CEVA HANDBOOK
OF POULTRY DISEASES

6 NEWCASTLE DISEASE

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DEFINITION

Newcastle Disease (ND) is a highly contagious disease which affects many domestic, companion and wild bird species and which, according to the viral strain and its tropism, provokes marked septicaemic and/or nervous signs with variable morbidity and mortality rate.

HISTORY AND SYNONYMS

Newcastle Disease was first recorded following the successful isolation and differentiation of the etiological agent from that of the fowl pest in 1927, after an outbreak in a farm near Newcastle (Doyle, 1927). In actual fact, the acute contagious disease with high mortality rate which struck birds in Java, Indonesia one year previously is now thought to be the first reported outbreak of the disease (Kraneveld, 1926). There are data for even earlier manifestations of a disease with similar signs and effects in central Europe (Halasz, 1912 in Alexander & Senne, 2008).

Other synonyms of the diseases are atypical fowl pest (Pseudopestis avium), Asian fowl plague and avian paramyxovirus type 1 infection.

In a recent review, a number of ND panzootics were recognized since 1926 (Alexander et al., 2004). The first probably originated in the Far East and spread slowly across the world. It took more than 20 years before this outbreak became a panzootic. The second ND panzootic began by the end of the 1960s and spread all over the world within 4 years (Hanson, 1972). The markedly different speed of ND spread between both outbreaks can be attributed to the development of the world poultry industry in the mean time, including extensive contact between poultry production companies (Alexander et al., 2004).

Other factors involved were the dominance of air transportation to international destinations and the increase in the transportation of caged birds.

By the end of the 1970s, antigenic and genetic evidence were found for a third panzootic outbreak, though the beginning of the processes remained unclear and was probably masked by the extensive application of vaccines since the mid 1970s (Alexander, 1997; Herczeg et al., 2001).

The fourth panzootic spread of ND was registered in the 1980s, affecting racing and show pigeons more than domestic poultry. By the end of the 1970s, pigeons were not routinely vaccinated and therefore were completely vulnerable to the ND virus. The infection among

pigeons probably originated in the Middle East (Kaleta et al., 1985), and by the mid-1980s had turned into a panzootic. Wild pigeons have also contributed to the spread of the disease in many countries, and in many cases it has remained endemic.

CHARACTERISTICS AND CLASSIFICATION OF THE PATHOGEN

The etiological agent of ND is an avian paramyxovirus 1 (APMV 1) or Newcastle disease virus (NDV).
It belongs to the Mononegavirales order, Paramyxoviridae family, Paramyxoviridae subfamily Avulavirus genus. The genus includes 9 serologically distinct paramyxoviruses with avian hosts, identified as Avian paramyxovirus 1÷9 (APMV 1÷9), (Lamb et al., 2000; Mayo, 2002). APMV 1 is the cause of Newcastle disease.
Newcastle disease outbreaks do not have to be reported to the OIE, provided the strain is velogenic: ICPI>0.7 a multiple basic sequence at the cleavage site (F).
NDV is composed of nucleocapsid and a lipoprotein envelope. It contains single-stranded, non-segmented spiral RNA. Virions are 160–250 nm in size and pleomorphic in shape (mainly spherical) (Zarkov, 2003). All isolated strains are morphologically, immunologically and antigenically similar. They possess a common group-specific antigen. Depending on their virulence, APMV-1 strains in chickens are classified into 3 pathotypes–velogenic, mesogenic and lentogenic. Velogenic strains are further subdivided into viscerotropic and neurotropic. Viscerotropic velogenic strains are sometimes called exotic or Asian. They are highly virulent for chickens, less virulent for turkeys and relatively apathogenic in psittacines Neurotropic velogenic strains result in acute nervous, sometimes respiratory signs and are fatal for chickens. They do not provoke intestinal lesions. Mesogenic NDV strains induce nervous and respiratory signs with low mortality rates. They are mainly used for vaccination of previously immunized birds.
Lentogenic NDV strains provoke a weak, sometimes subclinical

respiratory infection. They are used for vaccine production. Alexander et al. (2004) reported asymptomatic enteritis as a manifestation of avirulent infection, while the viral replication occurs mainly in intestines.

