MICROBIOLOGY

بسم الله الرحمن الرحيم

FINAL – Lecture 5

Rhinoviruses, Coronaviruses, Influenza and parainfluenza

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

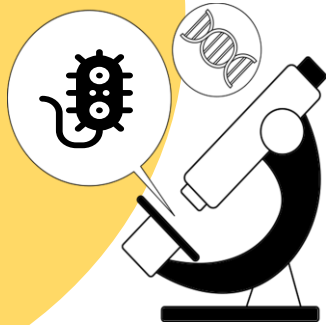
اللهم استعملنا ولا تستبدلنا

Written by:

- Abd AL Rahman Musa
- Mohammad AlHusami

Reviewed by:

- Laith Joudeh



Quiz on the previous lecture

ممكن تشعروا انه الكلام المضاف والمنقول من الدكتور مبالغ فيه وزيادة في هذا الملف ، ولكن كان ذلك حرصًا منا على إيصال كامل المعلومات وإيفاء المحاضرة حقها وعدم تفويت اي كلمة من الدكتور (كونه الدكتور جاب كثير اسئلة من كلامه بالميد) -((إن الله يحب إذا عمل أحدكم عملاً أن يتقنه))-
الكلام يحتوي إجابات على أسئلة الطلاب، ولكن وجب ذكر كل المعلومات التي انذكرت خلال المحاضرة.
بالتوفيق.

وَتَوَكَّلْ عَلَى الْحَيِّ الَّذِي لَا يَمُوتُ وَسَبِّحْ بِحَمْدِهِ ۚ وَكَفَىٰ بِهِ بِذُنُوبِ عِبَادِهِ خَبِيرًا

- **Quick recall:**
- In the previous lecture, we discussed **DNA** viruses from a clinical perspective, covering their properties, associated diseases, symptoms, and diagnostic methods. This lecture and subsequent ones will focus on **RNA** viruses.
- We've also studied Hepatitis viruses, most of which are RNA-based, except for Hepatitis B, which is a DNA virus. Despite this distinction, they were discussed together due to their similar clinical presentations.

Objectives

- Discuss the structure, properties, epidemiology, clinical presentation, laboratory diagnosis and treatment of the following viruses:

1. Rhinoviruses
2. Corona viruses
3. Influenza Virus
4. Parainfluenza viruses
5. Respiratory syncytial virus (RSV)

RNA viruses that cause common **respiratory** infections, which are similar in their clinical presentations.

Anatomy of Respiratory Tract

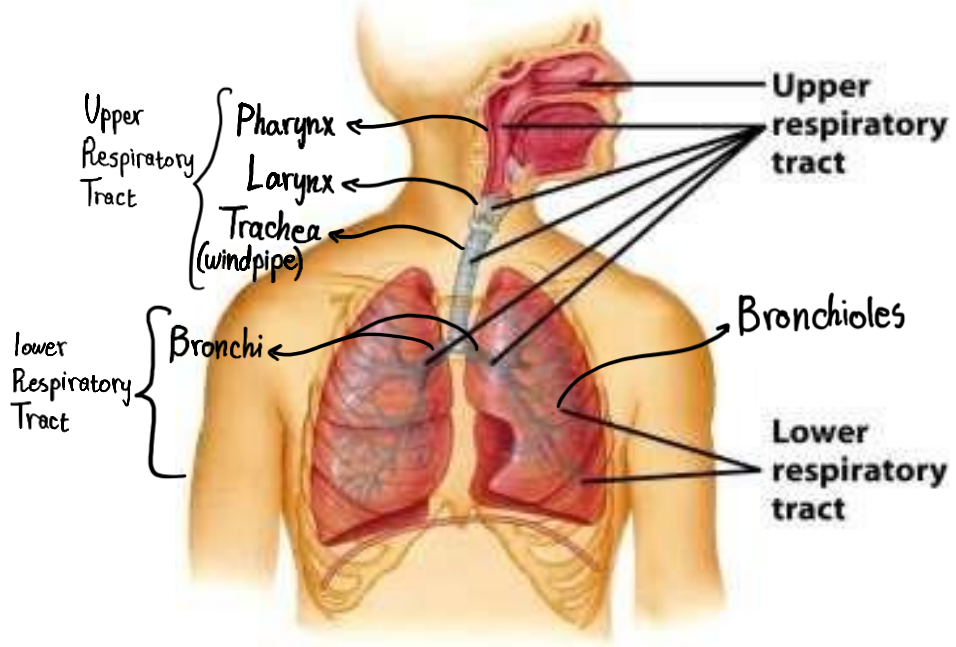
Divided into two main parts:

1. The upper respiratory tract:
   - Nasal cavity, sinuses, pharynx (Throat), and larynx (Voice box)
   - Infections are **fairly common**.
   - Usually nothing more than an **irritation.**

   Infections are usually self-limiting.
   - ✓ The upper respiratory tract (**URT**) ends with the larynx.
   - ✓ Sinusitis refers to an infection or inflammation of the sinuses, the air-filled cavities in the face.
   - ✓ Infections to the URT are common, but usually self limited and does not require any treatment.

Infections can either affect the upper respiratory tract (**URTI**) or the lower respiratory tract (**LRTI**).

The specific tissue involved in the infection may vary. For instance, an infection of the bronchioles (small air passages or tubes) differs from pneumonia, which primarily affects the parenchymal tissue of the lungs, including the alveoli.



bronchioles = smaller air passages connecting the bronchi to the alveoli.

