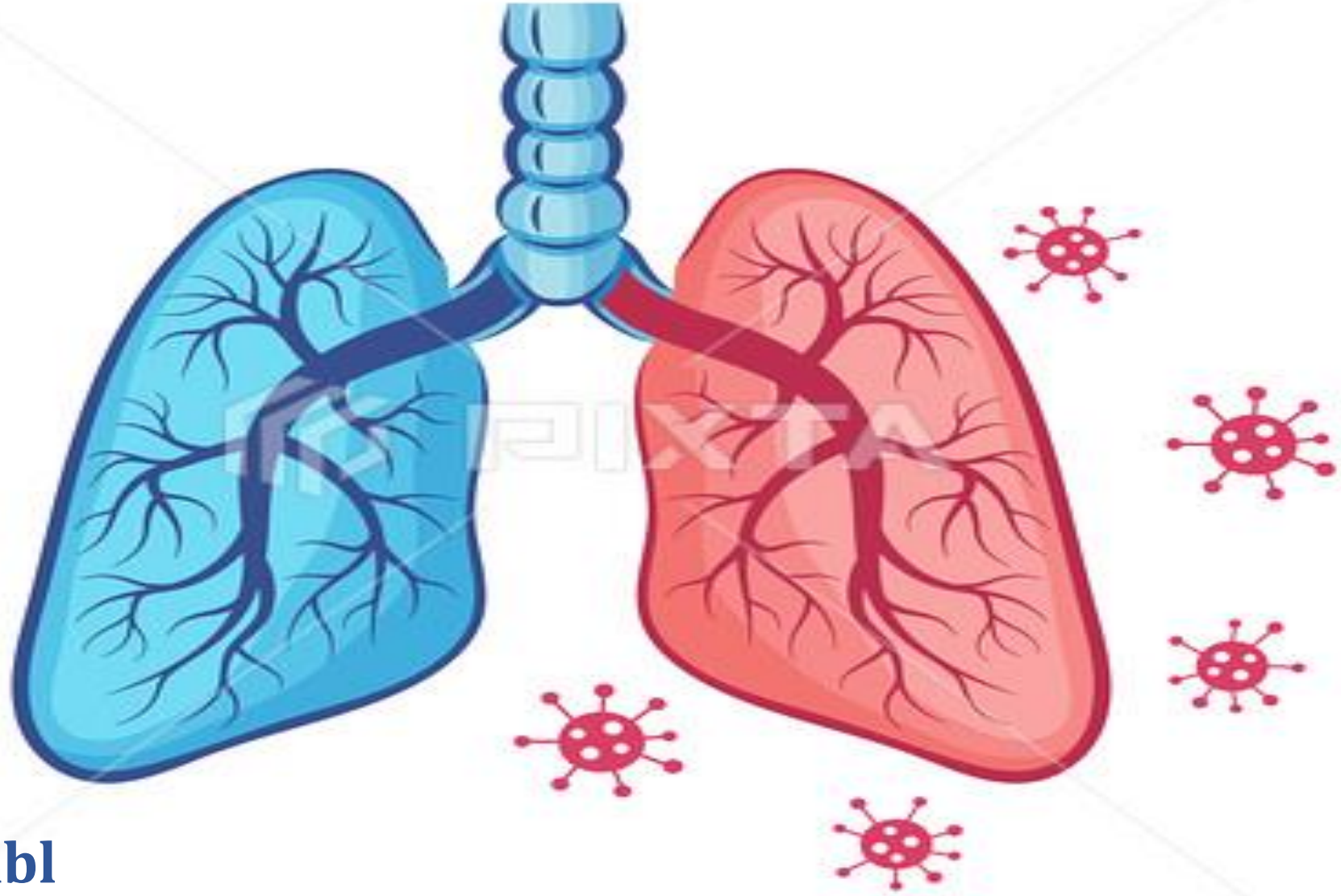
RESPIRATORY TRACT INFECTIONS - VII



By
Prof. Hala Tabl

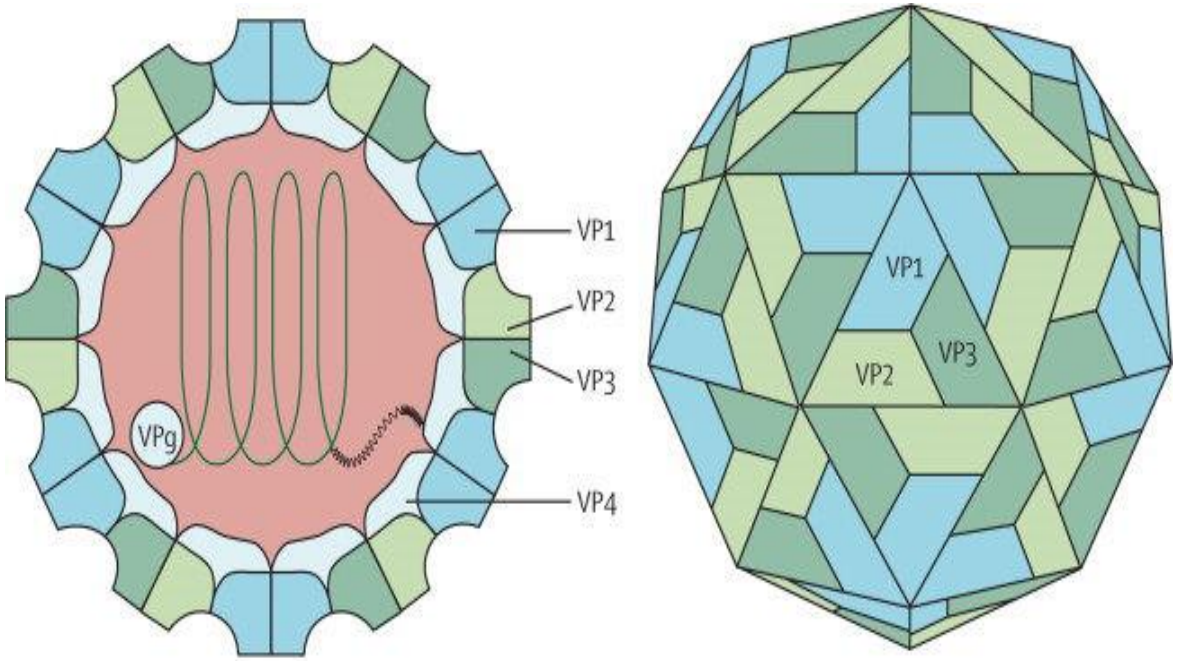
Common Cold Viruses

- **Common cold is the most common acute respiratory disease in humans.**
- **Coryza (sneezing, rhinorrhea with nasal obstruction, sore throat, dry cough ± low grade fever). The disease is self - limited.**
- **Infection occurs by droplet spread.**
- **Rhinoviruses are responsible for 30-50% of common colds, coronaviruses 10-30%.**
- **The rest are due to adenoviruses, enteroviruses, RSV, influenza, and parainfluenza viruses.**

RHINOVIRUSES

Morphological characters:

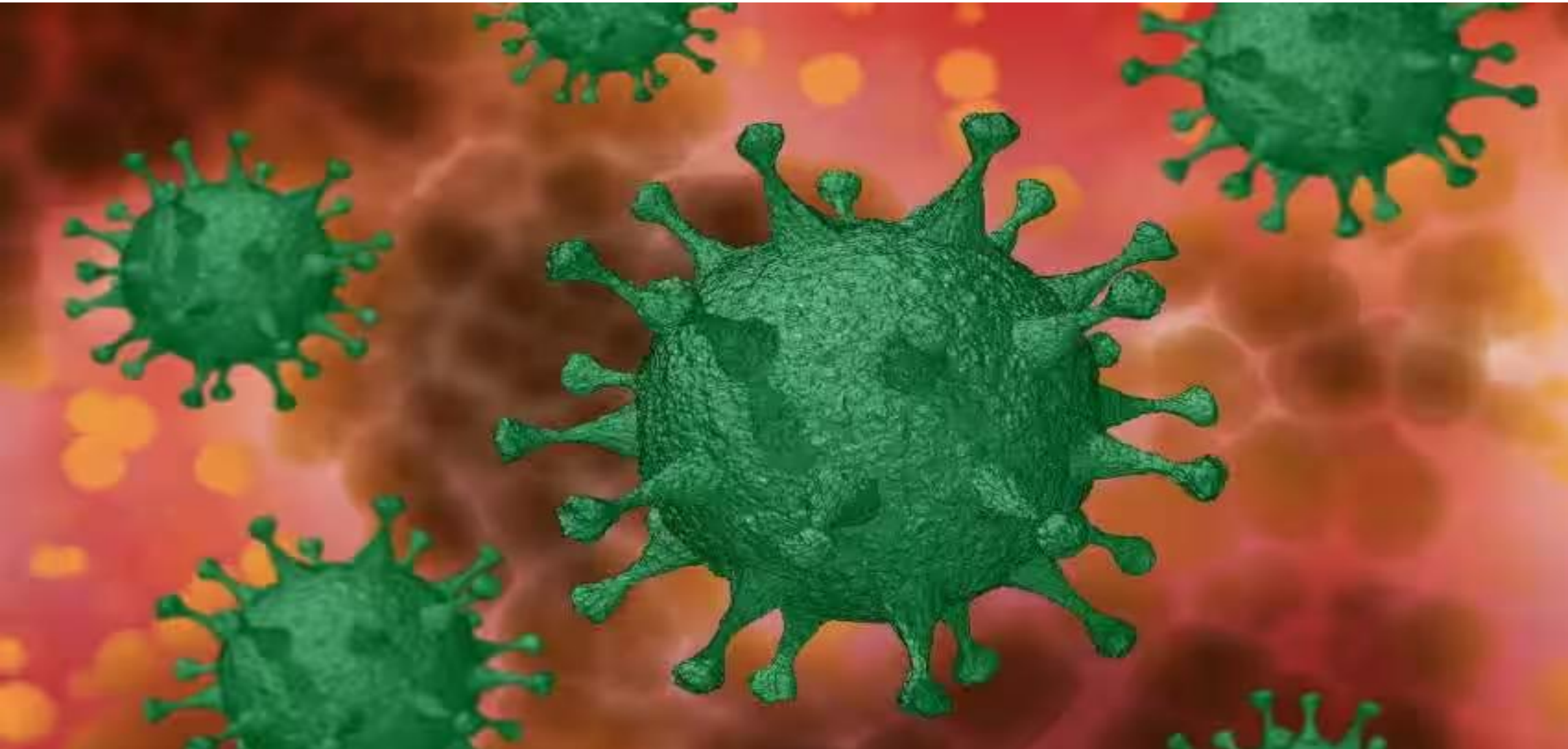
- Picornavirus family.
- **Small** 20-30nm.
- **Non-Enveloped** (Ether resistant).
- Icosahedral capsid symmetry.
- Genome: **ssRNA virus, +ve sense**.
- Replication occurs in the **cytoplasm**.



Epidemiology:

- There are more than 100 antigenic types.
- They are **the main cause** of common cold.
- **Grow best at 33°C**, which may partly account for their predilection for the cooler environment of the nasal mucosa.
- There is no long lasting immunity because of antigenic multiplicity of the viruses.

CORONAVIRUS (CoV)



Morphological characters:

- Medium sized, Spherical.

Genome:

- **Non-segmented** single-stranded RNA.
- **Positive-polarity** (**NO** RNA polymerase in the virion).

Helical symmetry.

Enveloped:

- Obtained from the endoplasmic reticulum, not from the plasma membrane.
- The envelope has large, widely spaced **club or petal shaped** spikes in the form of a **corona**.

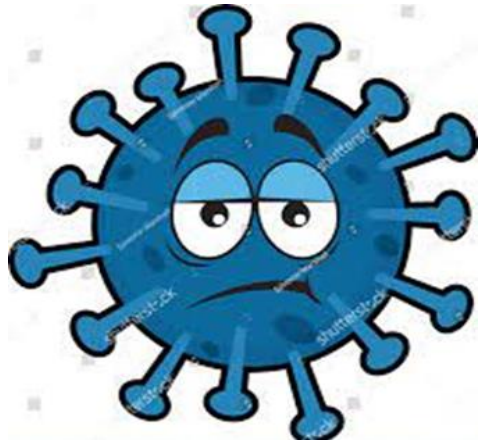
- Replication occurs in the **cytoplasm**.

Epidemiology:

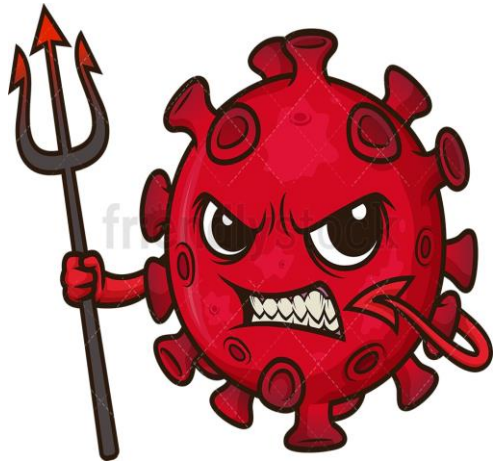
- There are four major antigenic groups of CoV; Alphacoronavirus & Betacoronavirus which contain both human and animal strains and Gammacoronavirus & Deltacoronavirus which contain only animal strains.
- There are **many animal CoV** and they suspected of being **a source for human infections**.
- There are **seven** serotypes of **human** coronaviruses:

- Four causing **upper** respiratory tract infections, such as the **common cold**.
- The other three cause **lower** respiratory tract infections, they are; **SARSCoV, SARSCoV2, and MERSCoV.**

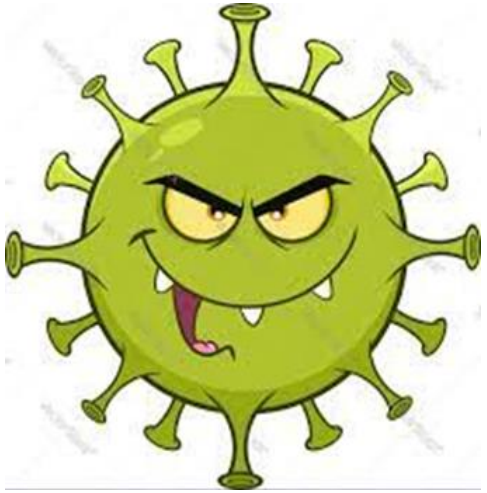
Coronaviruses are an important cause of the common cold, probably second only to rhinoviruses in frequency.
Infection by the common cold coronaviruses occurs worldwide and early in life.
Outbreaks occur primarily in the winter on a 2 to 3year cycle.
This seasonality is less dramatic than that of influenza virus.



In November 2002, a new strain originated in China and spread rapidly to other countries.
This virus caused Severe Acute Respiratory Syndrome (SARS) and so its name (SARSCoV).
Caused approximately 8300 cases and 785 deaths, a fatality rate of approximately 9%.
Bats & civets appears to be its animal hosts.



