Orthomyxoviridae

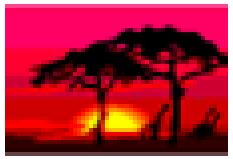
Orthomyxoviridae

Are a family of RNA viruses that includes six genera: Influenza virus A, Influenza virus B, Influenza virus C, Isavirus, Thogotovirus and Quaranjavirus. The first three genera contain viruses that cause influenza in vertebrates, including birds, humans, and other mammals. Isaviruses infect salmon; the thogotoviruses are arboviruses, infecting vertebrates and invertebrates, such as ticks and mosquitoes.

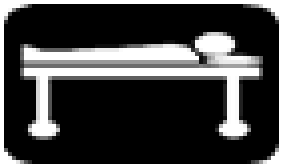
The orthomyxoviridae comprise the influenza viruses which are usually spread within a species by droplet or direct contact lead to upper respiratory infections. Some avian influenza viruses are more **pantropic** and cause fowl plague.

The orthos, Greek for "straight“whereas, **myxo,** Greek for “**mucus**"

Endemic: a disease that exists permanently in a particular region or population. Malaria is a constant worry in parts of Africa.



Epidemic: An outbreak of disease that attacks many peoples at about the same time and may spread through one or several communities.



Pandemic: When an epidemic spreads throughout the world.

pantropic virus; a virus that affects or has an affinity for many different kinds of tissue or organs, the ordinary strain of yellow fever virus, as distinguished from the neurotropic strain; has an affinity for different tissues.

Orthomyxoviridae

The Orthomyxoviridae are a family of RNA viruses that includes five genera:

1- Influenza virus A (infects birds, humans, and other mammals like, horses, swine, mink seals, and whales).

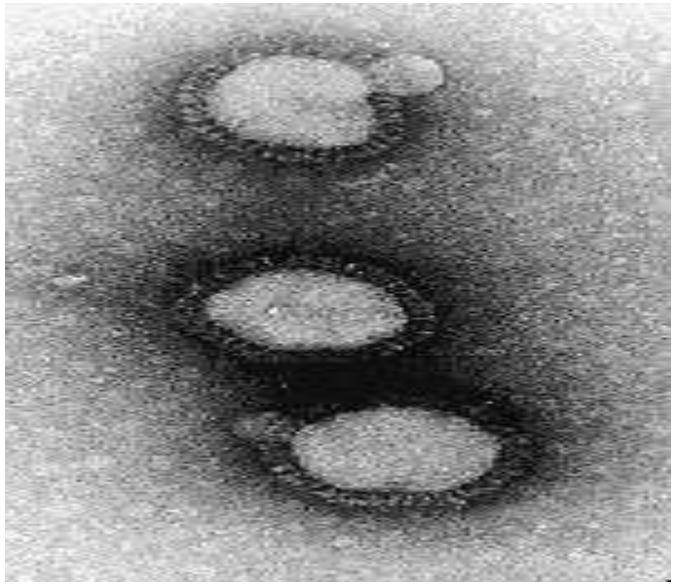
2-Influenzavirus B (infects humans only).

3- Influenzavirus C (infects humans and pigs).

4-Isaviruses: infect fish causes severe anemia of infected fish.

5-Thogotoviruses infect vertebrates and invertebrates, such as mosquitoes and sea lice.

6-Quaranjavirus: is a new genus of enveloped RNA viruses, one of six genera in the virus family *Orthomyxoviridae.*



Influenza viruses are divided into three types, A, B, C.

The type A viruses: are the most virulent human pathogens among the three influenza types and cause the most severe disease. The serotypes that have been confirmed in humans ordered by the number of known human pandemic deaths, are:

H1N1 caused Spanish Flu and Swine flu in 2009. (Spanish flu pandemic that swept the world in 1918, just as World War I ended, killed 25-40 million people more than the war itself.

H2N2 caused "Asian Flu“.

H3N2 caused "Hong Kong Flu", is a subtype of viruses that causes influenza (flu). Also H3N2 Viruses can infect birds and mammals. In birds, humans, and pigs the virus has mutated into many strains. H3N2 is increasingly abundant in seasonal influenza, which kills an estimated 36,000 people in the United States each year.

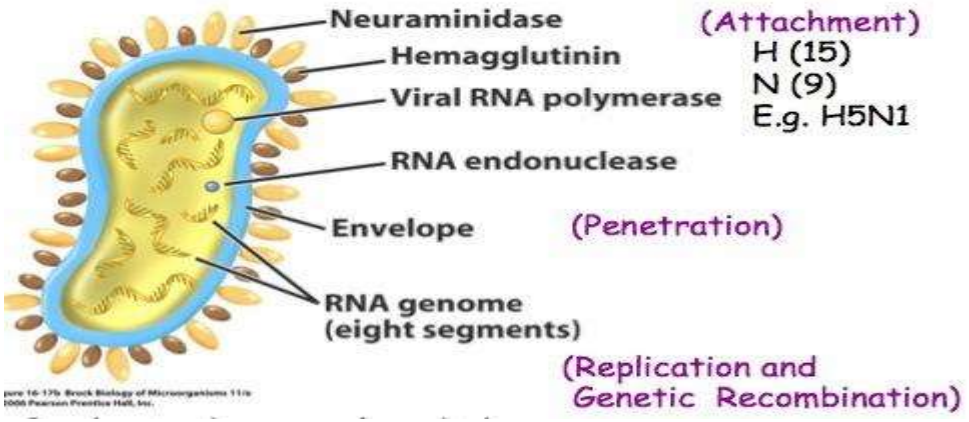
H5N1 is a pandemic threat, **highly pathogenic avian influenza . "bird flu"**

H7N7 has unusual zoonotic potential,(previously designated **equine influenza** viruses 1 and 2) cause respiratory disease in horses.

H1N2 is endemic in humans and pigs.

Type B virus:

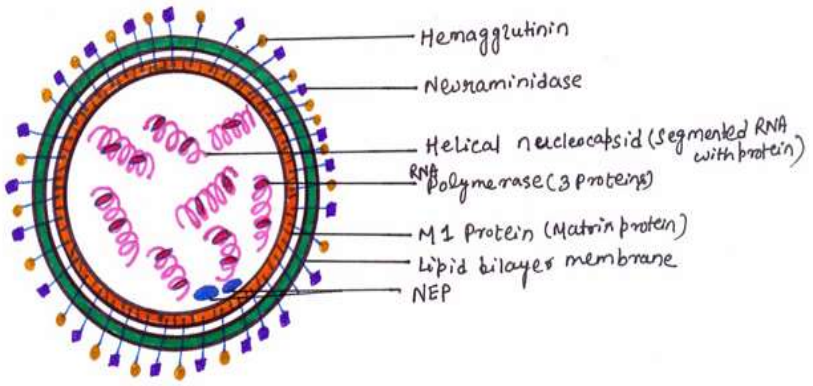
Is almost exclusively a human pathogen, and is less common than influenza A. The only other animal known to be susceptible to influenza B infection is the seal. This type of influenza mutates at a rate 2-3 times lower than type A and consequently is less genetically diverse with only one influenza B serotype. As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at early age. However, influenza B mutates enough that lasting immunity is not possible. This reduced rate of antigenic change, combined with its limited host range(inhibiting cross species antigenic shift), ensures that pandemics of influenza B do not occur.



Type C virus: The influenza C virus infects humans and pigs, and can cause sever illness and local epidemics. However, influenza C is less common than the other types and usually seems to cause mild disease in children.

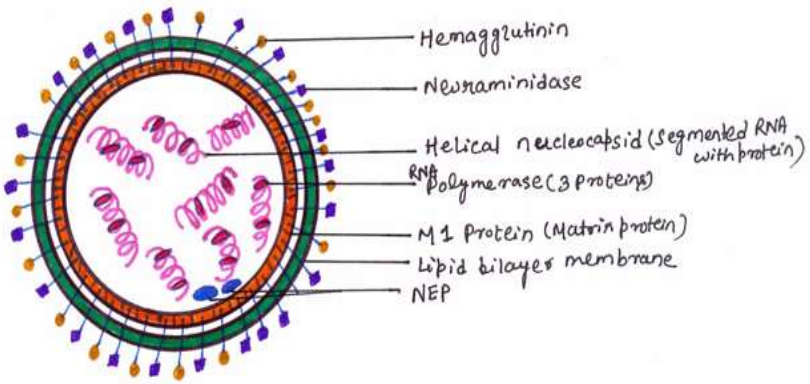
Influenza C viruses have only one type of glycoproteinpeplomer, consisting of multifunctional hemagglutinin-esterase molecules (HE).