2. The lower respiratory tract:
   - Consists of: **Lungs**, **bronchi**, **and bronchioles**
     - The lower respiratory tract (LRT) begins at the **trachea** (windpipe), which branches into two **bronchi**, each leading to a lung. These bronchi further divide into smaller **bronchioles**, which ultimately end in tiny air sacs called **alveoli** within the lungs.
   - Infections are **more dangerous**.
   - Can be very **difficult to treat**
     - Lower respiratory tract infections (LRTIs) are generally more severe and harder to treat than upper respiratory tract infections (URTIs). For example, pneumonia (an LRTI) tends to require more intensive treatment than sinusitis (a URTI).
   - The **most accessible system** in the body: Breathing brings in clouds of potentially infectious pathogens.
     - The respiratory system is the most vulnerable system to infections from microorganisms, including viruses. This vulnerability arises from its continuous exposure to inhaled air, which may carry airborne pathogens.
     - The gastrointestinal (GI) system is the second most accessible system in the body for microorganisms. Despite efforts to maintain food hygiene, ingested food often contains microorganisms. Depending on their quantity and pathogenicity, these microorganisms can bypass the body's natural defenses and cause an infection

Overview of Respiratory Tract Infections

➢ **Upper Respiratory Tract Infections (URTIs)**

- **Prevalence:**
  - Account for **30-50% of all infectious illnesses globally**.
  - Commonly seen in **outpatient settings** (e.g., clinics, ERs).
- **Causes:** Primarily caused by **viruses**.
- **Examples:**
  - Common cold
  - Influenza (flu)
  - Tonsillitis
  - Sinusitis
  - Pharyngitis
  - Laryngitis
- **Transmission:**
  - Spread through **respiratory droplets**, **direct contact**, and **contaminated surfaces**.
- **Key Fact:**
  - The **common cold** and **flu** are the most common viral infections affecting humans.

Overview of Respiratory Tract Infections

➢Lower Respiratory Tract Infections (LRTIs)

- **Prevalence:**
  - Constitute 20–30% of infections in hospitals (most common in inpatient settings).
- Examples:
  - Pneumonia (most common and severe).
- Impact:
  - Often more severe than URTIs due to involvement of deeper lung structures.

➢Combined RTIs (URTIs + LRTIs)

- Global Burden:
  - 40–60% of all infections worldwide.
  - 30–45% of all infections in hospitals.
- Healthcare Impact:
  - Respiratory infections are a major burden on healthcare systems globally, and they constitute a substantial portion of illnesses that doctors deal with.

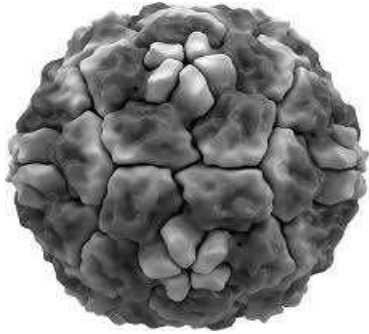
Common Viral Causes

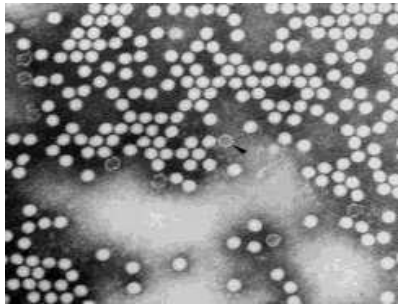
1. Rhinoviruses
2. Corona viruses
3. Influenza Virus
4. Parainfluenza viruses
5. Respiratory syncytial virus (RSV)

1. Rhinoviruses

- Family: Picornaviridae
- Genus : Rhinovirus
- **Unenveloped**
- More than **100** serotypes

- Small icosahedral particle, **20 - 30 nm** in diameter
- The viral genome is **ss-RNA**





Implications of Multiple Serotypes:

1. **High Frequency of Infection:**
   - Infections are extremely **common** and can occur **multiple times throughout life**, even **within the same year**.
2. **Serotype-Specific Immunity:**
   - Immunity developed against one serotype **does not protect** against others.
   - This explains the repeated occurrence of the **common cold (rhinitis)**, caused by rhinoviruses.
3. **Challenges in Vaccine Development:**
   - The large number of serotypes makes it **impractical to develop a vaccine**.
   - Our inability to develop effective serotype-specific immunity for all serotypes contributes to the virus' constant circulation in society.

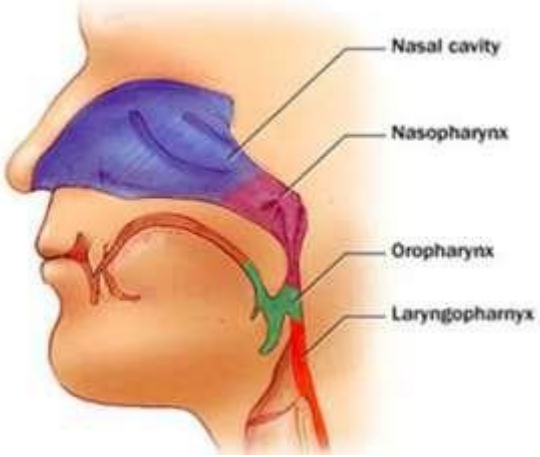
Hepatitis A virus has a single serotype, which makes vaccine development feasible and straightforward. Infection typically occurs only once, as recovery leads to lifelong immunity.

