RS

MICROBIOLOGY

MODIFIED NO. 2

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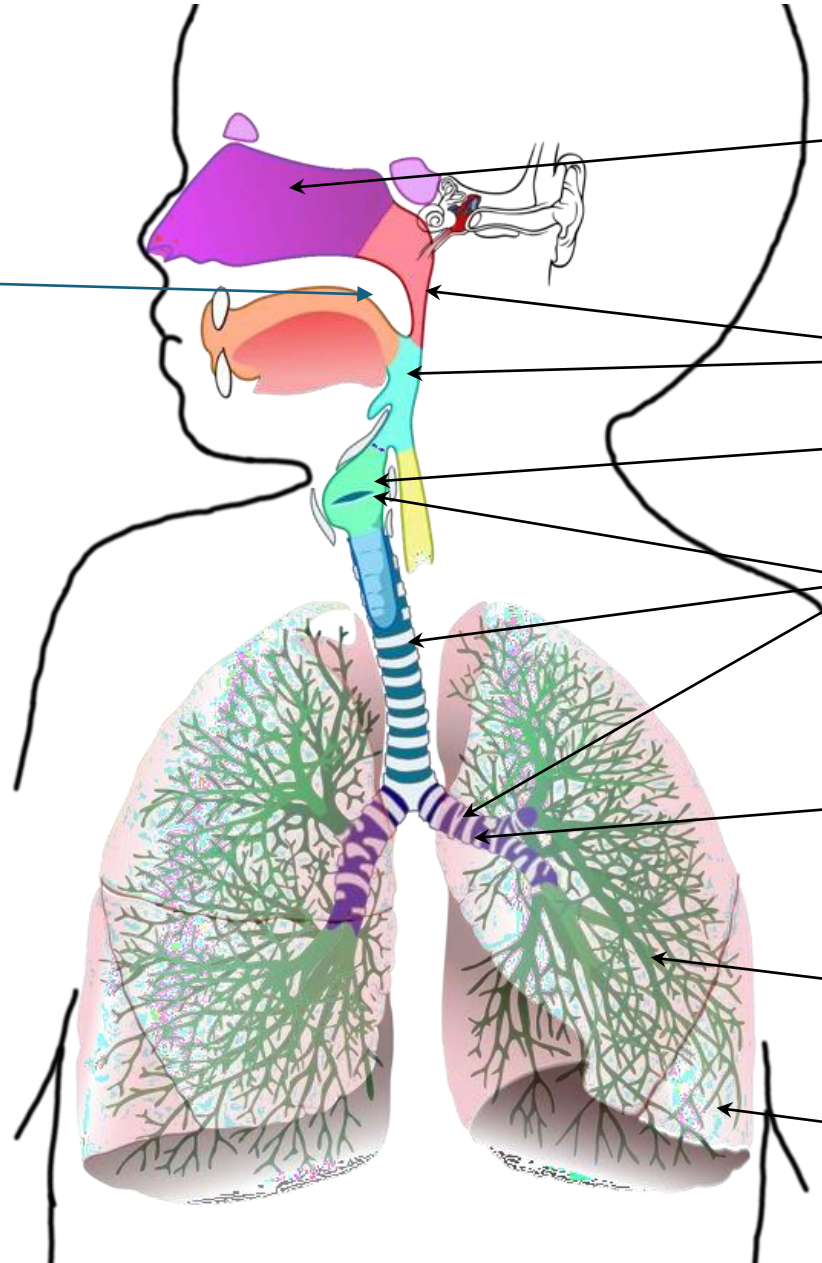
تدقيق: ميس قشّوع

الدكتور: حافظ المومني

Respiratory System Infections

Color code
Slides
Doctor
Additional info
Important

Anatomical Location of Viral Syndromes



EBV,CMV

Rhinitis
Common Cold
Rhinovirus, Coronavirus
Influenza

Pharyngitis
Sore Throat
Laryngitis
Adenovirus, Parainfluenza
Influenza

Laryngotracheobronchitis
Croup
Parainfluenza
Influenza

Bronchitis
Rhinovirus, Parainfluenza,
Adenovirus, Metapneumovirus
RSV, Coronavirus **Influenza**

Bronchiolitis
RSV (single serotype)
Metapneumovirus
Adenovirus **Influenza**

Pneumonia
All viruses **Influenza**

Influenza

- A common viral disease of the lower respiratory system caused by an **orthomyxovirus (the family of influenza virus)**
- 15-20% of world population
- 3-5 million sever cases
- 500000 death
- Influenza is pervasive worldwide and causes 3,000–50,000 deaths each year in the United States.
- Influenza infections are most typically characterized by **fever**, **chills**, and **body aches**. This is followed by symptoms similar to the common cold that may last a week or more

- Influenza is a widespread viral infection with a significant global impact. Approximately **15-20% of the world's population** is affected by the virus annually.