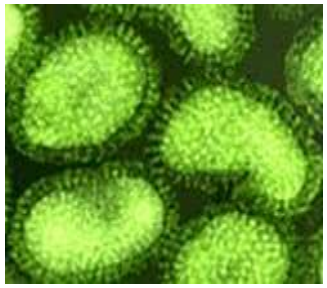
Genomic segments have a loop at one end and consist of a molecule of viral RNA enclosed within a capsid composed of helical symmetry arranged nucleoprotein (NP).



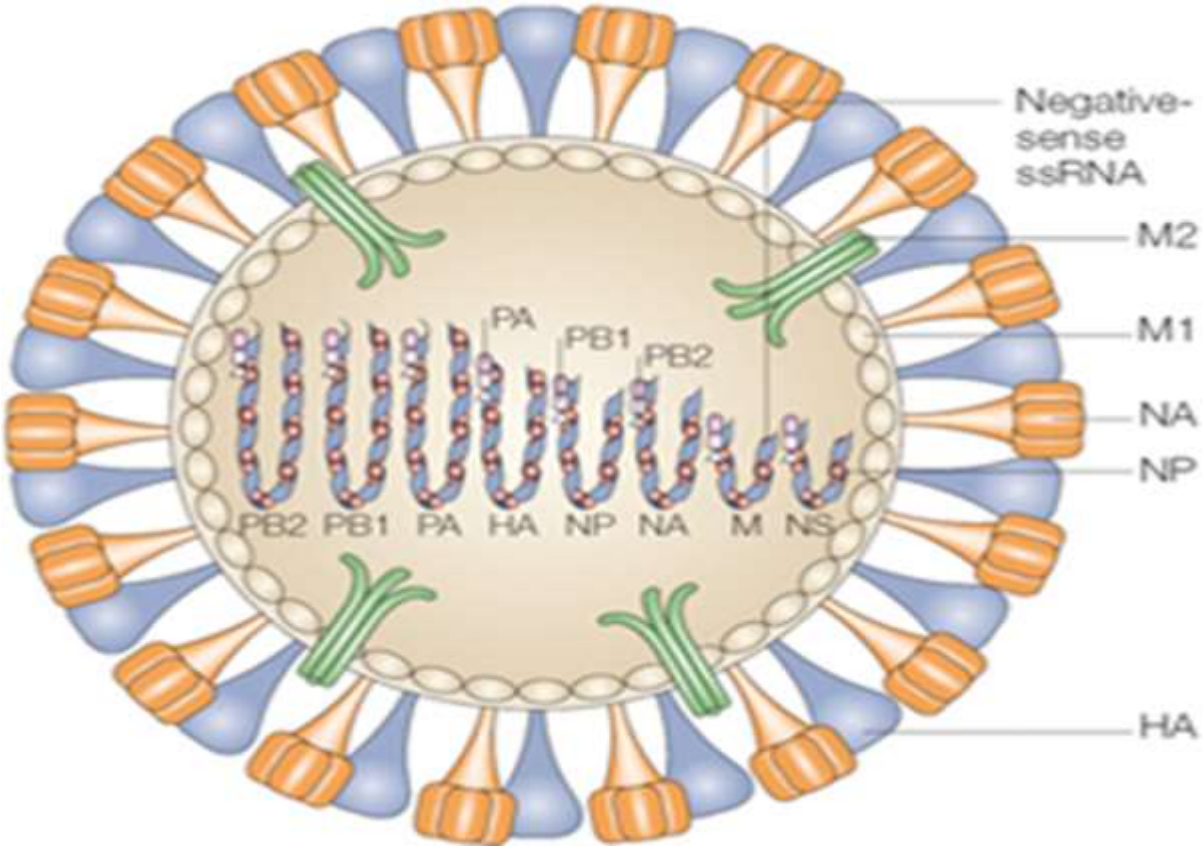
Structure

The influenza A virus particle or virion is 80-120 nm in diameter and usually roughly spherical, although filamentous forms can occur. Virions consist of an envelope with large peplomers surrounding eight (genera *Influenzavirus A and Influenzavirus B),* seven (genus *Influenzavirus C), or six (genus Thogotovirus)* helically symmetrical nucleocapsid segments of different sizes





Associated with the RNA are three proteins that make up the viral RNA polymerase (PB1, PB2, and PA).
Virion envelopes are lined by the matrixprotein (M1) and are spanned by a small number of ion channels composed of tetramers of a second matrixprotein, M2 spanning the lipid bilayer.



The genome in eight, seven, or six segments consists of linear negative-sense, single-stranded RNA,10-13.6 kb in overall size. Transcription and RNA replication occur **in the nucleus**, budding takes place on the plasma membrane.

Because of the segmented nature of the genome surface antigens, when a host cell is infected with two different influenza viruses, the progeny virus can be a mixture of both “parent” viruses.

Reassortment provides for increased biological variation that increases the ability of the virus to adapt to new hosts.

The appearance of variant viruses not only depends on genetic drift, i.e., point mutations (nucleotide substitutions, insertions, deletions), but also on genetic shift, i.e., genomic segment reassortment. Drift and shift of two genes.

Genetic Drift: Minor mutation in hemaglutinin or neuraminidase; does not require a new vaccine.

Genetic Shift :Major mutation in hemagluttinin or neuraminidase; need a new vaccine.

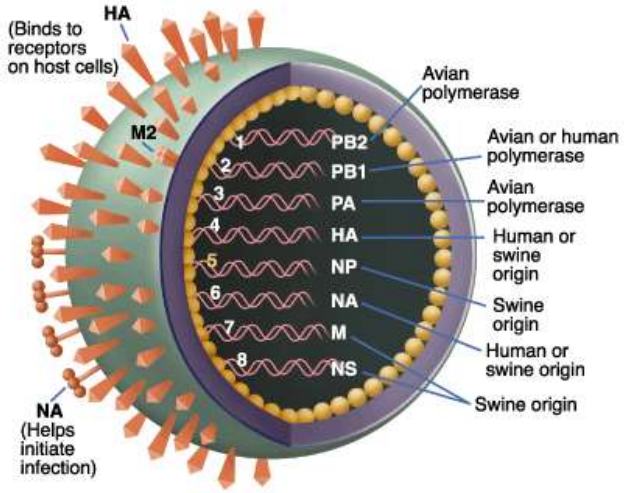
Unusually for a virus, the influenza A genome is not a single piece of nucleic acid; instead, it contains eight pieces of segamented negative-sense RNA (13.5 kilobases total) which encode 11 proteins (HA, NA, NP, MI, M2, NS1,NEP, PA, PB1, PB1-F2, PB2), the best characteristic of these viral proteins are hemagglutinin and neuraminidase, two large glycoproteins found on the outside of the viral particles.

Hemagglutinin is a lectin that mediates binding of the virus to target cells and entry of the viral genome into the target cell. By contrast,

Neuraminidase is an enzyme involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles.

The hemagglutinin (H) and neuraminidase (N) proteins are targets for antiviral drugs. These proteins are also recognized by antibodies, i.e. they are antigens. The responses of antibodies to these proteins are used to classify the different serotypes of influenza A viruses, hence the *H* and *N* in *H5N1.*

Influenza: Is a commonly called "**the flu**," is an illness caused by **RNA viruses** of the family ***Orthomyxoviridae,*** the influenza viruses infect the respiratory tract of many animals, birds, and humans.