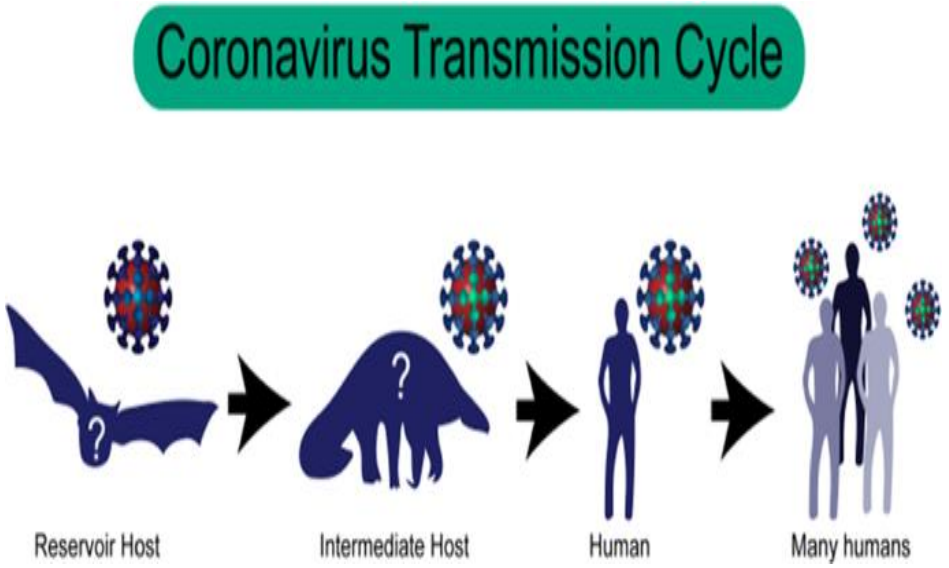
In 2012 to 2013, a new human coronavirus caused an outbreak of serious, often fatal pneumonia in Saudi Arabia and other countries in that region.
The disease is called Middle East respiratory syndrome (MERS), and the virus is called (MERSCoV).
Approximately 2400 cases with a mortality rate of 35%.
Bats and camels are its animal hosts.



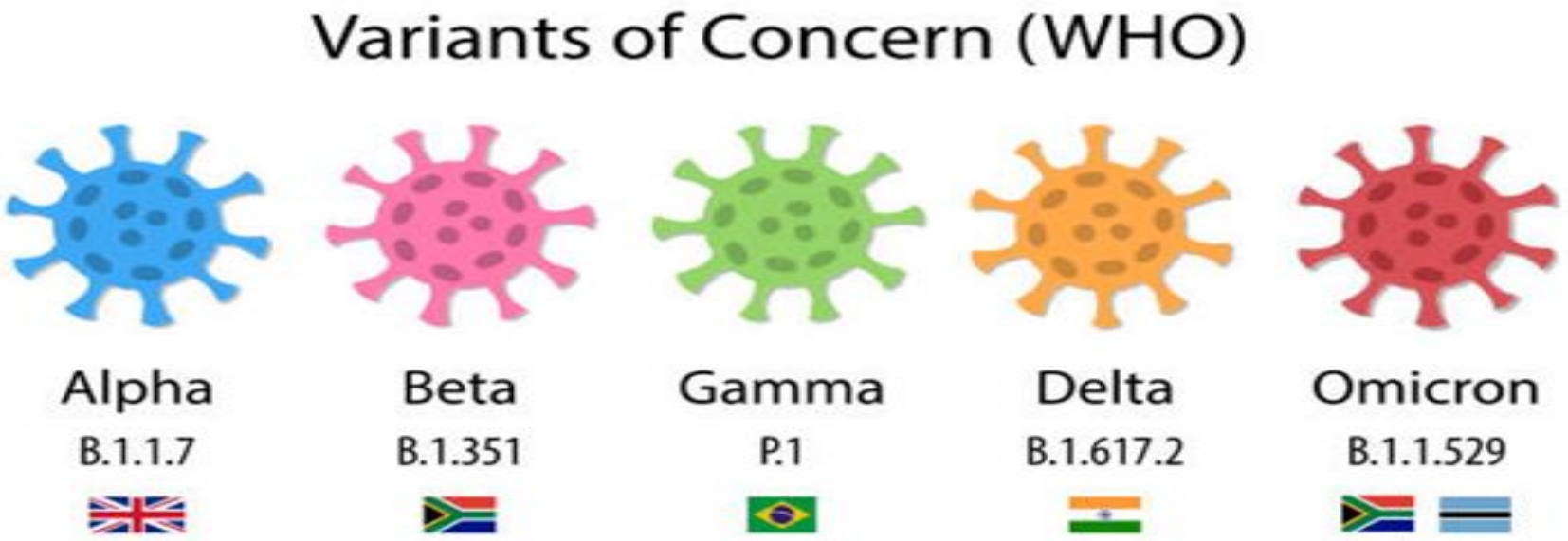
In December 2019, an outbreak of pneumonia in Wuhan, China caused by a new coronavirus was reported.
The virus named (SARSCoV2), and the disease is named (COVID19).
WHO declared it a global pandemic on March 11, 2020.
Caused approximately 628 million cases with fatality rate of approximately 3-4%.
Bats and pangolin are its animal hosts.

Coronavirus Global Pandemic in 2019
COVID19
(COVID stands for Coronavirus Disease and 19 stands for the year 2019)

- In December 2019, in Wuhan, China, a novel Coronavirus emerged. with spike protein antigens on its surface to which **NO one had antibodies**. The virus is named **SARSCoV2**.
- Based on genome RNA sequencing results, spike protein of SARSCoV2 closely resembles that of CoV of **bats** (the natural reservoir) and CoV of **pangolin** (second, intermediate reservoir).
- In May 2021, the original and the most accepted hypothesis that SARSCOV2 spread from an animal to people at a “wet animal” market in Wuhan, China was questioned. An alternative possibility that workers at the Virus Laboratory in Wuhan China may have been accidently infected and unintentionally spread the virus to others.
- This virus caused a **global pandemic** with millions of cases and millions of deaths.



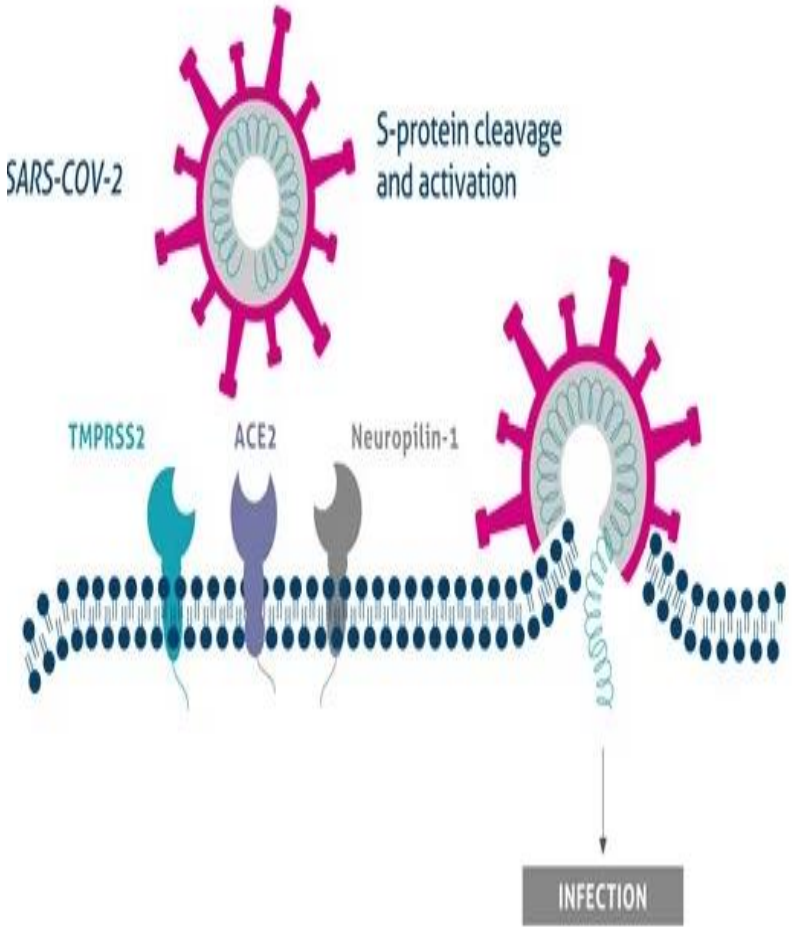
- Although, the number of cases and deaths from COVID19 declined significantly, mostly as a result of widespread immunization, subsequent waves of infections caused by **new viral variants Alpha, Beta, Gamma, Delta and lastly the Omicron (Variants of concern).**
- This increase in infections is the result of three factors, waning of the immunity induced by the vaccine, the delta and omicron variants that have increased transmissibility, and relaxation of public health measures such as masking.