The resistance of the virus is considerably higher at low temperatures. In frozen carcasses it remains active for up to 836 days at -20°C, in eggs at refrigerator temperatures for up to 538 days, in excreta away from light up to 17 days. If available on eggshells, it is completely inactivated during the incubation period. Direct sunlight, humid heat and rot kill the virus quickly (Arsov et al., 1984). It is resistant within the pH range from 2.0 to 10.0. The virus is rapidly inactivated by 2% quaternary ammonium salts, 2% formalin and 3% sodium hydroxide (Zarkov, 2003).

EPIDEMIOLOGY

In natural conditions, gallinaceous birds are the most vulnerable. Chickens are the most severely affected, whereas turkeys do not tend to develop severe clinical signs. The susceptibility of wild birds (quails, partridges, pheasants) is variable. Waterfowl (order Anseriformes) are usually subclinical NDV reservoir hosts, but some isolates did provoke outbreaks among geese in China during the 1990s. Outbreaks associated to APMV-1 in young cormorants (Phalacrocorax spp.) were observed in the USA and Canada during the 1990s (Wobeser et al., 1993). Such outbreaks in various geographic locations linked to genetically similar viruses are attributed to migrating birds that serve as reservoir hosts (Alexander et al., 1999). In a review of the existing literature published over a decade ago, cases of ND are reported in ostriches (order Struthioniformes) (Alexander, 2000).

Parrots and birds of prey are usually resistant to ND, but also may act as reservoir hosts. Other species known to be infected with NDV are gulls (order Charadriiformes), owls (order Strigiformes) and pelicans (order Pelecaniformes).

NDV has been isolated in penguins (order Sphenisciformes) as well (Thomazelli et al., 2010). Birds of all ages are affected, but poults are most vulnerable to infection. NDV

infection has been documented in over 240 avian species (Kaleta & Baldauf, 1988).

Sources of infection are diseased birds (mainly via respiratory discharge and faeces), dead birds' carcasses, asymptomatic carriers, contaminated frozen meat etc. Having analyzed the NDV spread in different epizootics, Alexander (1988) outlines the following routes of transmission: shipping of live birds (game birds, racing pigeons, commercial birds), contact with animals, poultry products, shipping of men and equipment, contaminated water and feed, airborne spread. There is evidence that in air removed by fans, NDV could be spread at a distance of 1600 m in calm weather and up to 3–5 km in windy weather (Arsov et al., 1984). The role of migrating birds in the long-distance transmission of the disease is also important. The infection is spread by faecal/oral and airborne routes. Diseased birds excrete a large amount of the virus in their faeces. Gallinaceous birds usually shed APMV-1 for 1–2 weeks, but psittacines could be reservoir hosts for several months or more than a year. The transmission between birds depends on virus infectivity (Alexander & Senne, 2008). These scientists argue for the possibility for vertical transmission of the virus (from parents to offspring). The role of wild birds in disease transmission is not significant in countries where poultry are reared indoors, but in free range rearing the probability for such a transmission to occur is rather high. Wild birds, especially waterfowl, can be reservoir hosts of lentogenic viruses. They may become more virulent if they become established in poultry.

Lentogenic or mesogenic APMV–1 in some pigeon populations are endemic and may become more virulent if transmitted to poultry flocks. Last but not least, backyard poultry play a key role in spreading the disease. This category includes poultry reared for eggs and meat by private owners, and cockerels used in fights, where such a tradition still exists.

This has notably been the cause of several ND foci and massive outbreaks of ND in recent years (Oreshkova et al., 2008; Alexander & Senne, 2008).

The incubation period is 56 days on the average, ranging from 2 to 15 days in naturally transmitted NDV and depending on the virulence of the strain, the susceptibility and the immune status of the host.

CLINICAL SIGNS AND PATHOLOGY

The clinical signs and the severity of lesions vary with the pathotype of the respective APMV–1 strain, host species and age, the occurrence of stressors etc. They are not specific enough to provide a consistent basis for ND diagnosing.

