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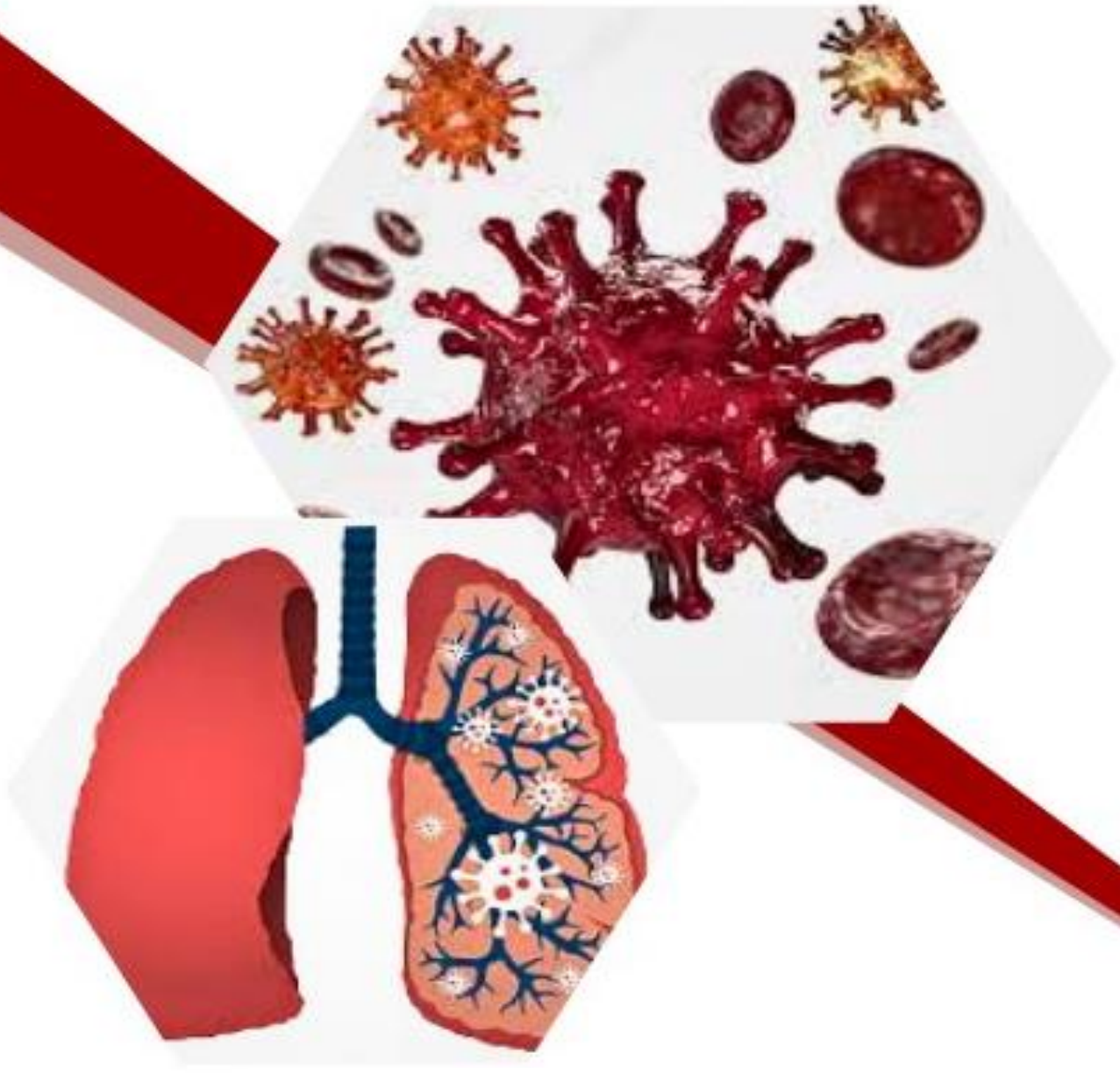
RS MICROBIOLOGY



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بسم الله الرحمن الرحيم
الحمد لله الذي علم بالقلم ، علم الإنسان ما لم يعلم ، والصلاة والسلام على نبي الأمم ، سيدنا محمد الأجل الأكرم ، وعلى آله وصحبه ، ومن تبعهم بإحسان إلى اليوم الأعظم

INFLUENZA

INFLUENZA: Acute respiratory tract illness caused by the influenza virus, characterized by constitutional symptoms such as fever, headache, myalgia, arthralgia, and possibly accompanied by local upper respiratory tract symptoms such as rhinorrhea, sneezing, and coughing.

At this level, differentiation between flu and the common cold, caused by rhinovirus, adenovirus, and parainfluenza virus, is essential.

The common cold is characterized by more prominent local upper respiratory tract symptoms like a runny nose, sneezing, coughing, and conjunctivitis, all indicating that the patient has the common cold. In contrast, a patient with the flu has more prominent myalgia, arthralgia, and may also experience local upper symptoms.

