

Vaccination against Avian Influenza as an aid to eradication

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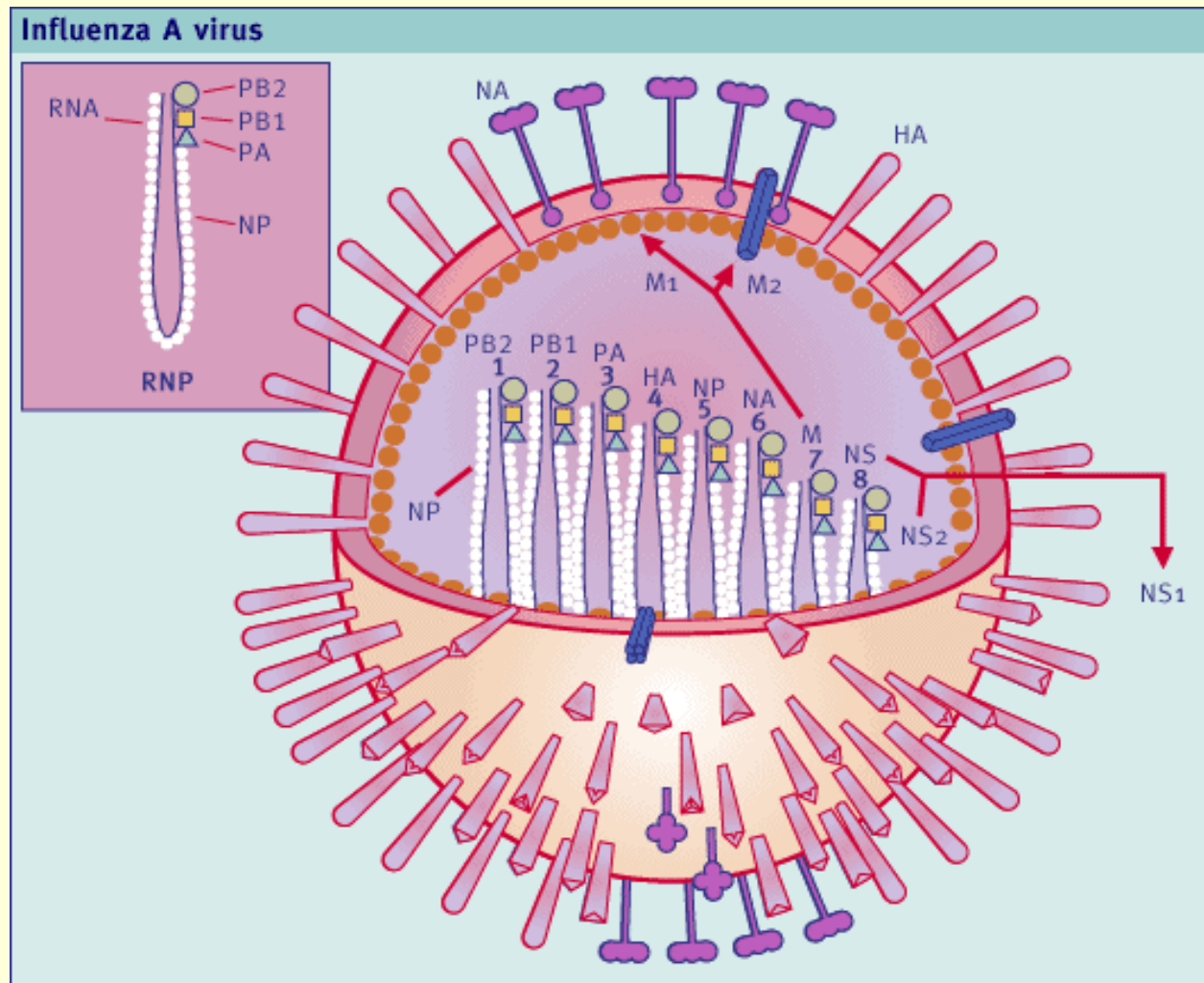


