# L:8 Virology

# Family: Orthomyxoviridae & Paramyxoviridae

By

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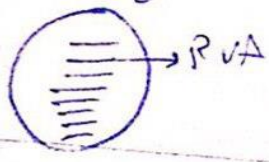
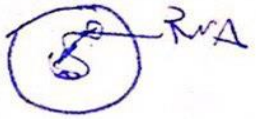
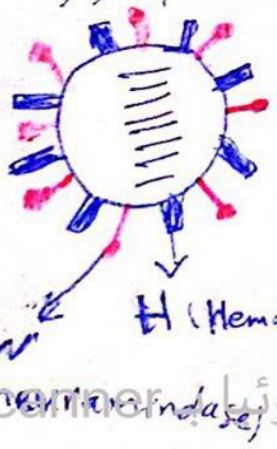
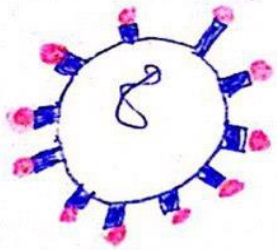
# Family Orthomyxoviridae& Paramyxoviridae

- Orthomyxoviruses are spherical, enveloped viruses containing a segmented RNA. Viruses in this family infect humans, and animal.
- **Structure**: Influenza virions are spherical, enveloped. Two types of spikes project from the surface: one is composed of hemagglutinin (H protein) and the second of neuraminidase (N protein). The RNA is composed of eight distinct segments of RNA.

| | Orthomyxoviridae | Paramyxo Viridae |
|---|---|---|
| ex: | ① Influenza virus A, B | ① - parainfluenza, mumps measels |
| N.A. | ② Segmented RNA (8 segment)   | ② RNA non segmented   |
| - spikes or glycoprotains | ③ - have two [H, N] separated glycoprotein   | ③ - have two [H, N] glycoprotins is Fusegenic  N+H at same glycoprotein |

**Influenza viruses: (Enveloped RNA Virus)**

****Influenza**: commonly known as "**the flu**", is an infectious disease caused by an influenza virus.

Influenza viruses belong to the **Orthomyxoviridae family** and are divided into types A, B and C, D. *Most cases due to Influenza A (cause a very bad cold). Influenza types A and B are responsible for epidemics of respiratory illness and death.

**Influenza type B viruses almost exclusively infect humans.

Influenza type C : is cause milder infection, less common than the other types and usually causes mild disease

influenza D virus, which infects pigs and cattle

**Structure of Influenza virus:**

****All influenza viruses are negative sense single stranded RNA(-ss RNA) viruses with a segmented genome.**

***Symptoms:

fever, chills, headache -muscle aches , feeling tired and weak,

sneezing, and stuffy or runny nose, sore throat and cough

Children may also have abdominal pain, nausea, diarrhea and vomiting

These symptoms typically begin two days after exposure to the virus and most last about a week

**Complications of influenza**

1) viral pneumonia, 2) secondary bacterial pneumonia, 3) sinus infections, 4) asthma , 5) heart failure.

***The hallmark of human influenza viruses is their ability to undergo **antigenic change** which occurs in the following two ways

- **Antigenic variability of influenza viruses**:
- In contrast to viruses such as polio or measles virus that have maintained antigenic stability since they were first isolated, influenza viruses have shown marked variation over the years in antigenic properties, specifically H and N proteins. Two distinct phenomena account for this observation: antigenic drift and antigenic shift.
- **Antigenic drift & Antigenic shift**
- **reassortment** of viral RNA segments

**** **Antigenic drift** – is a process of gradual and relatively continuous change in the viral HA and NA proteins. It results from the accumulation of point mutations in the HA and NA genes during viral replication.

***Both influenza type A and B viruses undergo antigenic drift, leading to new virus strains.

*The emergence of these new strains necessitates the frequent updating of influenza vaccine virus strains. Because antibodies to previous influenza infections may not provide full protection against the new strains resulting from antigenic drift,

This refers to minor antigenic changes of amino acid in H and N proteins that occur each year. Antigenic drift does not involve a change in the viral subtype. This phenomenon can be easily explained by random mutations in viral RNA and single or a small number of amino acid substitutions in H and N proteins.