- Out of these cases, there are **3-5 million severe cases**, where individuals experience serious complications. These severe cases are more likely to occur in vulnerable groups, such as the elderly, young children, and individuals with pre-existing conditions like chronic respiratory infections.

- Tragically, influenza is responsible for approximately **500,000 deaths** each year, highlighting the importance of prevention and treatment measures.

- The **clinical presentation** of influenza differs from that of the common cold, although there are some overlapping symptoms such as **cough**, **sneezing**, and **pharyngitis**.

- However, certain symptoms are more characteristic of influenza and help distinguish it from the common cold. These include **high-grade fever** and **chills**, which are typically more pronounced in influenza. Additionally, symptoms like **myalgia** (muscle pain), **arthralgia** (joint pain), **tiredness**, and **loose stools** tend to be **more severe in influenza** compared to the common cold, even though they may also occur in milder forms with the common cold.

Common Cold Vs Influenza

This is table its very important to compare between influenza and common cold

Sign/Symptom	Common Cold	Influenza
Fever	Low (37.2 °C [99 °F])	High (39 °C [102.2 °F])
Headache	Common	Common
Aches and pains	Mild	Severe
Fatigue	Slight	Severe
Nasal congestion	Common	Rare
Sneezing	Common	Rare

And diarrhea is more common with influenza

So, Myalgias, arthralgias, loose stool and high grade fever --> this is an influenza

- In general, influenza is self-limiting(7to 10 days). However, serious cases can lead to pneumonia and other complications that can be fatal. Such cases are more common in the very young and the elderly.
- The influenza virus is primarily transmitted by direct contact and inhalation of aerosols.

- When a person gets infected with influenza, the illness often resolves on its own. However, in some cases, complications may occur, such as **pneumonia** and **lower respiratory infections**.
- One of the most serious complications that can develop in some patients is **Reye's syndrome**, a rare but severe condition that primarily affects the liver and brain.

Reye syndrome

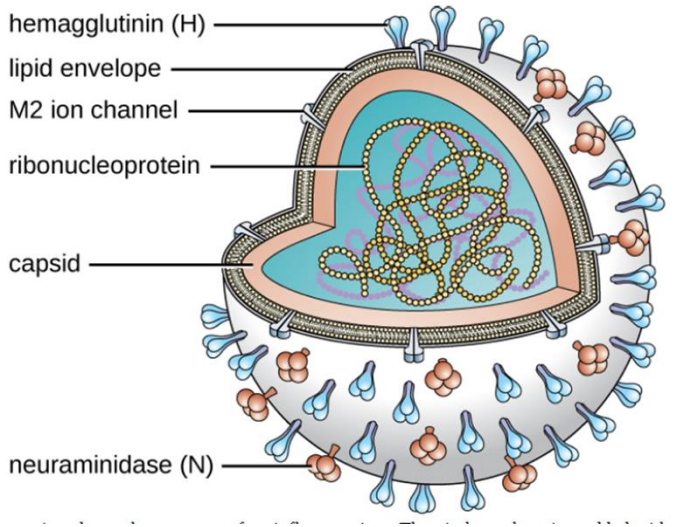
- A **complication of influenza** that occurs primarily in children and teenagers.
- Swelling in the liver and brain, and may progress to neurological damage, seizures, coma, or death.
- Reye syndrome may follow other viral infections, like **chickenpox and infleunza**, and has been associated with the use of **aspirin**.
- the CDC and other agencies recommend that aspirin and products containing aspirin never be used to treat viral illnesses in children younger than age 19 years.

- RS is primarily a children's disease, although it can occur at any age. It is often misdiagnosed. Symptoms may include:
  - Persistent or recurrent vomiting
  - Listlessness
  - Personality changes such as irritability or combativeness
  - Disorientation or confusion
  - Delirium
  - Convulsions
  - Loss of consciousness

- **Reye's syndrome** is a rare condition that typically affects children who have had influenza and were given aspirin. Although it is not a common complication, it is serious and can lead to liver and brain damage. The exact cause of Reye's syndrome remains unknown to this day.