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Avian Influenza

- n Family - *Orthomyxoviridae*, genus - *Influenzavirus A*
- n Typically spherical, sometimes filamentous
- n Surface covered with 2 types of glycoproteins
 - 4 Hemagglutinin (HA) – rod shaped trimer
 - 15-16 known HA proteins
 - Responsible for host cell entry
 - 4 Neuraminidase (NA) – mushroom shaped tetramer
 - 9 known NA proteins
 - Responsible for host cell exit
 - 4 Combination of HA and NA proteins gives the virus its characteristics / pathogenicity (highly pathogenic [HPAI] vs low pathogenic [LPAI])
 - Eg Avian Influenza: H5N1 (HPAI) and H5N2 (LPAI)
 - Eg Human Influenza (type B) H3N2
 - Eg Swine Influenza (type A or C) H1N1, H3N2
 - Eg Equine Influenza (type A) H7N7
- n Viral genome – 8 segments of -ve sense ss RNA
 - 4 Code for 10 proteins including 2 nonstructural proteins
 - 4 HA and NA coded by 1 segment each

Influenza A virus - Structure



The overall AI control strategy

- n **Biosecurity MUST be the first and central part of any AI control/ eradication strategy**
- n **It must be supplemented by appropriate monitoring programmes**
 - 4 Supported by the most recent OIE codes on the use of zoning and compartmentalisation for the maintenance of trade
- n **Flocks that become infected should be culled**

The role of vaccination

- n **Vaccination is not a “fire and forget” strategy**
- n **Vaccination requires the use of**
 - 4 Appropriately formulated vaccines (immunogenicity)
 - 4 Appropriately tested vaccines (QC)
 - 4 Appropriately applied vaccines (injectable versus mass administration)
- n **Vaccination can facilitate the maintenance of trade in an eradication programme via marker vaccination strategies**

The role of vaccination

- n **Vaccination can provide a cost effective alternative to mass slaughter policies when used within an overall control strategy**
- n **Vaccine banks can provide strategic insurance to minimise the financial consequences of mass culling for countries and poultry populations considered at lower risk of infection**
- n **Regardless of the approach, vaccination and vaccine requirements must be planned and forecasted to ensure appropriate quality standards are met.**

Possible approaches to vaccination

- **Routine** vaccination performed in endemic areas
- **Emergency** vaccination, which is implemented in the face of an epidemic
- **Preventative** (i.e. prophylactic) vaccination carried out if a high risk of virus incursions is identified

VACCINATION PROGRAMS

POSSIBLE SCENARIOS



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Bio-security



- n Automatic gate
- n Disinfection arc
- n Vehicles no admittance



Poultry production systems



Sector 1: Industrial integrated system
high level biosecurity



Sector 2: Commercial system
moderate to high biosecurity



Sector 3: Commercial system
low biosecurity



Sector 4: Village or backyard poultry
minimal biosecurity

AI vaccination

Possible scenarios

	Consideration of vaccination in each production sector			
Level of challenge	Sector 1	Sector 2	Sector 3	Sector 4
Negligible	No	No	No	No
Low	No	No	Yes	Yes
Moderate	No	Yes	Yes	Yes
High	Yes	Yes	Yes	Yes



Choice of vaccine

n Prophylaxis

- 4 Protection against both the major serotypes capable of causing HPAI is desirable – H5 and H7
- 4 The choice of isolates with sequences closely related to known circulating field viruses is an advantage
- 4 The use of master seed viruses with a similar H subgroup but heterologous and rare N is advantageous for DIVA purposes

n Emergency vaccination

- 4 Use of a product that contains an H antigen of the same H subgroup as the circulating field virus
- 4 The choice of isolates with sequences closely related to known circulating field viruses is an advantage
- 4 Any heterologous N containing vaccine is suitable

Choice of vaccine

n Inactivated vaccines

- 4 Efficacy in a wide range of target species
- 4 Duration of immunity
- 4 Require injection

n Live vectored vaccines

- 4 Day of age application
- 4 Limited duration of immunity
- 4 Injectable/ mass application options
- 4 Efficacy only in target species in which the vector will replication
- 4 Efficacy may be compromised in the face of a field challenge with vector virus
- 4 Efficacy may be compromised in the face of maternal antibodies