*__Antigenic shift__ – in addition to antigenic drift, __influenza type A virus__ can also undergo a more dramatic and abrupt type of change.

*A shift has occurred when an influenza type A virus emerges among humans bearing either a HA protein or a combination of HA and NA proteins that have not been circulating

***Antigenic shift results when two different flu strains combine and infect the same cell and their genomes combine to form a new subtype having a mixture of the surface antigens of the two or more original strains. This results in a sudden change in the virus, and can result in a pandemic strain

This phenomenon involves a much more dramatic change in the antigenic properties of the H and/or N proteins, and a change in subtype, for example, from H1N1 to H3N2. Antigenic shift occurs only infrequently, perhaps every ten or twenty years. For example, the appearance of a new, extremely virulent H1N1 virus, due presumably to antigenic shift, and H1N1 virus was replaced by subtype H2N2; in 1968, H2N2 was replaced by H3N2. Since 1977, multiple subtypes of influenza A have been circulating around the world.

**The serotypes of Influenza virus A that cause Pandemics of influenza during 20th century in humans are:**

H1N1, which caused Pandemic Spanish flu in 1918,

and Swine Flu in 2009

H1N2, endemic in humans, pigs and birds

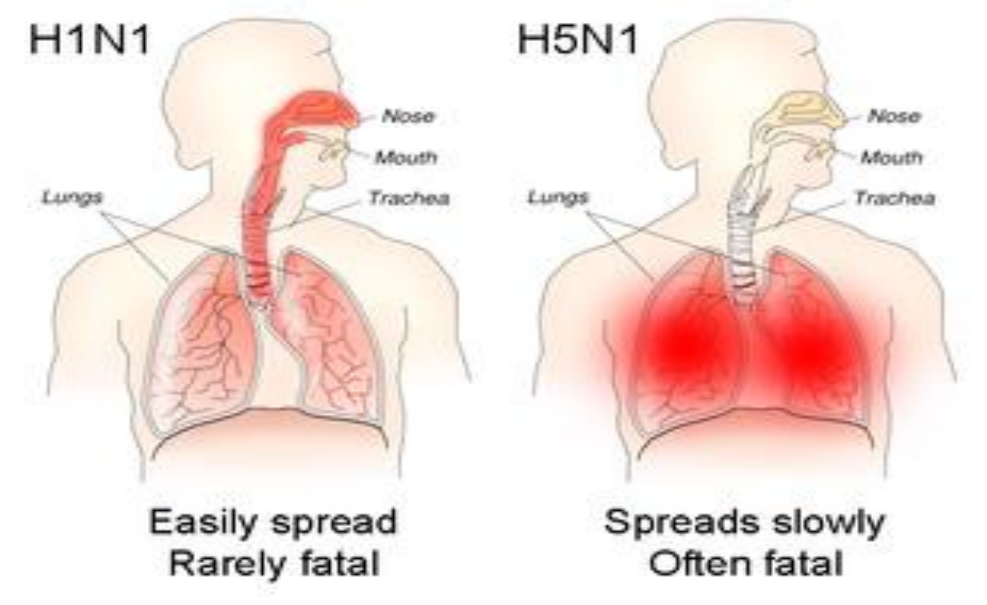
H2N2, which caused Asian Flu in 1957

H5N1, which caused Bird Flu in 2004

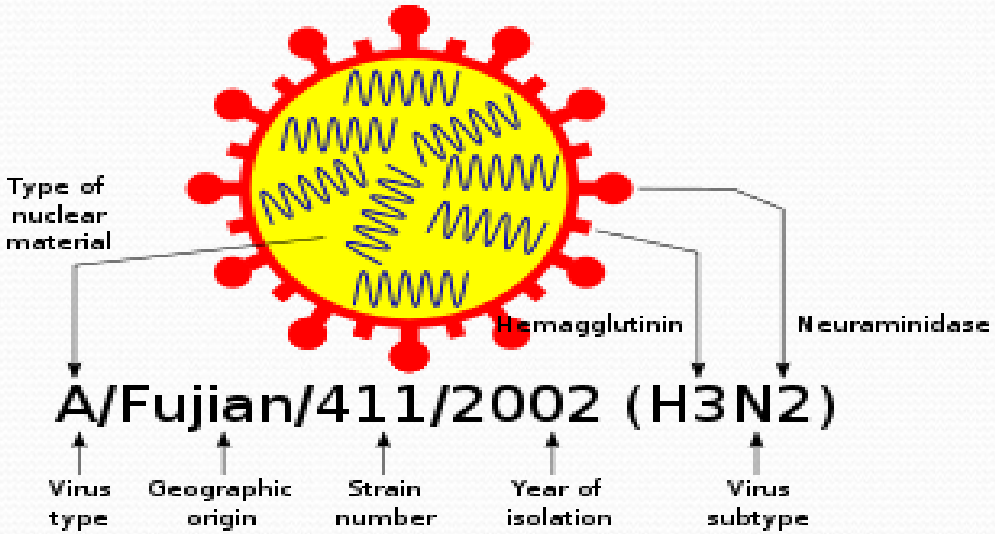
**Transmission of influenza:**

**Airborne**: virus-containing droplets and aerosols (airborne respiratory secretions) that are produced by coughing, sneezing or talking of infected person. Indirect transmission; contaminated fomites direct touching, kissing Children are an important factor in the spread of influenza in communities and households

- **Influenza control and prevention:**
- ****Influenza vaccines (**Annual vaccination**): Because influenza viruses are constantly changing, the seasonal influenza vaccines are updated and administered annually to provide the necessary protection.
- ****seasonal influenza vaccines**: contain a trivalent mixture of inactivated strains of the influenza viruses likely to circulate during the next influenza season.
- The influenza vaccine is recommended by the (WHO) for high-risk groups, such as :pregnant women, children aged less than five years, the elderly, health care workers, immunocompromised peoples as having AIDS, diabetes mellitus, malignant diseases as cancer




The different sites of infection (shown in red) of seasonal H1N1 versus avian H5N1. This influences their lethality and ability to spread.