Influenza virus

- The RNA genome
  - Seven or eight **segments**, each coated with ribonucleoprotein and encoding one or two specific viral proteins.
- The influenza virus is surrounded by a lipid membrane envelope, and **two of the main antigens** of the influenza virus are
  - The spike proteins hemagglutinin (H) and neuraminidase (N)
  - The hemagglutinin protein (for attachment) to bind to sialic acid receptors on host
  - Neuraminidase (for exit) , which cleaves sialic-acid receptors to allow progeny viruses to make a clean exit



- The difference in **serotypes** of the influenza virus is based on variations in the **H (hemagglutinin)** and **N (neuraminidase)** antigens. These antigens are surface proteins that play a crucial role in the virus's ability to infect host cells and evade the immune system.

The influenza viruses

- There are three genetically related influenza viruses, called A, B, and C.

	Influenza A virus	Influenza B virus	Influenza C virus
Severity	Severe	Moderate	Mild
Animal reservoir	Yes	No	No
Genome segments	8	8	7
Population spread	Epidemic and pandemic	Epidemic	Sporadic
Antigenic variation	Shift/drift	Drift	Drift

- The most virulent group is the influenza A viruses, which cause seasonal pandemics of influenza each year.
- Influenza A virus can infect a variety of animals, including pigs, horses and even whales and dolphins.
- Influenza B virus is less virulent and is sometimes associated with epidemic outbreaks.
- Influenza C virus generally produces the mildest disease symptoms and is rarely connected with epidemics.
- Neither influenza B virus nor influenza C virus has significant animal reservoirs.

- Influenza viruses undergo **antigenic variations**, which are changes in the surface antigens, particularly **hemagglutinin (H)** and **neuraminidase (N)**. These changes help the virus evade the immune system, leading to recurring outbreaks and epidemics. There are two main types of antigenic variation:

  1. **Antigenic Drift**:

  • This refers to **small, gradual changes** in the H and N antigens due to random mutations in the viral genome during replication.

  • These minor changes occur continuously over time and are the reason why seasonal flu vaccines need to be updated annually.

  • Antigenic drift causes **epidemics**, as the immune system of previously exposed individuals may not fully recognize the slightly altered virus.

  2. **Antigenic Shift**:

  • This is a **sudden, major change** in the H or N antigens, resulting in the emergence of a new influenza virus subtype.

  • Antigenic shift occurs when two different influenza viruses infect the same host cell, leading to a reassortment of their genetic material.

  • This process can result in a completely new strain of the virus, against which the population has little to no immunity.

  • Antigenic shift is responsible for **pandemics**, such as the H1N1 pandemic in 2009.

The influenza A viruses (The most severe one)

- The influenza A viruses
  - Have different subtypes (serotypes)
    - 18 known subtypes of hemagglutinin and 11 known subtypes of neuraminidase.
  - Influenza viruses are serologically characterized by the type of H (hemagglutinin) and N (neuraminidase) proteins that they possess.
  - there are certain strains or serotypes (combustion between H and N) that cause infection in human.
  - Of the nearly 200 different combinations of H and N, only a few, such as the H1N1 strain, are associated with human disease.
  - H2N2 and H3N3 don't cause infection.
  - The structure of H1N1 antigen differs from H2N2 antigen.