1. Rhinoviruses

- They replicate in the nasopharynx → Upper Respiratory Tract Infection
- Shed in large amounts in nasal secretion causing the rapid transmission
- The optimal temperature for their replication is **33-35 c** found in the nasal passages
  - This explains why rhinovirus infections are typically confined to the **URT**, where the nasal cavity's cooler temperatures are ideal for viral replication. In contrast, the LRT's warmer environment (approximately 37°C) is less favorable for rhinovirus survival and replication, preventing the infection from progressing further.
- Do not efficiently replicate at body temperature
  - Rhinovirus infections are strongly seasonal, occurring most frequently during the onset of winter and colder weather when cooler temperatures in the nasal passages favor viral replication.
  - Additionally, lower humidity levels during these seasons dry out the nasal mucous membranes, reducing their protective function and making it easier for viruses to invade. Indoor crowding, more common during cooler months, further facilitates the spread of respiratory viruses.

Rhinitis (common cold)

1. Rhinoviruses are responsible for **30-50%** of common colds
2. coronaviruses are responsible for **10-30%**.



- Although COVID-19 is the most recognized, **coronaviruses** existed before, causing only rhinitis. Then in the past 2 decades, **SARS** (2002-2003) and **MERS** (2012) emerged, then followed by SARS-CoV-2 that causes **COVID-19**.

- It is hypothesized that prior exposure to other coronaviruses, such as those causing the common cold, could provide partial cross-immunity to SARS-CoV-2 (COVID-19). This cross-reactivity occurs when the immune system, having encountered similar viruses before, recognizes and responds more effectively to SARS-CoV-2. This theory may explain why some individuals exposed to SARS-CoV-2 did not develop COVID-19, despite the virus's recency and high transmissibility.
- Studies have detected specific IgG antibodies against coronaviruses in individuals' blood, confirming prior exposure to other coronaviruses. This suggests that coronaviruses are not new, but their mutations and the diseases they cause, such as SARS-CoV-2, represent recent evolutionary developments.

Rhinitis (common cold)

- Common cold: inflammation of the nose and throat (nasopharynx)
- Symptoms **Mainly in the nose**

Most important Confined to the nose

- Watery nasal discharge.
- Sneezing.

  Protective body reflex that helps clear the nasal passages of irritants such as viruses. However, it increases the virus spread as the body tries to expel the virus.
- Mild sore throat (pharynx), causing mild pain when swallowing (odynophagia)
- Fever is not common

➢ Significant **fever is not common**, as it would **kill rhinoviruses**, which distinguishes them from influenza and other respiratory system diseases.

❖ Note: Infections typically affect all parts of the upper respiratory tract (URT) due to the close proximity and interconnectedness of its structures. Irritation in the nose often spreads to the pharynx, and bacteria or viruses in the pharynx can similarly affect the nose and vice versa.

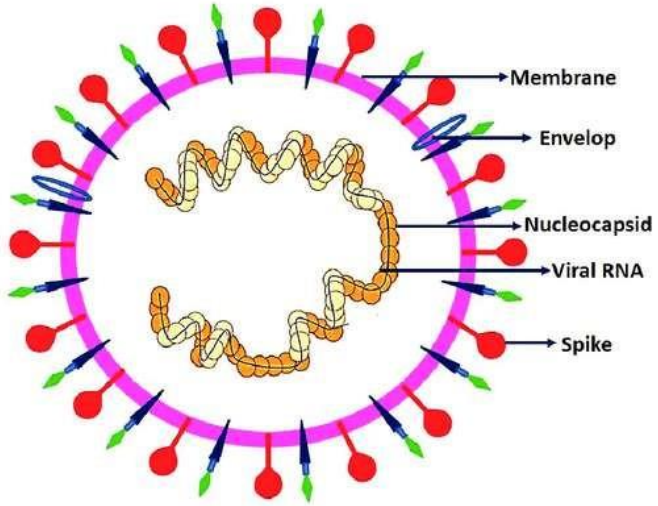
➢ Rhinitis primarily causes infection in the nose. In contrast, tonsillitis and pharyngitis affect the throat, causing inflammation with key symptoms of throat soreness and difficulty swallowing (dysphagia). These conditions may occasionally be accompanied by mild sneezing and nasal discharge, but these are not the primary symptoms, unlike in the common cold.

Rhinitis (common cold)

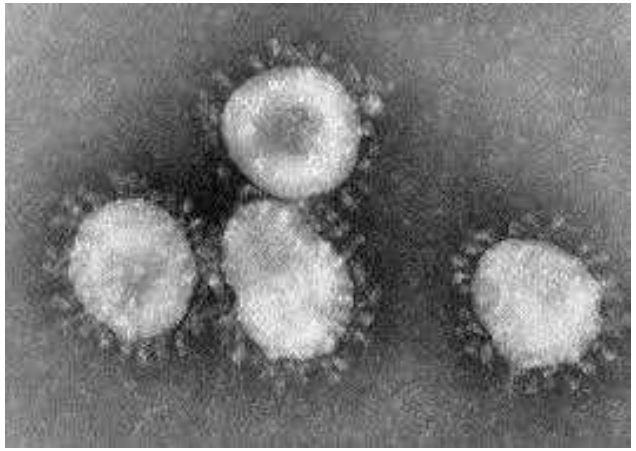
- It is a **highly contagious disease, high transmissibility rate**
- **Transmitted by inhalation** of respiratory droplets during sneezing and coughing and through contaminated hands Mainly respiratory but can be transmitted through hands.
- **No** lab **tests** are usually **required**, and **no treatment** is **required** only supportive treatment