Cell Receptors for SARSCoV2:

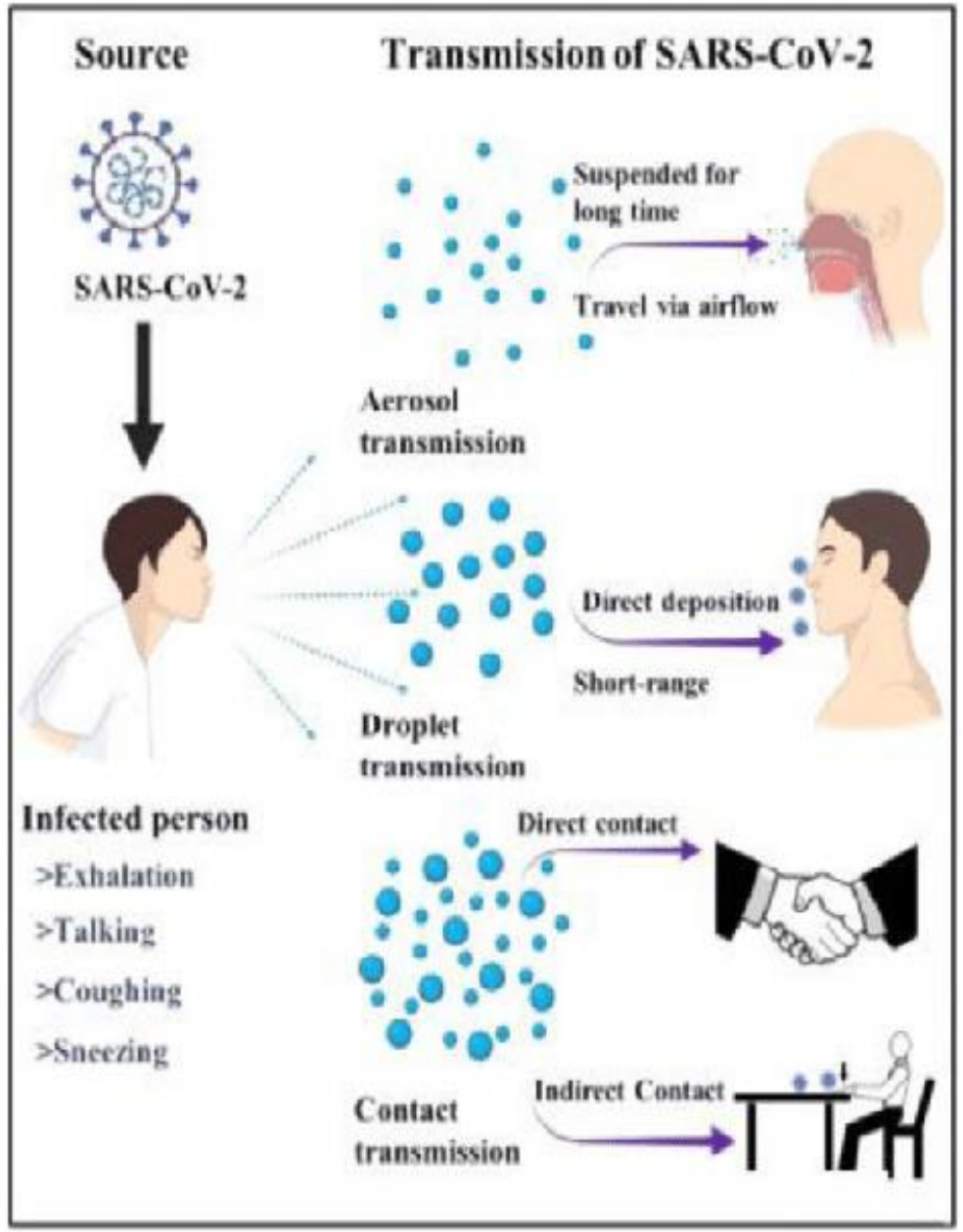
A) The main receptor is the ACE2 (angiotensin-converting enzyme 2) which is abundant on lung epithelial membrane.
Binding of the spike protein of the virus to the ACE2 receptor is the first step in the entry of the virus into the cell.
The relatively **low number of cases of COVID19 in children** is attributed to the low number of the ACE2 receptor displayed on their cells.

B) Another recently discovered receptor is neuropilin1 (NRP1) which is expressed abundantly in the respiratory and olfactory systems suggested that potentiates host cell entry.
Antibody to NRP1 prevents infection of the cell suggesting that it could be an additional target for drugs or vaccines.



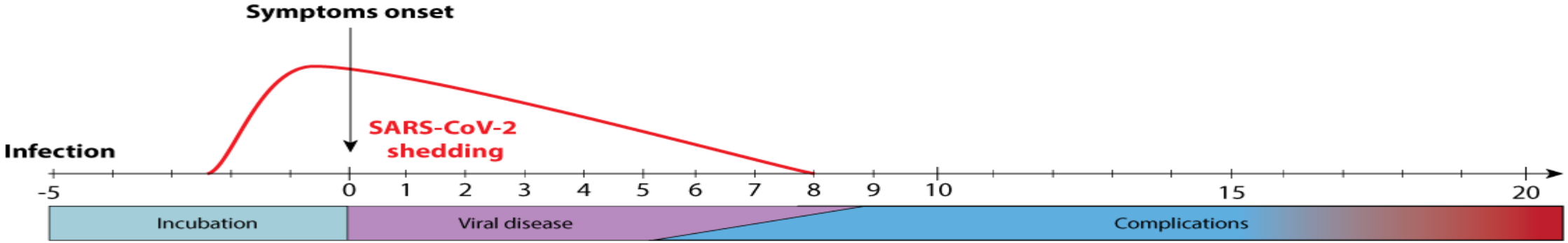
Methods of Transmission:

- The primary mode of transmission is inhalation of respiratory **droplets (> 5µm)** generated by coughing, sneezing, or talking (up to 1 meter).
- Respiratory **aerosols (< 5µm)** also play a role (aerosols are smaller than droplets so stay in the air longer and can be distributed over a distance of more than 6 feet by air currents).
- Transmission by **direct contact or indirect contact** with surfaces containing virus also occurs. Fingers transport the virus on the surface to the recipient's eyes, nose, or mouth.
- Virus is isolated in stool, but fecal-oral route does not seem to be an important route.
- **Virus survives on hands 15-30 minutes, 3 hours airborne and 2-3 days on plastic and stainless-steel surfaces.**



Shedding of virus by an infected patient (Infectiousness):

- Typically begins 2 to 3 days before symptom onset (asymptomatic transmission).
- Maximum with onset of symptoms.
- May continue after resolution of symptoms as well.
- A rough approximation is, therefore, about **10 days** after the time of infection.
- **Asymptomatic persons can also shed the virus.**



Seasonality: CoV exhibit less seasonality than do influenza virus. The increase in SARSCoV2 infections in the summer 2020 indicates that this virus is not exhibiting a drop off in infections during the warmer months, the way influenza does. Nevertheless, a worldwide study performed in January to March 2020 indicated a correlation of outbreaks of COVID19 within a narrow band of latitude with low temperature and low humidity.

