

# **SENSITIVITY OF VIRUSES TO PHYSICAL AND CHEMICAL EFFECTS**

## ➤ 1. Heat

- Viruses have very different sensitivities to changing temperatures.
- Enveloped viruses are more sensitive to rising temperatures than non-enveloped viruses.
- Likewise, it is known that viruses with icosahedral symmetry are more resistant to rising temperatures than viruses with helical symmetry.
- In general, the infectivity of viruses disappears within a few minutes at temperatures above 50°C. Many enveloped viruses become inactive within a few hours at room temperature (21-25°C) or 37°C.
- The main reason for the heat sensitivity of viruses is the denaturation of surface proteins.
- As the environmental temperature decreases, the resistance of viruses increases. Virus suspensions can be preserved for a long time by freezing or lyophilization.
  - Frozen viruses can be stored at (-20) °C or lower temperatures, and lyophilized viruses can be stored in the refrigerator (2-8 °C). Virus suspensions that will be stored for a very long time are kept at (-70) or (-196) °C.

## ➤ 2. pH

- Viruses should ideally be maintained at physiological pH. Many viruses maintain their infectivity between pH values of 5.0-9.0. Most enteric viruses are not affected by acidic pH values, but alkaline pH values (>9.0) negatively affect all viruses.

## ➤ 3. Radiation

- Radiation sources such as ultraviolet rays, X-rays, etc. inactivate viruses. These rays act directly on the viral nucleic acid.

#### ➤ 4. Photodynamic inactivation

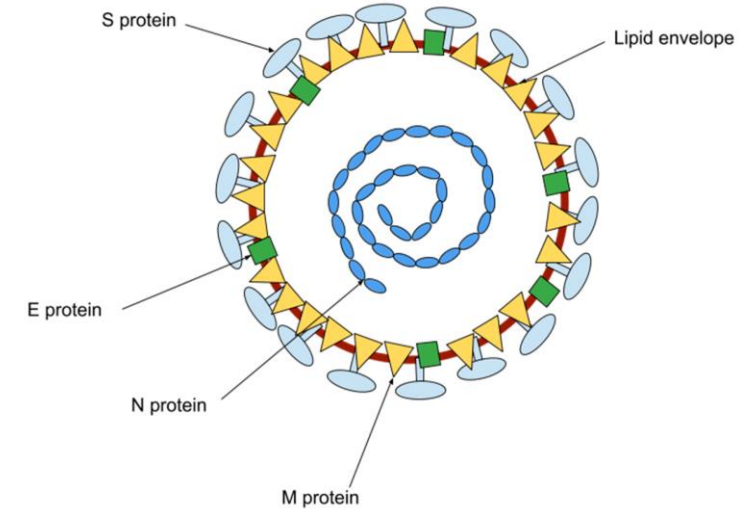
- Vital dyes such as neutral red, proflavin and toluidine blue can penetrate into the virion at varying levels.
- These dyes, which subsequently bind to viral nucleic acid, can increase the rate of inactivation of the virus by sunlight.
  - This is especially important when purifying the virus using plaque testing.

#### ➤ 5. Stabilization with salt solutions

- Salt solutions such as  $MgCl_2$ ,  $MgSO_4$ , and  $Na_2SO_4$  increase the resistance of many viruses to high temperatures.
  - For example, salt solutions prepared at 1M concentration can extend the resistance of viruses at 50°C for 1 hour.
  - This feature is important in the identification of viruses and in increasing the resistance of live virus vaccines to environmental conditions.

## ➤ 6. Sensitivity to lipid dissolvers

- Due to the high content of lipids in the structure of the envelope, the infectivity of enveloped viruses is affected by ether and chloroform. The same effect applies to detergent derivatives. The sensitivity of poxviruses, which are enveloped viruses, to ether varies.



## ➤ 7. Formaldehyde

- Formaldehyde affects the viral nucleic acid and eliminates the infectivity of the virus.
- Single-stranded viral nucleic acids are much more sensitive to formaldehyde than double-stranded ones.
- Since its negative effect on viral proteins is limited, formaldehyde can be used as an inactivating substance in the preparation of inactive vaccines.
- Due to its inactivating effect, the use of formaldehyde should be strictly avoided when sending samples for virus diagnosis.

## ➤ 8. Other chemicals and antibacterial agents

- The infectivity of viruses is not affected by antibiotics and sulfonamides.
- It is generally accepted that quaternary ammonium compounds and phenol-derived compounds affect viruses at low levels.
- Organic iodine preparations have limited effectiveness against viruses. High levels of chlorine compounds can affect viruses.
- Alcohol (ethanol, isopropyl alcohol) has limited activity against non-enveloped viruses.
- One of the most effective chemicals in virus inactivation is bleach.