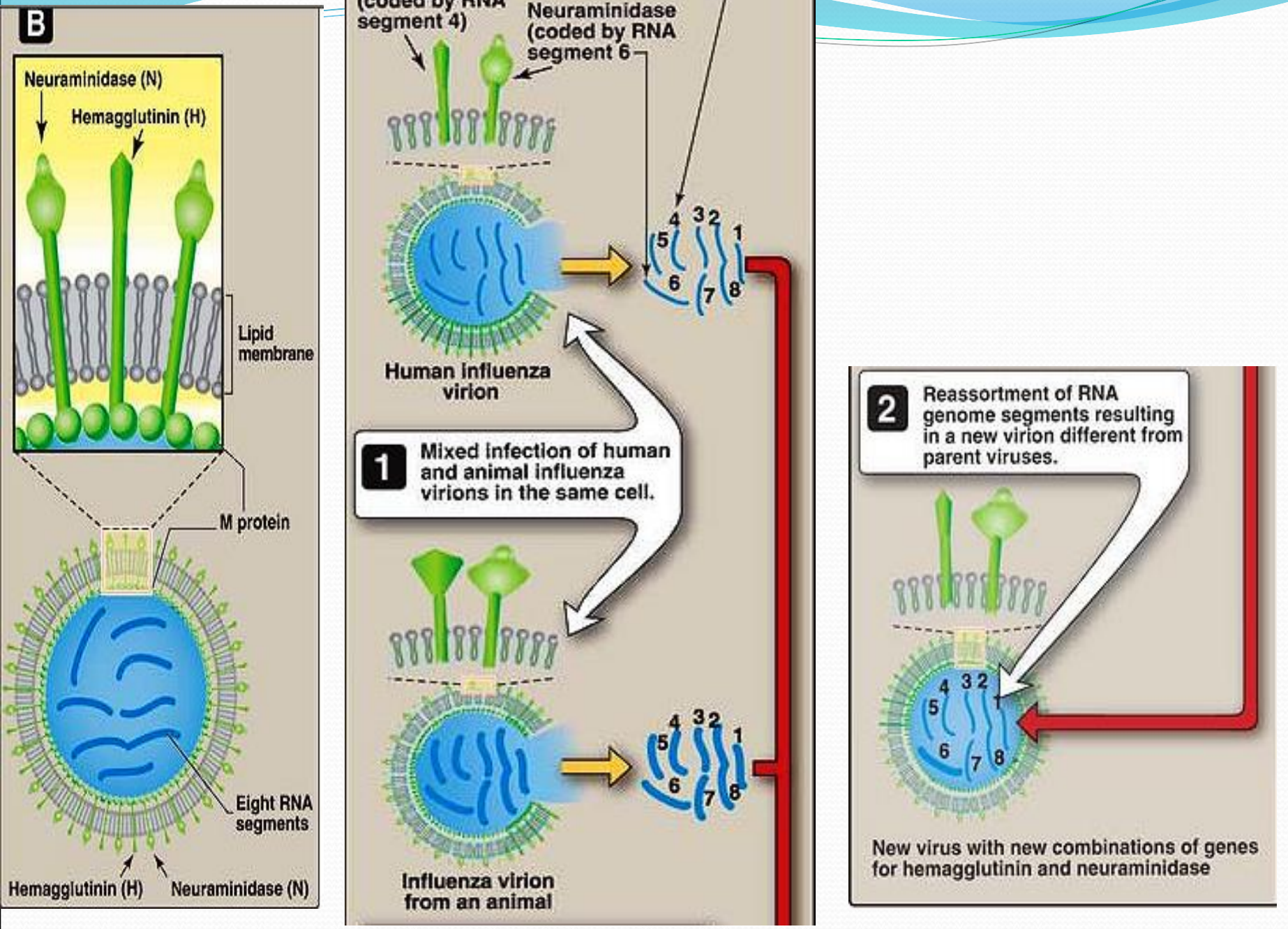



Influenza virus nomenclature (for a Fujian flu virus)

**The molecular basis of antigenic variation:** The dramatic changes associated with antigenic shift result from **reassortment** of viral RNA segments, a process observed with all RNA viruses having a segmented genome. Reassortment results when a cell is infected with two genetically distinct influenza viruses; the genomic RNAs of both parental viruses are replicated, and progeny viruses are assembled that contain genomic RNA segments from one of the parental viruses, and other genomic segments from the second parent (Figure). In this way, new viruses can be generated that differ from both parents.

- **Diagnosis:** Specific test is the quantitation of HI (hemagglutination inhibition) antibodies.

**Treatment**: Amantadine, rimantadine, Zanamivir & oseltamivir.


B
Neuraminidase (N)
Hemagglutinin (H)
Lipid membrane
M protein
Eight RNA segments
Hemagglutinin (H)
Neuraminidase (N)
Hemagglutinin (coded by RNA segment 4)
Neuraminidase (coded by RNA segment 6)
Human influenza virion
1
Mixed infection of human and animal influenza virions in the same cell.
Influenza virion from an animal
2
Reassortment of RNA genome segments resulting in a new virion different from parent viruses.
New virus with new combinations of genes for hemagglutinin and neuraminidase

- **Paramyxoviridae**
- The genera include; **parainfluenza** viruses (which cause upper respiratory tract infections), the **mumps** virus, the **measles** virus, and **respiratory syncytial virus** (a major respiratory tract pathogen). Paramyxoviruses are spherical, enveloped particles that contain a nonsegmented, and have envelope. The first, the HN protein (H, and N), is involved in the binding of the virus to a cell; measles virus lacks the neuraminidase activity. The second, the F protein (fusion), functions to fuse viral and cellular membranes, thus facilitating virus entry into the cytoplasm where viral replication occurs.