Pathogenesis & Clinical Findings:

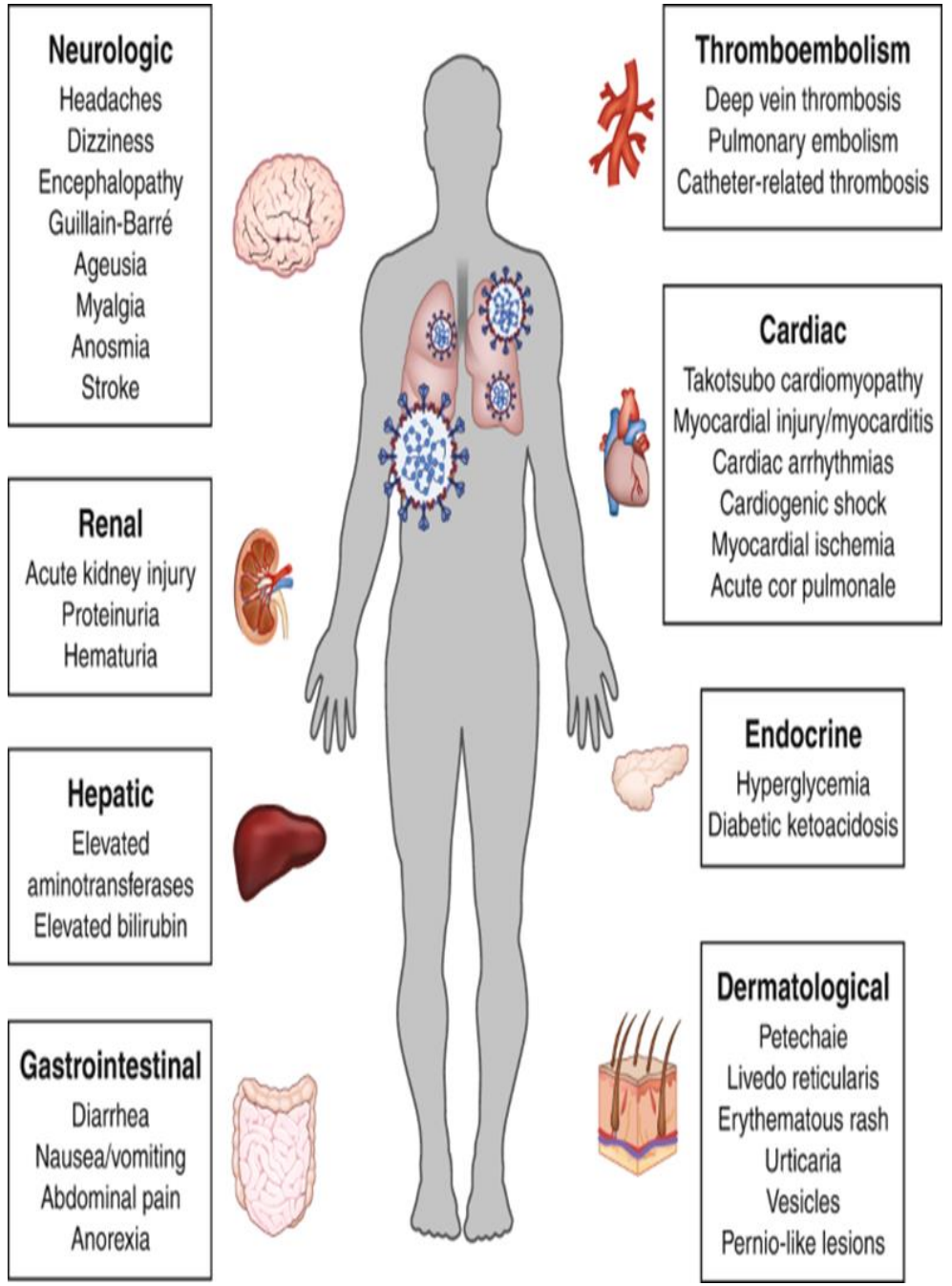
- **The incubation period:** ranges from 2 to 14 days with a mean of 5 days.
- **General manifestations:** such as fever, chills, myalgia, fatigue and headache.
- **Respiratory manifestations:** dry cough and **shortness of breath**.

- **The respiratory manifestations are likely to have two pathogenic mechanisms:**

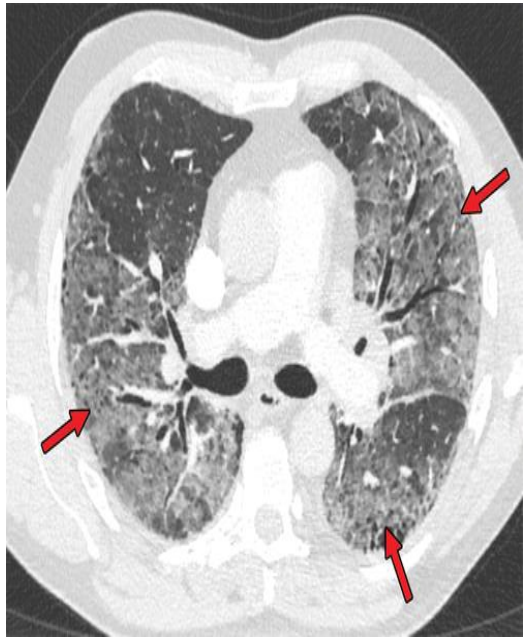
- One is the killing of alveolar cells by the virus. Accumulated cell debris blocks diffusion of oxygen into the capillaries resulting in **hypoxia**.
- The other is an immune mediated **"Cytokine Storm"** resulting in further damage to the alveolar membrane and ARDS (**Acute Respiratory Distress Syndrome**).

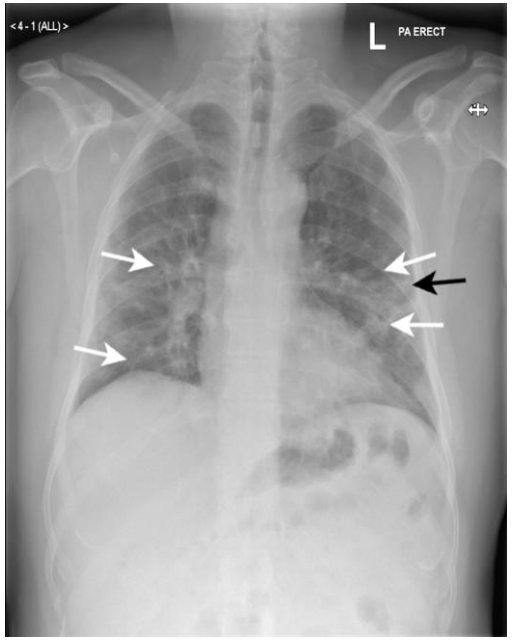
Extra-pulmonary manifestations:

- **Neurological:** Abnormal smell **(anosmia, parosmia)** and abnormal taste **(dysgeusia)** are the initial symptoms in some patients. These are important diagnostic features of COVID19.
- **GIT:** Nausea, vomiting, and diarrhea have occurred in some patients.
- **Cardiac:** A severe myocarditis with symptoms resembling a myocardial infarction has occurred in some patients.
- **Thrombo-embolism:** in some patients leading to an increased risk of stroke.
- Many of these findings are caused not by the virus directly but by the overproduction of cytokine release, **"Cytokine Storm"** triggered by the viral infection.