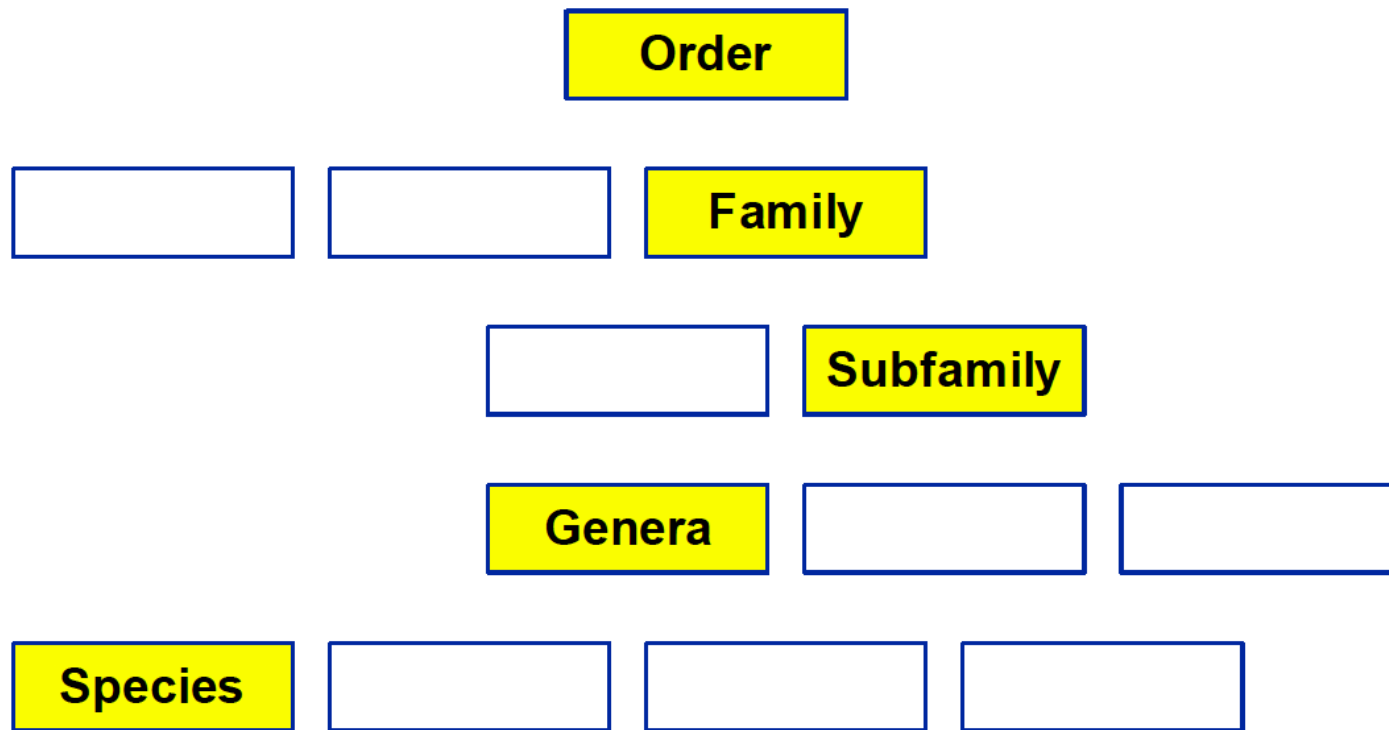
# **Virus Classification and Taxonomy**

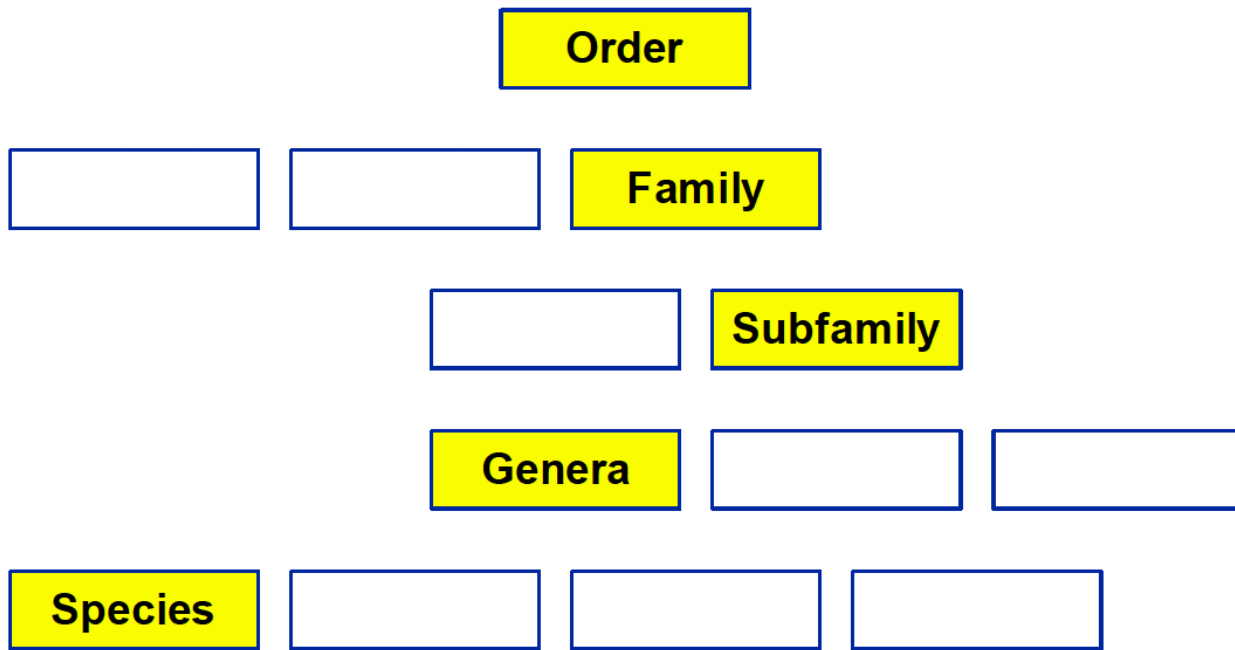
- It is necessary to define all viruses existing in nature (plant, animal and bacteria) with standard parameters.
- It allows the determination of the structural and chemical compositions of viruses.
- International Committee on Taxonomy of Viruses (ICTV)



# How to Classify Viruses?

- Family often the highest classification. Ends in -viridae.
- Many families have subfamilies. Ends in -virinae.