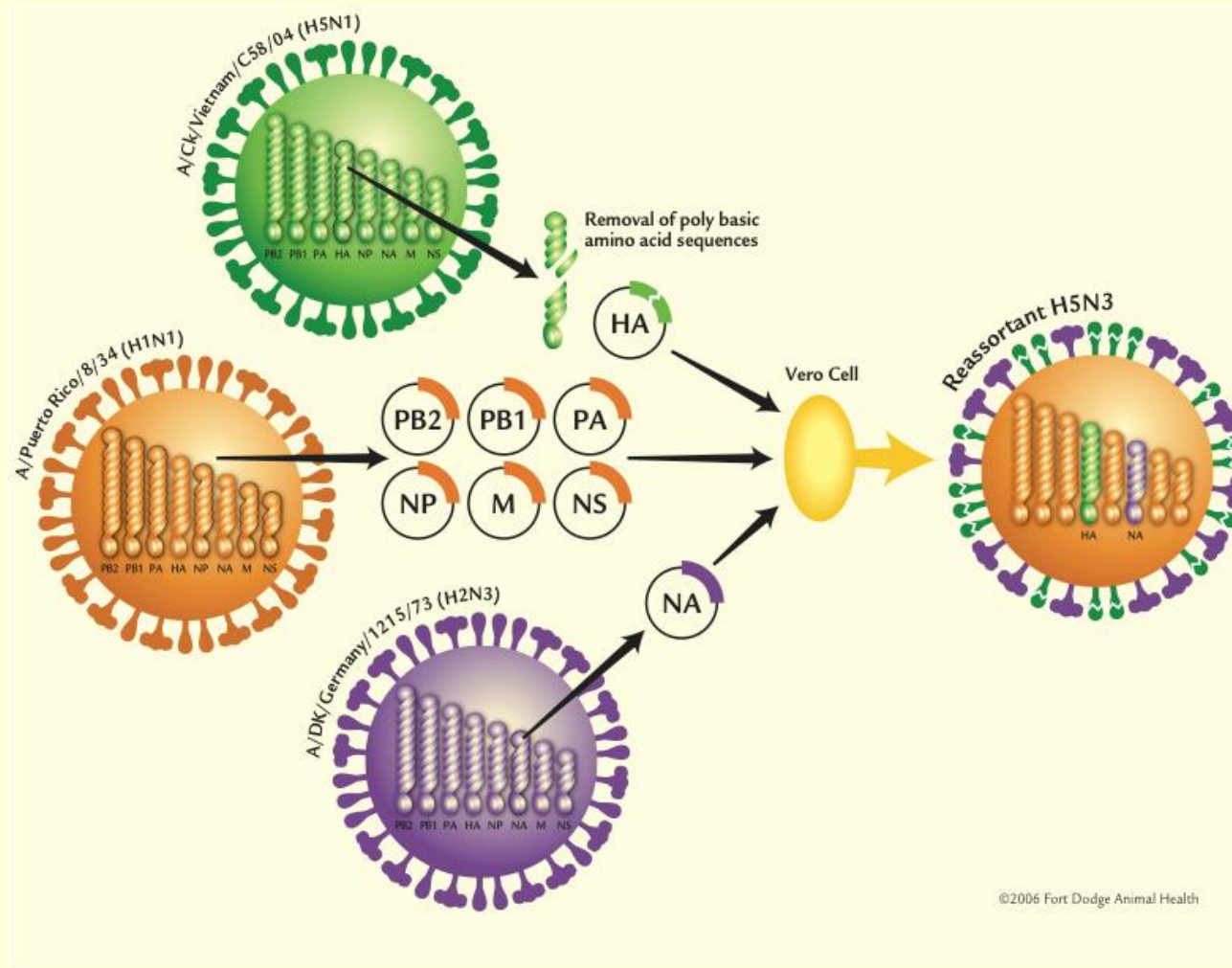
Derivation of Reverse Genetics (H5N3) vaccine

- n **HA gene from recent Asian outbreak**
 - 4 Allows optimum protection against current endemic H5N1 strain
 - 4 Through reverse genetics technology high path virus modified to low path while retaining protective ability

- n **NA gene selected for differentiation from wild type infections**
 - 4 N3 versus N1

- n **PR8 “backbone” well characterized and studied to be safe and efficient in cell culture**

Reverse Genetics (H5N3) vaccine- Outline



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The diagnosis of AI

- n **The presence of influenza type A viruses (GSA diagnostics against the M and NP) are determined by**
 - 4 Agar Gel Immuno-Diffusion (AGID) (high specificity, lower sensitivity)
 - Chickens and turkeys
 - NOT waterfowl – no precipitating antibodies
 - 4 Enzyme Linked Immuno-Sorbent Assay (ELISA) (high sensitivity, lower specificity)
 - Seropositivity to influenza A in water fowl is a normal finding
- n **Molecular methods**