  - **Clinical** diagnosis only, and specific treatment is not given at all.
  - **Supportive** treatment is given to patients, such as: **decongestants** like **pseudoephedrine** and **antihistamines**, over-the-counter **pain relievers** like **acetaminophen** (Panadol) or **ibuprofen** (Advil), cough suppressants, and throat lozenges.
  - **Vitamin C** is recommended for patients too, and some tablets are designed for common cold or flu symptoms that contain acetaminophen and antihistamines.
  - Medications for **fever** are **not given** as it is not common. Some recommendations to prevent transmission to others are also given.
  - Patients are advised to stay hydrated by drinking enough fluids, rest and drink warm fluids to soothe throat soreness.
  - Common cold lasts a few days and does **not** present **systemic** manifestations like **fever**, joint pain (**arthralgia**), **myalgia** (muscle pain) or severe **fatigue**, which are symptoms of flu.

2. Coronaviruses ⟷ Originally, it caused rhinitis

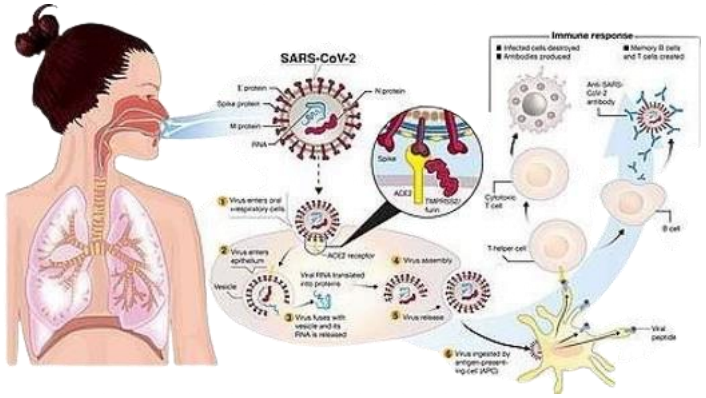


1) Family: **Coronaviridae**
2) **Irregular** in shape
3) **Enveloped** with club-shaped glycoprotein spikes. Most COVID-19 vaccines target the **spike protein (S protein).**
4) Spike protein is important for **attachment** and **immunity**
5) **Helical nucleocapsid**
6) The viral genome is **ss-RNA**



Corona Diseases

check next slides for further notes



- Coronaviruses can cause common cold, SARS-CoV-1 and MERS-CoV, and recently COVID-19 Mutations of common cold coronaviruses
- COVID-19 disease causes by SARS-CoV-2
- Transmission by air droplets and direct contact
  - **SARS-CoV-1** (thought to have originated from **birds** and transmitted to humans) caused SARS outbreak mainly in east **Asian** countries. There was significant fear that it might escalate into a pandemic. No known cases since 2004.
  - MERS-CoV appeared in the **Middle East** and was believed to have originated from **camels** and then transmitted to humans, it spread mostly in Saudi Arabia and UAE.

SARS-CoV is thought to have transmitted from bats, but the doctor said otherwise.

Corona Diseases check next slides for further notes

- Symptoms:
  - Fever or chills (**systemic** manifestations)
  - cold-like symptoms
  - dry cough (indicates reaching the lungs)
  - shortness of breath (indicates reaching the lungs)
  - loss of taste or smell (common in COVID-19)
  - Fatigue
  - Headache
  - Vomiting
  - diarrhea.

Explanation of Symptoms

- The main **receptor** of coronavirus is the angiotensin-converting enzyme 2 (**ACE2**) receptor found mainly in **lungs**. Therefore, it causes symptoms in both **URT** and **LRT**.
- **Loss of taste or smell**: COVID-19 has a wide range of symptoms, including loss of taste or smell which are **neurological** manifestations, caused by inflammation affecting nerves carrying taste or smell signals. While most people **regain** their sense of taste and smell within a few weeks, a small percentage of individuals experience **long-term** or **permanent** impairment because of permanent damage to **nerve endings**.
- Research suggests that persistent loss of smell may be linked to ongoing immune responses and damage to the cells supporting olfactory neurons and taste bud cells.
- **Vomiting and diarrhea** caused by the virus moving from the pharynx to the **GI**, causing irritation and inflammation (ACE2 receptors are found in the lining of the stomach and intestines allowing it to infect cells in the GI and cause inflammation and tissue damage).

Corona Diseases

- Complications: acute respiratory distress syndrome
  - Most common complications (especially during COVID-19 pandemic) is **ARDS**, caused by the immune system being overworked resulting in **excessive cytokines** production and exacerbating symptoms, and can be **fatal**.
  - Mechanism/Pathophysiology of ARDS: Injury to the alveolar-capillary barrier, excessive inflammatory response, fluid accumulation in alveoli, loss of surfactant, hypoxemia, fibrosis and scarring.
  - **Other complications** of COVID-19: permanent loss of taste or smell, post-COVID **fibrosis** of the lungs resulting in permanent damage to the lungs.