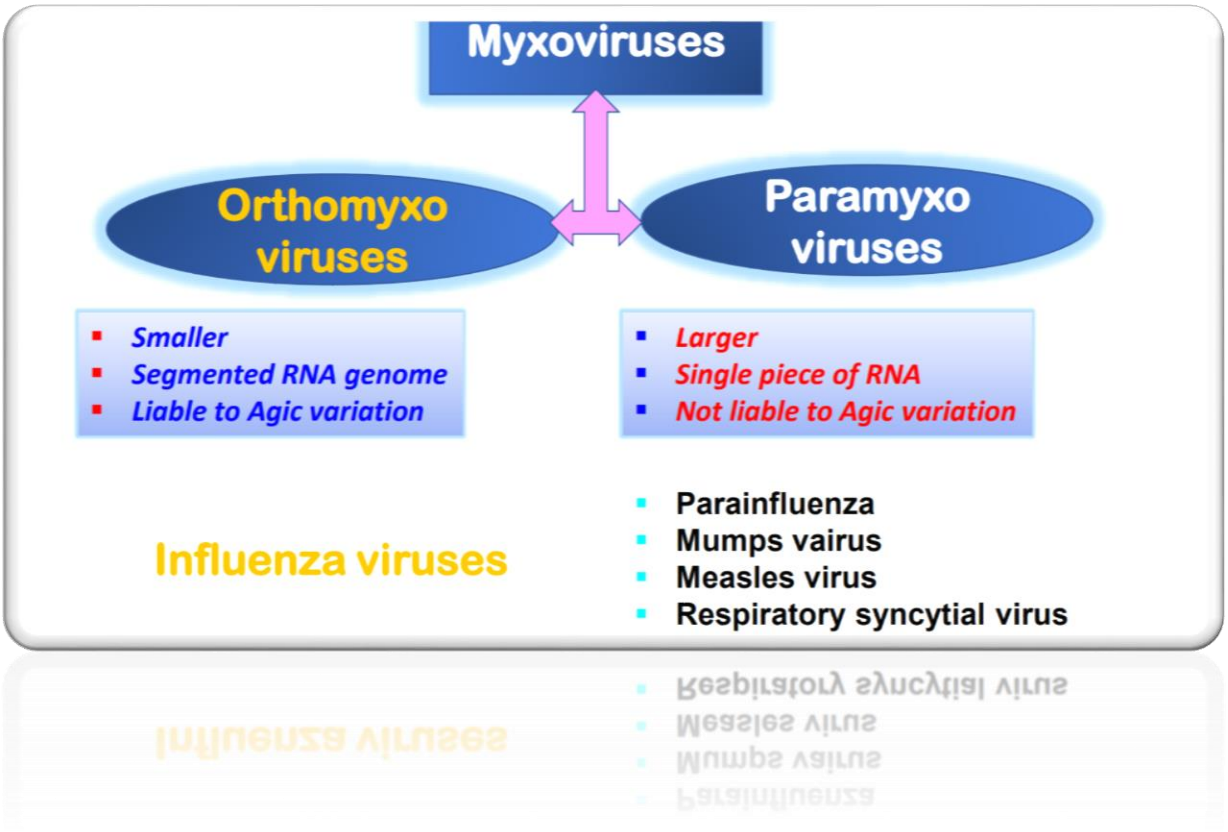
Influenza viruses are considered important because they exert strain and stress on the medical sector, especially in winter, and may have an impact on economic sectors.

All of them are considered emerging and re-emerging diseases, closely related to antigenic variation phenomena that occur with influenza viruses, such as antigenic shift and antigenic drift.
Antigenic shift is responsible for influenza pandemics, emerging when there is a new subtype of influenza type A virus that is not covered by the seasonal influenza vaccine.

INFLUENZA SYMPTOMS ARE CONSIDERED MORE CONSTITUTIONAL RATHER THAN LOCALIZED.

There is no viremia with influenza viruses, and the symptoms are related to cytokines release, mainly IL-1, IL-6,Il-8 , TNF-A, and IL-A.
Influenza virus is considered one member of the Myxovirus family and named by this name because they have an affinity for mucus, 'MUCIN,' found in the respiratory tract and GI tract.
Avian influenza sheds the virus in their feces.

However, in humans, it is mainly found in the upper respiratory tract to a lower extent in the lower respiratory tract.