Diagnosis:



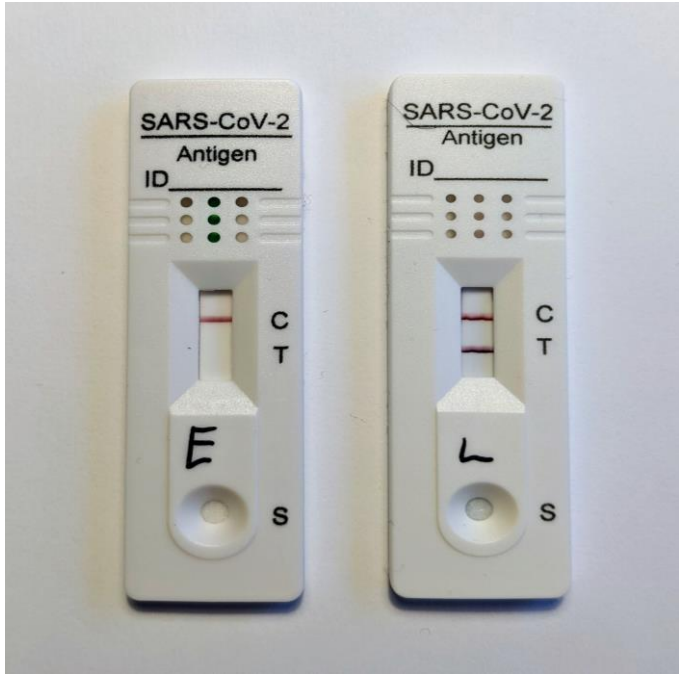


A) Clinical findings.

B) Radiological findings: Consolidation and "groundglass" infiltrates appear in X-ray and CT scan. It is not specific for COVID-19 and may overlap with other infections.

C) Laboratory tests: Nasopharyngeal swabs

- **RT-PCR** to detect viral RNA, it is **very sensitive and specific.**
- **Immunoassay** to detect viral antigen
  - ✓ ELIZA
  - ✓ Immunochromatography: rapid, inexpensive but less sensitive than PCR.



Treatment

A) Non specific supportive & symptomatic treatment:

- **Analgesic antipyretic e.g. paracetamol** (Ibuprofen increases ACE2 which could worsen COVID-19 infections, WHO warns against it).
- Supplemental **oxygen** and respiratory support "mechanical ventilators" may be needed in severe cases.

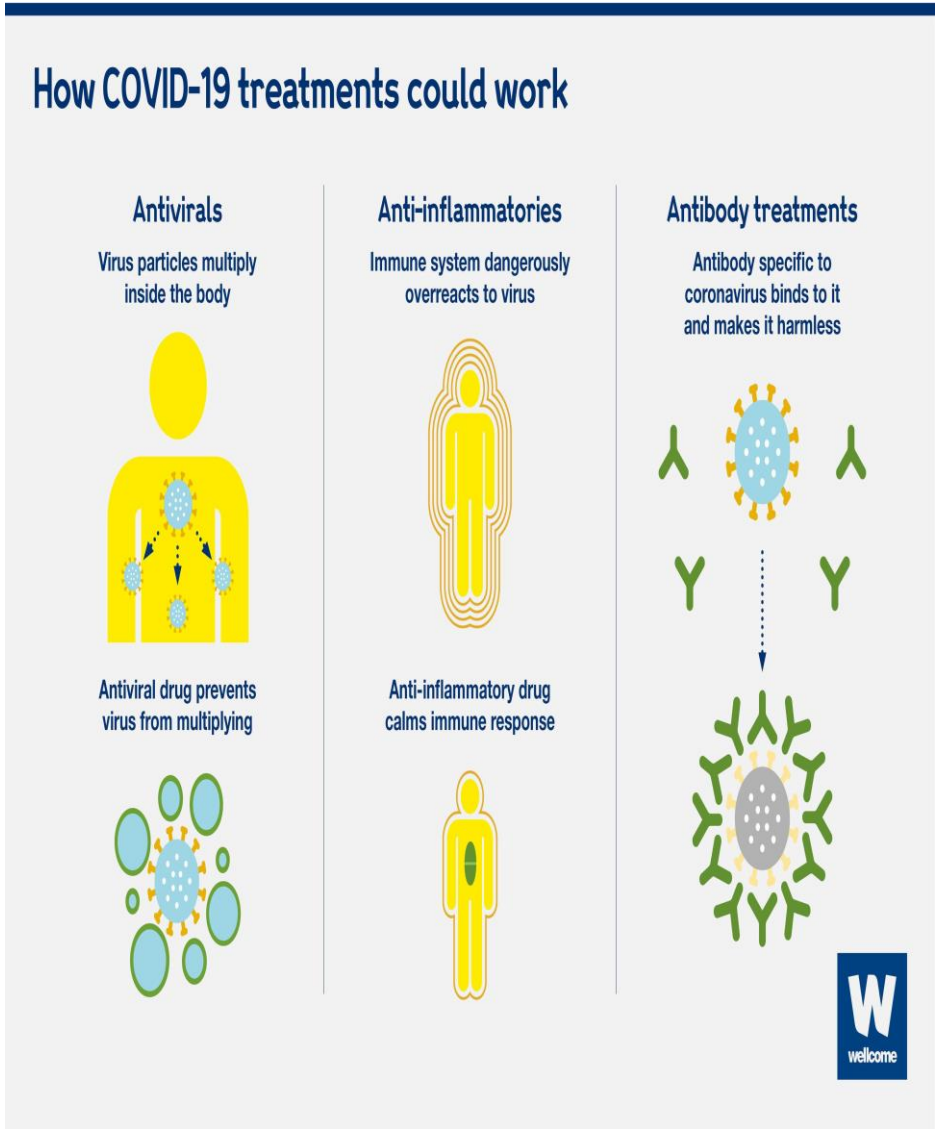
B) Specific therapeutic modalities: 3 main lines

a) Antiviral drugs: Inhibit viral replication

1. Remdesivir (inhibits viral RNA polymerase).
2. Nirmatrelvir & ritonavir (Paxlovid) (protease inhibitor).
3. Molnupiravir (cytosine analog).

b) Monoclonal antibodies directed against spike protein.

c) Drugs inhibit (Cytokine Storm) e.g. Corticosteroids.