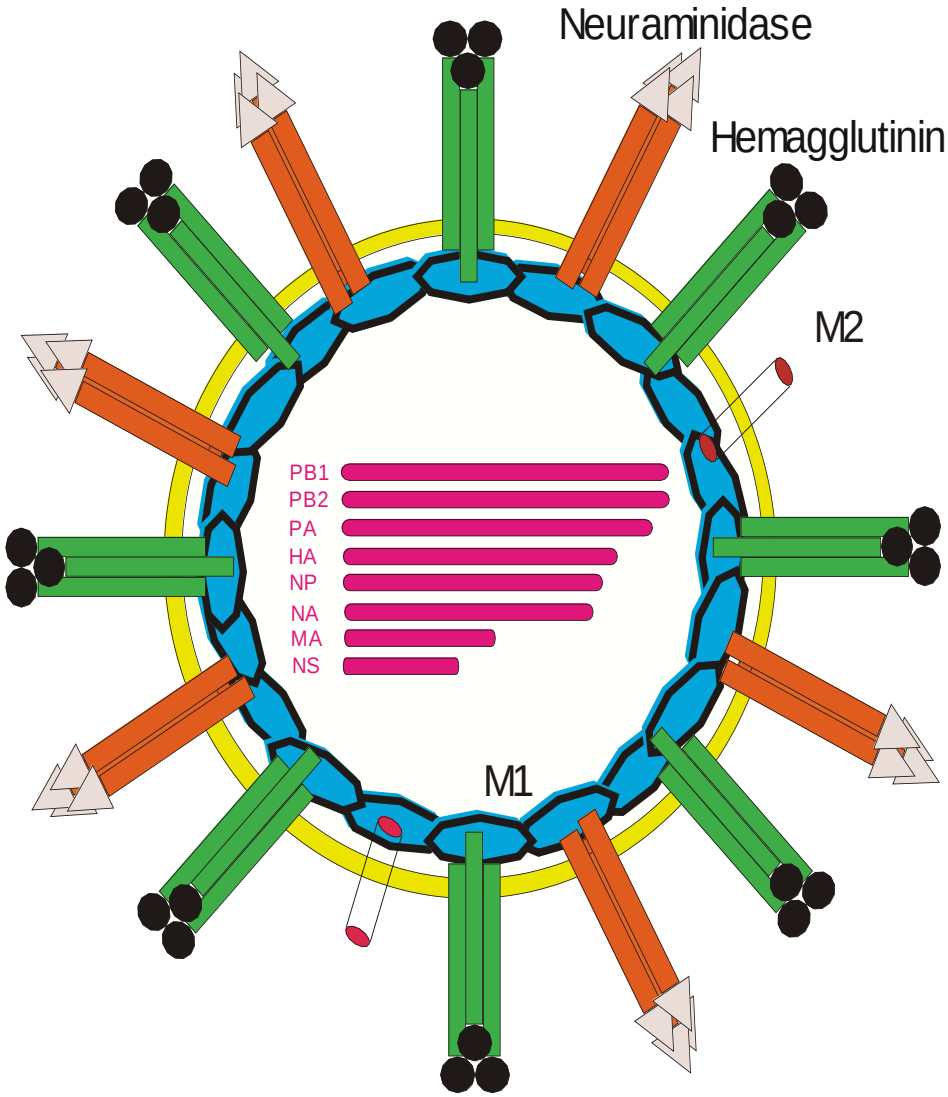


Influenza virus

Negative sense RNA

Single stranded

Segmented



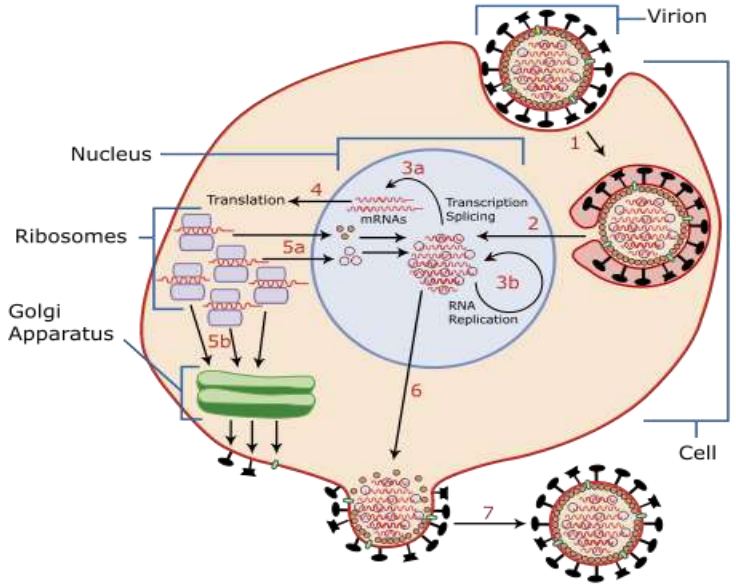
16 Hemagglutinin subtypes

9 Neuraminidase Subtypes

Replication cycle

Orthomyxoviridae viruses are one of the only RNA viruses that replicate in **the nucleus**. This is because the machinery of orthomyxo viruses cannot make their own mRNAs.

Typically, influenza is transmitted from infected mammals through the air by coughs or sneezes, creating aerosols containing the virus, and from infected birds through their droppings. Influenza can also be transmitted by saliva, nasal secretions, feces and blood.



Classification

Viruses are further categorized by their **host** (swine, horses, birds, etc.),
geographic origin, strain number, and **year of isolation.**
The full description of influenza named as follow…

★★★★

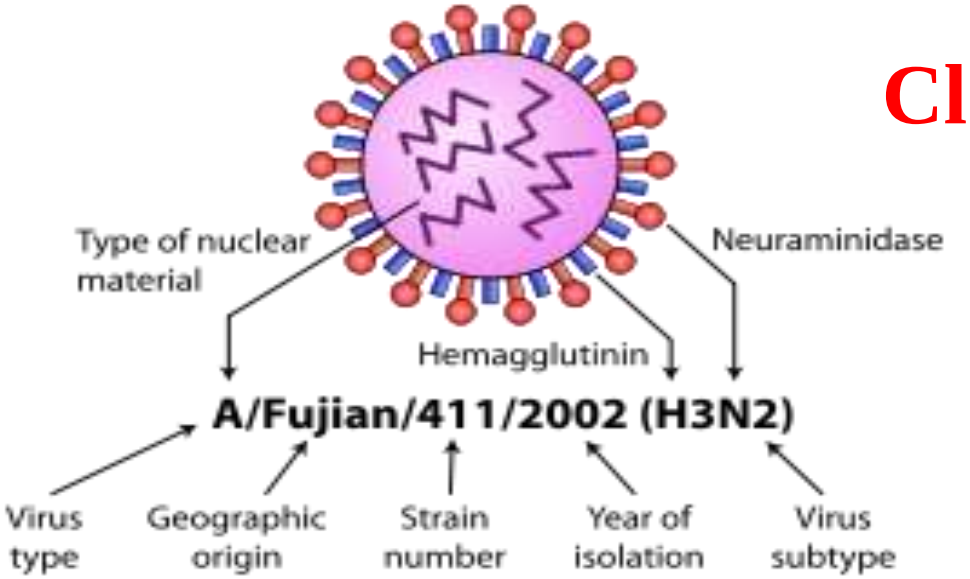
Influenza virus ***A/equine/Prague/1/65 (H7N7),*** *which record type (A), species or origion(**equine**), geographic location (**Pargue**),strain or laboratory reference number (1), year of isolation (**1965**), subtype of H (**H7**), subtype of N(**N7**).*
whereas virulence of isolate not included.
Other sample, **A/equine/Miami/I/63 (H3N8),**

Classification

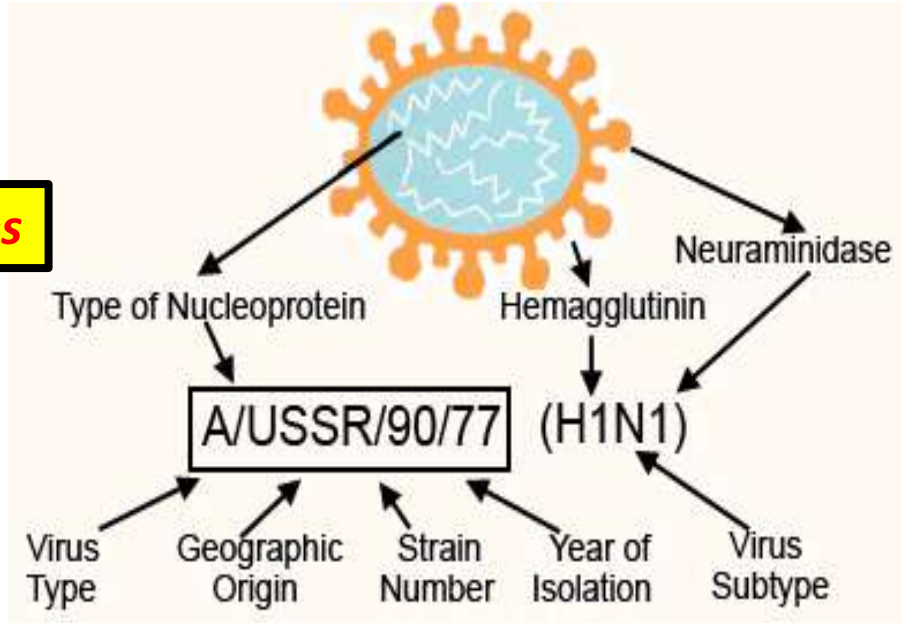
A/swine/Iowa/15/30 (HIN1), the prototypic strain of **swine** influenza virus Influenza virus.