- **Mumps virus**:

is **RNA virus** in the family **Paramyxoviridae.**

Mumps used to be one of the commonly acquired childhood infections. Adults who escape the disease in childhood could also be infected. In the prevaccine period, mumps was the most common cause of viral encephalitis. Complete recovery may be. The virus is spread by respiratory droplets. Although about one third of infections are subclinical, the classic clinical presentation and diagnosis center on infection and **swelling of the salivary glands, primarily the parotid glands**. However, infection is widespread in the body and may involve not only the salivary glands but also the pancreas, CNS, and testes. Orchitis or **testicles** (inflammation of the testis) caused by mumps virus may cause sterility. .

**Transmission of Mumps virus**,

Airborne disease, Mumps is **very contagious**: transmit by inhalation or oral contact with direct contact with infected respiratory **droplets** or secretions, **saliva**. , or fomites contaminated by saliva, and possibly urine.

Mother-to-child transmission has been observed in various forms.

**The most common symptoms of mumps that may be seen in both adults and children:** Approximately 30% of infections are sub-clinical (asymptomatic)

***Parotitis** : cause pain in the parotid glands (immediately in front of the ears)and pain in the salivary glands (in the front of the neck) or Difficulty chewing.

***Deafness** may improve with time but is usually permanent.

****Infection can be prevented** with **Vaccination**:.

****Mumps vaccines**: **MMR vaccine**: (use live attenuated viruses):which protects against **Mumps, Measles and Rubella**, is the most commonly used mumps vaccine.

**Mumps vaccination which provides protection against Mumps , Measles, Rubella, Chickenpox, and Shingles.

*isolating infected individuals.

*The virus is rapidly inactivated by organic solvents such as chloroform and ether, UV light and formaldehyde.

- **Measles virus**

Measles virus is transmitted by sneeze or cough-produced respiratory droplets **or <u>airborne spray</u>** to mucous membranes in the upper respiratory tract or conjunctiva. spreads easily from one person to the next through the <u>coughs and sneezes</u> of infected people (direct contact with mouth or nasal secretions).Humans reservoir are the only natural hosts of measles virus. Monkeys may infected

The virus is It is a **<u>highly contagious</u>**, and almost all infected individuals develop a clinical illness. Measles virus replicates initially in the respiratory epithelium and then in various lymphoid organs. Measles begins with a prodromal period of fever, upper respiratory tract symptoms, and conjunctivitis. 2 to 3 days later, specific diagnostic signs develop; first, Koplik spots (small white spots with bluish-white centers on a red background on bright red mucous membranes of the mouth and throat) and then a generalized **macular rash**, beginning at the head and traveling slowly to the lower extremities. Soon after the rash appears, the patient is no longer infectious.

***Measles signs and symptoms:** Measles virus infects the respiratory system: Symptoms may appear (7 -14) days after contact with the virus, and last within 7-10 days.

1.high fever 2. runny nose 3.Cough, 4. red, watery eyes (inflamed eyes) 5. Koplik's spots

1. The **rash** appears (three to five days after the start of symptoms) as **flat red spots** on the **face** at the hairline and spreads downward to the neck, trunk, arms, legs, and feet
2. The incubation period is approximately 10–12 days from exposure to the onset of fever and 14 days (with about a range of 7–18 days) from exposure to the onset of rash.

****Complications of measles**

The major morbidity and mortality caused by measles are associated with complications of infection, especially those affecting the lower respiratory tract and the CNS. This is an autoimmune disease associated with an immune response to myelin basic protein.

**other Complications include**:

1. Ear infection
2. Bronchitis
3. Pneumonia
4. Encephalitis
5. Pregnancy problems (such as miscarriage, stillbirth, and premature delivery)

Less common complication seizures, blindness, or inflammation of the brain

The genetic variation does **not** appear to be **biologically significant**, as **all genotypes are neutralized by measles vaccine**-induced antibodies.

