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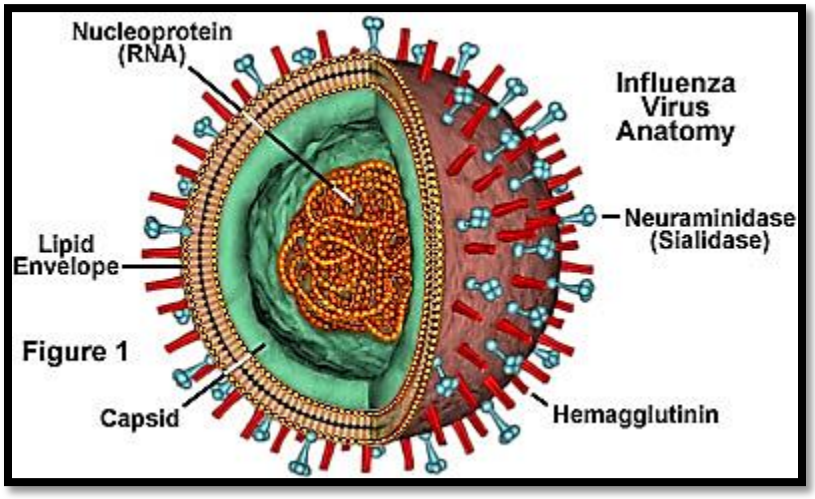
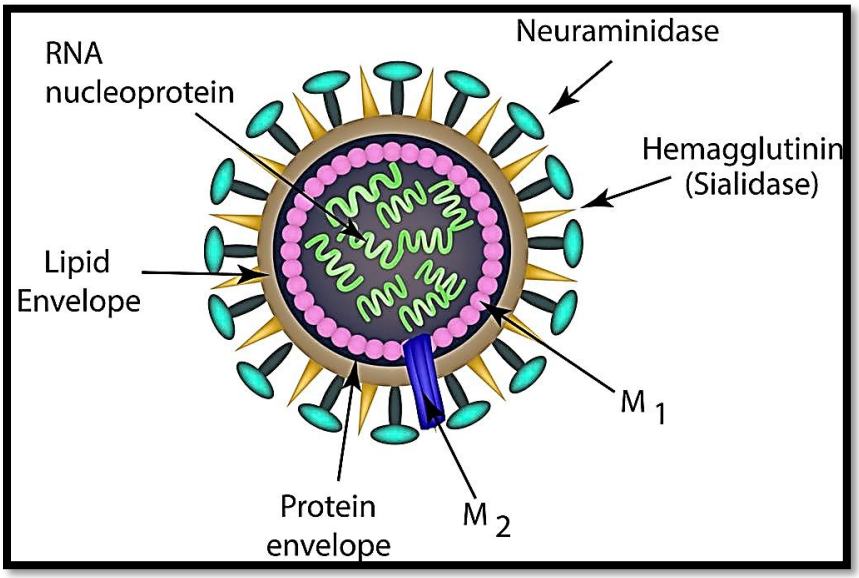
Avian influenza

Agent, Infection, and Disease: Avian influenza (AI) is caused by type A influenza virus classified into 16 hemagglutinin (H1–H16) and nine neuraminidase (N1–N9) subtypes. Most infections are subclinical in poultry, but some low pathogenicity (LP) AI strains (H1–12) have produced respiratory disease, diarrhea, and/or drops in egg production. High pathogenicity (HP) strains (H5 and H7 strains) produce severe systemic disease in gallinaceous poultry but variable disease and mortality in waterfowl. Low pathogenicity avian influenza (LPAI) viruses are found worldwide in wild aquatic birds. H5Nx HPAI viruses and H9N2 LPAI viruses has exposed vulnerabilities in disease prevention and control systems especially within large, complex bio-insecure production and market chains.

Etiology:

Avian influenza viruses are classified in the family Orthomyxoviridae, genus Influenza virus A. Virions are typically spherical to pleomorphic (100 nm) but can be filamentous with lengths up to several hundred nm. The surface is covered by two types of glycoprotein projections (10–14 nm in length and 4–6 nm in diameter): (1) rod-shaped trimers of hemagglutinin (HA), and (2) mushroom-shaped tetramers of neuraminidase (NA). The viral genome is composed of eight segments of single-stranded, negative sense RNA that code for a minimum of 10 or up to 17 proteins depending on the strain.



