more or less normal (Fig. 1). Two birds out of a total of 120 birds sampled from the treatment group had a titre below 2^4. Assuming that a titre of 2^4 represented a positive response, this finding means that the vaccine coverage, here defined as the percentage of birds with a titre equal to or higher than 2^4, was >95%. The vaccine coverage using a cut-off value of 2^5 was approximately 90%.

In the native chicken flocks (4 farms; 9 flocks in total), 24% of the birds had a titre of 2^1 at the end of production, after two vaccinations. We estimated the average titre of the remaining 76% of the birds, which did respond (Fig. 2). The average titre in these birds was $2^{4.4}$ (SD $2^{2.3}$). In this group, 51% of samples had a titre above 2^4, thus a much lower coverage was achieved, and this was exacerbated because the number of non-responders was much higher than among the layers in the treatment group.
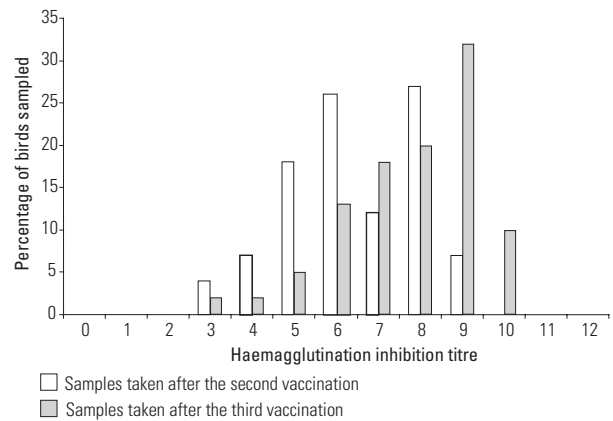

☐ Samples taken after the second vaccination
▨ Samples taken after the third vaccination

Fig. 1
Distribution of HI antibody titres in samples from layer flocks in the treatment group that were collected after two and three vaccinations

Control group

The average titre of birds in layer flocks after the second vaccination was $2^{5.8}$ (SD $2^{3.7}$). This calculation was based on samples collected from chickens of all four layer farms. In one of these flocks, very few sampled birds developed a titre. In this flock a vaccine of unknown origin had been used. The average titre in this particular flock was $2^{0.4}$ (SD $2^{0.9}$) with a coverage of 0%. The average titre of the three other flocks was $2^{7.6}$ (SD $2^{2.2}$) with a coverage (at a titre of 2^4) of approximately 93% after the second vaccination.

The average coverage in the native chicken flocks was 50%. The average titre in the native chicken flocks in the control group was $2^{2.9}$ (SD $2^{2.4}$).

Ring zone

The average titre in the 1 km ring around the flocks in the treatment group after two vaccinations was $2^{2.6}$ (SD $2^{2.7}$).
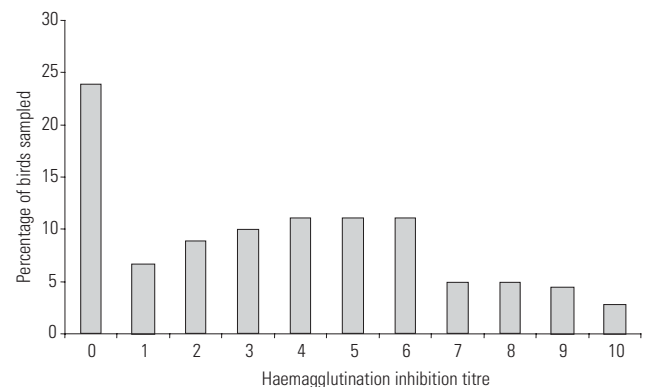

Fig. 2
Distribution of HI antibody titres in samples from native chicken flocks in the treatment group after two vaccinations, collected at the end of the production period

The vaccination coverage (percentage of birds with a titre of 2^4 or above) was 38%. The coverage estimated using this cut-off titre in the 1 km ring around the flocks in the control group was 12%.