**Measles virus is viable for less than 2 hours at ambient temperatures

****The aerosolized virus remains infectious for 30 minutes or more.**

****It is heat-labile and is inactivated after 30 minutes at 56°C.**

the virus appears to **survive in freeze-drying relatively well** and, **When freeze-dried with a protein stabilizer, can survive storage for decades at -70°C.

**The virus is **inactivated by solvents**, such as **ether** and **chloroform**, by **acids (pH less than 5), alkalis (pH greater than 10)**, and by **UV** and **visible light.**

It is also susceptible to many **disinfectants,** including **1% sodium hypochlorite, 70% alcohol** and **formalin.**

- **prevention :**
- ***Immunity following natural infection is believed to be **lifelong,**
- ***Vaccination** with measles vaccine has been shown to be protective for **at least 20 years**
- ****Vaccination** with **measles, mumps, and rubella (MMR) vaccine** (provides around 93 percent protection), It also protects against mumps and rubella.
- In developed countries, it recommends that all children get the MMR shot at 12 months after birth and adults should get one if they didn't have it as a child.
- The MMR shot is safe and effective at preventing measles.

- **Rubella virus {German measles or three-day measles}.**
- Respiratory secretions of an infected person are the primary vehicles for rubella virus transmission. Rubella causes a mild clinical syndrome that is characterized by a generalized maculopapular rash and occipital lymphadenopathy. In most cases, these symptoms may be hardly noticeable, and the infection remains subclinical. The clinical significance of rubella lies not in the primary infection described above, but rather in the fact that when a woman is **infected during pregnancy**, there can be severe damage to the developing fetus, especially in the first trimester (**congenital rubella**). This damage can include congenital heart disease, cataracts, hepatitis, or abnormalities related to the CNS, such as mental retardation, motor dysfunction, and deafness.

The familyof **Rubella is Matonaviridae**, The genome, single-stranded RNA of positive polarity (+ve sense) (+ssRNA)which is enclosed by an **icosahedral** capsid.

**Transmission of** Rubella is **Airborne disease**, spread from one person to the next through the air via coughs of people who are infected.

People are infectious during the week before and after the appearance of the rash. Only humans are infected

****Vertical (Congenital) mother to fetus**

**Signs and Symptoms of Rubella:**

In children, the disease is often mild and in half of people is asymptomatic. A **rash** may start around 2weeks after exposure and last for 3 days. It usually starts on the face and spreads to the rest of the body. The rash is sometimes itchy and is not as bright as that of measles.

****Swollen lymph glands behind the ears and in the neck are the most characteristic clinical feature.**

A fever, sore throat,& fatigue may occur. In adults joint pain is common.

Fetal damage resulting from rubella infection is preventable by MMR vaccine. This vaccine preventing congenital rubella because it reduces the reservoir of the virus in the childhood populations, and also ensures that women reaching childbearing age are immune to rubella infection.

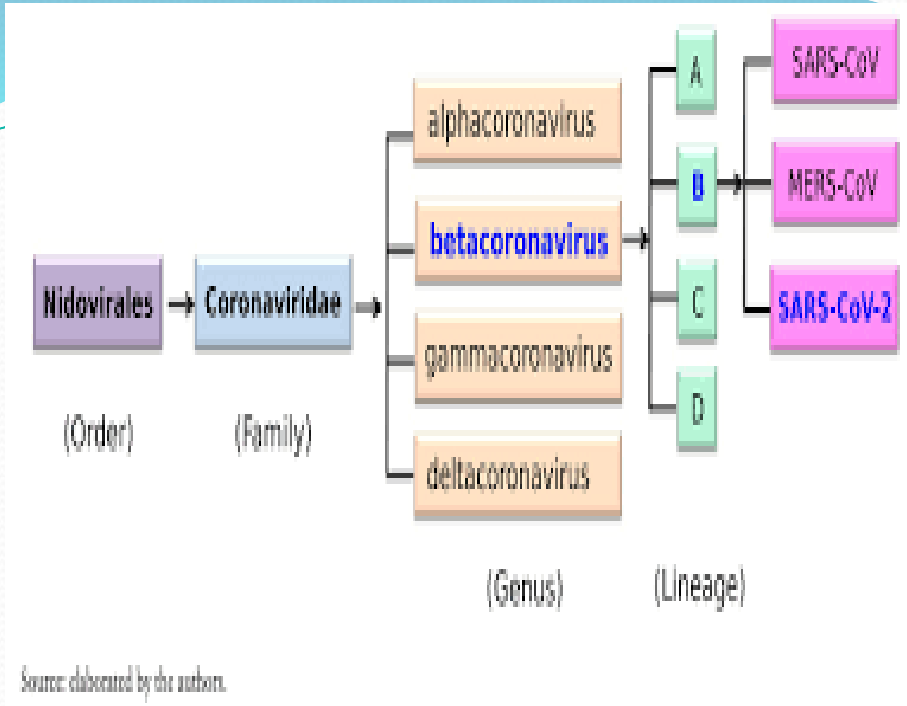
**Complications may include:** bleeding problems, testicular swelling, encephalitis, and inflammation of nerves.