Diagnosis of Corona Diseases

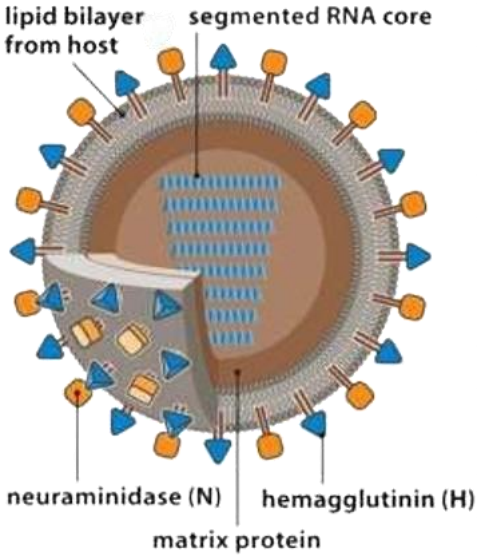
Through:

- RT-PCR
  - **Reverse Transcription PCR** since it is an **RNA** virus, and we use **real-time** PCR (qPCR).
- Chest X-ray
- CT-scan
  - Clear signs of COVID-19 using CT-scan in diagnosis, also used in follow-up visits to check for lung damage and fibrosis.
- **Other diagnostic tests used:**
  - CBC test (higher-than-normal)
  - Liver enzymes
  - ESR tests
    - ESR test: Erythrocyte Sedimentation Rate, an inflammatory indicator.

Corona Diseases

- Treatment: debatable and none specific
  - One of the first treatments given was **Chloroquine (antimalarial),** which turned out to be **ineffective**.
  - **Azithromycin** and multiple **antiviral** drugs were tried, but all **failed** to be effective in treating COVID-19.
  - **Corticosteroids** are a viable option for cases of **ARDS** which has a clear clinical indication. They are not a treatment, but rather **immunosuppressants** (potent anti-inflammatory drugs) that **inhibit** the **cytokine storm**, which helps control the symptoms and improves clinical outcomes.
  - No well-proved treatment of COVID-19 was found effective.
- Vaccinations are available
  - Vaccinations are available with an efficacy of 70-80%, primarily aimed at reducing severe cases rather than completely preventing infections. They significantly lower hospitalization rates, often approaching zero in vaccinated individuals.
  - However, vaccines provided short-term immunity (6-12 months), which required booster doses.
  - COVID-19 remains present today, with variant X currently circulating. As a result of widespread immunity—achieved through vaccination and prior infections—significantly reducing the severity of the disease, hospitalization and mortality rates are now extremely low. However, the virus continues to circulate in society.

6. Influenza Virus



- Influenza virus is an **orthomyxovirus**
- Segmented **ssRNA** virus
- **Spherical**/ovoid, 80-120 nm diameter (relatively large)
- The **outer surface** of the particle consists of a lipid envelope from which project prominent glycoprotein spikes of **two types:**

1. Haemagglutinin (HA): Can agglutinate RBCs used for viral attachment and fusion, and it elicits (trigger) neutralizing protective antibody responses
   - When a flu virus enters the body, it triggers the production of IgA antibodies, to neutralize the hemagglutinin (HA) spikes.
2. Neuraminidase (NA): Enzyme that uses neuraminic (sialic) acid as a substrate. Important in releasing mature virus from cells
   - Neuraminidase inhibitors are given as a treatment.
   - Recall: influenza virus orders the cell to present neuraminidase on its surface, allowing it to capture the neuraminidase spikes as well as a part of the cell membrane when leaving the cell.

Types of influenza virus

- Three types: A, B, and C
  - **Type A** undergoes antigenic **shift and drift**. This group is the cause of epidemics and pandemics and has an avian intermediate host (IH).
    - Antigenic shift is more dangerous than antigenic drift as it causes a bigger change in the genome
    - Antigenic shift → Responsible for pandemics.
  - **Type B** undergoes antigenic **drift only**. This group causes epidemics and has no IH. Human-to-Human mode of transmission.
  - **Type C** is relatively **stable**. This group does not cause epidemics and causes mild disease.
- Subtypes (serotypes):
  - According to antigenicity of HA and NA, influenza virus is divided into subtypes such as **HnNm** (H1N2, et al).
  - H1 → special Haemagglutinin structure , H2 → different Haemagglutinin structure and so on…

IH: Intermediate host, NA: Neuraminidase, HA: Haemagglutinin

Antigenic shift and drift

- **Antigenic shift:**
  - Reassortment of genes is a common feature of **Influenza A**, but **not** B or C.
  - When two different "A" viruses infect the same cell, their RNA segments can become mixed during replication, resulting in a new virus strain to which the body has no existing immunity.
  - Requires 2 different viruses to enter the body at the same time (low chance but possible).
  - New viruses produced in this way may survive due to a selective advantage within the population.
    - 1918 H1N1: "Spanish Influenza" 20-40 million deaths
    - 1957 H2N2: "Asian Flu" 1-2 million death
    - 1968 H3N2: "Hong Kong Flu" 700,000 deaths

Whenever the viruses shift, they produce a new strain that causes a new pandemic

There are variations among these shifts (not all shifts are the same).

- **Antigenic drift:**
  - Constant mutations in the RNA of influenza which lead to polypeptide mutations. Remember that not all mutations cause changes (silent mutations).
  - Changes are less dramatic than those induced by Shift.
  - It doesn't result in a new strain; therefore, no pandemics arise.