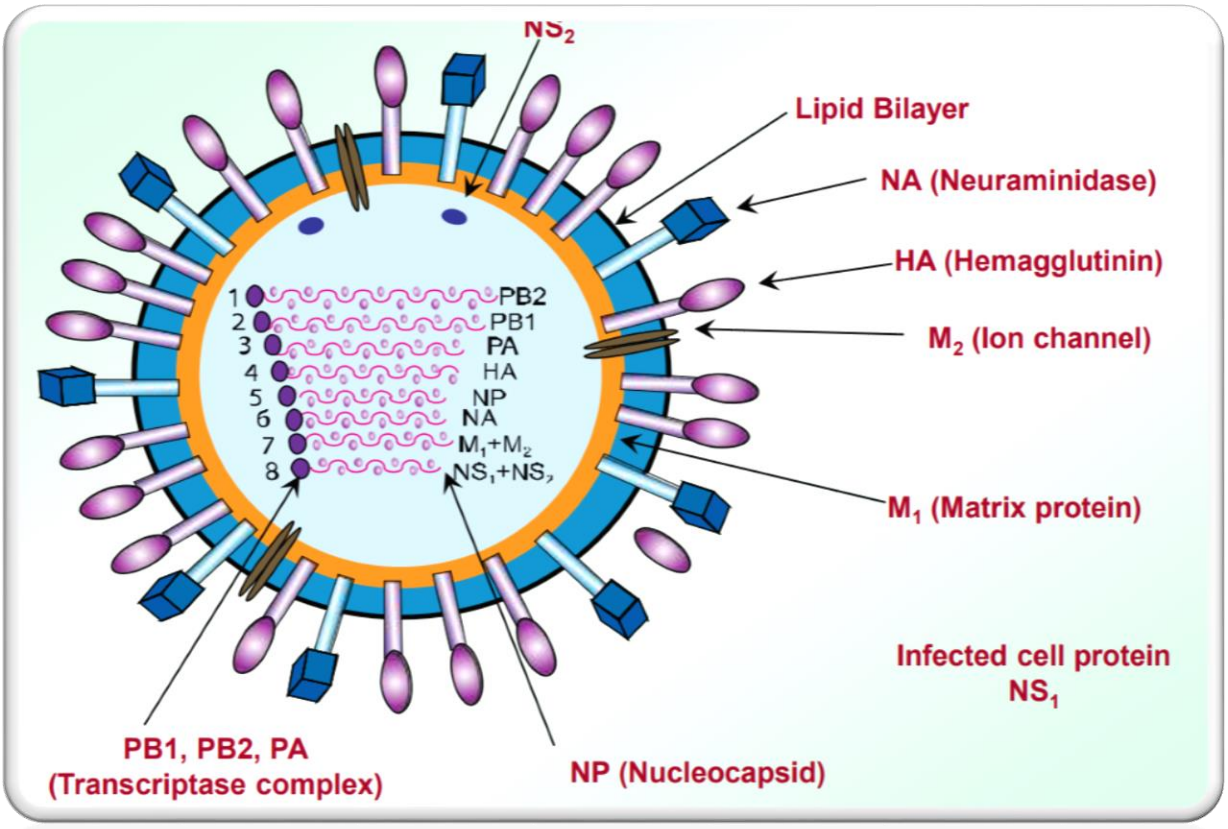


Genetic reassortment occurs when a cell is affected by two parental viruses from different species, allowing for the exchange of genetic material. This phenomenon occurs for every segmented genome.

Respiratory syncytial virus (RSV) is a more common cause of bronchiolitis in children and infants. There are four types of influenza viruses: A, B, C, and D. Influenza D primarily affects cattle and may infect humans, but it cannot cause illness. Among these, Type A is the only one that causes antigenic shifts and is considered the only one capable of causing pandemics. Three conditions are necessary for a pandemic to occur: the emergence of a new subtype A influenza virus, the ability to cause significant illness in humans, and most importantly, the ability to sustain and transmit the virus between humans and susceptible individuals.

All circulating strains are avian influenza, and Type A can cause infection in humans and other species, while Types B and C only cause infection in humans.

In terms of structure, influenza viruses are pleomorphic, spherical-shaped, and contain mRNA segments.
They also possess spike proteins, namely hemagglutinin and neuraminidase, and are enveloped. Types A and B have eight segments, while Types C and D have seven segments, lacking the neuraminidase segment.
The determination of illness-causing influenza types in humans is based on core antigens, specifically nucleoproteins, ribonucleoproteins, and matrix proteins.
These antigens are antigenically unrelated, leading to no cross-reactivity between them.



