United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

May 24, 2018

Virulent Newcastle Disease Virus (vNDV)

Case Definition

1. General disease/pathogen information

Newcastle disease (ND) is a contagious and often fatal disease that affects over 250 bird species that is caused by infection with virulent strains of Newcastle disease virus (vNDV). Clinical signs vary and can include respiratory, neurological, reproductive, and intestinal signs. The severity of disease produced varies with the host species and the strain of the virus, with chickens being the most susceptible and waterfowl the least susceptible. In humans, the virus causes a temporary mild conjunctivitis and influenza-like symptoms. The World Organization for Animal Health (OIE) has defined ND (historically called Exotic Newcastle disease [END] in the United States) as an OIE-notifiable disease, based on its potential for rapid spread, serious economic consequences, and impact on the international trade of poultry and poultry products.

1.1. *Etiologic Agent:* Newcastle disease virus is a negative-sense, single-stranded RNA virus also known as avian paramyxovirus-1 (APMV-1). It is a member of the family Paramyxoviridae, genus *Avulavirus*. There are many different serotypes of avian paramyxovirus, with APMV-1 being the most important for poultry. APMV-1 viruses are categorized into five pathotypes according to the OIE, which characterize virulence as well as tropism: asymptomatic (no apparent disease), lentogenic (low virulence viruses), mesogenic (moderate virulence), and viscerotropic vs neurotropic velogenic (virulent) based upon pathogenicity experiments performed in chickens. While these definitions remain important descriptors, APMV-1 viruses are currently reported in the U.S. as either low virulent (e.g. lentogenic viruses) or virulent (comprising mesogenic and velogenic viruses). The OIE defines Newcastle disease as an infection with a vNDV characterized by either an intracerebral pathogenicity index (ICPI) of 0.7 or greater in day-old chickens, or the presence of multiple basic amino acids at positions 113- 116 of the C-terminus of the fusion (F2) protein (either arginine (R) or lysine (K)), plus phenylalanine (F) at residue 117 of the F1 protein.

1.2. *Distribution:* ND is endemic in a number of countries in Asia, Africa, and the Americas. Commercial poultry in the U.S. and Canada are free of vNDV. Outbreaks of vNDV occurred in California, Nevada, and Arizona in 2002-2003 and in Texas in 2003. Virulent NDV has not been detected in U.S. commercial poultry since 2003.

1.3. *Clinical signs:* Clinical signs can vary significantly from high levels of morbidity and mortality to sub-clinical infections depending on viral strain, host species, age of host, co-infection with other organisms, physiologic and environmental stress, and immune status. General clinical signs include respiratory distress, decreased egg production, depression, neurological signs, and diarrhea.

1.3.1. *Chickens:* Chickens are one of the most susceptible species to disease caused by vNDV infection. Poorly protected or unprotected flocks infected with vNDV typically experience high death losses within 24-48 hours with no apparent clinical signs. Birds that survive beyond 12-14 days may experience permanent neurological signs and/or permanent reproductive impairment. Vaccinated birds often experience marked drops in egg production with eggs that are misshapen, abnormally pale, rough, or thin-shelled with watery albumin. Infections with low virulent strains typically cause respiratory signs, decreased feed and water consumption, and a small decline in egg production.

Virulent strains may be viscerotropic or neurotropic. Viscerotropic strains cause hemorrhagic lesions in the intestinal tract, with conjunctival edema (at 2-3 days) and depression, and may result in sudden death regardless of vaccination status. Infection with neurotropic strains causes neurologic signs such as muscular tremors, leg and wing paralysis, torticollis, and opisthotonos, with death after 5-7 days. It is important to note that viscerotropic strains may also cause neurologic signs such as muscle tremors and torticollis; however, neurotropic strains rarely cause gastrointestinal hemorrhagic lesions in absence of other pathogens.

1.3.2. *Turkeys:* In general, turkeys tend to be less susceptible to APMV-1 infections. When infected, they may experience high morbidity, but clinical disease is less severe and mortality is lower.

1.3.3. *Other birds:* Upland game birds occasionally have severe clinical signs when affected with vNDV. Psittacine species exhibit variable susceptibility to vNDV and have the potential to chronically shed virus.

1.3.4. *Species-adapted strains:* APMV-1 viruses from pigeons are variants referred to as pigeon paramyxovirus-1 (PPMV-1). While these viruses typically have virulent fusion cleavage sites, chickens infected with PPMV-1 demonstrate variable clinical disease; however, if found in poultry, these viruses are reportable under the current OIE definition. A species-adapted virus is also found in double crested cormorants. These lineages are distinguishable by genomic sequence.

1.4. *Incubation period*: The incubation period in poultry ranges from 2-15 days with an average of 2-6 days in chickens infected with virulent strains. Time until disease onset depends upon host species, viral strain and dose, age and immune status of the host, presence of other infections, and environmental conditions.

1.5. *Differential diagnosis:* The differential diagnosis for Newcastle disease includes other causes of septicemia, enteritis, respiratory disease, and/or neurological disease.

1.5.1. *Viral diseases:* highly pathogenic avian influenza, laryngotracheitis, fowl pox (diphtheritic form), Pacheco's disease, avian metapneumovirus, infectious bronchitis**.**

1.5.2. *Bacterial diseases:* fowl cholera, psittacosis (chlamydiosis), mycoplasmosis, salmonellosis (especially in pet birds), botulism (especially in cormorants)

1.5.3. *Other:* aspergillosis, management errors such as deprivation of water, feed, air

1.6. *Transmission and reservoir:* Transmission can occur directly and indirectly from infected birds to susceptible birds. Infection can occur through direct contact with fecal excretions and respiratory secretions of infected birds. Contaminated feed, water, premises, and other fomites allow for indirect transmission. Vaccinated poultry may serve as a source of transmission if acutely infected and introduced to a susceptible flock. Virus can be shed throughout the incubation period and into convalescence. Illegally imported psittacine species, some of which may not show clinical signs, have served as sources of vNDV infection to domestic poultry. Survival of NDV in the environment is prolonged from days to months in the presence of organic matter, and up to years in feather follicles or temperatures <0°C. However, the virus is destroyed rapidly by dehydration and by the ultraviolet rays in sunlight.

