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Live newcastle disease virus vaccines.

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References cited:
BE-A- 853 923
GB-A- 2 062 461
US-A- 2 798 835


AMERICAN JOURNAL OF VETERINARY RESEARCH, vol. 17, April 1956; L.E. HANSON et al., pp. 294-298&NUM;

AVIAN DISEASES, vol. 11, 1967; C.W. BEARD, pp. 399-406&NUM;

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Description

The invention relates to live Newcastle Disease virus (NDV) vaccines for poultry, to a method of preparing the same and to a new NDV strain.

NDV is a disorder of the respiratory tract, the laying system, the intestines and the central nervous system, frequently occurring in poultry.

The disease causes great economical losses in poultry farming. In addition to mortality of animals, the disease causes respiratory and nervous symptoms, and in layers decrease of production as result of damage to the laying system.

The disease is controlled by vaccinating the animals with a live or an inactivated vaccine. For example, vaccinations with live vaccines based on among others the Hitchner-strain or the De La Sota-strain have been carried out for a considerable period of time already. Although the use of vaccines based on the said known NDV strains is comparatively safe and effective, it has been found that in the vaccination of young chickens a strong vaccination reaction nevertheless occurs when the vaccination is done with a strain which provides a good protection. On the other hand the protection is not complete when vaccination is carried out with a strain which causes little vaccination reaction. In this connection the maternal immunity plays an important role since, for causing the vaccination in chickens with a maternal immunity to be effective, vaccination strains are required which cause a considerable vaccination reaction.

Another disadvantage of the NDV vaccines based on the known strains is that vaccination with combination vaccines against ND and infectious bronchitis (IB) is not possible due to the occurrence of unacceptably strong vaccination reactions.

Document BE-A-853 923 describes Newcastle Disease Viruses of strain P/77/8 which are derived from strain P/76/5. Viruses of strain P/77/8 markedly differ from viruses of strain NDW in the thermobility of their hemagglutinin. The hemagglutinin of strain P/77/8 viruses is strongly thermostable, whereas NDW hemagglutinin is thermostable, and hence is more nearly resembling viruses of pathogenic Newcastle Disease viruses such as the Essex strain viruses which, however, are not suited for vaccine applications.

US-A-2 798 835 relates to Newcastle Disease Viruses in general, of which only the Blacksburg B-1 strain is mentioned explicitly. This Newcastle Disease Virus strain B1 (if administered alone, as a vaccine) was described to possess poor efficacy, particularly in birds with maternally derived antibodies (G. Bennejan et al (1978); Avian Pathology 7, 15-27). In contrast, vaccination with the NDW virus strain according to the present invention was shown to provide a good protection of chickens with a high maternal immunity.

GB-A-2 062 461 relates to Newcastle Disease Virus of the Russian strain a-Bor-74NGNKKI. This strain also is much less efficacious than the strain according to the present invention. The Russian strain should be administered twice to young chickens, in order to attain adequate protection (see p2, left column, lines 15-24 of GB-A-2 062 461 whereas the Examples of the present application demonstrate adequate protection of 1-day-old chickens upon a single vaccination.

It has now been found surprisingly that ND vaccines which do not have the disadvantage mentioned here inbefore are obtained when the NDV strain used is the strain NDW which is registered at the CNCM of the Institut Pasteur, in Paris, under number T-781.

It has been found that live vaccines based on the strain NDW are completely safe and readily efficacious, also for the protection of chickens having a high maternal immunity. Therefore, vaccine according to the invention may be used already at an age of 1 day.

It has furthermore been found that a generally known problem which occurs when vaccines are administered which contain more than one live virus component, namely the fact that the combined viruses become less immunogenic due to a mutual interaction (so-called interference, see Am.J.Vet.Res. 36 (1965), p. 4, 524 and 525; and Avian Diseases 12 (1968), p. 577) does not occur when the NDW-strain is combined with other live virus strains.

The NDW virus strain can be processed in a manner known per se to a vaccine suitable for administration. Such a vaccine may be administered to chickens from the age of 1 day or at a later date, even when they have a high maternal immunity, if desired in combination with one or more IB-virus strains. The administration may be carried out, for example, by means of a spray or eyedrops.