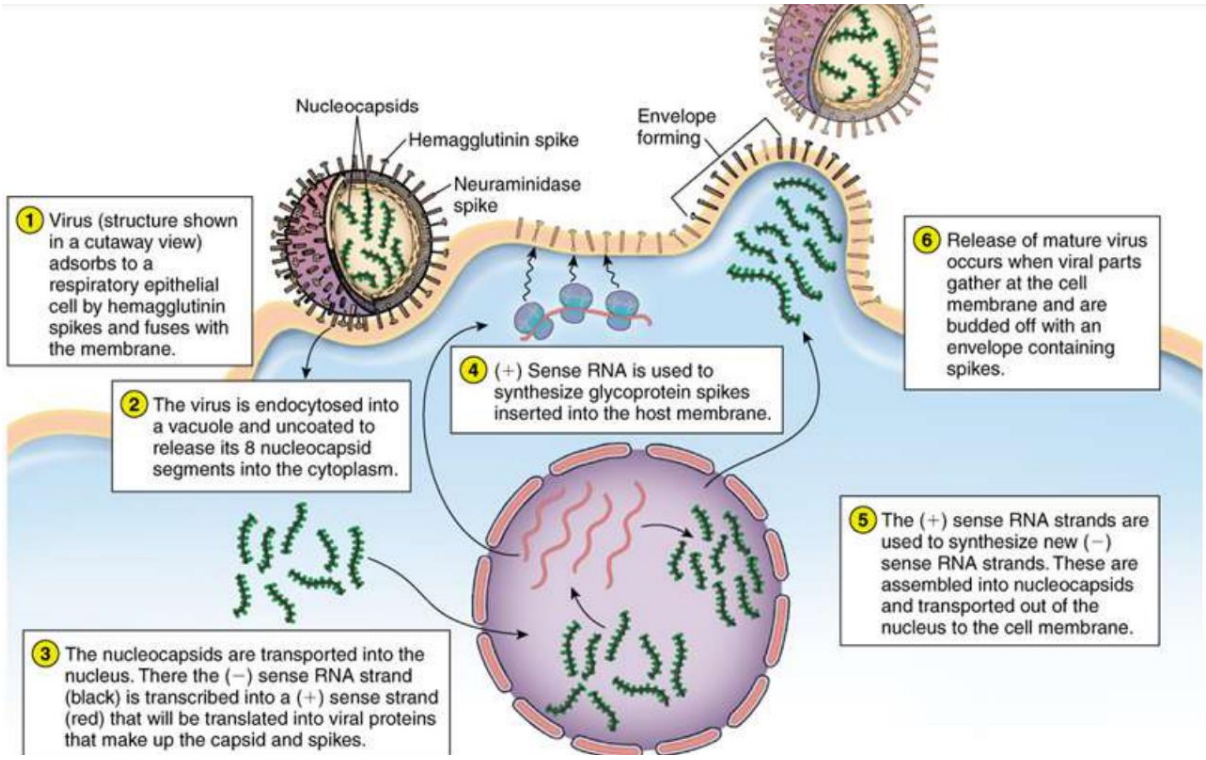
PB2, PB1, and PA collectively form the transcriptase complex. In the past, the primary line of treatment involved M2-ion channel inhibitors, specifically amantadine. However, these inhibitors are no longer considered effective in current treatments for two reasons: they cannot work against type B, and type A strains have developed resistance.
In type A influenza, various subtypes are identified, while for types B and C, lineages are used in naming.

Spike proteins play a crucial role in the pathogenesis of the influenza virus. Hemagglutinin, named for its ability to agglutinate red blood cells from various animal species, initiates the replicative cycle by attaching to host cells through glycoproteins containing sialic acid. This attachment is followed by the internalization of the virus.
Antibodies against Hemagglutinin are neutralizing antibodies and are considered a deterrent against influenza.
Seasonal vaccines provide immunity against influenza for months by targeting these antibodies.

Neuraminidase operates at the end of the replicative cycle, facilitating the budding of the virion from the host cell.
This process involves detaching the attachment between the flu virus and neuraminic acid, a type of sialic acid. Neuraminidase plays a crucial role in navigating through mucus secretions, contributing to primary and secondary pneumonia.
This ability gives the virus the potential to be fatal in certain high-risk groups. Despite this, antibodies against neuraminidase play a minimal role in countering influenza.