Virus detection

An outbreak of H5 virus infection occurred on one farm in the treatment group approximately 4 weeks after the second vaccination, as demonstrated by a positive PCR test and virus isolation in embryonated eggs. The farm had 95 sheds containing poultry, of which five were included in the trial. The outbreak seemed to have started in one of the sheds containing growers that had not been included in the trial. Poultry in two sheds included in the trial were affected 1 week after the second vaccination (aged 12 to 13 weeks). The average titre just before virus introduction was approximately $2^{5.2}$ (SD $2^{1.3}$); the percentage of samples with a titre $>2^4$ was 80%. The other sheds in the trial were culled at 57 to 62 weeks of age, and no additional information about these sheds was available. The virus that caused the outbreak was isolated from the sentinel birds and was confirmed to be HPAI H5 by PCR. Preliminary RNA sequence analysis performed at Bbalivet showed that the strain was similar to A/Ch/WJ/PWT-WIJ/06, which was isolated on Java in 2006 (13). No H5 virus was detected on the other farms that participated in the trial.

Discussion

The aim of this study was to study the effectiveness of vaccination against H5N1 AI under field conditions by measuring antibody titres in the HI test and detecting outbreaks of H5 virus infection. The vaccine coverage of a flock was estimated from the titre values. Sentinel birds that were not vaccinated against AI were used to record major H5N1 outbreaks in the flocks included in the trial, and were also necessary for correct interpretation of the antibody titres. Without this DIVA surveillance system it is impossible to be sure whether the measured titres result from vaccination, infection with H5 subtype viruses, or a combination of the two.

The average titre after two vaccinations of layers in the treatment group was $2^{5.9}$ and the coverage, here defined as the percentage of samples with a titre of 2^4 or above, was more than 95%. This trial demonstrates that, with locally produced homologous vaccines, high antibody titres and a high coverage could be reached, at least in layer flocks. Philippa *et al.* (10) used a different cut-off value for vaccine effectiveness. They used a titre of >40, a value that is considered to be protective and to reduce virus replication in humans, in a situation in which challenge experiments were not ethical. For similar reasons Philippa *et al.* (10)

assumed that vaccinated zoo birds with a titre of 1:40 or greater would be protected. After three vaccinations the coverage obtained using this cut-off value was approximately 90%. It would be helpful to have more data on the relationship between titre and protection against virus transmission, as has been described for Newcastle disease (17).

An important aim of vaccination is to reduce the transmission of virus within and between flocks. The reproduction ratio R, the average number of secondary cases caused by one infectious animal (6), is a frequently used measure of transmission of pathogens. If R is larger than one, the infection will spread. This measure can also give an indication of the critical fraction of immune birds that is required to prevent major outbreaks in a flock (6). If the percentage of vaccinated birds in a flock is 1–1/R, the virus can be eliminated by vaccination. For H5N1 virus within a poultry flock the R has been estimated to be about 2.3 to 2.6 (16). From the reproduction ratio, the critical fraction of immune birds is estimated to be approximately 60% if a perfect vaccine is used. Assuming that HI titres >40 are sufficient to reduce the reproduction ratio to 0, the coverage of 90% achieved in the layer flocks in the treatment group of this study seems to be sufficient. It should be realised, however, that the vaccine is probably not perfect, and R values may differ between flocks. A level of coverage higher than 60% is therefore advisable.

The titres of the samples from native chickens were lower, and more birds on these farms did not have a detectable titre. It has been suggested that native chickens may be less responsive to vaccination. The lower responses were explained by concurrent diseases or immunosuppressive infections at the time of or after vaccination, but the underlying mechanism of the lower response needs to be explored. It is necessary to study the transmission of the virus in native chickens using vaccination challenge experiments under controlled conditions.