Example:	Example:
Mononegavirales	Herpesvirales
Orthomyxviridae	Herpesviridae
-	Alphaherpesvirinae
Influenzavirus A	Varicello <u>virus</u>
Avian influenza virus	Bovine Herpes virus 1 (BHV1)

# Parameters of classification

## A. Virion properties

- Virion size
- Virion shape
- Presence of envelope
- Symmetry and structure of capsomer

## B. Genome properties

- Type of nucleic acid (DNA or RNA)
- Type of strand (single or double)
- Linear or circular
- Polarity (+ or -)
- Number of segments

### C.Properties of proteins

- Number of proteins
- Size of proteins
- Functional properties
- Amino acid sequence

### D.Replication properties

- Replication strategy
- Characteristics of transcription

### E.Physical Properties

- pH stability
- Thermal stability
- Cation ( $Mg^{+2}$ ,  $Mn^{+2}$ ) stability
- Stability to solvent and detergents

### F.Biological properties

- Serologic relations
- Host spectrum (natural and experimental)
- Tissue tropism, pathology and histopathology
- Transmission mode
- Vector based relations
- Geographical distribution

Baltimore classification	
Group	Characteristics
I	Double-stranded DNA
II	Single-stranded DNA
III	Double-stranded RNA
IV	Single-stranded RNA (+)
V	Single-stranded RNA (-)
VI	Single-stranded RNA with reverse transcriptase
VII	Double-stranded DNA with reverse transcriptase

One classification scheme was developed in the 1970s by Nobel laureate David Baltimore. The **Baltimore classification system** categorizes viruses **based on the type of nucleic acid genome and replication strategy of the virus**. The single-stranded RNA viruses are classified into positive strand (+) and negative strand (-).

**Positive-strand** (also positive-sense or plus-strand) RNA is able to be immediately translated into proteins; as such, messenger RNA (mRNA) in the cell is positive strand.

**Negative-strand** (also negative-sense or minus-strand) RNA is not translatable into proteins; it first has to be transcribed into positive-strand RNA.

Baltimore also considered viruses that are able to **reverse transcribe**, or create DNA from an RNA template.

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# International Committee on Taxonomy of Viruses: ICTV

## Official Taxonomic Resources



**ICTV Taxonomy Browser**

Search and browse the virus taxonomy



**Master Species List**

MSL: Spreadsheet of all current species



**Virus Metadata Resource**

VMR: Virus exemplars for every species

### Taxonomy Browser

This taxonomy browser provides access to the current virus taxonomy. This page will be updated whenever a new taxonomy release has been approved by the ICTV.

[Taxonomy Search](#)
[Taxonomy Browser](#)
[Download Current Taxonomy Spreadsheet \(MSL\)](#)

Unless the "Select to search across all ICTV releases" button is checked below, your search will be against the taxonomy release indicated below the search box (or below the search result set, if present). To search against the current release, refresh the page.

Search taxonomy...

Select to search across all ICTV releases

#### Virus Taxonomy: 2022 Release

EC 54, Online meeting, July 2022  
 Email ratification March 2023 (MSL #38)  
 6 realms, 10 kingdoms, 17 phyla, 2 subphyla, 40 classes, 72 orders, 8 suborders, 264 families, 182 subfamilies, 2818 genera, 84 subgenera, 11273 species

Expand ranks to show  Hide ranks above

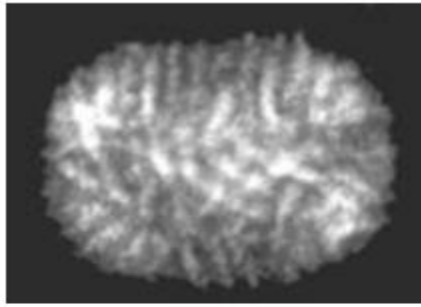
- + Realm: *Adnaviria*
- + Realm: *Duplodnaviria*
- + Realm: *Monodnaviria*
- + Realm: *Riboviria*
- + Realm: *Ribozyviria*
- + Realm: *Varidnaviria*
- + Class: *Naldoviricetes*
- + Family: *Alphatellitidae*
- + Family: *Ampullaviridae*
- + Family: *Anelloviridae*

- There are a variety of ways by which viruses could be classified, however, including virion size, capsid structure, type of nucleic acid, physical properties, host species, or disease caused.
- Because of this challenge, **the International Committee on Taxonomy of Viruses (ICTV)** was formed and has been the sole body charged with classifying viruses since 1966.
- Taxonomy is the science of categorizing and assigning names (nomenclature) to organisms based on similar characteristics, and the ICTV utilizes the same taxonomic hierarchy that is used to classify..