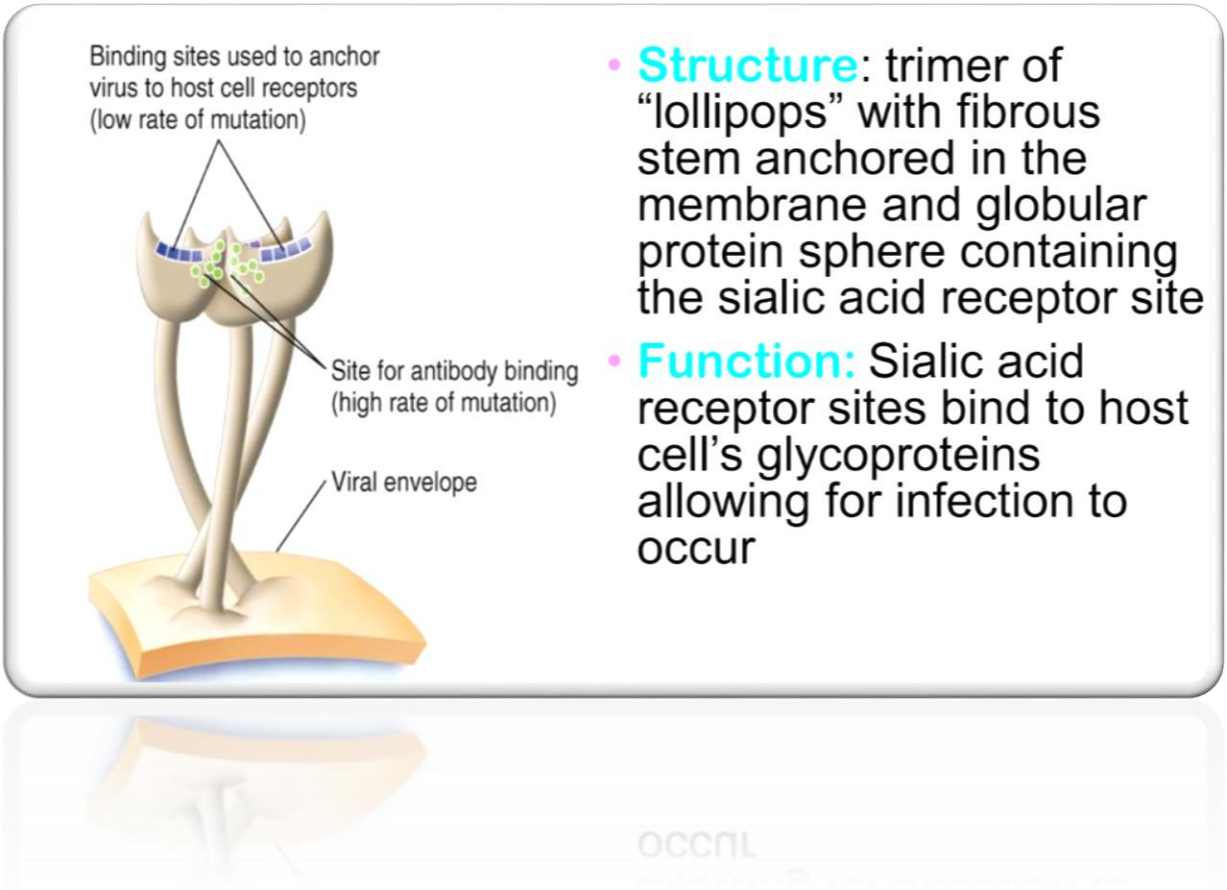
The replicative cycle of the influenza virus begins with receptor-mediated endocytosis, facilitated by the attachment of hemagglutinin to sialic acid. The virus enters the cell as an endosome, and in the acidic environment, H1 and H2 undergo cleavage and activation, leading to fusion. Subsequently, there is uncoating of proteins, allowing the viral genetic material to enter the nucleus.

Birds can shed the virus in their feces for up to two weeks, and if it finds a suitable environment, the virus can remain infectious for an extended period, lasting up to three months.