Velogenic strains induce a severe, usually fatal disease in chickens. The disease can appear suddenly without clinical symptoms, with a high death rate.

Viscerotropic NDV strains provoke general signs such as lethargy, somnolence, difficult breathing, feed refusal, comb cyanosis, prostration and death. This pathotype of APMV-1 does not always cause respiratory signs. Sometimes conjunctivitis, eyelid swelling and profuse greenish or white diarrhoea may be observed. At a later stage, nervous symptoms may be manifested as torticollis, opisthotonus, leg and wing paralysis and abnormal circling *(Fig. 1)*. Consequently, a sharp reduction in egg laying rate, eggs with watery albumen, deformation and discoloration of eggshells can occur. The death rate can reach 100% in non-vaccinated chicken flocks (Alexander & Senne, 2008).

Neurotropic NDV strains cause a severe respiratory disease with sudden onset, followed by nervous signs after 1-2 days. The morbidity rate can be up to 100%, and the death rate about 50% in adults and up to 90% in young birds. This form of ND is most common in the USA (Alexander & Senne, 2008). In birds that survive the disease, usually after 1-2 weeks, permanent neurological lesions are observed.

In general, mesogenic NDV strains induce a disease characterized by low mortality, respiratory and occasional nervous clinical signs.

Lentogenic NDV strains can provoke less serious respiratory symptoms (dyspnea, rhales, sneezing) in young chickens, while adults usually remain asymptomatic. Co-infection with other pathogens may induce more severe signs. In other susceptible bird species, clinical signs are usually weaker and may differ from those observed in chickens. In young ostriches, for instance, ND is manifested in the form of depression and nervous symptoms, whereas adults remain asymptomatic (Alexander, 2000).

POST MORTEM LESIONS

Major gross lesions are observed only in cases provoked by viscerotropic velogenic NDV strains, but they may just as well be absent. In general, this form of ND is characterized by septicaemic effects manifested as haemorrhages in the mucous coating of the entire alimentary tract (from the beak to the vent) and necrotic diphtheritic lymph tissue lesions (caecal tonsils and Peyer's patches).

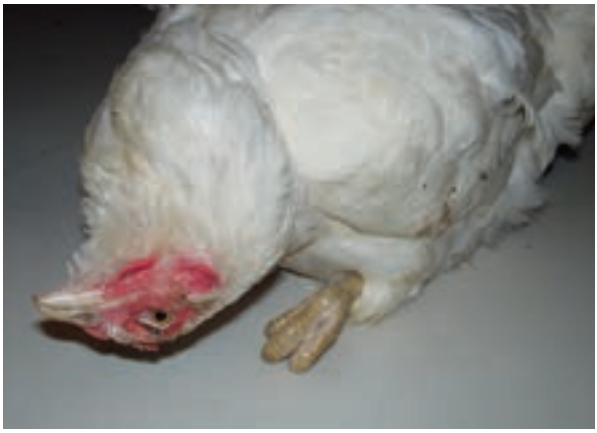


Fig.1
Nervous signs manifested as torticollis and abnormal circling.

Fig.2

The haemorrhages seen on proventricular mucosa are impressive. Multiple petechiae, and more rarely small ecchimoses, are found mainly around the mucous gland orifices.

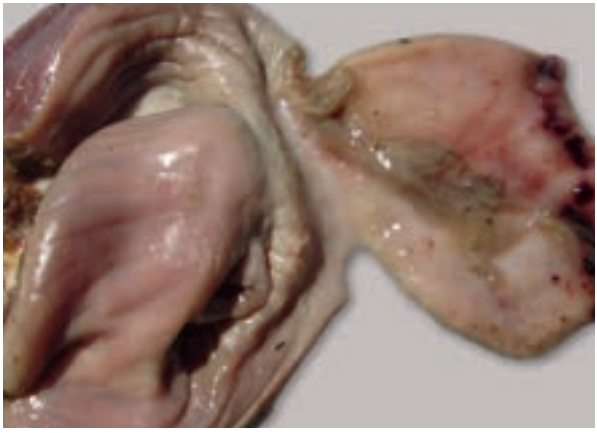


Fig.3

Sometimes, the haemorrhages are concentrated on the boundary between oesophagus and proventriculus.