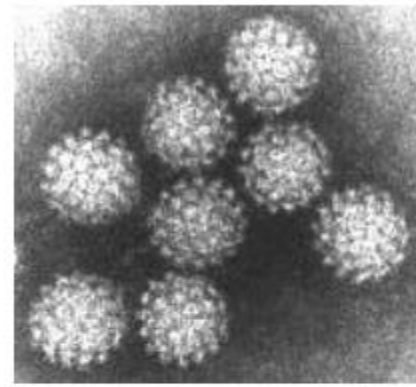
# You should know!!!

## Families of DNA Viruses

- Adenoviridae
- Hepadnaviridae
- Herpesviridae
- Parvoviridae
- Papovaviridae
  - Poxviridae



Poxvirus



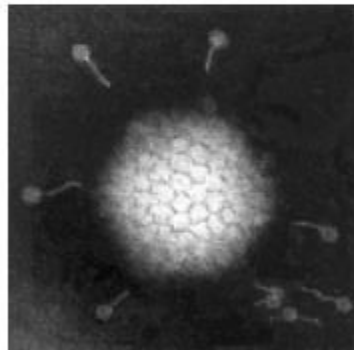
Papovavirus



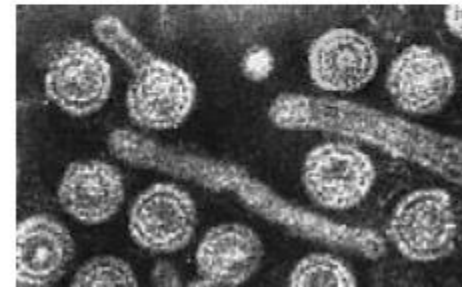
Herpesvirus



Parvovirus



Adenovirus



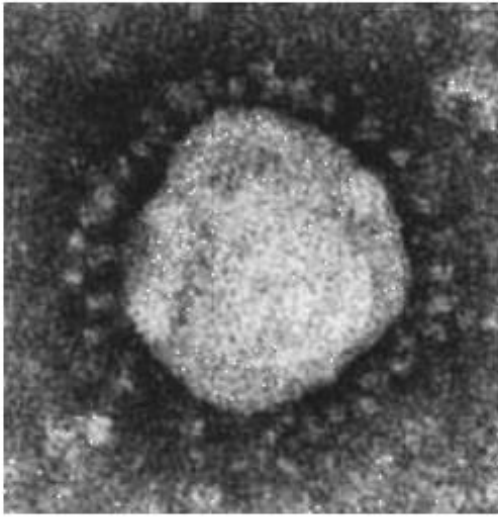
Hepadnavirus



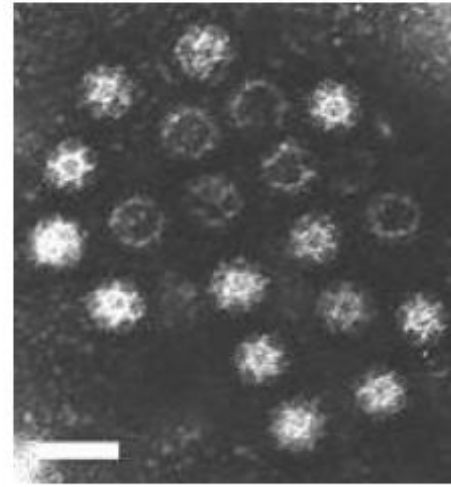
# You should know !!!

## Families of RNA viruses

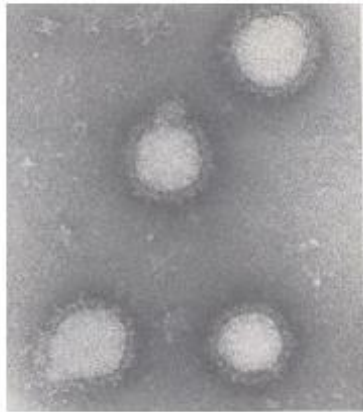
- Arenaviridae
- Bunyaviridae
- Caliciviridae
- Coronaviridae
- Flaviviridae
- Filoviridae
- Orthomyxoviridae
- Paramyxoviridae
- Picornaviridae
- Rhabdoviridae
- Reoviridae
- Retroviridae