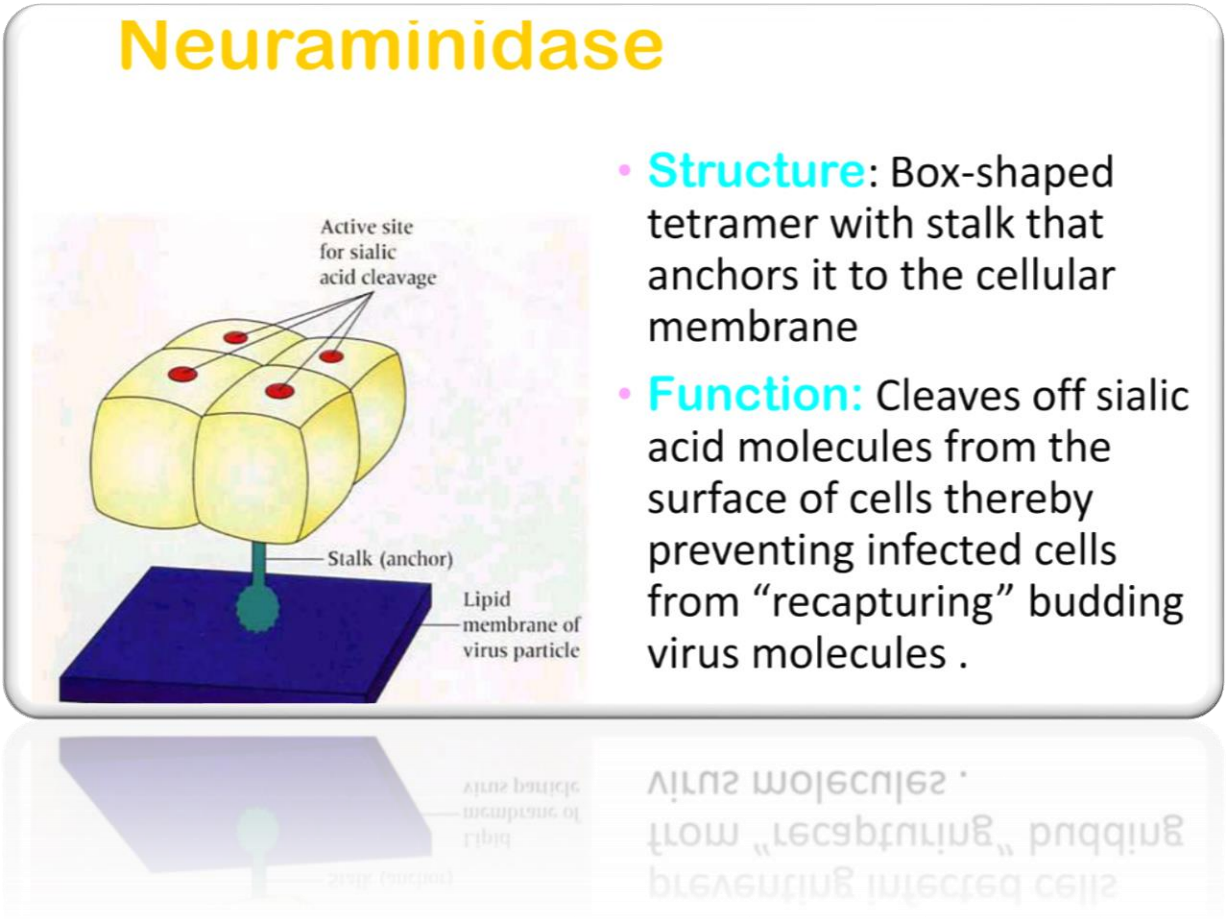


A negative-sense mRNA virus undergoes replication in the nucleus, and assembly occurs at the host cell's lipid membrane.

Type A influenza can infect humans, mammals, and birds, making it capable of genetic shifts due to its extensive reservoirs in wild hosts. This ability contributes to the potential for pandemics.
Type B can cause milder disease in humans, exhibits a lesser ability for antigenic variation, and may lead to epidemics but lacks the potential to cause pandemics.
Type C, being the most stable, has minimal ability to cause antigenic variations, and its impact is typically limited to sporadic outbreaks.



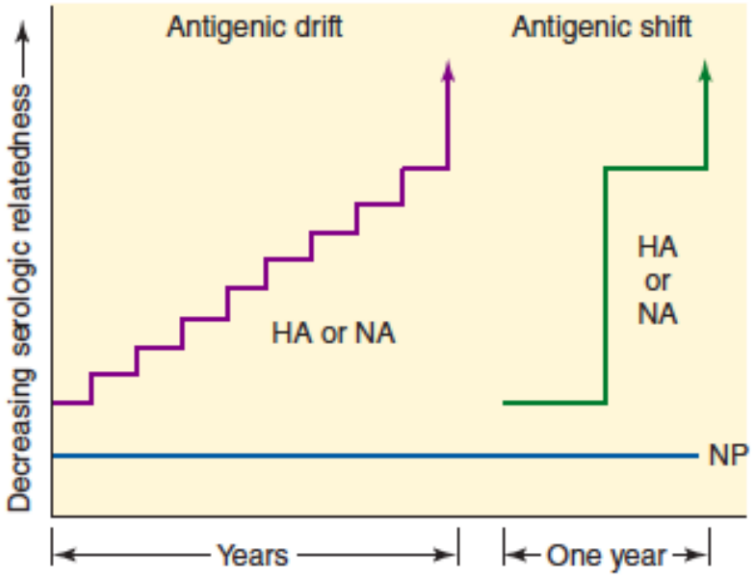
The binding sites that anchor the virus to the host cell are not highly variable, while the neutralizing antigens against glycoproteins have highly variable binding sites.



Antigenic variation in influenza involves surface glycoproteins encoded by genetic segments within the virus. If the same host cell, such as in a swine-mixing bowl, gets infected by two different viruses, genetic mixing can occur, involving segments like HN and N.
This process is not limited to hemagglutinin and neuraminidase.

There are two types of genetic variation. The first, genetic shift, results in major sudden changes, leading to new subtypes and the potential for pandemics. This phenomenon is exclusive to Type A influenza. Notably, the 1918 Spanish flu (H1N1) was the first recorded influenza pandemic, followed by subsequent shifts like the Chinese one (H2N2), Hong Kong (H3N2), and more recently, Russia.

The second type of antigenic variation is antigenic drift, involving mild, minor changes that can occur in Types A, B, and C. It happens through spontaneous mutations in the nucleus, affecting amino acid sequences over an extended period. The concept of original antigenic sin suggests that a new subtype may face immunity from previously immunized individuals, potentially preventing pandemics.
Both genetic shift and drift have the potential to cause new influenza subtypes.