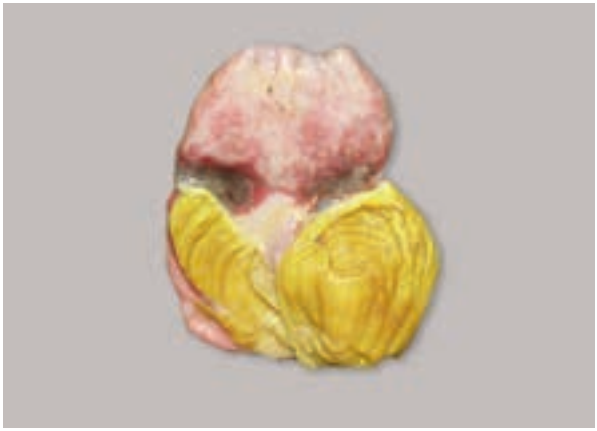


Fig.4

In other cases, haemorrhages are concentrated to form a continuous or discrete line on the boundary between proventriculus and gizzard.

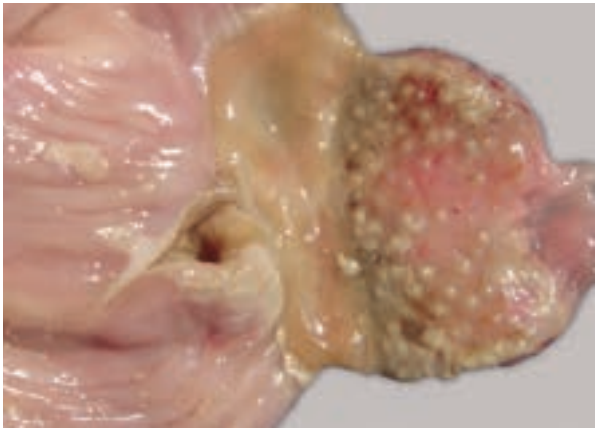


Fig.5

The gastric mucosa is usually oedematous and covered with thick mucus and fibrinous deposits.

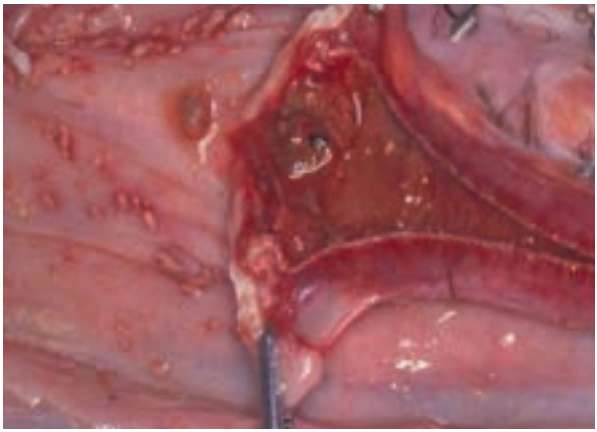


Fig.6

The mucous coating of the buccal cavity, the nasopharynx and the proximal oesophagus are oedematous, hyperaemic and often present superficial focal diphtheritic deposits.

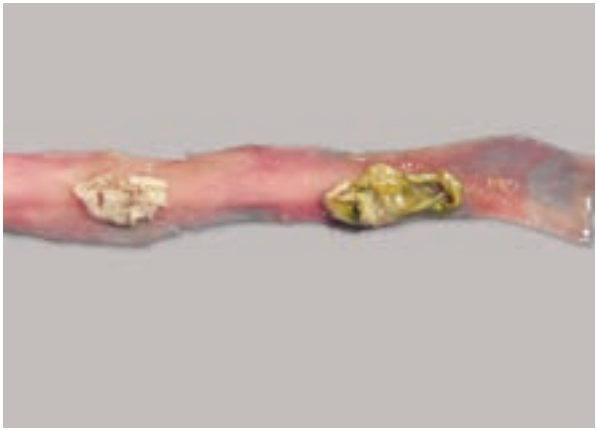


Fig.7

Catarrhal inflammation of the mucosa of the entire intestinal tract, with distinct focal necrotic diphtheritic lymph tissue lesions.