Influenza virus infections

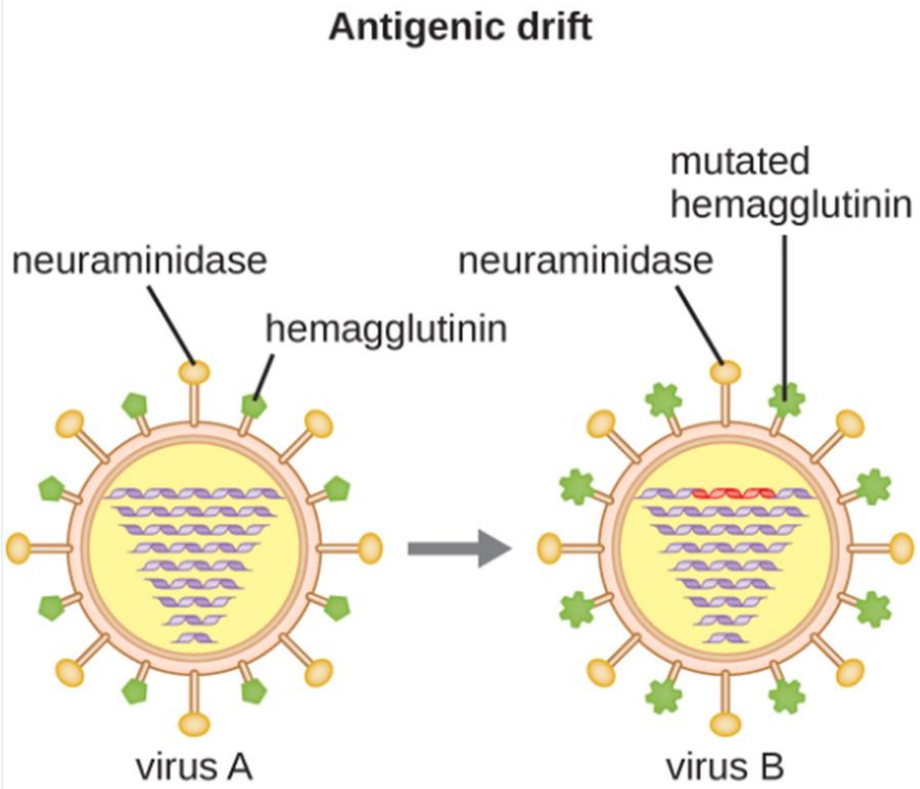
- Elicit a **strong immune response**, particularly to the hemagglutinin protein
- The clinical presentation of sever immune response is Sever Influenza Infection with more severe symptoms such as high grade fever.
- Although the strong immune response helps in the development of antibodies against the virus, Unfortunately, the antigenic properties of the virus change relatively rapidly, so new strains are evolving.
- When an influenza virus gains a new hemagglutinin or neuraminidase type, it is able to evade the host's immune response and be successfully transmitted, often leading to an epidemic. So every year, we are facing a new serotype that differs from the serotype of the previous year as a result of changing H and N antigen.

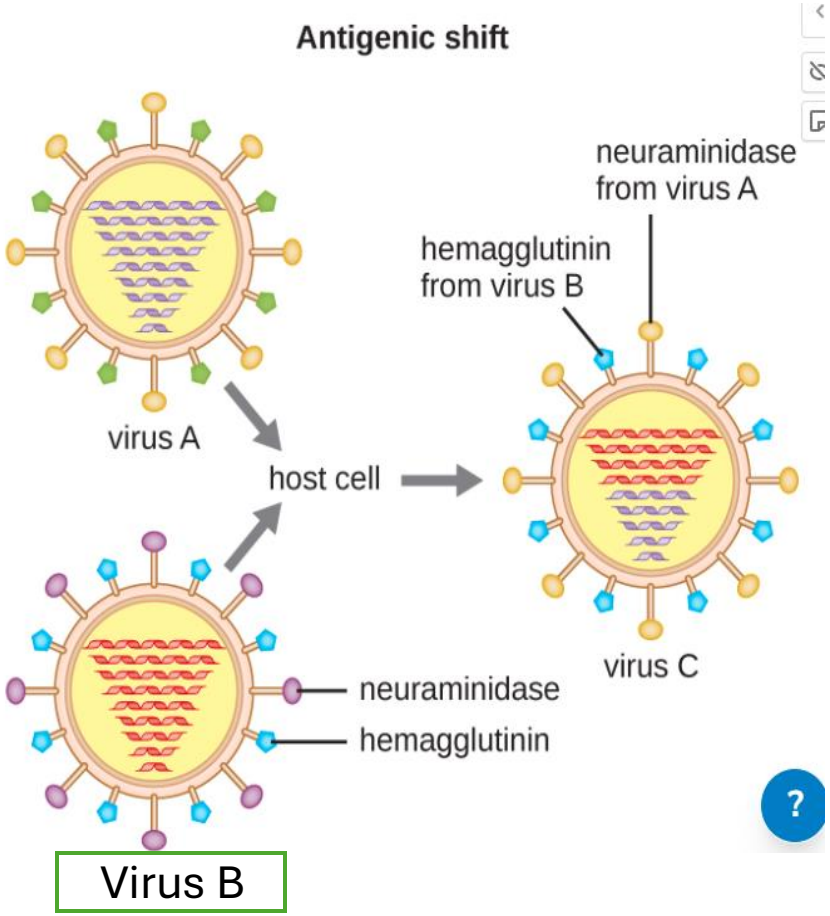
Evolutionary changes

- **Drift:** Minor change
- **Shift:** Major change

- Antigenic Variation in influenza viruses
  - Two types of antigenic variations: Antigenic **drift** and Antigenic **shift**
- Antigenic drift is the result of point mutations (change in one amino acid) causing slight changes in the spike proteins hemagglutinin (H) and neuraminidase (N).
- Although antigenic drift result in minor changes to viral antigens, the body lacks immunity to the newly generated viral antigens.
- Antigenic shift is a major change in spike proteins due to gene reassortment.
  - Influenza viruses swap gene segments. This genetic exchange is possible due to the segmented nature of the viral genome
  - Occurs when two differing influenza viruses co-infect a cell.
  - When two viruses infect the same cell, genetic changes can occur as they exchange segments with each other through a process known as **reassortment**.