Influenza (Flu)

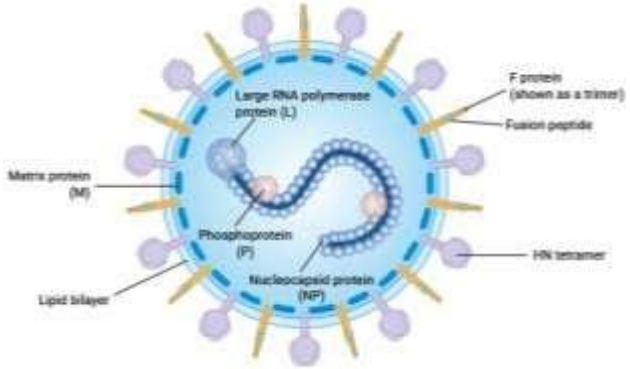
- Can occur as pandemics due to antigenic shifts or Epidemics through antigenic drifts or sporadic cases
- Transmission is by **respiratory droplets**
- Occur more frequently in the winter
- Symptoms:
  1. Fever, headache and myalgia → major signs of influenza.
  2. cough and rhinitis

     Both influenza (flu) and the common cold have similar clinical presentations, as they primarily affect the upper respiratory tract (URT). However, the presence of fever and systemic manifestations, such as fatigue (شعور بالإرهاق), body aches, and chills, strongly suggest influenza rather than the common cold.

Influenza (Flu)

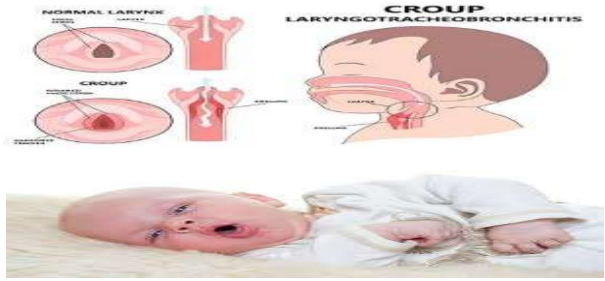
- Diagnosis: Nasopharyngeal aspirates, throat, and nasal swabs are normally used for antigen detection, RT-PCR for viral RNA, virus isolation and serology.
  - Influenza can often be clinically diagnosed in young, otherwise healthy individuals based on typical symptoms. However, in elderly individuals, diagnostic tests are usually required.
- Neuraminidase inhibitors (Tamiflu) - are now the drugs of choice. Affect the different types of influenza (A, B, C) differently.
- Vaccines are available annually with efficacy of (40-50%) → due to shifts and drifts.

3. Parainfluenza viruses



- Family: Paramyxoviridae
- Large, 150-300 nm in diameter
- Pleomorphic with helical nucleocapsid
- Enveloped with two glycoprotein spikes, HN and F
  - The HN has both hemagglutinine and neuraminidase activities used for attachement
  - The F (fusion), mediates cell entry by the fusion process
- The viral genome is **ss-RNA**
- 5 subtypes: 1, 2, 3, 4a and 4b
- Transmission: respiratory droplets, winter months.
- It occurs in children (below 3 years).

Croup



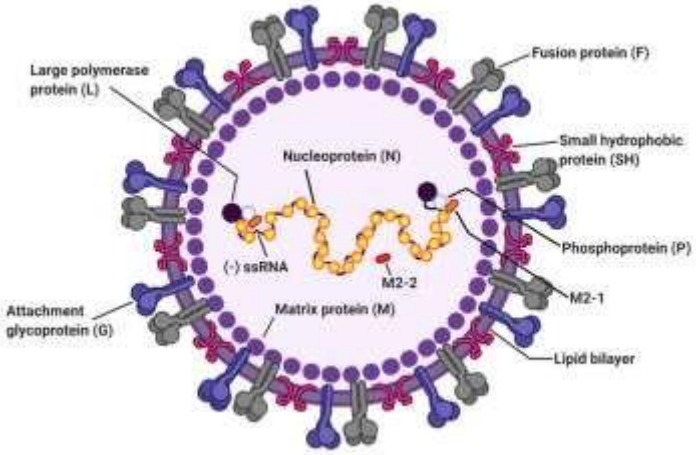
- Acute inflammation of the larynx and trachea in infants and young children characterized by swelling of the epithelial cells lining the airway, so that the airways narrows, and breathing becomes difficult.
- Symptoms: afebrile, early runny nose, (harsh cough + inspiratory stridor), and hoarse voice. These features are particularly useful for clinical diagnosis, as the cough has a distinct "barking" sound caused by narrowing of the larynx due to edema and increased secretions.
- Symptoms subside within 1 or 2 days.
  - Croup can become life-threatening in infants if the inflammation spreads further into the respiratory system, causing severe shortness of breath or even complete closure of the larynx. In such cases, treatment involves inserting breathing tubes to secure the airway and administering corticosteroids.

Croup Diagnosis and Treatment

- Diagnosis:
  - Clinical diagnosis is the rule.
  - Lab: Detection of Antigen, Virus Isolation, and Serology
- Treatment: it is self-limiting and benign
  - No specific antiviral chemotherapy is available.
  - Severe cases should be admitted and placed in oxygen tents.
  - Severe respiratory obstruction may require endotracheal intubation and tracheotomy
  - No vaccine is available.

4. Respiratory syncytial virus (RSV)

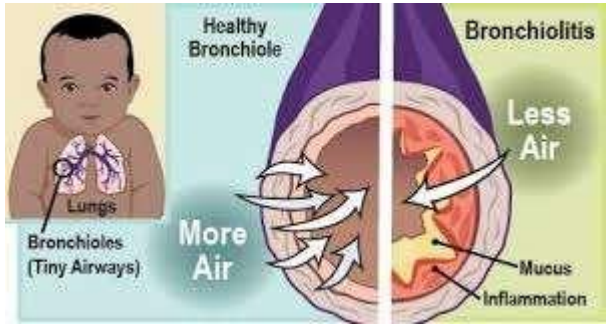
- Family: Paramyxoviridae
- Large, 150-300 nm
- Pleomorphic, helical nucleocapsid
- Enveloped with two glycoprotein spikes:
  - The G protein, lacks hemagglutinins and neuraminidase activities. Attachment protein
  - The F, Mediates cell entry, by the fusion process
- The viral genome is ss-RNA
- Most common cause of severe lower respiratory tract disease in infants, responsible for 50-90% of Bronchiolitis and 5-40% of Bronchopneumonia. In older children and adults, the symptoms are much milder.