Fig.8

Diphtheritic plaques are grey-yellowish in colour and vary in size from several millimetres to 1-2 cm in diameter. Usually, their shape is elliptical and elongated.

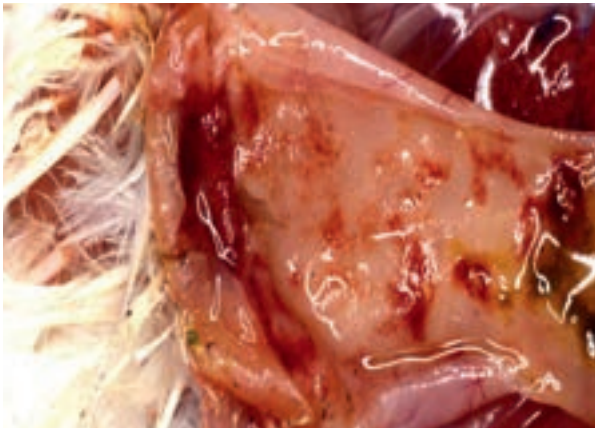


Fig.9

Haemorrhagic cloacitis is often observed. Mucous coat haemorrhages vary from petechiae to ecchimoses and are usually covered with mucus.

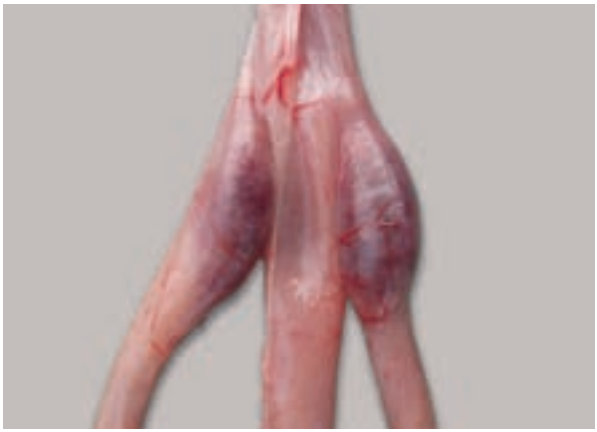


Fig.10
Enlargement and haemorrhages of caecal tonsils are common findings.

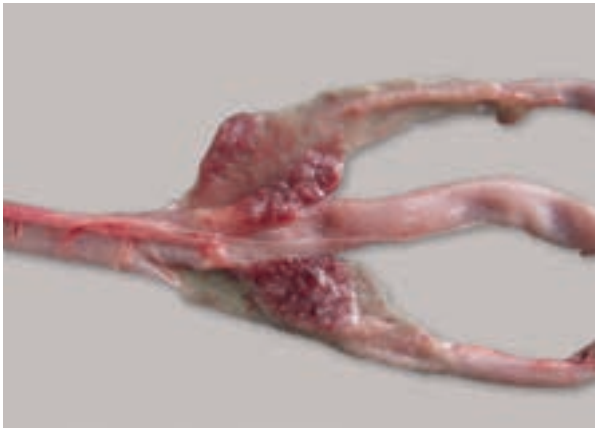


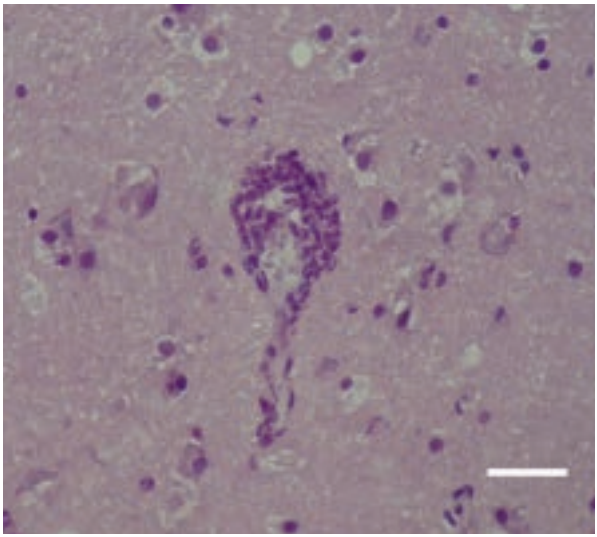
Fig.11
Haemorrhagic necrotic tonsilitis (caecal tonsils)

Fig.12

Paramyxovirosis in pigeons is clinically manifested, with clinical signs indistinguishable from those of ND. In this photograph – torticollis.