The diagnosis of AI – The determination of the H subtype

- n HI testing
 - 4 Confirm positivity to notifiable AI first
 - H5, H7
 - 4 Use two antigens of the same H type but with different N types (e.g. H5N1 and H5N9)
- n A sample is considered positive if it causes inhibition of haemagglutinating activity of 4HA units at a titre of at least 1:16
- n Low degree cross reactivity with other H types can be observed due to N group homology
- n Example: A serum is positive to H9N2 at a titre of 1:256. If tested with H5N2 antigen, a positive inhibition can results at 1:8. When tested with an H5N9 antigen, the sample will be negative
- n Molecular methods

DIVA Systems

n Differentiation of Infected from Vaccination Animals

n Achievable by three basic means

- 4 Unvaccinated sentinels
- 4 Live vectored vaccines that do not express M and NP proteins
- 4 Inactivated vaccines that do not trigger immune responses to non structural proteins
- 4 Inactivated heterologous neuraminidase vaccination and detection

DIVA Systems

n Sentinels

- 4 A useful part of any market vaccination strategy
- 4 Difficult to manage in many countries due to their ability to be switched
- 4 The use of breeds of a different colour is encouraged
- 4 The non vaccination of cockerels to act as sentinels in village chicken farming is also encouraged

n Live vectored vaccines that do not express M and NP proteins

- 4 Use of standard AGID and ELISA tests facilitates the marker strategy
- 4 Disadvantages relate to the efficacy of pox vectored vaccines in the face of maternal antibodies and field challenge
- 4 Disadvantages relate to the lack of replication of the vector in key species
 - Ducks and turkeys

DIVA Systems

- n **Inactivated vaccines that do not trigger immune responses to non structural proteins**
 - 4 Field infection results in replicating virus that generates an immune response to non structural proteins
 - 4 Experimental development of diagnostic tests has demonstrated promising results
 - 4 Difficulties with the nature and duration of the immune response
 - Progressive truncation throughout the course of infection leading to changing immunogenicity
 - 4 Not yet validated fully

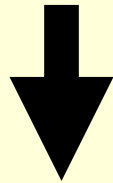
DIVA Systems

n **Achieved by heterologous neuraminidase vaccination**

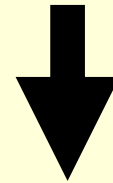
- 4 The N of the vaccine antigen is different to that of the field virus
- 4 Diagnostics against the field virus N prove freedom from field virus infection
- 4 This test is certified by the OIE and EU and can facilitate export
- 4 Associated detection systems
 - Immunofluorescence testing
 - Neuraminidase inhibition testing
 - Positive results should be used as an indicator to kill the flock
 - Appropriate testing schemes are essential

Monitoring Measure in the Vaccination Area

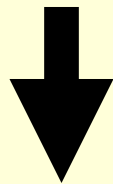
Farms where Vaccination is Practised



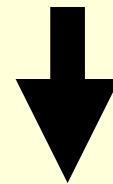
Monitoring vaccine efficacy



Monitoring epidemiological
Situation (all farms)



- 30 farms where vaccination is practised
- HI test
- 20 vaccinated birds/farm/month



- Every 30 – 45 days
- Serological – DIVA test
- 10 sentinel animals/farm
- Virological methods – VI, PCR

Replication kinetics of AI viruses vary with pathotype, poultry species and farming system



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Key objective

- n **To create virus negative populations**
- n **To identify these by appropriate monitoring**
- n **To maintain the negative status of these populations by**
 - 4 Raising the minimum infectious dose (vaccination)
 - 4 Decreasing the level of viral challenge (management and biosecurity)
- n **Ideal vaccines must be able to:**
 - 4 **Prevent clinical disease AND virus shedding in commercial poultry species**
 - 4 **Prevent virus shedding in reservoir species (ducks)**
 - 4 **Contain a DIVA strategy**
- n **Many commercial vaccines prevent clinical signs only and contain no DIVA strategy!**

Avian influenza: control strategies

Reservoirs



Poultry production systems



Monitoring and surveillance

- Reduction (not increase) of poultry density
- Avoid mixing of different species
- Improve hygienic standards (biosecurity, training, etc.)
- Monitoring and surveillance
- Contingency plans (vaccine banks)

- Risk communication
- Emergency or long term vaccination