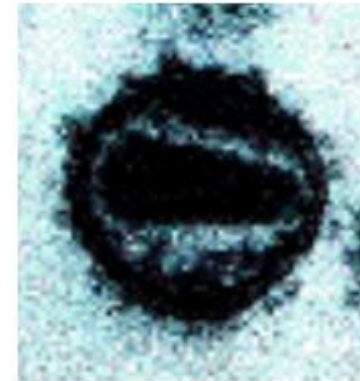
Coronavirus



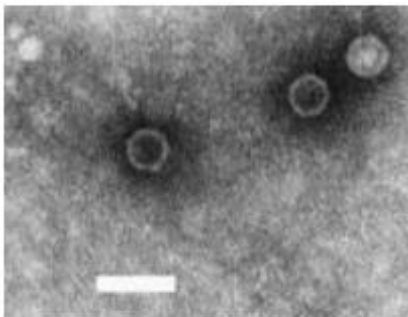
Calicivirus



Flavivirus



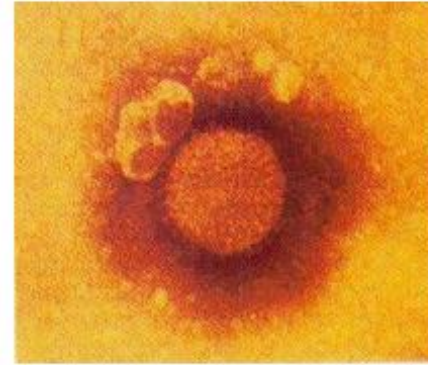
Retrovirus



Picornavirus



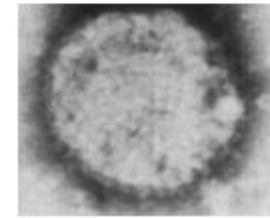
Paramyxovirus



Arenavirus



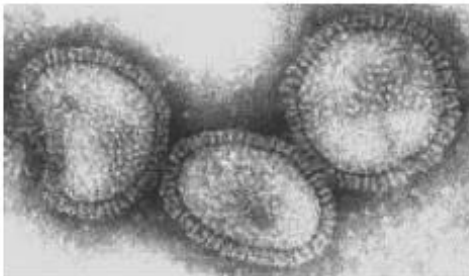
Rhabdovirus



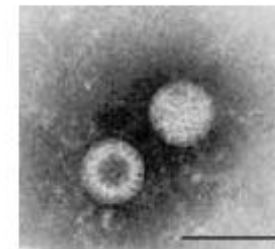
Bunyavirus



Filovirus



Orthomyxovirus



Reovirus

# Viral Genetics

# 1. Mutation

- Permanent (transmitted between generations) changes that occur in the virus genome (nucleic acid) are called Mutation.

Irreversible changes in virus genome called as **mutation**.

- Mutations;

It is the most important way viruses exist in nature.

It is more common in RNA viruses than in DNA viruses (WHY????).



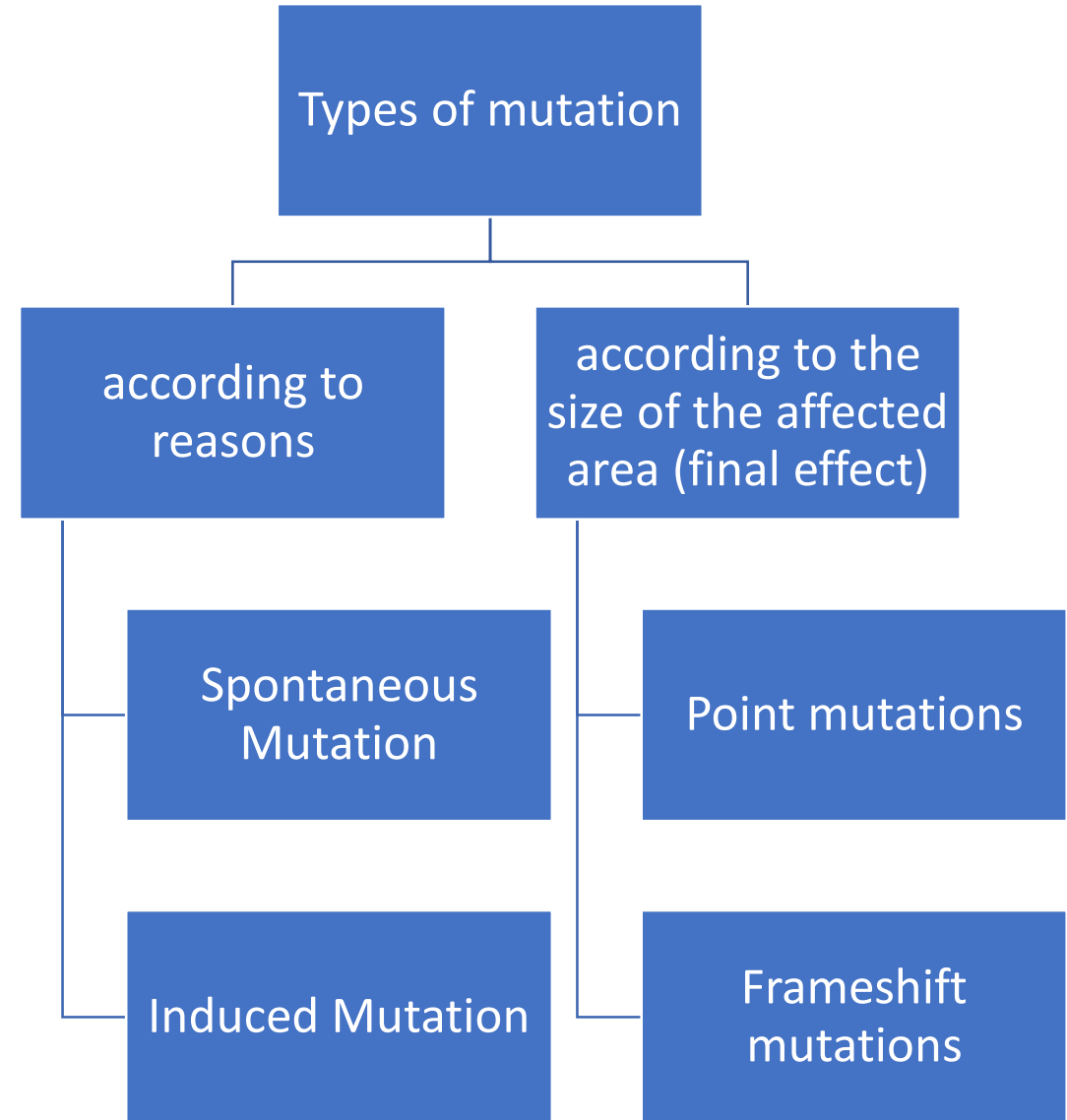
- DNA viruses have mutation rates similar to those of eukaryotic cells because, like eukaryotic DNA polymerases, **their replicatory enzymes have proofreading functions**.
- The RNA viruses, however, lack a proofreading function in their replicatory enzymes, and some have mutation rates that are many orders of magnitude higher.
- The mutation rate in DNA viruses is approximately 1 million times lower than in RNA viruses.