- **Antigenic shift Mechanism**:
- The viral RNA segments mix (reassortment), producing a new subtype with a novel combination of surface proteins (e.g., hemagglutinin [H] and neuraminidase [N] in influenza viruses).





Virus B

- **Antigenic drift:** point mutation results in minor change. Note that A and B viruses look alike.

Antigenic shift: reassortment between 2 viruses infect the same cell.
Subtypes like **H1N1** (swine flu) and **H5N1** (avian flu) typically result from **antigenic shift**. This process occurs primarily in animals, where different strains of viruses can mix and produce new variants.

- The rate of antigenic variation in influenza viruses is very high, making it difficult for the immune system to recognize the many different strains of Influenza virus.
- Although the body may develop immunity to one strain through natural exposure or vaccination, antigenic variation results in the continual emergence of new strains that the immune system will not recognize.
  - This is the main reason that vaccines against Influenza virus must be given annually.
- Each year's influenza vaccine provides protection against the most prevalent strains for that year, but new or different strains may be more prevalent the following year.
- The effectiveness of influenza vaccine is about 50%, and it is indicated only for high risk groups like elderly.

  - Ever year there is a new virus strain

Spanish flu

- **The most lethal influenza pandemic in recorded history** occurred from 1918 through 1919.
- An **antigenic shift** involving the recombination of avian and human viruses
  - A new H1N1 virus.
- Killed as many as 40 million to 50 million (High mortality rate).
- Although it is called “Spanish flu”, it actually Originated in the United States.
- the conditions of World War I greatly contributed to the spread of this disease.
  - Crowding, poor sanitation, bad hygiene and rapid mobilization of large numbers of personnel and animals facilitated the dissemination of the new virus once it appeared.

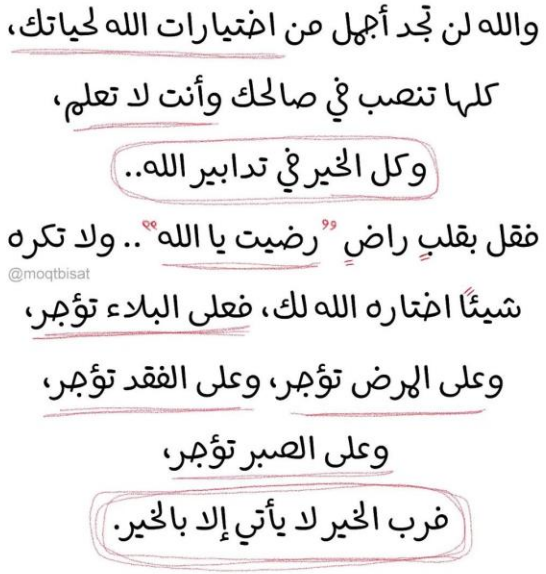
Bird Flu (Avian Influenza)

- H5N1
- Cause **severe** respiratory symptoms.
- People who work with poultry, water fowl (like geese and ducks) and livestock are most at risk.
- Infected animal's body fluid
- Causes lower respiratory tract infection, mainly viral pneumonia.
- It's extremely rare for it to spread from person to person mostly it spreads from animals to humans.

H1N1 swine flu

- H1N1 flu to be a pandemic in 2009
- Results from antigenic shift.
- It differs from H1N1 Spanish flu.
- That year the virus caused an estimated 284,400 deaths worldwide. In August 2010, WHO declared the pandemic over
- It's called swine flu because it's similar to a flu virus that affects pigs (swine), it infects humans also.
- The virus leads to a lung (respiratory) disease in pigs.

Feature	Influenza (Seasonal Flu)	Bird Flu	Swine Flu
Host Species	Humans	Birds	Pigs and humans
Human Impact	Widespread, annual	Rare in humans	Widespread in pandemics
Mortality Rate	Relatively low	Very high	Similar to seasonal flu
Transmission	Person-to-person	Contact with birds	Person-to-person
Vaccination	Annual flu vaccine	Limited experimental vaccines	Covered in flu vaccines



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	10	entry	exit
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!