A/Hong Kong/1/68 (H3N2), the virus that caused the human pandemic of 1968 (when the host of origin is not specified it indicates human origin.

Classification



Noimanclature of influenza viruses



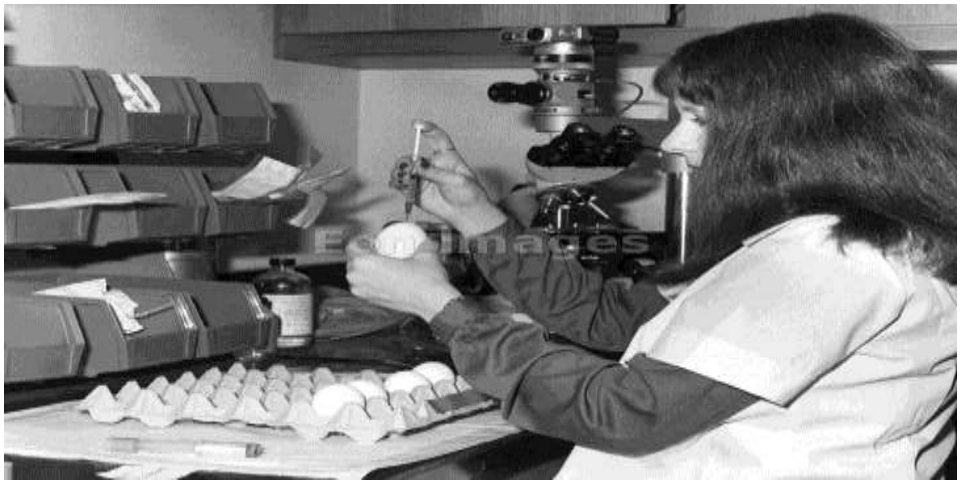
Physical-Chemical properties

Influenza viruses are sensitive to heat (56 ˚C at 30 minutes), acid (pH 3), drying, detergents and disinfectants and do not survive in the external environment.

Cultivation and Cytopathic effect

1-Influenza viruses are routinely grown to high titer in the allantoic cavity of 10-days fertile eggs.

2-Some influenza isolates grow in cell cultures and yield cytopathic effect characterized by cells rounding and later detachment from the flask. Eggs are therefore still used for isolation of virus and preparation of vaccines.



Equine Influenza

Is highly contagious and spreads rapidly among naive horses. Horses 1–5 yr old are the most susceptible to infection. The disease caused by strains of influenza A that are enzootic in horse species. Equine influenza occurs globally, and is caused by **two main strains** of virus: equine-1 (H7N7) and equine-2 (H3N8).

The differentiation of equine influenza from other equine respiratory diseases was established in 1956 when influenza virus ***A/equine/Prague/1/56 (H7N7)*** *(equine influenza* virus 1) was isolated in an epidemic in central Europe and subsequently in the United States; a second virus, **A/equine/Miami/I/63 (H3N8)** (equine influenza virus 2), was first isolated in 1963. Since then, the disease has been reported in horses and also in donkeys and mules in all parts of the world except Australia, New Zealand, and Iceland.

H3N8 virus has been identified in all recent outbreaks; the last outbreak caused by subtype H7N7 virus was in 1979, but antibody has been detected in unvaccinated horses since then, suggesting that the virus still circulates. H3N8 virus has undergone only modest genetic drift since it was first isolated, yet it continues to cause disease and to affect the performance of racehorses.

Pathogenesis

Influenza virus replicates within **respiratory epithelial cells,** resulting in **destruction of tracheal and bronchial epithelium and cilia**. Cough develops early in the course of infection and may persist for several weeks. Nasal discharge, although scant and serous initially, may become mucopurulent due to secondary bacterial infection.

Mildly affected horses recover uneventfully in 2–3 wk; severely affected horses may convalesce as long as 6 mo. Recovery may be hastened by complete restriction of strenuous physical activity. Respiratory tract epithelium takes ~21 days to regenerate; during this time, horses are susceptible to development of secondary bacterial complications such as pneumonia, pleuropneumonia, and chronic bronchitis.

Clinical Findings and Lesions

1-The incubation period of influenza is ~1–3 days.

2-High fever (up to 106°F [41.1°C]),

3- Serous nasal discharge, submandibular lymphadenopathy, and coughing that is dry, harsh, and nonproductive

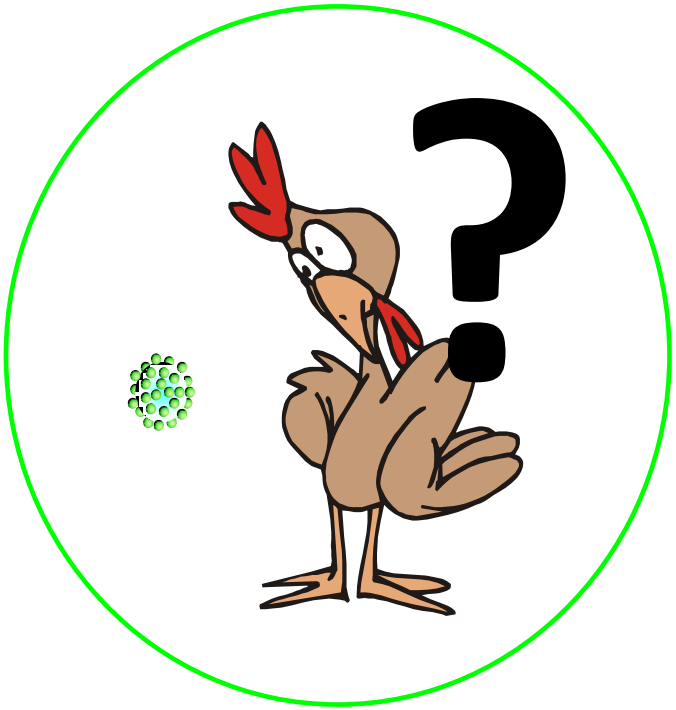
4-Depression, anorexia, and weakness are frequently seen.

5- Clinical signs usually last <3 days in uncomplicated cases.

Complications are minimized by restricting exercise, controlling dust, providing superior ventilation, and practicing good stable hygiene. Primary complications of vasculitis, myositis, and myocarditis are seen infrequently.

AVIAN INFLUENZA

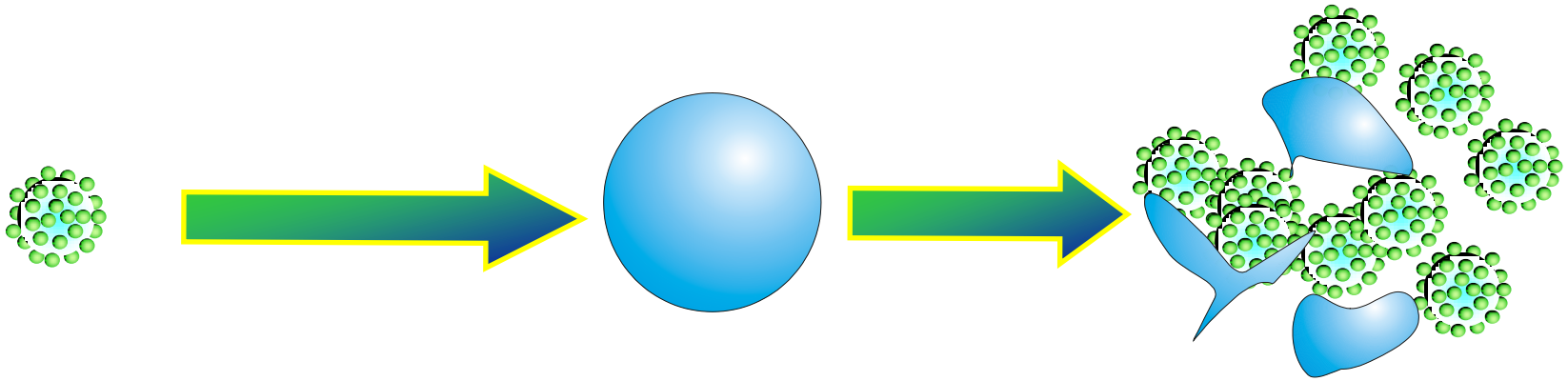
AIV: A Viral disease of Domestic and Wild Birds characterized by the full range of responses from almost no signs of the disease to very high mortality. The incubation period is also highly variable, and ranges from a few days to a week (3 to 7 days).