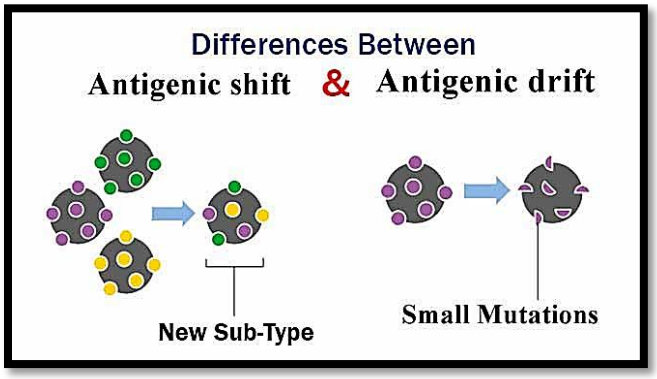


Antigenic Variation of Strains—Drift and Shift:

As has been demonstrated with seasonal human influenza viruses (H1N1 and H3N2), influenza A viruses have a high frequency of antigenic variation in the surface glycoproteins (HA and NA) because of two phenomena, drift and shift.

Antigenic drift in influenza viruses arises from point mutations in the HA and/or NA genes that results in antigenic changes in the coding proteins.

Antigenic shift arises from reassortment between influenza gene segments coding the surface proteins, most importantly the HA, and occurs when two influenza viruses infect the same cell. Most significantly, novel HA and/or NA antigen combinations emerge in the infected population because of the lack of preexisting immunity. Reassortment of internal gene segments occurs frequently, may affect the phenotype of the virus.



Pathogenicity Tests:

HPAI viruses have an IVPI in six-week-old chickens greater than 1.2 or, as an alternative, cause at least 75% mortality in four- to eight-week-old chickens infected intravenously. H5 and H7 viruses which do not have an IVPI of greater than 1.2 or cause less than 75% mortality in an intravenous lethality test should be sequenced to determine whether multiple basic amino acids are present at the cleavage site of the haemagglutinin molecule.

Mechanisms of Cellular Pathobiology:

Based on morphologic and biochemical evidence, AI viruses exert pathological effect on avian cells by two mechanisms: necrosis or apoptosis.

Necrosis has been identified in many cell types including renal tubule cells, pancreatic acinar epithelium, cardiac myocytes, adrenal cortical cells, and pulmonary epithelial cells in chickens.

Necrosis has been associated with intense virus replication and demonstration of abundant AI viral nucleoprotein in the nucleus and cytoplasm. Apoptotic cell death has been demonstrated most often in lymphocytes.

Pathogenesis of the Infectious Process:

In poultry, the process begins by inhalation or ingestion of infectious LPAI or HPAI virions. Because trypsin-like enzymes in respiratory and intestinal epithelial cells allow cleavage of the surface hemagglutinin, multiple replication cycles occur in respiratory and/or intestinal tracts with either type of virus. In gallinaceous poultry, the nasal cavity is a major site of initial replication.

With HPAI viruses, after initial replication in respiratory epithelium, the virions invade the submucosa, entering capillaries. The virus replicates within endothelial cells and spreads via the vascular or lymphatic systems to infect and replicate in a variety of cell types in visceral organs, brain, and skin. Alternatively, the virus may become systemic before having.

Transmission and Carriers:

Avian influenza virus is shed from the nares, mouth, conjunctiva, and cloaca of infected birds into the environment because of virus replication in the respiratory, intestinal, renal, and/or reproductive organs. HPAI viruses can also be detected in epidermis including feathers, feather follicles, and glands such as preen gland resulting in environmental contamination.

Incubation Period:

The incubation periods for the various diseases caused by these viruses range from as short as a few hours in intravenously inoculated birds to 3 days in naturally infected individual birds and up to 14 days in a flock. The incubation period is dependent on the dose of virus, the route of exposure, the species exposed, and the ability to detect clinical signs.

Clinical Signs:

The pathotype of AI virus (LP or HP) has a major impact on the clinical manifestation of the disease. However, clinical signs of disease are extremely variable and depend on other factors including host species, age, sex, concurrent infections, acquired immunity, and environmental factors.

Low Pathogenicity Avian Influenza Viruses:

Most infections by LPAI viruses in wild birds produce no clinical signs. However, in experimental studies in mallard ducks, LPAI virus infections suppressed T-cell function and produced a one-week depression in egg production.

In domestic poultry (chickens and turkeys), clinical signs reflect abnormalities in the respiratory, digestive, urinary, and reproductive organs. The most frequent signs represent infection of the respiratory tract and include mild to severe respiratory signs such as coughing, sneezing, rales, rattles, and excessive lacrimation. In layers and breeders, hens may exhibit increased broodiness and decreased egg production.

In addition, domestic poultry will exhibit generalized clinical signs including huddling, ruffled feathers, listlessness, decreased activity, lethargy, decreased feed and water consumption, and occasionally diarrhea. Emaciation has been reported but is infrequent because AI is an acute, not a chronic disease. Secondary infections can exacerbate clinical disease and increase mortalities.

High Pathogenicity Avian Influenza Viruses:

In wild and domestic waterfowl, most HPAI viruses replicate to a limited degree and produce few clinical signs. The major exception to this rule are some H5Nx HPAI viruses which can infect and cause clinical disease including neurological signs, depression, anorexia, and sudden death.