Bronchiolitis

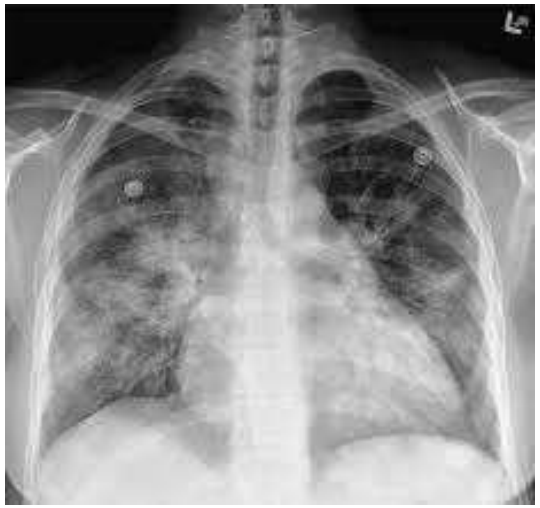
The doctor will explain the remaining 2 slides the next lecture

- Inflammation of the bronchioles in infants and young children. Bronchioles become inflamed, edematous and obstructed by mucous .
- Respiratory syncytial virus (RSV) and parainfluenza virus type 3 are the major cause of bronchiolitis in infants.
- Symptoms:
  - Usually preceded by URT symptoms.
  - Expiratory obstruction.
  - Expiratory wheezing.
  - Respiratory distress (difficult & labored breathing).
  - Hypoxia and cyanosis
- Most cases are mild, recover completely & do not require hospitalization. Increasing respiratory distress, cyanosis, fatigue or dehydration are indication for hospitalization.
- Diagnosis is usually clinical and no specific treatment and no vaccination is available.