The invention will now be described in greater detail with reference to the ensuing experiments.

EXPERIMENT I

Efficacy of vaccination with strain NDW

24 Birds taken from a group of 1-day-old broilers were used for the determination of the maternal immunity according to the HI-method. The mean titer was found to be $2\log 10.7$.

43 chickens were vaccinated with $10^5$log $5.4$ ELD$_{50}$ per bird by means of spray vaccination. 3 and 6 weeks after vaccination 21 and 22 birds, respectively, were subjected to a challenge infection with $10^5$log $6$ ELD$_{50}$ of Herts 33 virus, administered ocularly, per bird. As a control, at the time
of challenge, 2 SPF chickens, 1 week older than the broilers, were added and also challenged.

After the challenge at 3 weeks post vaccination, all 21 birds survived, while after the challenge at 6 weeks post vaccination 20 out of 22 birds survived. The SPF controls died.

It appears from this experiment that the vaccination with the strain NDW of chickens having a high maternal immunity provides excellent protection against an infection with virulent ND virus throughout the fattening period.

EXPERIMENT II

Efficacy of vaccination with the NDW-strain as a component of an ND/IB combination vaccine

48 broilers having a mean maternal antibody titer of $10^5$ HU units were vaccinated by means of spray at the age of 1 day with a combination vaccine consisting of $10^5$ EID$_{50}$ NDW and $10^5$ EID$_{50}$ H120/84-3 per dose.

3 and 6 weeks post vaccination 23 and 25 birds, respectively, were subjected to an ocular challenge with $10^5$ ELD$_{50}$ of Herts 33 virus per bird. As a control, at the time of challenge, 2 SPF chickens were added and also challenged.

After the challenge at 3 weeks post vaccination, 21 out of the 23 animals survived. After the challenge at 6 weeks post vaccination all 25 birds survived. The SPF controls died.

It appears from this experiment that the NDW-strain administered as a component of an ND/IB combination vaccine provides an excellent protection against infection with virulent ND virus throughout the fattening period. This is in spite of the high maternal antibody titre of the chickens at the time of vaccination.

EXPERIMENT III

Efficacy of vaccination with the NDW-strain as a component of an ND/IB combination vaccine

25 birds were taken from a group of 75 day-old broilers for the determination of the maternal antibody titer according to the HI-method. The mean titer was found to be $10^5$ B.7. The remaining chickens were divided into two groups of 25. The first group was vaccinated with a combination vaccine NDW/H120/84-3 in a manner identical to that of experiment 2. The second group formed the non-vaccinated control group. One bird from this group died in the period before challenge. Both groups were infected 32 days post vaccination with $10^5$ ELD$_{50}$ of Herts 33 virus per bird. Two SPF chickens of approximately 6 weeks old were added and also challenged.

1 out of the 25 vaccinated birds died after challenge. 21 out of the 24 non-vaccinated controls died. The SPF controls died.

It appears from this experiment that the NDW strain as a component of an ND/IB combination vaccine provides an excellent protection against infection with virulent ND virus, which confirms the conclusion of experiment 2.

EXPERIMENT 4

Small field trial

1-day-old broilers were distributed over a number of pens and vaccinated with Poultvac IB Primer (IB-strain H120/84-3) or with a combination vaccine consisting of Poultvac IB Primer and NDW vaccine. A few pens were not vaccinated serving as a control group. Each pen housed 400 chickens.

The trachea lesion score, determined at 10 days post vaccination, was
- 0.0 for the non-vaccinated birds
- 0.1- 0.6- 0.7- 1.1 for the birds vaccinated with IB Primer (4 groups of 10 birds each)
- 0.0- 0.0- 0.2- 0.8 for the birds vaccinated with IB Primer/NDW combination (4 groups of 10 birds each)

The mean ND HI titer, determined at 0, 3 and 6 weeks post vaccination was
- 8.2 (maternal immunity) 4.0 and 4.0, respectively, for birds vaccinated with IB Primer,
- 8.2, 5.2 and 6.4, respectively, for the birds vaccinated with IB Primer/NDW combination

The average weights, determined at 6 weeks after vaccination, showed no significant differences between the groups.