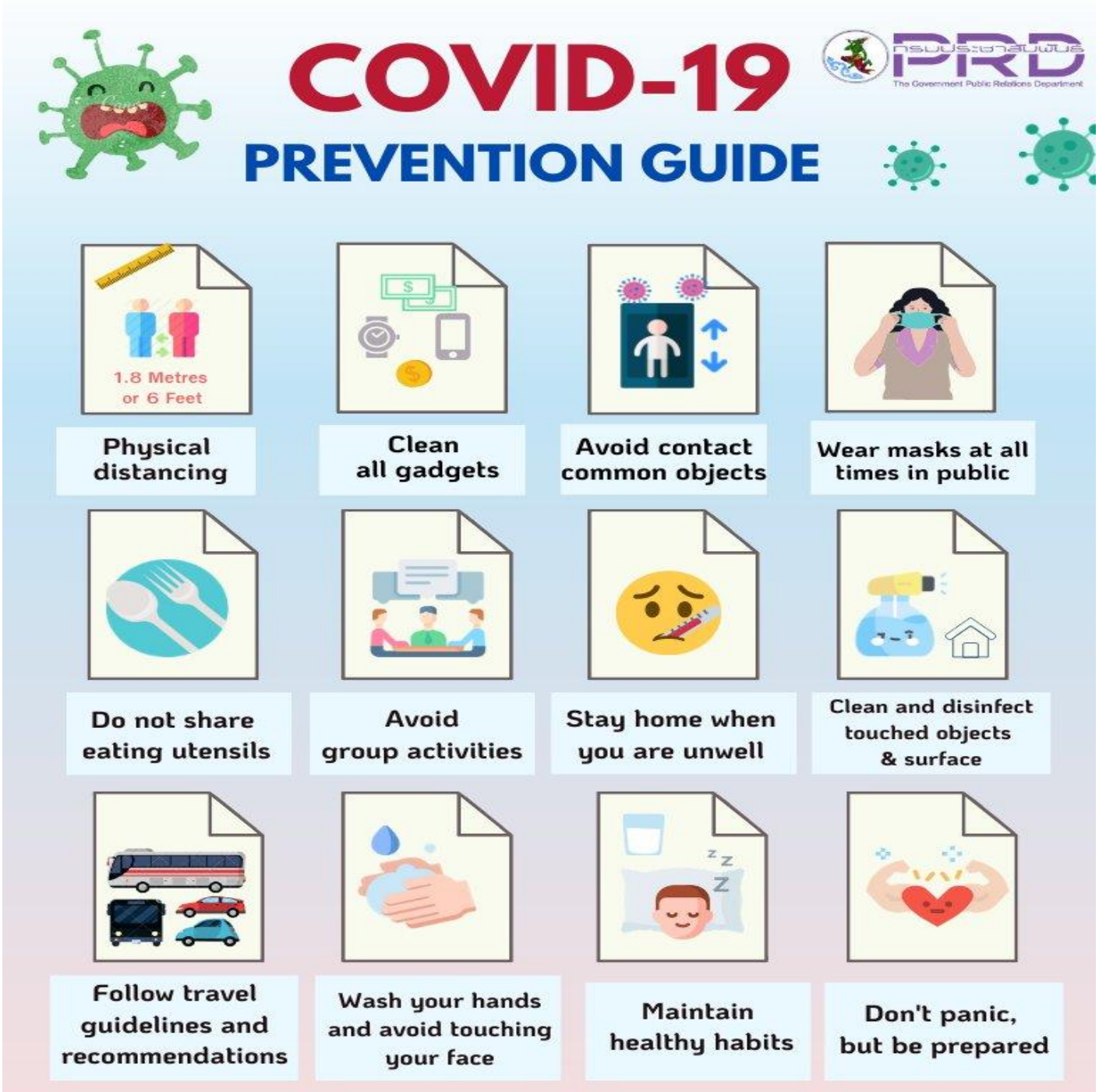


Prevention:

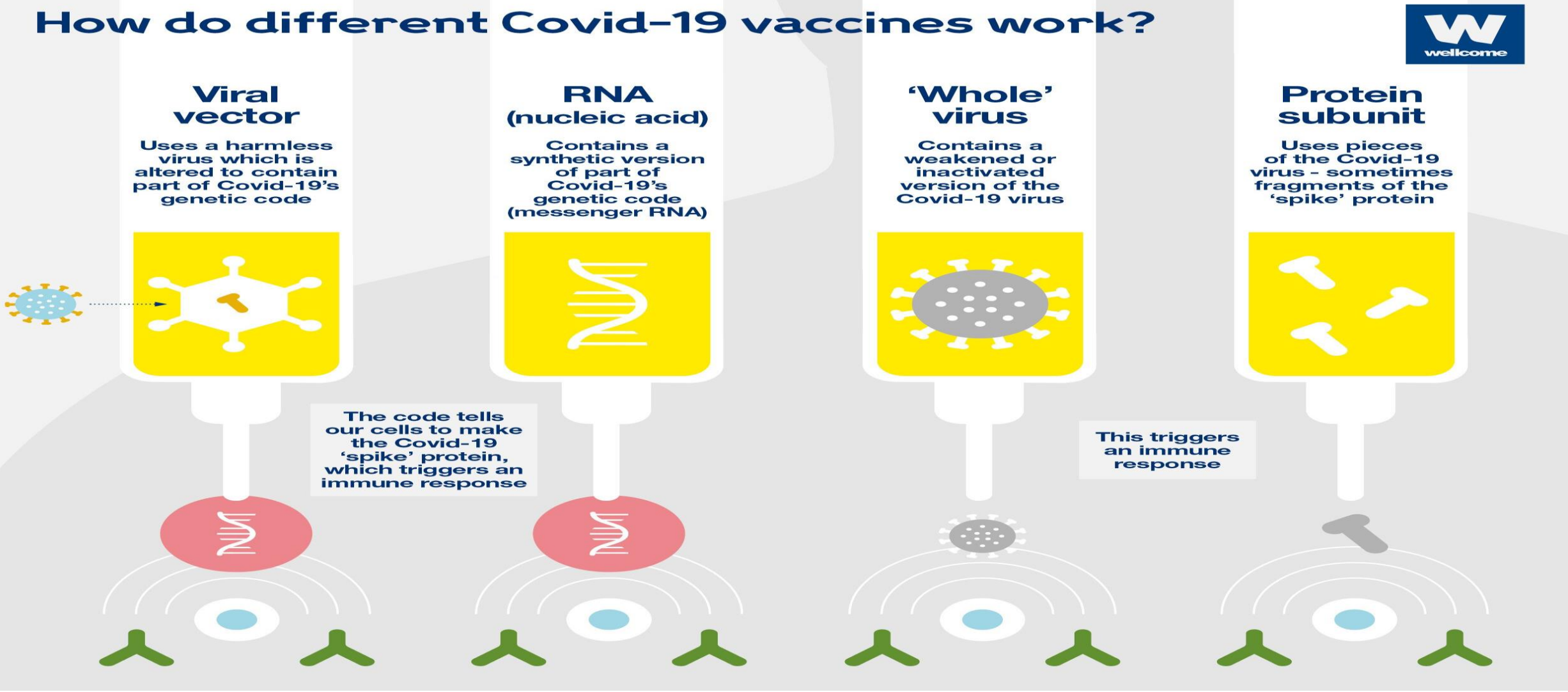
A) Follow prevention guidelines.

N.B., If a person has been significantly exposed and is asymptomatic, a **quarantine period of 10 to 14 days** is recommended.

B) Vaccination



How do different Covid-19 vaccines work?