Avian Influenza

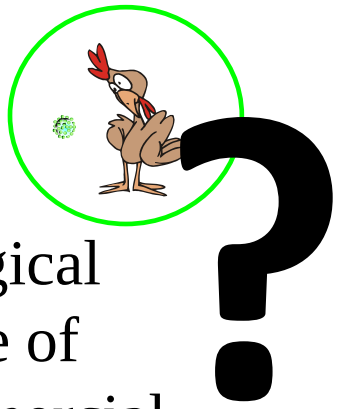
Bird flu (avian influenza) is a disease caused by an influenza virus that primarily affects birds.
The disturbing form of influenza in chickens known as "fowl plague" was recognized as a distinct disease entity as early as 1878.

What is AI



Virus Cell Replication

The isolation of an **avian influenza virus** in 1901 preceded the discovery of **mammalian and human influenza viruses**, but it was not until 1955 that it was recognized that avian and mammalian influenza viruses are **closely related**.



From the **1970s** onward, avian influenza came into ecological focus when surveillance indicated the ubiquitous presence of viruses in waterfowl and the risk these birds pose to commercial chicken industries.

A very large epidemic centered in the broiler industry of Pennsylvania in **1983**, which cost **61**$ million to control, brought substance to this risk. A repeat of this kind of epidemic in the commercial broiler industry of Mexico in the **1990s** showed that the risk continues. **The first human case** of illness from **highly pathogenic avian influenza** was identified in **1997**, and more than 560 cases have been identified since then, with deaths worldwide exceeding 300 cases.

Avian Influenza

The epidemic was linked to chickens and classified as avian influenza A (H5N1). Human cases of avian influenza A (H5N1) have since been reported in Asia, Africa, Europe, Indonesia, Vietnam, the Pacific, and the near East. Hundreds of people have become sick with this virus. Slightly more than 60% of those who became ill have died.

Distrbution

These viruses occur naturally among wild migratory aquatic birds worldwide and can infect domestic poultry and other bird and animal species. Wild aquatic birds are the natural reservoir and can be infected with avian influenza A viruses in their intestines and respiratory tract, but usually do not get sick. However, avian influenza A viruses are very contagious among birds and some of these viruses can sicken and even kill certain domesticated bird species including chickens, ducks, and turkeys.

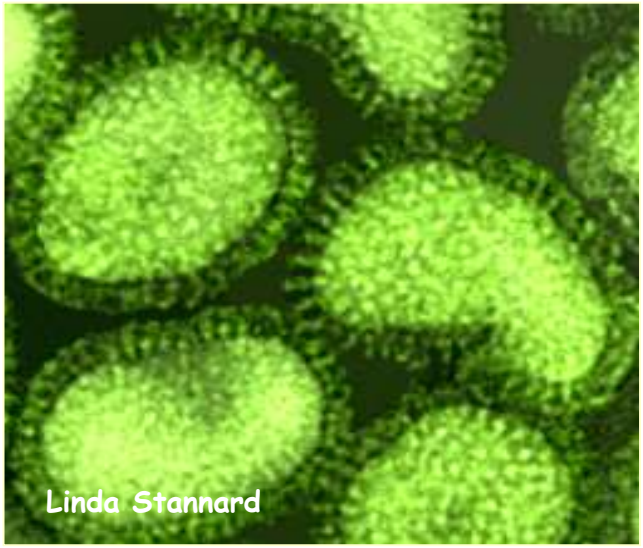
Aetiology of Avian Influenza

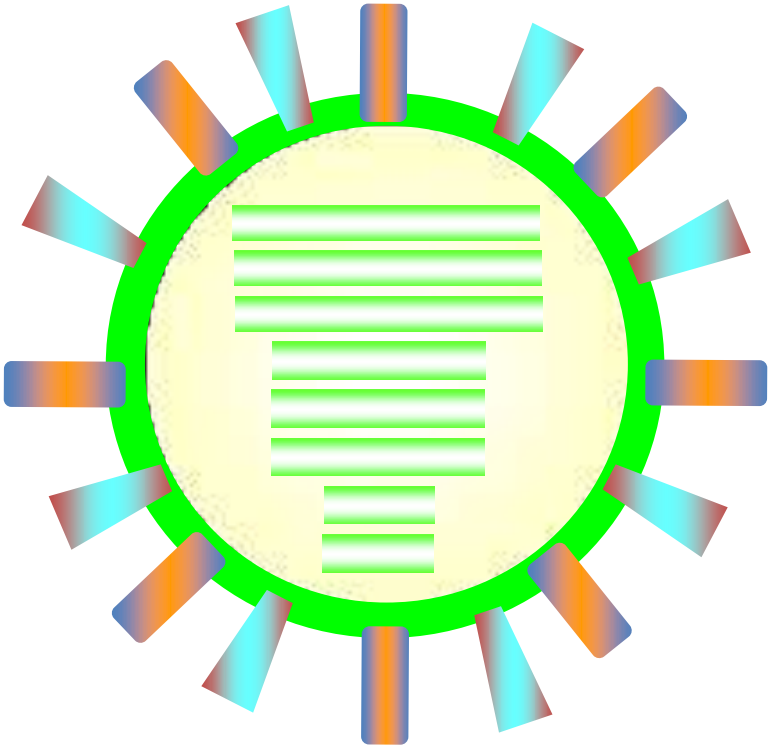
Influenzavirus A genus of the Orthomyxoviridae family. They are enveloped, negative stranded RNA viruses. Influenza A viruses can be divided into **15 Haemagglutinin** (H) antigens. **9 Neuraminidase (N)** antigens.

Excessive antigenic variability brought about by genetic reassortment in host cells.

Avian influenza virus not infected human, but they do tend to exchange genetic material with other influenza viruses infectious to humans and develop into new viral strains.

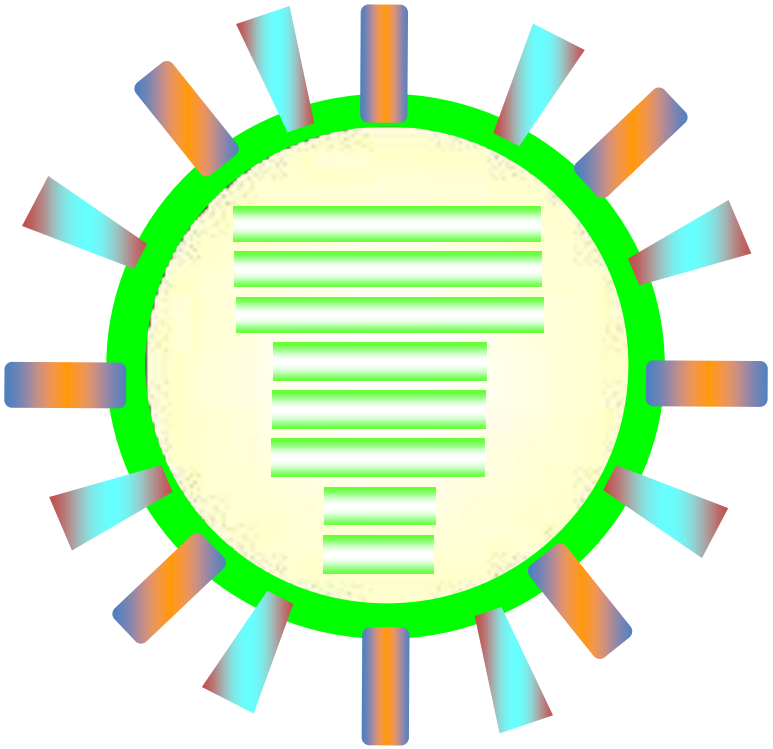
What is AI



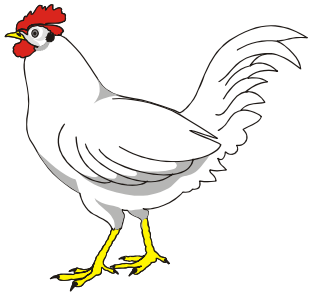


- Haemaglutinin (15)
- Neuraminidase (9)