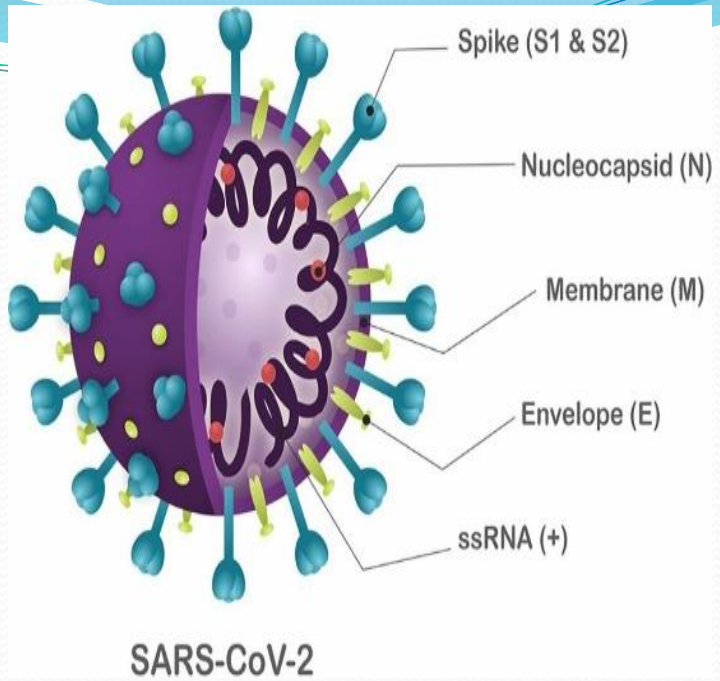
**Infection during early pregnancy may result in:**
a miscarriage or a child born with congenital rubella syndrome (CRS).
Babies with CRS may spread the virus for more than a year.

Symptoms of CRS manifest as problems with: the eyes such as cataracts, or **blindness,** deafness, as well as affecting the heart and brain. or other life-threatening organ disorders.
Problems are **rare** after the 20th week of pregnancy.

**Prevention:** (MMR) vaccine are now recommended, the first at twelve to eighteen months, the second at four to twelve years. single dose of vaccine gives more than 95% long-lasting immunity, which is similar to that induced by natural infection.

- **Coronaviruses:**
- -Coronaviruses are a family of viruses found in people and animals causing a range of illnesses from the common cold to severe respiratory infection.
- **Human coronaviruses types:**
- **SARS-CoV** (the beta coronavirus that causes **Severe Acute Respiratory Syndrome** ( **SARS**) in southern China in 2002/2003.
- **MERS-CoV** (the beta coronavirus that causes **Middle East Respiratory Syndrome** (**MERS**) in the Arabian Sundian in 2012 camel
- **SARS-CoV-2** (the novel coronavirus that causes **Coronavirus Disease 2019** (COVID-19) outbreak.
- **General structure of human Coronavirus:**
- ***Belong to subfamily :**Coronavirinae** in the **family of Coronaviridae** and the subfamily contains 4 genera: **Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus**.
- ***The genome of CoVs (27–32 kb) is a **single stranded positive-sense RNA** (+ssRNA) which is larger than any other RNA viruses.
- **The **nucleocapsid** protein (N) formed the **capsid** outside the genome and the genome is further packed by an ****envelope** which is associated with three structural proteins: **membrane protein (M), spike protein (S), and envelope protein (E) .**




| Figure:Classification of coronaviruses | Figure:structure of SARS-CoV-2 |
| --- | --- |