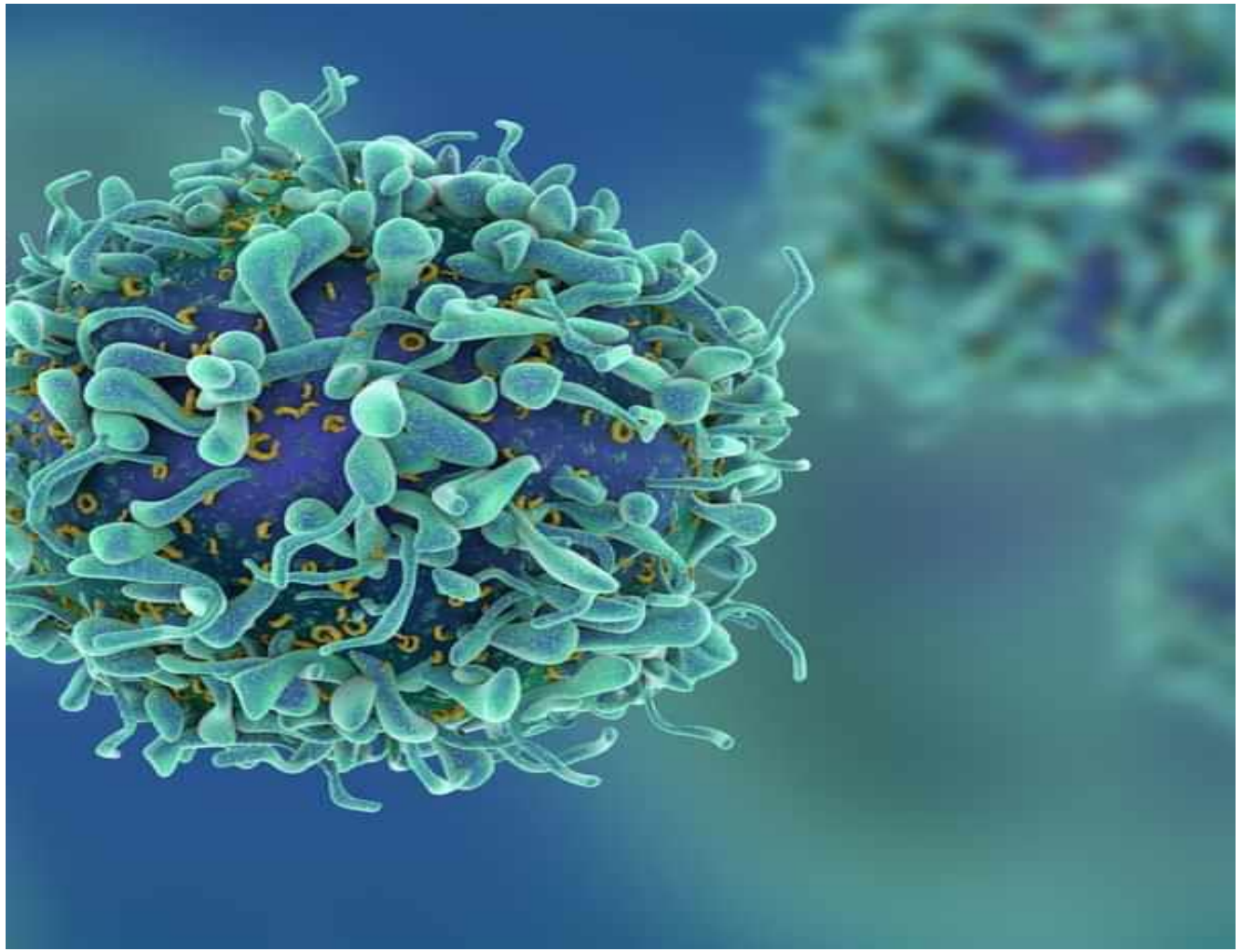
Viral pneumonia

- Inflammation of the lung and alveoli
- RSV and parainfluenza virus type-3 are the major cause of infantile pneumonia
- Symptoms: usually preceded by the URT symptoms
  - Fever
  - Chills
  - Pharyngitis
  - Cough
  - Shortness of breath
  - Muscle aches
  - Fatigue
  - Chest pain



- Prognosis: Most cases are mild and get better without treatment
- Some cases are more serious and require hospitalization
- Complications: Respiratory failure and heart failure

Quiz on this lecture



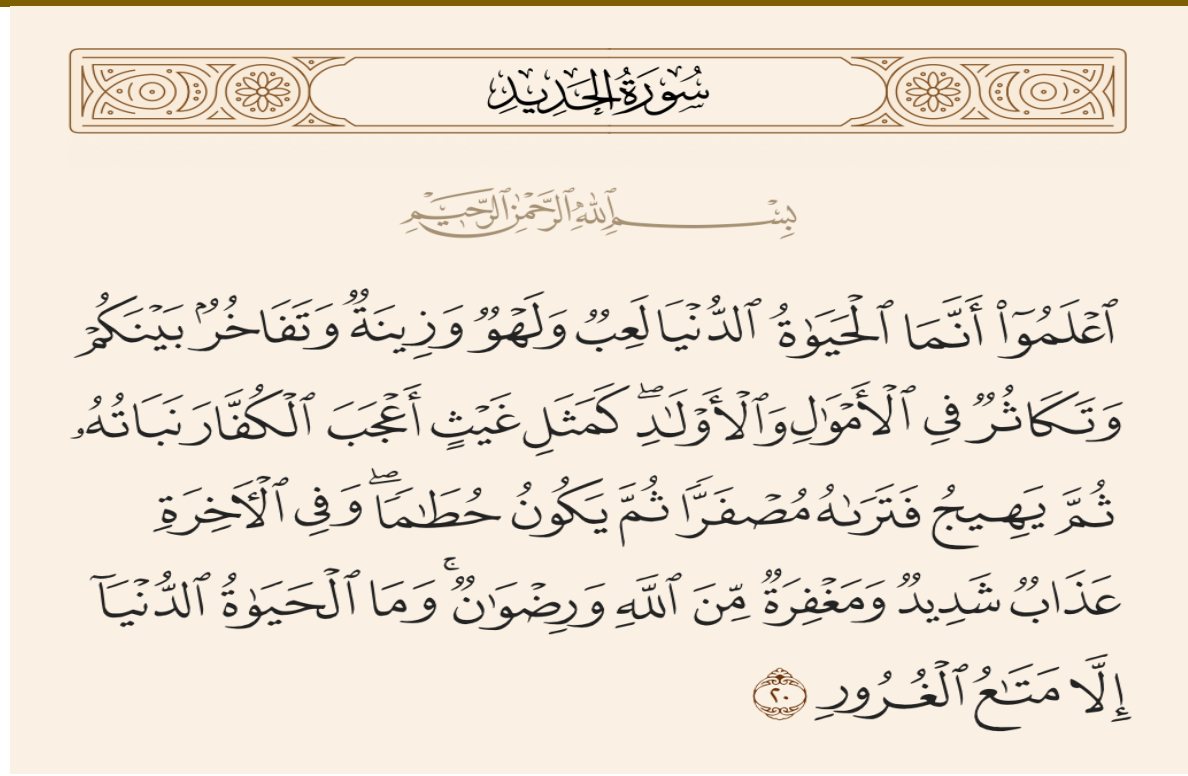
For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:



سُورَةُ الحَدِيدِ

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

اعْلَمُوا أَنَّمَا الْحَيَاةُ الدُّنْيَا لَعِبٌ وَلَهْوٌ وَزِينَةٌ وَتَفَاخُرٌ بَيْنَكُمْ
وَتَكَاثُرٌ فِي الْأَمْوَالِ وَالْأَوْلَادِ ۖ كَمَثَلِ غَيْثٍ أَعْجَبَ الْكُفَّارَ نَبَاتُهُ
ثُمَّ يَهِيجُ فَتَرَاهُ مُصْفَرًّا ثُمَّ يَكُونُ حُطَامًا ۖ وَفِي الْآخِرَةِ
عَذَابٌ شَدِيدٌ وَمَغْفِرَةٌ مِنَ اللَّهِ وَرِضْوَانٌ ۚ وَمَا الْحَيَاةُ الدُّنْيَا
إِلَّا مَتَاعُ الْغُرُورِ ﴿٢٠﴾

كم غافِلٍ عَن حِياضِ المَوتِ في لَعِبٍ يُمسي وَيُصبِحُ رَكّاباً لِما هَوِيا...
وَمُنقَضٍ ما تَراهُ العَينُ مُنقَطِعٌ ما كُلُّ شَيءٍ يُرى إِلّا لِيَنقَضِيا

https://www.instagram.com/reel/DDqT5EKzp5B/?utm_source=ig_web_copy_link Well deserved