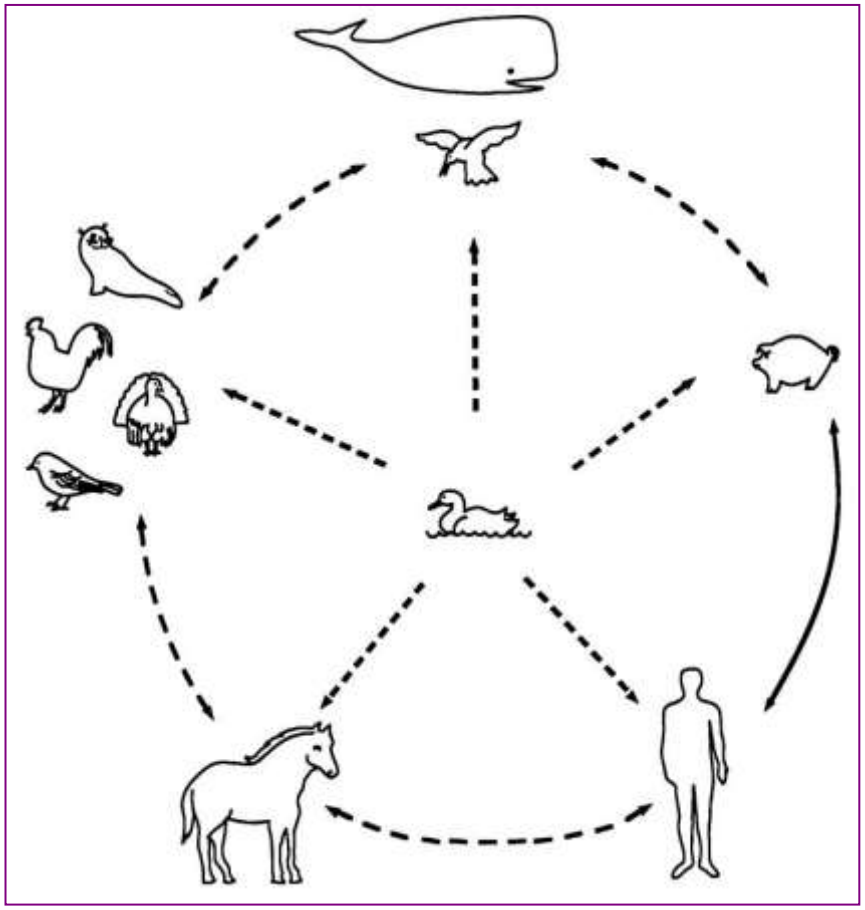
What is AI



H-Highly
P-Pathogenic
A-Avian



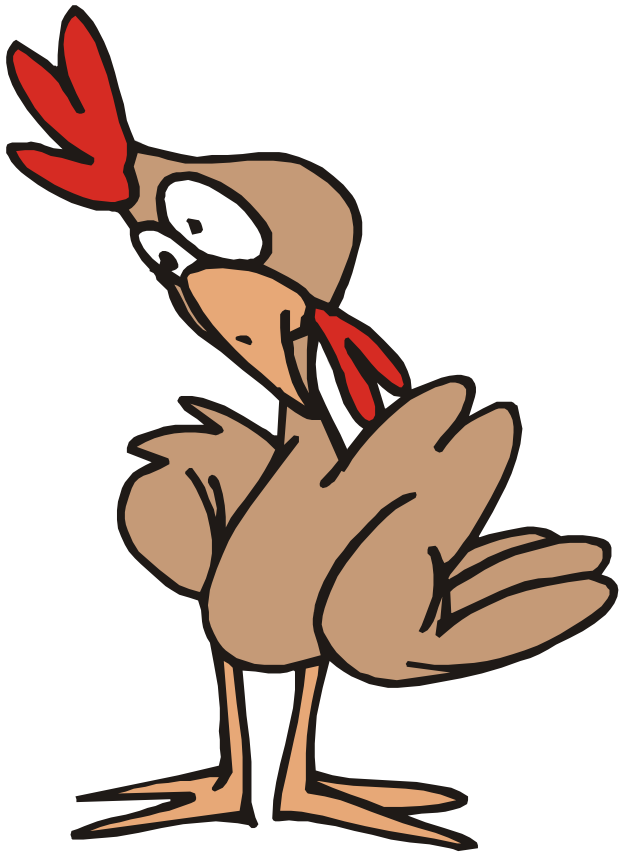
Role of wild birds



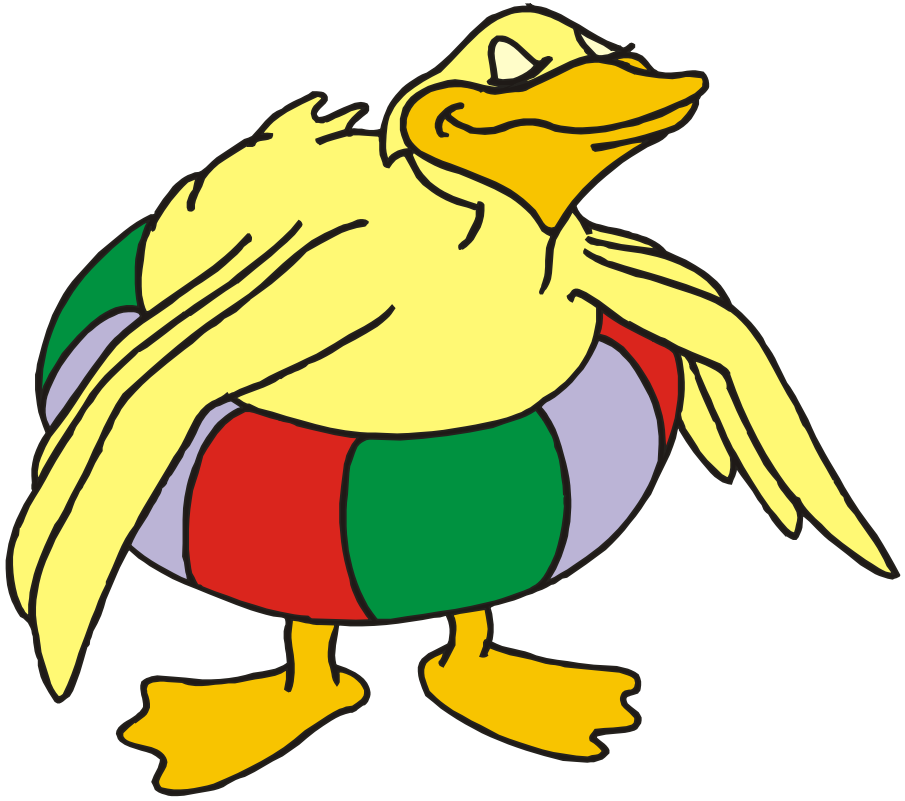
- Type A - wild and domestic birds, humans, pigs, horses and marine mammals.
- Types B & C - humans, less severe disease

Waterbirds (ducks, gulls and shorebirds) are the natural reservoir

H5N1 - Who's spreading it?



Poultry?



Wild birds?

The greatest variety of Avian Influenza viruses has been isolated from wild birds, particularly from waterfowls. Serve as reservoirs and gene pools. These birds perpetuate only viruses of low pathogenecity. Natural host of AI viruses to which the viruses are well adapted.
Waterfowls are resistant to the disease induced by HPAI viruses

Domestic Poultry does not appear to be the natural host of these viruses, therefore the degree of adaptation to the host is low and this could possibly explain why documented virus mutation has virtually always occurred in domestic poultry.