A challenge with virulent ND virus, strain Herts 33/56, carried out at 4, 5 and 6 weeks post vaccination, resulted in a protection of 90%, 100% and 92%, respectively, in the group vaccinated with IB Primer/NDW combination vaccine. The group vaccinated with IB Primer, as well as the non-vaccinated group, were entirely unprotected against an infection with virulent ND (0% protection) at all three occasions.

A challenge with virulent IB virus, carried out 4 weeks post vaccination, both with the strain Voet and with a virulent strain D274, resulted in
- a protection of 100% against Voet and 90-100% against D274 for the birds vaccinated with IB Primer
- a protection of 100% against Voet and 60-100% against D274 for the birds vaccinated with IB Primer/NDW combination
- no protection (both strains 0% protection) for the non-vaccinated birds. From this experiment it appears that the NDW strain as a component of an IB/ND combination vaccine
- is fully harmless
- provides an excellent protection against infection with virulent ND virus
- does not interfere with the remaining components of the vaccine, so that these also remain fully efficacious.

Claims
Claims for the following Contracting States:
AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

1. A live vaccine against Newcastle Disease, characterised in that it comprises a virus of the strain NDW registered at the CNCM of the Institut Pasteur in Paris, under number I-781.

2. A vaccine as claimed in Claim 1, characterised in that it comprises a quantity of virus $>10^{10}$ log 5.5 EID$_{50}$ per dose.

3. A vaccine as claimed in Claim 1 or 2, characterised in that it comprises also one or more infectious bronchitis virus strains.

4. Virus strain NDW registered at the CNCM of the Institut Pasteur in Paris, under number I-781.

Claims for the following Contracting States:
ES, GR

1. Use of the Newcastle Disease virus of strain NDW registered at the CNCM of the Institut Pasteur in Paris, under number I-781 in the preparation of a live vaccine against Newcastle Disease.

2. Use according to claim 1 characterized in that a quantity of virus is used of more than $10^{10}$ log 5.5 EID$_{50}$ per dose.

3. Use according to claim 1 or 2 characterized in that additionally also viruses of one or more Infectious Bronchitis virus strains are used.

Patentansprüche
Patentansprüche für folgende Vertragsstaaten:
AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE


2. Impfstoff nach Anspruch 1, dadurch gekennzeichnet, daß er auch einen oder mehrere infektiöse Bronchitisvirusstämme umfaßt.


Patentansprüche für folgende Vertragsstaaten:
ES, GR


2. Verwendung nach Anspruch 1, dadurch gekennzeichnet, daß eine Virusenmenge von mehr als $10^{10}$ log 5.5 EID$_{50}$ pro Dosis verwendet wird.

3. Verwendung nach Anspruch 1 oder 2, dadurch gekennzeichnet, daß zusätzlich auch Viren eines oder mehrerer infektiöser Bronchitisvirusstämme verwendet werden.

Revendications
Revendications pour les Etats contractants suivants:
AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

1. Vaccin vivant contre la maladie de Newcastle, caractérisé en ce qu’il comprend un virus de la souche NDW, enregistrée auprès du CNCM, à l’Institut Pasteur de Paris, sous le numéro I-781.

2. Vaccin selon la revendication 1, caractérisé en ce qu’il comprend une quantité du virus supérieure à $10^{10}$ log 5.5 EID$_{50}$ par dose.

3. Vaccin selon la revendication 1 ou 2, caractérisé en ce qu’il comprend aussi une ou plusieurs souches du virus de la bronchite infectieuse.


Revendications pour les Etats contractants suivants:
ES, GR

1. Utilisation de virus, appartenant au virus de la maladie de Newcastle de la souche NDW, enregistrée auprès du CNCM, à l’Institut Pasteur de Paris, sous le numéro I-781, pour pré-
parer un vaccin vivant contre la maladie de Newcastle.

2. Utilisation selon la revendication 1, caractérisée en ce qu'on utilise une quantité du virus supérieure à $10^{5.5}$ EID₅₀ par dose.

3. Utilisation selon la revendication 1 ou 2, caractérisée en ce qu'on utilise en outre aussi des virus d'une ou plusieurs souches du virus de la bronchite infectieuse.