An outbreak of AI occurred in one of the layer flocks in the treatment group. It is believed that the outbreak started in one of the sheds on the farm that was not included in the treatment group. As a result of the increase in the number of birds in the affected shed that were shedding virus, the dose of virus to which the birds in the flock that were included in the treatment group was exposed may have been very high. The level of virus challenge was probably much higher than that to which birds in sheds located in a remote area would have been exposed. In addition, this farm may have been infected by an antigenic mutant strain like the A/Ch/WJ/PWT-WIJ/06 strain. Vaccination challenge studies have shown that most vaccines currently licensed in Indonesia do not provide optimal protection against this strain (13). Based on preliminary sequencing, the virus isolated from this flock was similar to the A/Ch/WJ/PWT-WIJ/06 strain. Given that an outbreak

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occurred only in a flock of the treatment group, one could infer at first sight that vaccination in this group was less effective than in the control group. This cannot be concluded, however. First, it is obvious that the number of outbreaks is far too low to be of any statistical significance. Second, farms were not randomly allocated to the two groups, either treatment or control, because participation was entirely voluntary. Therefore, we cannot exclude the possibility that, among other factors, farm management differed substantially between the two groups.

When monitoring HI antibodies induced by vaccination it is essential to ensure that the antibodies are the result of vaccination only and are not caused by infection with an H5 subtype virus, or a combination of vaccination and infection. The possible contribution of infection can only be excluded by using the DIVA principle (12, 19). The DIVA strategy used in this trial was based on the use of sentinel birds; we could not use antibodies against the neuraminidase protein because a homologous neuraminidase vaccine was used. It seems reasonable to assume that the risk of outbreaks of HPAI attributable to the presence of sentinels is negligible, as only a few birds in each shed were sentinels. Moreover, direct contact between the sentinels and the vaccinated birds did not occur, as they were all housed in cages. Data from transmission trials has shown that no indirect virus transmission occurs (4); therefore it seems unlikely that the sentinels on the outbreak farm initially contracted the infection and were responsible for the subsequent extensive spread of the virus. Many farmers are of the opinion that sentinels are at high risk of infection with AI. The level of knowledge of farmers and veterinarians with respect to the risks inherent in the use of sentinels and the value of adequate surveillance systems in the control of AI should therefore be improved. This may contribute to the adoption of DIVA vaccination campaigns and improvement of the current surveillance strategies.

The number of farms included in this study was much lower than calculated for the power analysis. One of the reasons was that farmers were reluctant to participate, and much time and effort was expended on visiting farms and informing the farmers of the trial. In addition to this, the treatment was not allocated randomly, as some farmers were willing to cooperate only when they could apply their own vaccination programme. The programme set up to inform farmers and try to convince them to join the trial experienced difficulties, especially in convincing farmers to implement the DIVA strategy using sentinel chickens. Farmers were worried about the risk of these sentinels being a source of infection to other chickens in the flock.

The small sample size means that it is impossible to draw conclusions about the effectiveness of vaccination in relation to virus transmission between flocks, to perform statistical analysis or to make statistical inferences from the results of this trial. In addition, the owners of backyard chickens did not always respond to the vaccination campaign, and there was a lack of support from the government of the villages. Moreover, flock owners were not convinced that repeated vaccinations were necessary, and were afraid that vaccination may lead to increased mortality. The whole vaccination procedure was time consuming because field officers had to catch many of the chickens to be vaccinated.

Nevertheless, we learned important lessons from this trial about the antibody responses that can be induced by vaccination in the field, about the quality of the laboratory test procedures, and finally about various aspects of the organisation and implementation of a surveillance programme in Indonesia. The surveillance system, based on the DIVA principle, also showed that farms can remain free from H5N1 virus during their production cycle. These and other lessons can be of use for other organisations involved in the planning and implementation of surveillance and control programmes for AI.