Influenza Nomenclature

1 2 3 4 5 6 7

A/Chicken/Pennsylvania/1370/83 (H5N2)

1 2 3 4 5 6 7

1) Antigenic type

2) Isolate host of origin

3) Geographic location

4) Isolate reference

5) Year of isolation

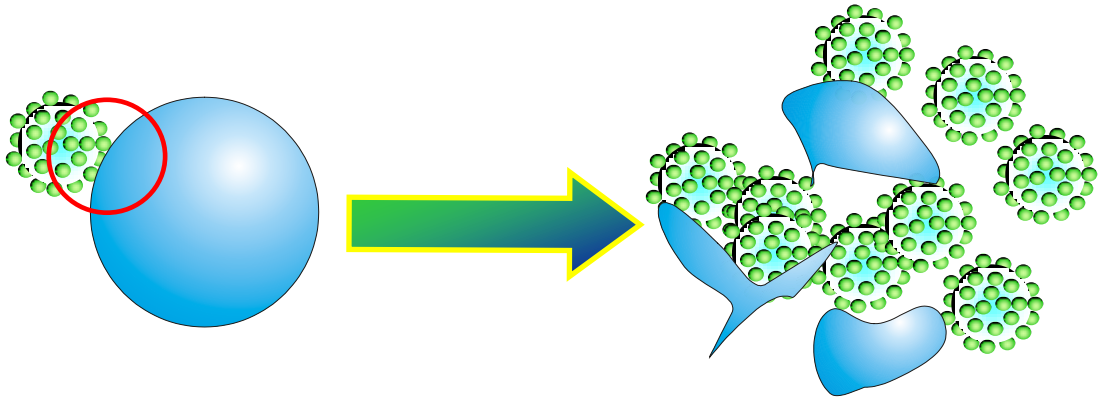
6) Hemagglutinin subtype

7) Neuraminidase subtype

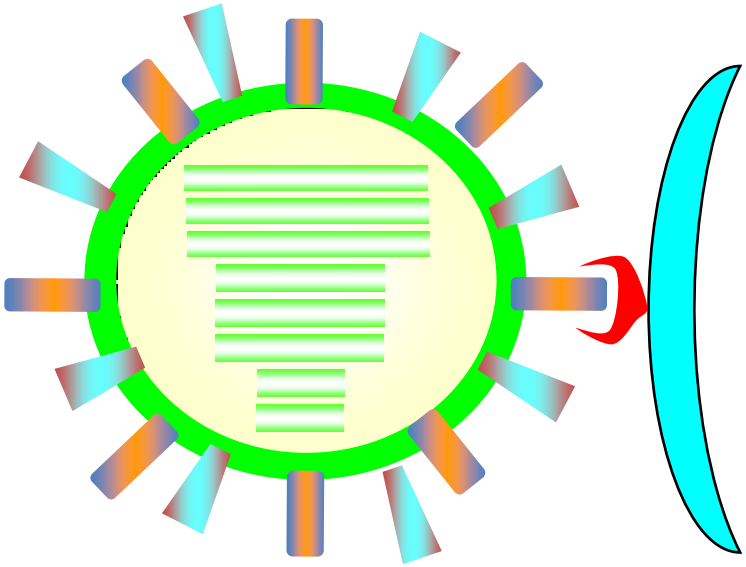
Geographic Range of Avian Influenza

- **Most reported isolations have been from North America, Europe and Asia.**

A few isolations from Australia Africa, and South America. No reported isolations Antarctica.



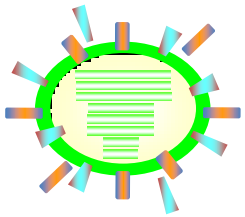
Virus Receptor



Cell membrane

PANDEMIC

Human disease that spreads beyond large regions (e.g. between continents)



1) Subtype

2) Illness

3) Transmissible

Differential Diagnosis

- Infectious Bronchitis
- TRT/APV
- Newcastle Disease
- Respiratory viruses – Mixed infections

Avian Influenza in Poultry

- AIV is not normally found in **domestic** ducks, chickens and turkeys
- Transmission of AIV from wild birds to domestic poultry species occurs commonly (ducks>turkeys> chickens)
- AIV on rare occasions may become established in chickens and turkeys and result in serious disease outbreaks
- AIV once adapted to chickens and turkeys can be difficult to eradicate.

Highly Pathogenic Avian Influenza

- Systemic, rapidly fatal disease of poultry
- Only **H5 and H7** subtypes are recognized to cause HPAI
- **OIE** List A Disease-outbreaks are reportable
- **HA** cleavage site critical virulence factor
- Low pathogenic H5 and H7 AI viruses can mutate into the highly pathogenic form of the virus

Diagnosis

1. Clinical Signs
2. Virus Isolation and Characterization
3. Serology
4. PCR
5. Histopathology and Immunochemistry

BIOSECURITY

- DEFINITION : all procedures used to prevent the introduction of disease
- OBJECTIVES :

  - prevent the entry of disease

  - control the spread of disease

BIOSECURITY IS EVERYONE'S RESPONSIBILITY!

Prevention

1- Practice proper sanitation and good hygiene during handling of poultry and poultry production.

2-Wear masks, safety glasses and gloves.

3-Avoid unnecessary contact with live, sick or dead birds.

4-Cook chickens until boiling temperature (exceeds 71 degrees).

5- Wash eggs thoroughly with soapy water, rinse and thoroughly cook.

What is the government doing

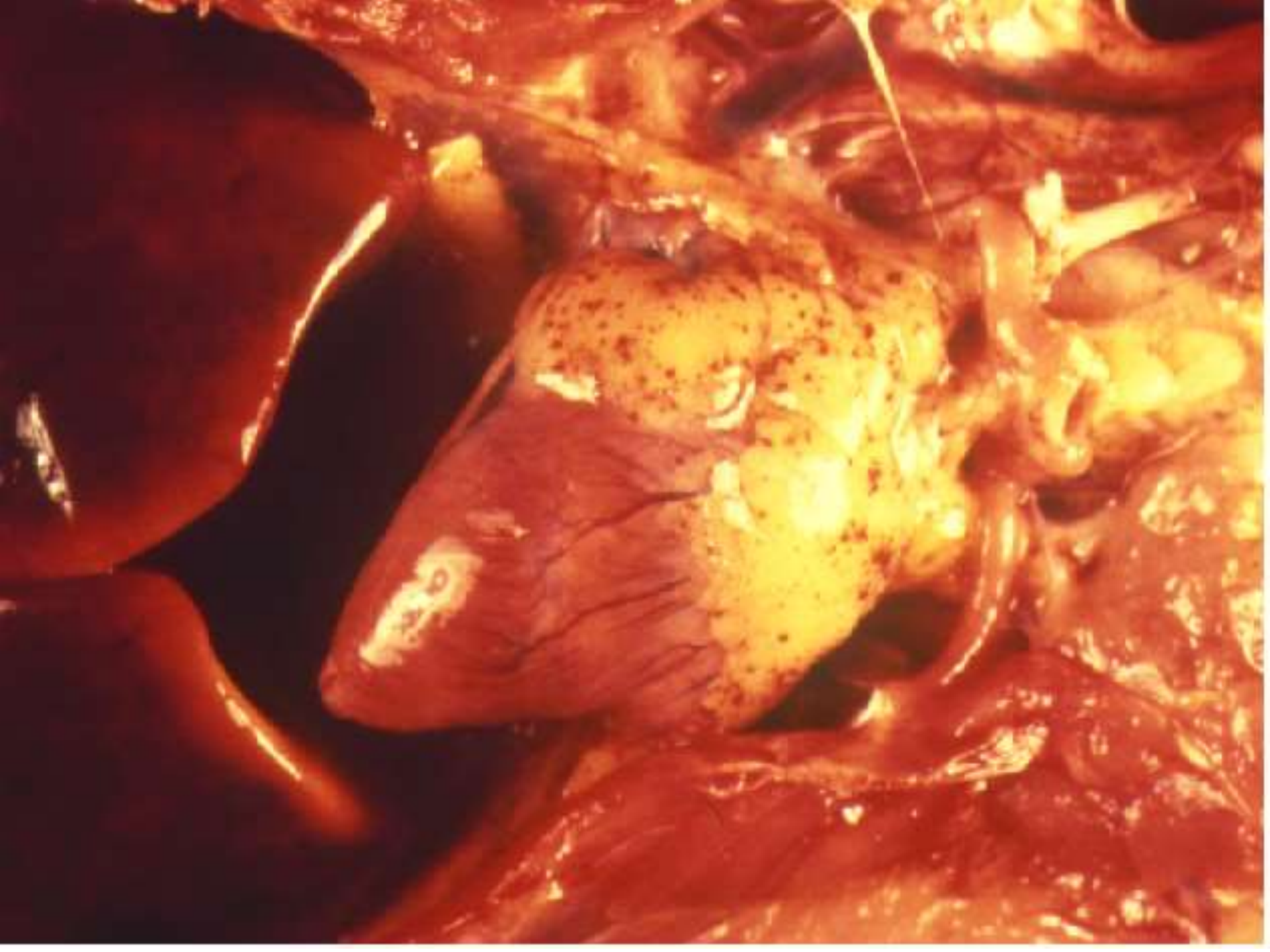
Government over the globe need to corperate and develop detection system and control measures to prevent the spread of AI.