The standard nomenclature system for influenza virus isolates includes crucial information such as type, host of origin, geographic origin, strain number, and year of isolation. For human isolates, like A/Hong Kong/03/68(H3N2), the host of origin is not indicated, whereas it is specified for others, as seen in A/swine/Iowa/15/30(H1N1).

There are 18 subtypes of HA (H1–H18) and eleven subtypes of NA (N1–N11), found in various combinations across birds, animals, and humans. Six HA (H1–H3, H5, H7, H9) and three NA (N1, N2, N7) subtypes have been identified in humans.

The receptor for the virus is found on alveolar cells, epithelial cells, mucous-secreting cells, and macrophages. Systemic manifestations result from cytokine release, and notably, there is no viremia.

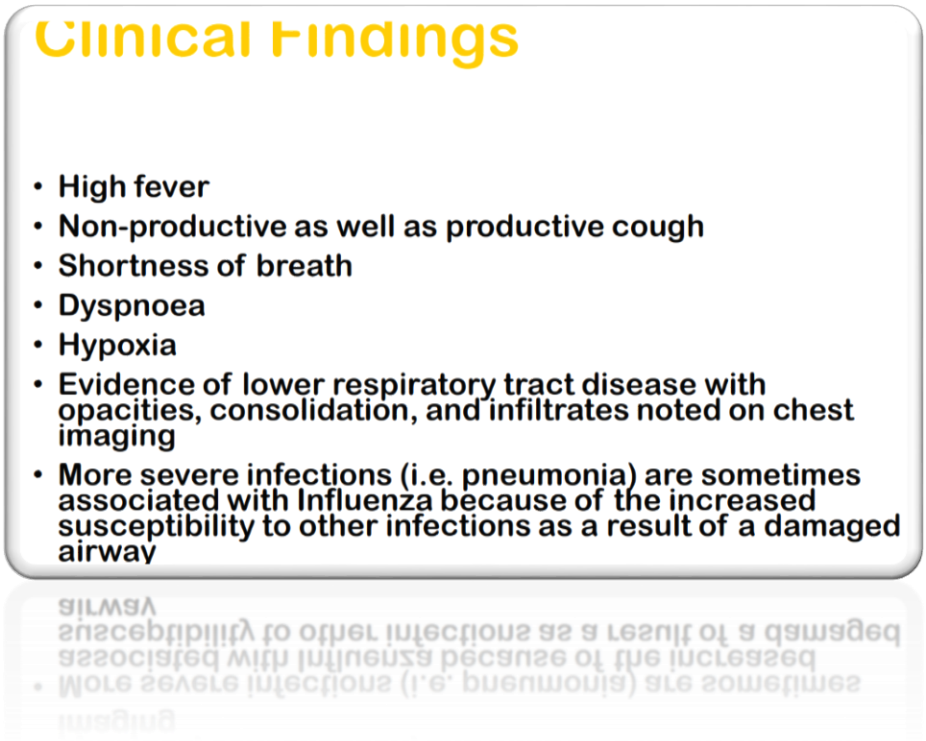
In the past, culture was the gold standard for diagnosis.

Influenza, being highly contagious, can spread through droplets, airborne particles, and both direct and indirect modes of transmission.

The reproductive number (R note), indicating how many people an infected individual can transmit the virus to, is estimated to be about 2 for influenza, similar to the coronavirus.

Hands are considered porous, and the virus can remain viable for about six hours on them, while on non-porous surfaces, it can persist for up to 48 hours. The shedding of the virus typically begins one to two days before the onset of fever, peaks 1-2 days during symptoms, and gradually declines over about five days until it ends. Importantly, shedding correlates well with symptoms.

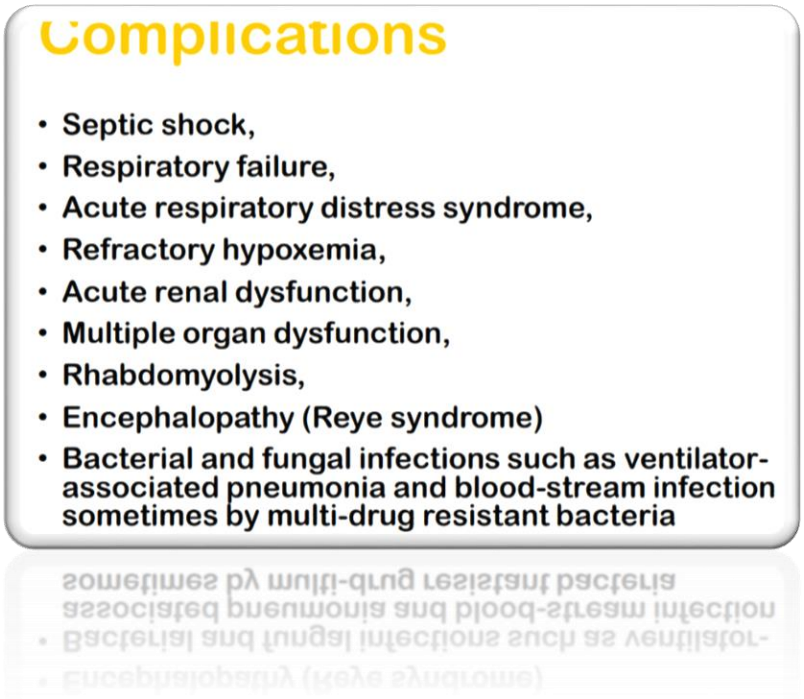
Patients often complain of constitutional symptoms as the primary manifestation of the illness. These symptoms may be accompanied by local upper respiratory symptoms, and a non-productive cough is also possible. Individuals at high risk may be vulnerable to superimposed bacterial or fungal infections.