# Types of Mutation

- **Spontaneous Mutation:** Occurs spontaneously under natural conditions
- **Induced Mutation:** It is done for certain purposes under laboratory conditions (vaccines, weapons).

In addition, two kinds of mutation have been described based on mechanism of occurrence and final effect;

- Point mutations
- Frameshift mutations



# Point mutation

- This was characterized by single nucleotide change in the genome and relevant amino acid.
- It is a mutation that is based on the incorrect mapping or change of any nucleotide on the genome and is characterized by only a single amino acid change.
- A point mutation occurs in a genome when a single base pair is added, deleted or changed.
  - While most point mutations are benign, they can also have various functional consequences, including changes in gene expression or alterations in encoded proteins.

5' - **ATG GGC GAG TCC CGA AAA TGG CAC CCG CTA** -3'

Met Gly Glu Ser Arg Lys Trp His Pro Leu



5' - **ATG GGC GAC TCC CGA AAA TGG CAC CCG CTA** -3'

Met Gly Asp Ser Arg Lys Trp His Pro Leu





## Nucleotide Changes

- Transition mutations

- Pirimidin -Pirimidin

$T \rightarrow C$   $C \rightarrow T$

Purin -Purin

$A \rightarrow G$   $G \rightarrow A$

- Crossed mutations

- Pirimidin -Purin

$T \rightarrow A$   $T \rightarrow G$   $C \rightarrow A$   $C \rightarrow G$

- Purin -Pirimidin

$A \rightarrow T$   $A \rightarrow C$   $G \rightarrow T$   $G \rightarrow C$

# Frameshift Mutations

- A frameshift mutation in a gene refers to **the insertion or deletion** of nucleotide bases in numbers that are not multiples of three.
- An insertion or deletion of a nucleotide in the frame occurs so that the entire sequence after the gene's point of action changes significantly, affecting the amino acid sequence of interest.
- This is important because a cell reads a gene's code in groups of three bases when making a protein.
- Each of these **“triplet codons”** corresponds to one of 20 different amino acids used to build a protein.
- If a mutation disrupts this normal reading frame, then the entire gene sequence following the mutation will be incorrectly read.
- **This can result in the addition of the wrong amino acids to the protein and/or the creation of a codon that stops the protein from growing longer.**

## 1. Nucleotide insertion

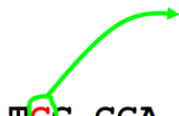
5' - **ATG GGC GAG TCC CGA AAA TGG CAC CCG CTA** -3'  
Met Gly Glu Ser Arg Lys Trp His Pro Leu

A  
↓

5' - **ATG GGC GAG TAC CCG AAA ATG GCA CCC GCT** -3'  
Met Gly Glu Try Pro Lys Met Ala Pro Val

## 2. Nucleotide deletion

5' - **ATG GGC GAG TCC CGA AAA TGG CAC CCG CTA** -3'  
Met Gly Glu Ser Arg Lys Trp His Pro Leu



5' - **ATG GGC GAG TCC GAA AAT GGC ACC CGC TAT** -3'  
Met Gly Glu Ser Glu Asn Gly Thr Ala Try

# Mutagens

## 1. Chemical Mutagens

### A. Base analogs

- 5-bromourasil (Urasil)
- 2-aminopurin (Adenin)

### B. Agents changing nucleic acid

- Nitrous acid ( $\text{HNO}_2$ )  $\text{A} \rightarrow \text{H}$
- Hydroxylamine ( $\text{NH}_2\text{OH}$ )  $\text{C} \rightarrow \text{U}$