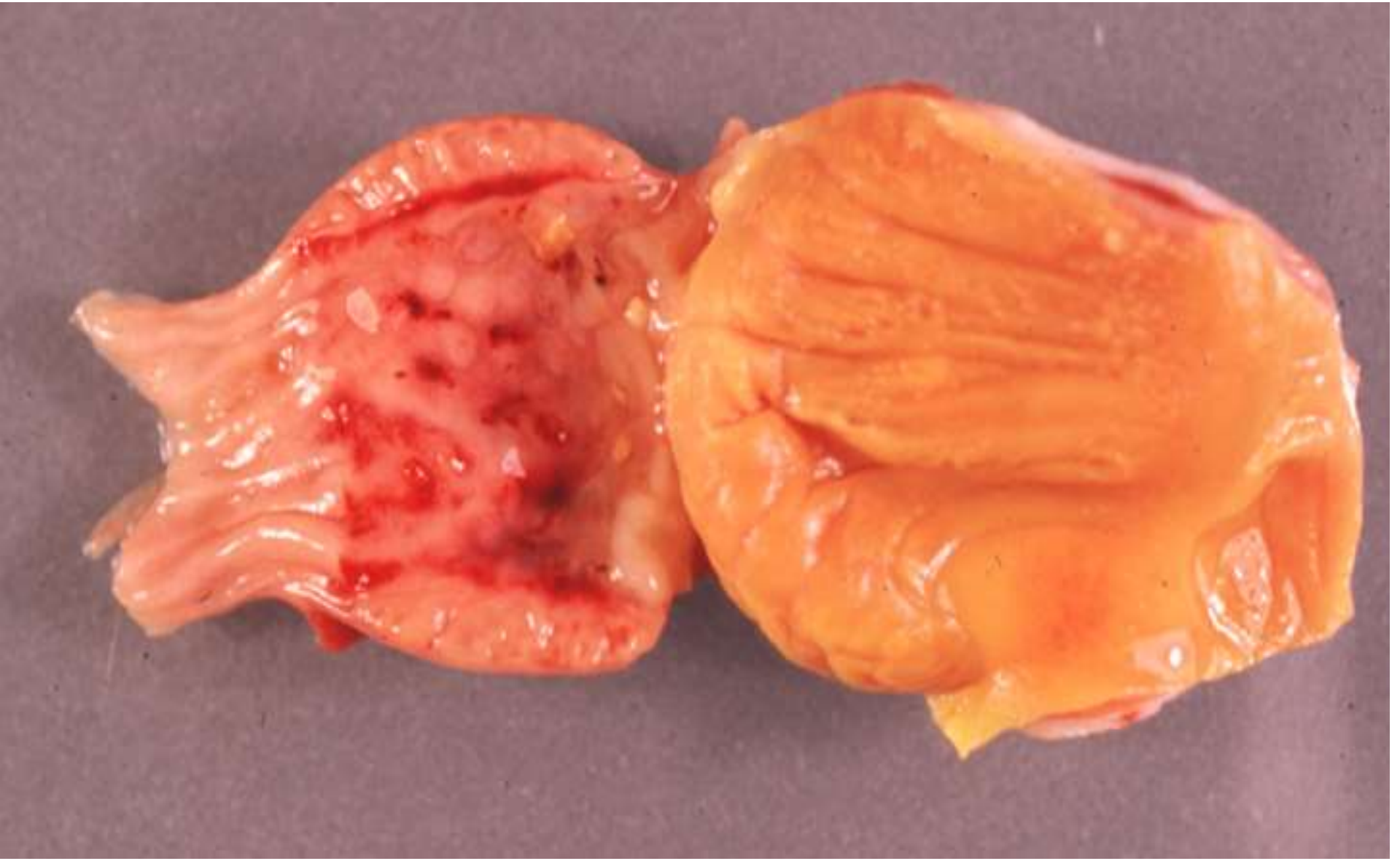
Clinical Features

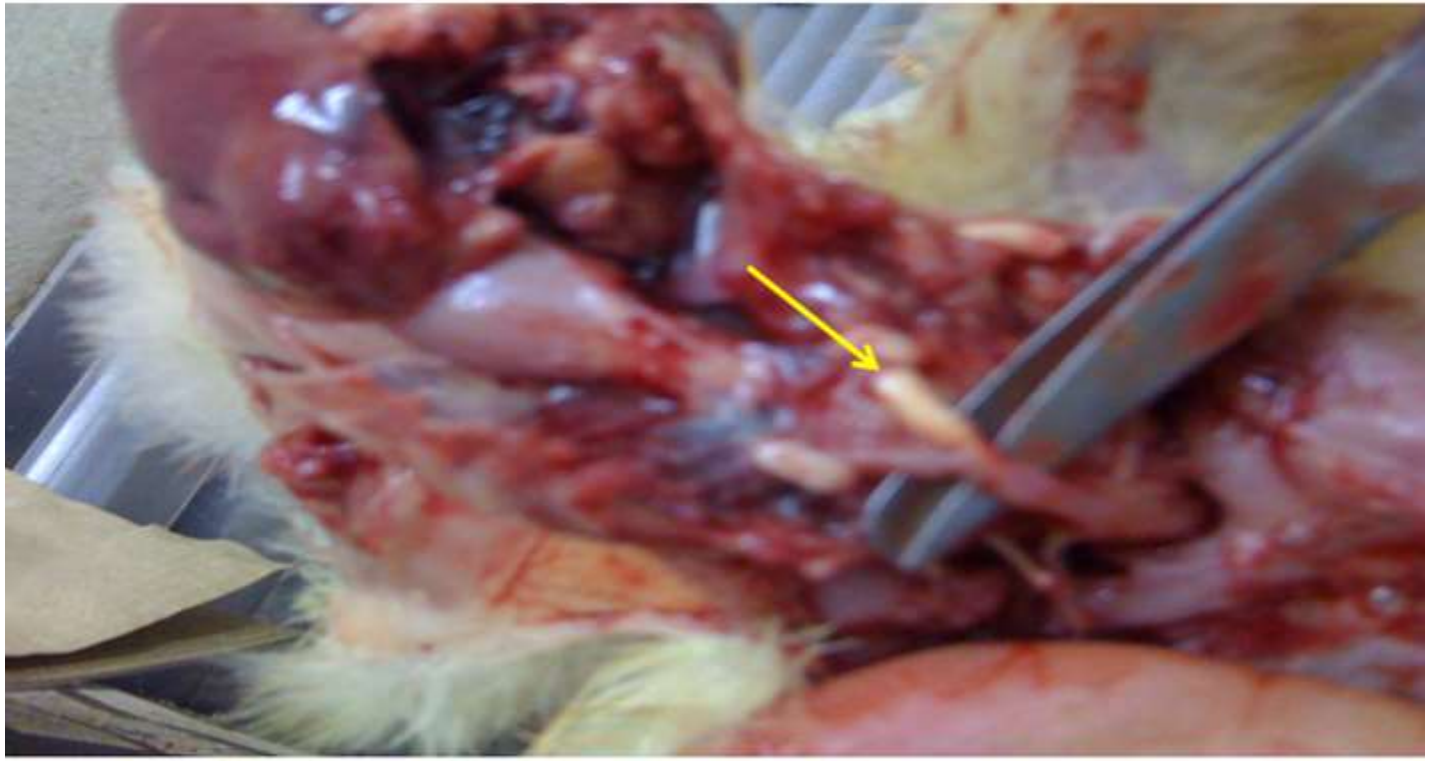
The disease caused in chickens and turkeys by highly pathogenic avian influenza viruses has historically been called "fowl plague."

Highly virulent strains cause sudden death without prodromal symptoms.

If birds survive for more than 48 hours (which is more likely in older birds), there is a cessation of egg laying, respiratory distress, lacrimation, sinusitis, diarrhea, edema of the head, face and neck, and cyanosis of unfeathered skin, particularly the comb and wattles.







Emergence of HPAI

LPAI H5 or H7 virus
transmitted to poultry

LPAI virus circulates in
poultry with mild disease

LPAI Virus Mutates to HPAI
with severe disease