In domestic chickens, turkeys, and related galliformes, clinical signs reflect virus replication and damage to multiple visceral organs, and cardiovascular and nervous systems. However, clinical manifestations vary depending on the extent of damage to specific organs and tissues (i.e., not all clinical signs are present in every bird).

If the disease is less fulminating and birds survive for 3–7 days, individual birds may exhibit nervous disorders such as tremors of the head and neck, inability to stand, torticollis, opisthotonus, and other unusual positions of head.

Pathology:

Gross Lesion

Gross lesions have been extremely variable with regard to their location and severity, depending greatly on the host species, pathogenicity of the infecting virus, and presence of secondary pathogens.

Low Pathogenicity Avian Influenza Viruses

In poultry, the most frequent lesions are in the respiratory tract, especially sinuses, and are characterized as catarrhal, fibrinous, serofibrinous, mucopurulent, or fibrinopurulent inflammation. The tracheal mucosa can be edematous with congestion and occasionally hemorrhages. Tracheal exudates may vary from serous to caseous, with occasional occlusion of airways and resulting asphyxiation. Fibrinous to fibrinopurulent air sacculitis may be present.

The infraorbital sinuses may be swollen with muco-to-mucopurulent nasal discharge. Fibrinopurulent bronchopneumonia can result when accompanied by secondary pathogens such as *Pasteurella multocida or Escherichia coli.*

Catarrhal to fibrinous inflammation may be noted in the air sacs and peritoneal cavity, and egg yolk peritonitis may be observed. Catarrhal-to fibrinous enteritis may be observed in the ceca and/or intestine, especially in turkeys. Inflammatory exudates may be found in the oviducts of laying birds, and the last few eggs laid

will have reductions in calcium deposition within the eggshells. Resulting eggs may be misshapen and fragile with loss of pigmentation.

The oviduct may be edematous and contain catarrhal-to-fibrinous luminal exudates before undergoing involution. Swollen kidneys occurred and were accompanied by visceral urate deposition ("visceral gout").

Highly Pathogenic Avian Influenza Viruses

In poultry, HPAI viruses produce a variety of edematous,hemorrhagic, and necrotic lesions in visceral organs and the skin. Although, when death is per-acute, no gross lesions may be observed. In chickens, swelling of the head, face, upper neck, and feet may be observed which results from subcutaneous edema and may be accompanied by petechial-to-ecchymotic hemorrhages. Periorbital edema may be seen. Necrotic foci, hemorrhage, and cyanosis of the non-feathered skin have been reported especially wattles and combs.

Lesions in visceral organs vary with virus strain but most consistently are represented by hemorrhages on serosal or mucosal surfaces and foci of necrosis within parenchyma of visceral organs. Especially prominent are hemorrhages on the epicardium in pectoral muscles, and in mucosa of the proventriculus and ventriculus.

necrosis and hemorrhage in Peyer's patches of the small intestine were common as was reported with outbreaks.

With most HPAI viruses, necrotic foci are common in pancreas, spleen, and heart, and occasionally in liver and kidney. The kidney lesions may be accompanied by urate deposits. Lungs have focal ventral-to-diffuse interstitial pneumonia with edema. The lungs can be congested or hemorrhagic. The cloacal bursa and thymus are usually atrophic. Splenomegaly is frequent in birds infected with H5N1.

Microscopic:

In severe cases, the pneumonia may be diffuse with air capillary edema. Heterophilic-tolymphocytic tracheitis and bronchitis have been common, the LPAI viruses produced heterophilic-to-pyogranulomatous sinusitis, bronchitis, and pneumonia with necrosis of respiratory epithelium.

The most consistent and most severely affected tissues are brain, heart, lung, pancreas, and primary and secondary lymphoid organs. Lymphocytic meningoencephalitis with focal gliosis, neuronal necrosis, and neuronophagia are

common, but edema and hemorrhage may be seen. Focal degeneration to multifocal-diffuse coagulative necrosis of cardiac myocytes has been reported. AI virus replication include necrosis in skeletal myofibers, kidney tubules, vascular endothelial cells, corticotropic cells of adrenal, and pancreatic acinar cells.

Diagnosis.

Reverse transcription-polymerase chainreaction (RT-PCR) is commonly used to diagnose avian influenza infections, with type A.

In embryonating chicken eggs, is still recommended to allow full characterization of an isolate. Pathotype is determined by sequencing and/or in vivo tests (intravenous pathogenicity test).

Serologic detection of exposure to AI virus utilizes enzyme-linked immunosorbent assay (ELISA) (type A), agar gel immunodiffusion (type A), and/ or hemagglutination-inhibition (HI) tests (H sub type specific).

The control

Biosecurity is the primary preventive measure but weaknesses in biosecurity systems results in infection on some farms. Virus elimination is the preferred strategy for HPAI and H5/H7 LPAI control when outbreaks occur in previously AI-free countries or areas. Vaccination is also being used as a preventive and emergency control measure for both LPAI and HPAI.