Oxford-AstraZeneca
Johnson & Johnson

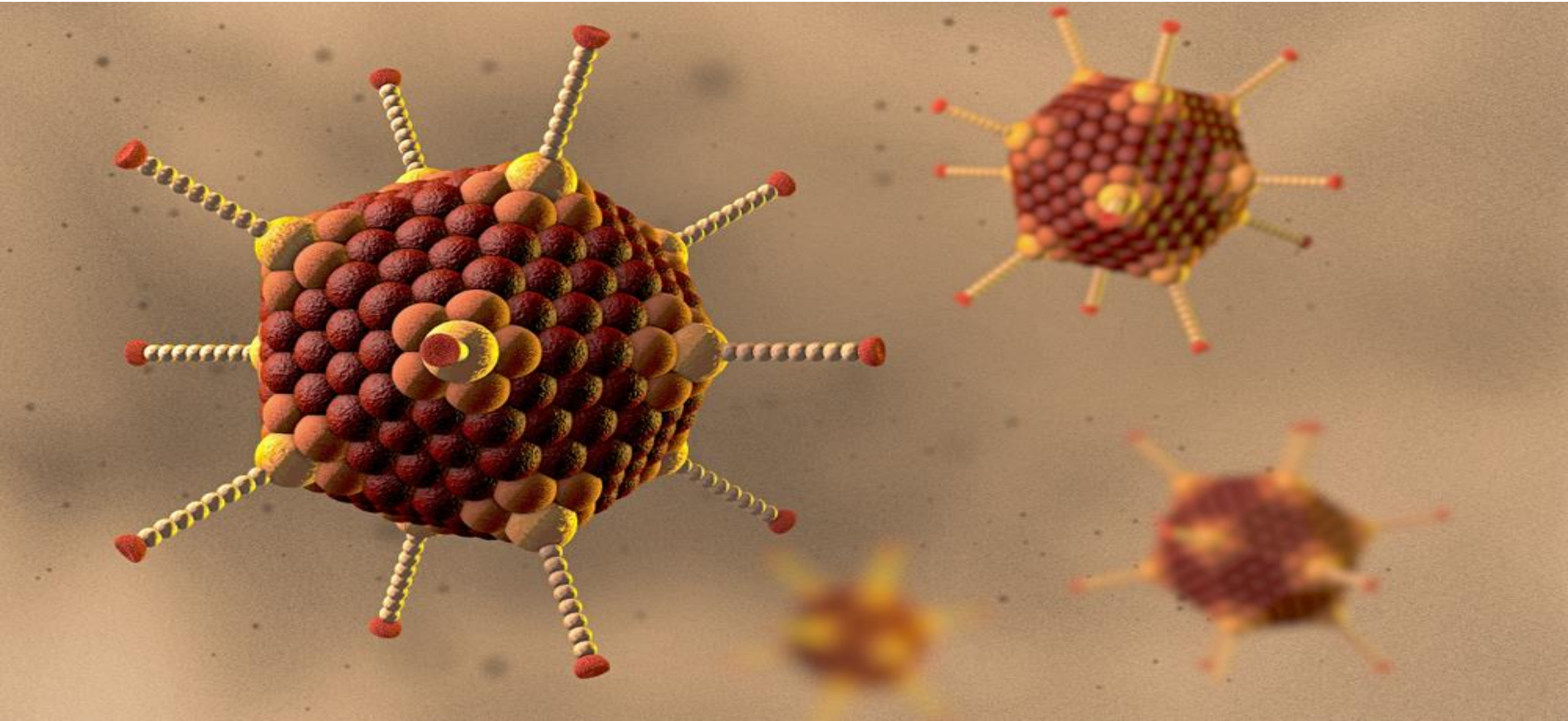
Pfizer–BioNTech
Moderna

Sinopharm
Sinovac

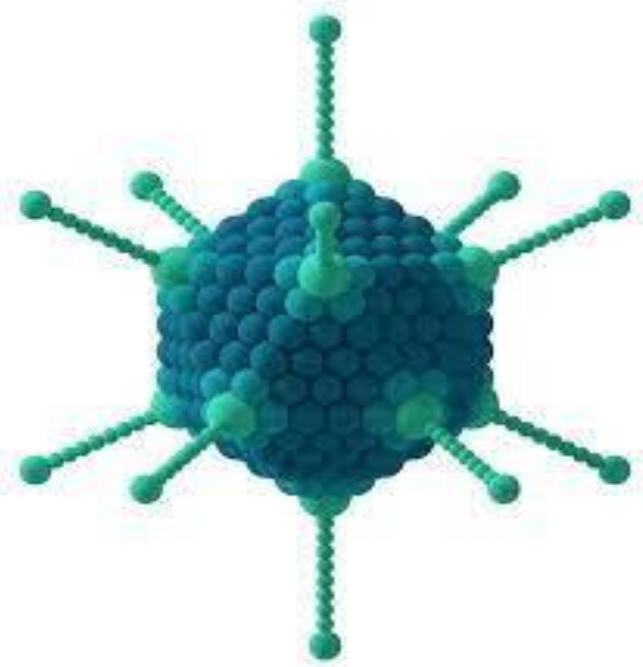
Novavax,

Open end.....

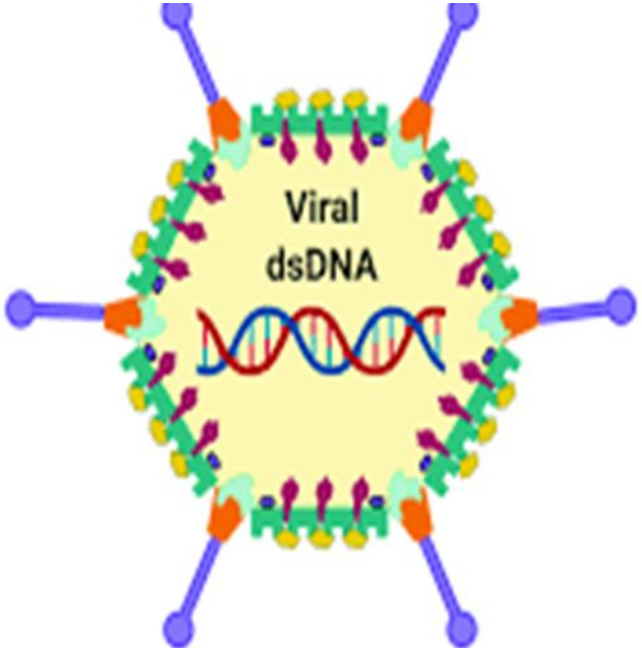
ADENOVIRUS



Classification & Morphological characters:



- Adenoviridae family, genus Mastadenovirus.
- **Non-Enveloped.**
- Icosahedral capsid symmetry.
- Genome: **Double stranded Linear DNA**
- Virion has unique “Spike" or “Fiber” projecting from each of 12 vertices of the capsid. The fiber is the organ of attachment and is a hemagglutinin.
- Replication occurs in the **nucleus**.
- There are 57 accepted human adenovirus serotypes classified into seven groups (A to G).
- Respiratory diseases are caused by (Adenovirus group B & C).



Pathogenesis & Epidemiology:

- Adenoviruses have a pronounced affinity for the mucous membranes of the respiratory tract, alimentary tracts, conjunctiva and for lymphoid tissue (adenoidal and tonsillar tissues of the throat) where the virus may be **latent** for long periods.
- Adenoviruses are transmitted by several mechanisms: aerosol droplet, fecal–oral route, and direct inoculation of conjunctivas by tonometer or fingers.
- Adenovirus infections are endemic worldwide, but outbreaks occur among recruits e.g. military recruits.

Clinical findings:

Adenovirus causes a variety of diseases:

1- Respiratory infections: Adenoviruses invade the mucosa of the upper & lower respiratory tract (especially types **3,4,7&21**):

- Pharyngitis.
- Pharyngo-conjunctival fever may occur in outbreaks in summer camps (swimming pool conjunctivitis).
- Common cold, coryza.
- Pneumonia.

2- Eye infections: conjunctivitis and keratoconjunctivitis **“pink eye”.**

3- Gastroenteritis in infants.

4- Acute hemorrhagic cystitis in children.

Laboratory Diagnosis:

1) PCR
2) Antigen detection by IF.
3) Virus Isolation: Specimens are inoculated into HeLa cells. The virus detected and typed by hemagglutination-inhibition and/or neutralization with type-specific antisera.
4) Serology: Detection of specific Ab.

Treatment & Prevention:

- There is no specific antiviral therapy.
- Three live, monovalent vaccines against serotypes 4, 7, and 21.
  -Used only by the military (not for civilian use).

Thank you