### C. Alkylating agents

- Nitrosoguanidin
- Etilmetan sulfonat
- Metilmetan sulfonat

### D. Acylizing agents

### E. Intercalating agents

## 2. Physical Mutagens

### A. Heat and pH

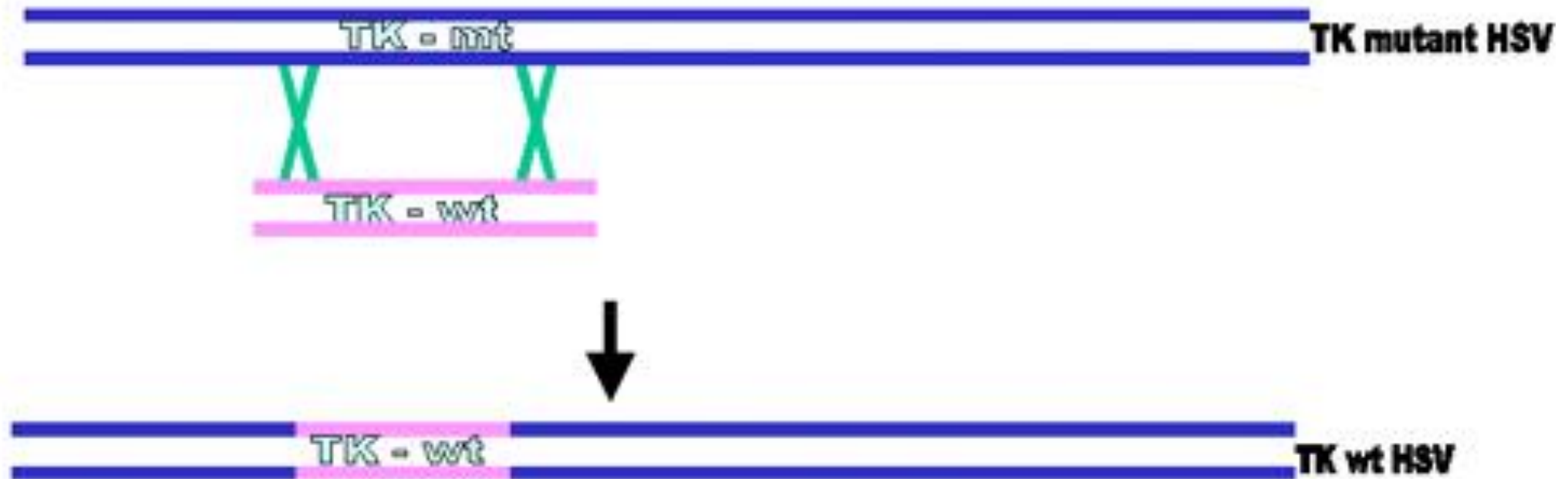
### B. Rays

- Ionized (X and gamma)
- Non-ionized (UV)

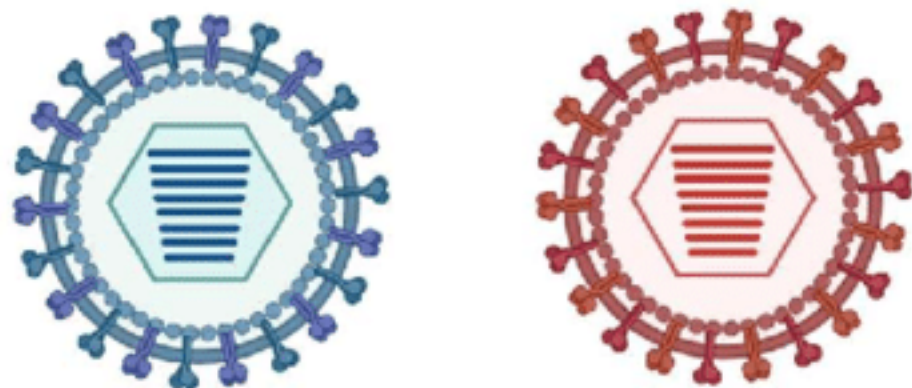
## 2. Recombination

- If two different viruses infect the same host cell, there may be mutual changes between the nucleic acid base sequences of these viruses.
- These changes, which are reflected in the newly synthesized nucleic acid, are defined as recombination. The new virus that emerges as a result of recombination is called recombinant virus.
  1. Intramolecular recombination: It describes partial or total gene changes between virus genomes that infect the same cell. Mostly seen in dsDNA viruses, e.g. herpesviruses .
  2. Genetic reassortment: It describes the segment exchange between viruses with two segmented genomes that infect the same cell. Seen in segmented RNA viruses. For example, Influenzaviruses

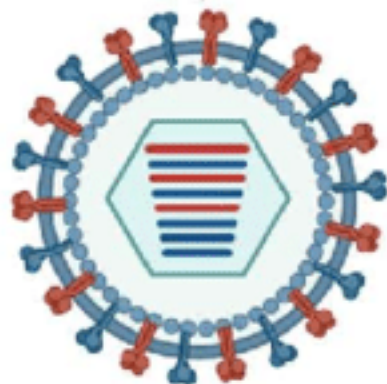
## marker rescue



(A)