## Mode of Transmission of Coronaviruses:

**SARS-CoV in human is thought to arise from **bat SARSr-CoV, and **palm civets being intermediate hosts. Direct transmission routes from bats to humans have also been postulated.

**MERS-CoV, is thought to be transmitted to humans from infected **dromedary camels** (possibility ,animal-to-human and human-to-human )transmission

**Interspecies transmission from **zoonotic sources** can occur by viral spillover events during direct or indirect contact between humans and reservoir hosts.

## COVID-19:

Several clusters of pneumonia cases of unknown causes were reported in Wuhan city, Hubei province, China, in December 2019.

***The causative agent of this pneumonia was the **severe acute respiratory syndrome coronavirus-2** (**SARS-CoV-2**). اسم الكامل لفايروس الكورونا

***the diseases was termed: **Coronavirus Disease-2019 (COVID-19).**

***SARS-CoV-2 forms a distinct lineage with Bat-SARS-like coronaviruses that belong to the order Nidovirales family **Coronaviridae**, genus Betacoronavirus

**COVID-19 is a **zoonotic disease** (***Bats** are thought to be a natural reservoir for SARS-CoV-2.)

**SARS-CoV-2 has a distinctive spikes, giving the virions the appearance of a **solar corona**.

- **Symptoms of COVID-19:**
- Symptoms of a COVID-19 infection may appear 2-14 days after being exposed to the virus. Symptoms range from mild to severe respiratory illness. The most common symptoms include:
- Fever
- Cough
- Shortness of breath or difficulty in breathing
- Tiredness/fatigue
- While less common, individuals with COVID-19 may have following additional symptoms:
- Aches and pains
- Sore throat
- Nasal congestion
- Runny nose
- Diarrhea
- nausea/vomiting myalgia
- Olfactory and/or gustatory dysfunctions
- Anosmia may be the sole presenting symptom in approximately

***Diagnosis of COVID-19:**

Real-time reverse transcriptase-polymerase chain reaction (**RT-PCR) assay**, High-throughput genome sequencing

**Serological** evaluation of anti-viral immunoglobulin (IgM) and (IgG)

X-ray : The lung X-ray (CXR) generally shows bilateral infiltrations but may be normal in the early phase of the disease.

-The chest CT scan.

***Transmission of COVID-19:**

***Airborne**:virus-containing droplets and aerosols(airborne respiratory secretions) that are produced by coughing, sneezing or talking of infected person.

**Indirect transmission; contaminated fomites

**direct touching, kissing

**Prolonged exposure to an infected person (being within 6 feet for at least 15 minutes) and briefer exposures to individuals who are symptomatic (eg, coughing) are associated with higher risk for transmission, while brief exposures to asymptomatic contacts are less likely to result in transmission.

- **Prevention of COVID-19:**
- Practice social distancing (about 6 feet or more)
- Wash your hands
- Wear a mask
- Restrict your travel
- *****Vaccination : include the following types of *****Vaccines:**
- Sinopharm vaccine
- Pfizer-BioNTech
- Moderna
- Novavax
- Janssen Johnson & Johnson’s vaccine
- AstraZeneca

- **Treatment of COVID-19**
- **According to the recommendation guideline the specialist doctor depend on the patient's condition in treatment determination
- Treatment may be:
- **A**. **Plasma and antibodies** obtained from the convalescent patients have been proposed for use in treatment.
- **B. Remdesivir** is a nucleotide pro drug of an adenosine analog. It binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely, (aged ≥12 years and weighing ≥40 kg)