Conclusions

A clinical trial was carried out to monitor vaccine-induced HI titres, vaccination coverage and the number of outbreaks of HPAI H5 in poultry flocks. The trial was only small-scale, and this prevents the drawing of conclusions about the effectiveness of vaccination in AI control in Indonesia. Nevertheless, valuable experience was obtained in the operation of veterinary services, sample handling, quality assurance of laboratory testing, and the implementation of a DIVA surveillance strategy using sentinel birds that were not vaccinated against AI. The results and experiences of this trial may help to develop and improve future surveillance and control strategies in Indonesia and in other countries in the region.

Acknowledgements

Étude de terrain pour évaluer l'efficacité de la vaccination contre l'influenza aviaire en Indonésie

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Résumé
Une étude de terrain a été réalisée afin de déterminer l'efficacité de la vaccination contre la souche H5N1 du virus de l'influenza aviaire hautement pathogène (IAHP) en Indonésie. L'essai clinique, de portée limitée et basé sur un prototype, a porté sur deux groupes de poulets, le premier comprenant des cheptels traités suivant une procédure standardisée et ayant reçu au moins deux doses vaccinales d'un vaccin H5N1 sélectionné, et le second (groupe de contrôle) comprenant des cheptels traités suivant des procédures non standardisées décidées par l'éleveur. Chaque groupe consistait en six cheptels de poules pondeuses ou de poulets autochtones. Les titres d'anticorps inhibant l'hémagglutination (IH) ont été déterminés en se basant sur un échantillonnage régulier ; la surveillance du foyer reposait sur l'utilisation d'oiseaux sentinelles non vaccinés contre l'influenza aviaire. Après trois vaccinations, le groupe traité présentait des titres élevés d'anticorps, avec près de 90 % des poules pondeuses exhibant un titre d'anticorps IH supérieur à 40. Bien qu'aucune conclusion ne puisse être tirée quant à une éventuelle diminution de la transmission virale, il a été constaté que 11 élevages sont restés indemnes durant la période d'observation ; en outre, l'étude a montré la faisabilité d'un programme de surveillance fondé sur la différenciation entre animaux infectés et animaux vaccinés (DIVA).

Mots-clés
Différenciation entre animaux infectés et animaux vaccinés (DIVA) – Indonésie – Influenza aviaire hautement pathogène – Oiseau sentinelle non vacciné contre l'influenza aviaire – Surveillance – Vaccination.
■

Ensayos sobre el terreno para evaluar la eficacia de la vacunación contra la influenza aviar en Indonesia

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Resumen
Los autores describen un estudio sobre el terreno realizado en Indonesia para determinar la eficacia de la vacunación contra la cepa H5N1 del virus de la influenza aviar altamente patógena. Se llevó a cabo un ensayo clínico limitado, con carácter experimental, utilizando un grupo de tratamiento normalizado, en el que las bandadas fueron vacunadas como mínimo dos veces con una vacuna

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anti-H5N1, y un grupo de control con bandadas sometidas a un tratamiento no normalizado, que se dejaba a discreción del criador. Cada grupo constaba de seis bandadas, compuestas por aves ponedoras o pollos nativos. Tras un muestreo sérico ordinario se determinaron los niveles de anticuerpos por inhibición de hemaglutinación (IH) y se estableció una vigilancia de posibles brotes con aves centinela no vacunadas contra la influenza aviar. Después de tres vacunaciones se obtuvieron títulos elevados de anticuerpos en el grupo de tratamiento: alrededor de un 90% de las ponedoras presentaba un título de IH superior a 40. Aunque no cabe extraer conclusiones respecto a la reducción de la transmisión del virus, el estudio demostró que 11 explotaciones permanecían libres de influenza aviar durante el periodo de observación, y que es posible instituir un programa de vigilancia basado en la discriminación entre animales infectados y vacunados (DIVA: *differentiating infected from vaccinated animals*).

Palabras clave
Centinela no vacunado contra la influenza aviar – DIVA – Indonesia – Influenza aviar altamente patógena – Vacunación – Vigilancia.

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