1.7. *Epidemiology:* Morbidity of unvaccinated chickens infected with vNDV strains can reach 100 percent, and mortality ranges from 70-100 percent. Many other avian diseases present with clinical signs similar to vNDV; therefore, laboratory testing is necessary to distinguish between diseases. The virulence of the affecting strain is also important and OIE-designated assays should be performed to determine virulence of vNDV; virulent strains can be maintained in pigeons and cormorants. Viruses of low virulence may be detected as US poultry are typically vaccinated with live NDV vaccines and other low virulence viruses may circulate in wild birds, especially wild waterfowl.

2. Laboratory criteria: OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2018, Chapter 2.3.14. *Newcastle Disease.*

2.1. *Agent isolation and identification:* Samples of choice are tracheal, oropharyngeal, or cloacal swabs (or feces) from live birds. From dead birds, tissues (lung, spleen, trachea, intestine, and brain) as well as pools of organs and feces, are appropriate specimens. Tests include the isolation or culture of the virus in embryonated chicken eggs (appropriate cell culture may be used per the OIE Manual of Diagnostic Tests), and real-time reverse transcriptase polymerase chain reaction (rRT-PCR) for detection of the virus or the viral genome. Viral isolates can be identified by the hemagglutination (HA), hemagglutination inhibition (HI), and real-time reverse transcriptase polymerase chain reaction (rRT-PCR) tests. APMV-1 viruses, especially those with moderate to high titers, may cross-react in the HI tests with other APMV viruses, most specifically APMV-2, -3, and -7.

2.2. *Pathogenicity Assessment*: The intracerebral pathogenicity index (ICPI) in 24-40-hour-old chicks from specific pathogen free (SPF) eggs is the definitive assessment for virulence per OIE. The OIE allows for confirmation of virus virulence by amino acid sequence analysis of the fusion protein cleavage site, but molecular methods are not sufficient evidence for lack of virulence.

2.3. *Serological tests*: Use clotted blood or serum for enzyme-linked immunosorbent assay (ELISA) or HI. Antibodies are detectable 6 to 10 days after infection.

3. Case definition:

3.1. *Suspect case:* Domesticated bird or flock having:

3.1.1. Clinical signs compatible with ND; **OR**

3.1.2. Detection of APMV-1 by rRT-PCR; **OR**

3.1.3. Epidemiological information indicating exposure to vNDV.

3.2. *Presumptive positive case:* A suspect case (as in 3.1) with detection of vNDV by the fusion-target rRT-PCR test at a laboratory designated by the Secretary of Agriculture; NOTE – a negative virulent test in the face of clinical signs requires further virus characterization by sequence and/or in vivo testing.

3.3. *Confirmed positive case:* Domesticated bird or flock from which:

3.3.1. vNDV has been identified at the National Veterinary Services Laboratories (NVSL) by:

3.3.1.1. Presumptive positive (as in 3.2) with confirmation of multiple basic amino acids (either directly via protein or by deduction through sequencing) in the fusion gene at the C-terminus of the F2 protein and phenylalanine at residue 117, which is the N-terminus of the F-1 protein. The term 'multiple basic amino acids' refers to at least three arginine or lysine residues between residues 113 and 116; **AND/OR**

Failure to demonstrate the characteristic pattern of amino acid residues as described above would require virus isolation and further characterization by an in vivo test.

3.3.1.2. The vNDV has an ICPI in day-old chicks (Gallus gallus) of 0.7 or greater.

4. Reporting criteria: Virulent ND is a U.S. foreign animal disease (FAD) and OIE-notifiable disease. OIE reporting is limited to infections in poultry as defined by the OIE.[1] Follow standard FAD procedures according to Veterinary Services Guidance Document 12001 (formerly VS Memorandum No. 580.4). Suspect cases reported to State Animal Health Official or Assistant District Director (ADD).

[1] OIE definition of poultry: all domesticated birds, including backyard poultry, used for the production of meat or eggs for consumption, for the production of other commercial products, for restocking supplies of game, or for breeding these categories of birds, as well as fighting cocks used for any purpose.

Birds that are kept in captivity for any reason other than those reasons referred to in the preceding paragraph, including those that are kept for shows, races, exhibitions, competitions or for breeding or selling these categories of birds as well as pet birds, are not considered to be poultry.

References:

1. *Foreign Animal Diseases.* The United States Animal Health Association. Seventh Edition. 2008.
2. Iowa State University: Center for Food Security and Public Health. *Newcastle Disease*. Available online at www.cfsph.iastate.edu/Factsheets/pdfs/newcastle_disease.pdf
3. Merck Online Veterinary Manual. Newcastle Disease in Poultry. Available online at http://www.merckmanuals.com/vet/poultry/newcastle_disease_and_other_paramyxovirus_infections/newcastle_disease_in_poultry.html?qt=newcastle disease&alt=sh
4. OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2018. Chapter 2.3.14. *Newcastle Disease.* Available online at http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.03.14_NEWCASTLE_DIS.pdf
5. OIE Terrestrial Animal Health Code 2018. Chapter 10.9. *Newcastle Disease*. Available online at http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_nd.htm