Fig.13

Paramyxovirosis in a pigeon –opisthotonus.



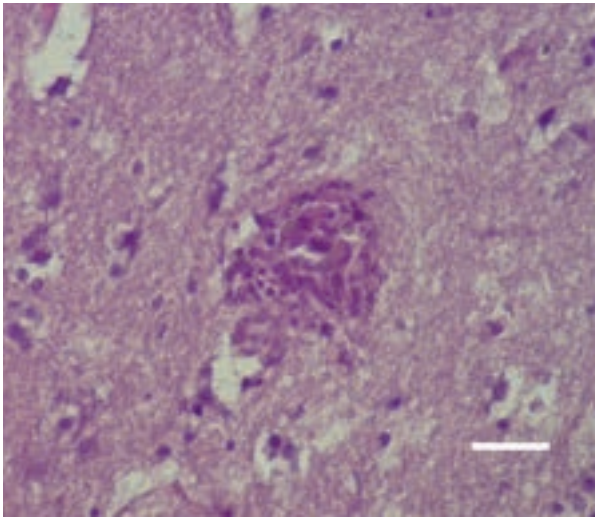


Fig.14 & 15

Non-purulent encephalitis. Perivascular microglial proliferation. H/E, Bar = 30 µm.

DIAGNOSIS

A tentative diagnosis can be made with reference to the disease history, and clinical and morphological signs but laboratory confirmation is essential.

Sample collection

In the collection and transportation of samples, all safety measures to prevent the spread of the disease must be observed. Taking into consideration the predilection sites of virus replication, it is advisable to collect samples from the respiratory (tracheal swabs) or intestinal (cloacal swabs) tracts. From fresh carcasses, intestinal content or faecal masses may be also collected. Oronasal swabs or viscera after necropsy (especially caecal tonsils, spleen etc.) are also appropriate specimens. Samples should be kept cold (with ice packs) and swabs placed in a suitable transport medium. The same types of specimen are suitable for express diagnostics by means of reverse transcription real - time polymerase chain reaction (rRT–PCR), (Oreshkova et al., 2008).

For serological analysis, blood sera or blood clots can be used.

Laboratory methods

a) Isolation and identification of APMV-1 from affected birds by inoculation of 9-11-days old chick embryos, followed by:

- Haemagglutination inhibition with virus-specific antiserum
- Haemagglutinating activity test

b) Serological test:

- Haemagglutination inhibition test
- ELISA

c) Direct detection of viral antigens:

- Immunohistochemical techniques for detection of viral antigens in organs and tissues (Lockaby et al., 1993).
- Immunofluorescence techniques for thin tracheal sections (Hilbink et al., 1982).
- Immunoperoxidase technique on thin sections (Hamid et al., 1988).

d) Molecular techniques:

- Express diagnostics by means of reverse transcription real-time polymerase chain reaction (rRT – PCR), (Bustin, 2000; Aldous et al., 2001).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis is required to distinguish disease induced by viscerotropic velogenic APMV-1 strains from cases with septicaemic signs, enteric lesions and respiratory and/or nervous signs. The lack of a pathognomonic gross lesion for ND impedes the differentiation of the disease. The detection of haemorrhages in the proventriculus is not always associated with ND. The same type of haemorrhages may be observed in other infectious diseases (clostridiosis); intoxications (coumarin derivatives); mycotoxicoses (fusariotoxins with caustic effect).