Primary influenza pneumonia exhibits a direct and rapid progression, with the patient's symptomology worsening over time rather than improving. If there are window periods, they are typically brief, lasting no more than a few hours.

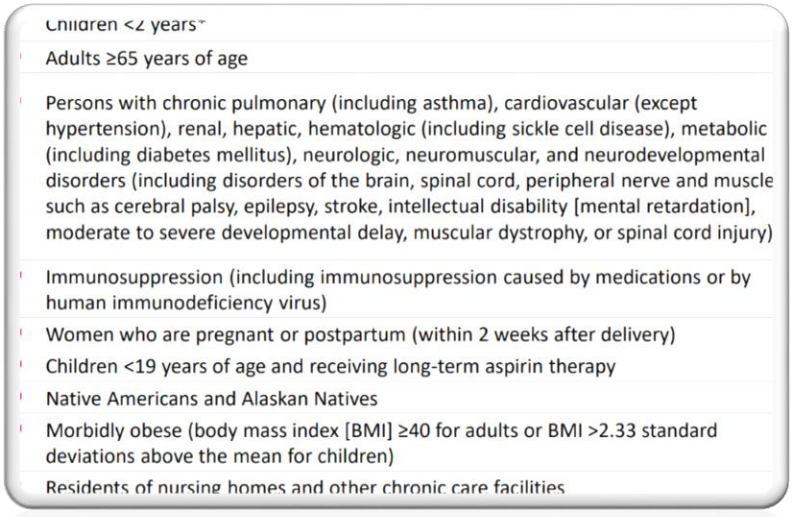
Secondary bacterial pneumonia, on the other hand, involves a mixed infection of both viral and bacterial agents. What distinguishes it from primary influenza pneumonia is a longer window period, potentially extending beyond the initial

few hours. lasts up to 4 or 5 days after the onset of influenza then return back to become worse.



Reye Syndrome is characterized by acute encephalopathy and acute fatty liver changes. It typically occurs in children and teenagers aged 5-15 years, and an important factor associated with its development is the use of aspirin during or after recovering from influenza or flu-like illnesses.

Groups at high risk for influenza complication:



The gold standard for diagnosing influenza is RT-PCR, which can be completed within one hour using swab samples, searching for genes encoding the influenza virus. In the past, culture was used, involving monkey eggs and hemagglutination assays, but this method was time-consuming. Additionally, serology, involving the use of antibodies, is another important diagnostic approach for influenza.

Influenza vaccines come in various forms, such as killed or live attenuated viruses, whole virus, or subunits focusing on components like HA (hemagglutinin) and NA (neuraminidase). Vaccination is the primary strategy against influenza, offering protection for about 6-8 months. Due to the virus's mutability, a new formula is administered annually, with a current trend towards split and quadrivalent vaccines. Two main types are inactivated subunit (TIV), administered intramuscularly, and live attenuated vaccine (LAIV), administered intranasally. They are both trivalent, but current formulations are quadrivalent, including two subtypes of A (H1N1 and H3N2) and two lineages of B influenza virus (Yamagata and Victoria).

For drug interventions, M2 inhibitors like amantadine and rimantadine were used in the past, but currently, neuraminidase inhibitors like Tamiflu (oral) and oseltamivir (IV) are preferred. Administered within 48 hours of symptom onset, these drugs are crucial in halting replication and spread. Prophylaxis is also a key consideration.

Avian Influenza affects various avian species, with wild birds serving as natural reservoirs. In exotic birds, it can be a silent infection with virus shedding in feces for two weeks, while domesticated birds show severe signs. Avian influenza can be transmitted to humans but typically ends after infecting a few individuals. Different types, including low pathogenic (LPAI) and highly pathogenic (HPAI), exist in avians. Mathematical models and poultry vaccines are used to predict and manage potential pandemics.

Swine Influenza, caused by type A influenza viruses (H1N1 subtype), is a respiratory disease in pigs that occasionally leads to human infections. Transmission to humans has been reported but was historically limited and not sustained beyond three people.