Other diseases with septicaemic lesions that should be considered with regard to the differential diagnosis of ND include: fowl cholera, salmonelloses, mixed necrotic enteritis infection, Avian influenza and small intestine coccidiosis etc. Those accompanied with respiratory signs should be distinguished from infectious bronchitis, swollen head syndrome in broiler breeders, diphtheritic form of fowl pox, laryngotracheitis etc. Some production systems flaws, as the inadequate ventilation, should be also taken into consideration.

PREVENTION AND CONTROL OF ND

The biosecurity measures required to prevent ND outbreaks include specific and non-specific disease control procedures. Specific control includes flock vaccinations, and the general control - compliance to a number of technological principles.

Vaccinations

Vaccinations can prevent the clinical signs of ND in birds, but not necessarily the replication and spread of the virus (Parede & Young, 1990; Guittet et al., 1993). At present, immunoprophylaxis against ND uses live and inactivated vaccines.

Live vaccines

Conventional live vaccines contain lentogenic (Hitchner-B1; La Sota etc.) or mesogenic (Roakin, Komarov, Mukteswar) attenuated viral strains. Vaccines prepared from lentogenic strains provide a shorter period of immunity, and require revaccination. Vaccines using mesogenic strains result in the build-up of a prolonged immunity, but they are less safe and can prove fatal, especially in birds without primary immunity achieved using lentogenic vaccinal strains. Such vaccines are used as a secondary option only in countries where ND is endemic (Alexander & Senne, 2008).

Live vaccines are used mainly by less expensive mass application techniques. Aerosol application is an easy means to vaccinate many birds in a short time. Caution should be taken to use an appropriate size of aerosol particles in order to avoid a respiratory reaction in the birds (Allan et al., 1978). Another means to apply live vaccines is via drinking water. Water properties (temperature, pH, purity) that could inactivate the vaccinal virus should be considered. At present, a number of stabilizers that prolong the survival of the virus are available. For small, privately-owned farms or backyard fowl, vaccine application can be performed using eye drops.

Inactived vaccines

Usually a 10-20% infective allantoic suspension with various strains such as B1, La Sota, Roakin etc., inactivated by addition of formalin etc. and mixed with adjuvant. Now, oil-emulsion adjuvants are used. Vaccines are injected intramuscularly or subcutaneously.

Advantages and disadvantages of live and inactivated vaccines:

Live vaccines result in the rapid build-up of local immunity, so non-vaccinated birds may become immunized by viral transmission from vaccinated birds. Inactivated vaccines are safe, and can be used in circumstances when the application of live vaccines is impossible and provide a high antibody levels for a long period of time (Alexander & Senne, 2008).

A disadvantage of live vaccines is that they can provoke disease, depending on environmental and other conditions. They also risk being neutralized by chemicals and heat,

or may be contaminated by other pathogens. One major flaw of inactivated vaccines is the laborious application process (individual injection of each bird) and thus the high costs entailed (Alexander et al., 2008).

Non-specific control

Biosecurity is essential for protection from ND at the farm level. It begins with planning the location where the farm will be built. A sufficient distance between premises should be provided to avoid concentration of birds. Flocks should not come into contact with domestic birds whose health status is not known, with pet birds (particularly psittacines), and with wild birds (pigeons, cormorants etc.). Farm workers should minimize contacts with birds outside the farm. Hatcheries should be isolated from poultry farms. The collection of dead bird carcasses and their destruction is of utmost importance.

In cases of ND outbreak, the eradication measure are simple: quarantine of the farm and personnel; depopulation of all infected and exposed birds, general cleaning and disinfection of premises using suitable sanitizers; APMV-1 can be also inactivated by heat (600 C or 1400 F) for 30 min or formalin. The role of darkling beetles (Alphitobiusdiaperinus) as APMV-1 vectors is acknowledged (Hosen et al., 2004), but that of flies, although not firmly proven, should not be underestimated. Farms should be left empty for a number of weeks (the exact time may vary according to the climate, the season and other factors) before a new batch of birds is stocked.

A new generation of vaccines has recently been made available in the field, based on the recombinant technology. These vaccines are much safer than live vaccines and therefore they dramatically reduce the respiratory post-vaccination reactions.

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