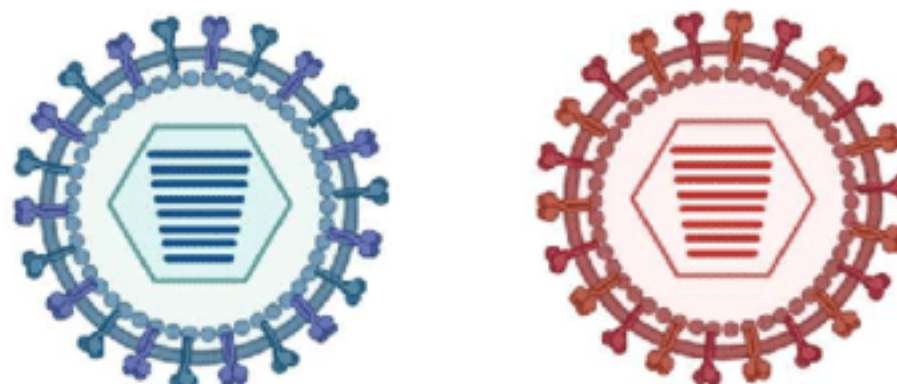


Reassortment

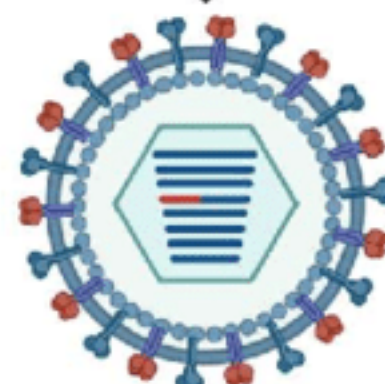


E.g. Influenza Viruses

(B)

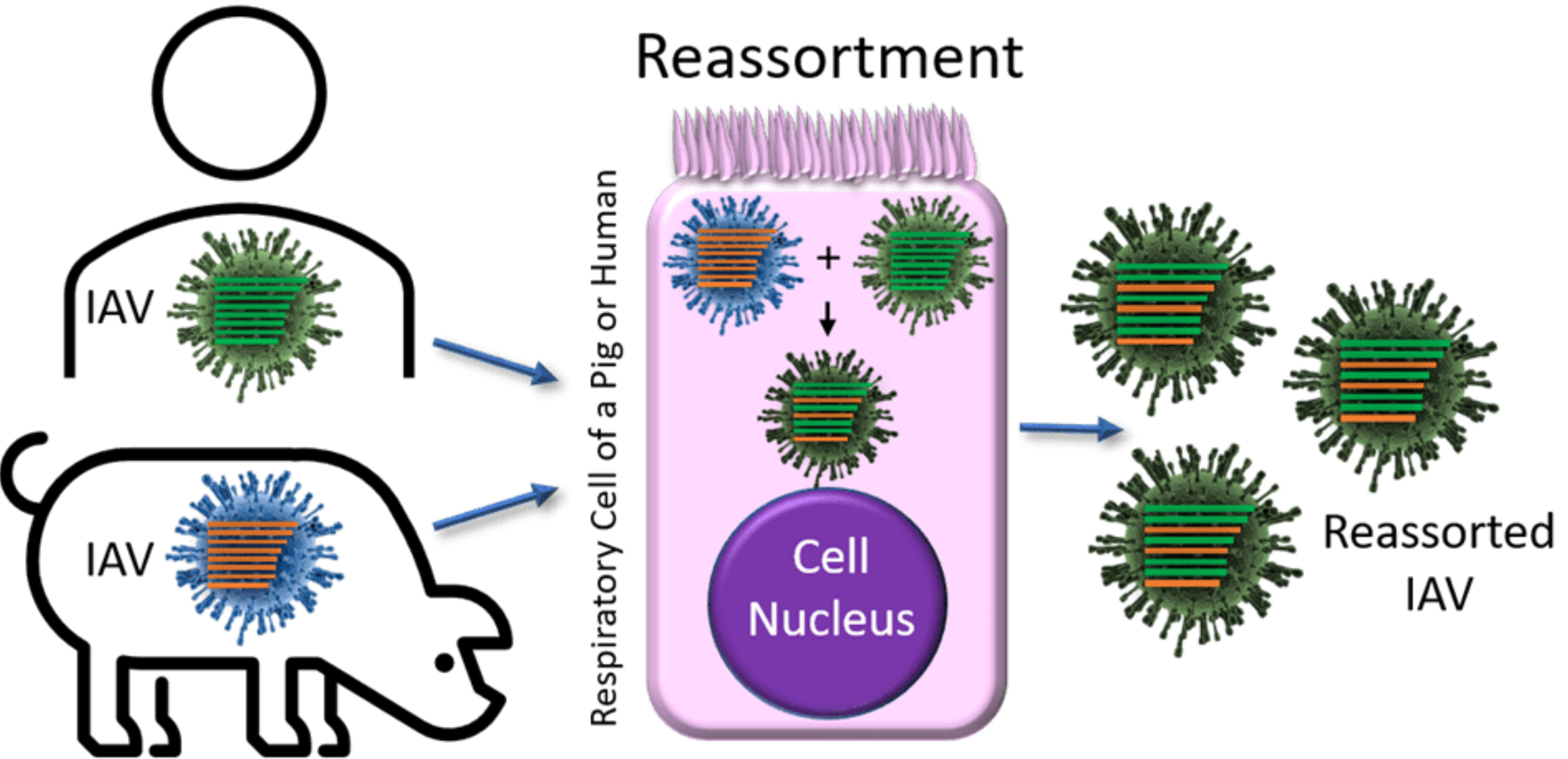


Recombination



E.g. Human Immunodeficiency Virus (HIV) and Enterovirus D68 (EV-D68)

# Genetic Reassortment

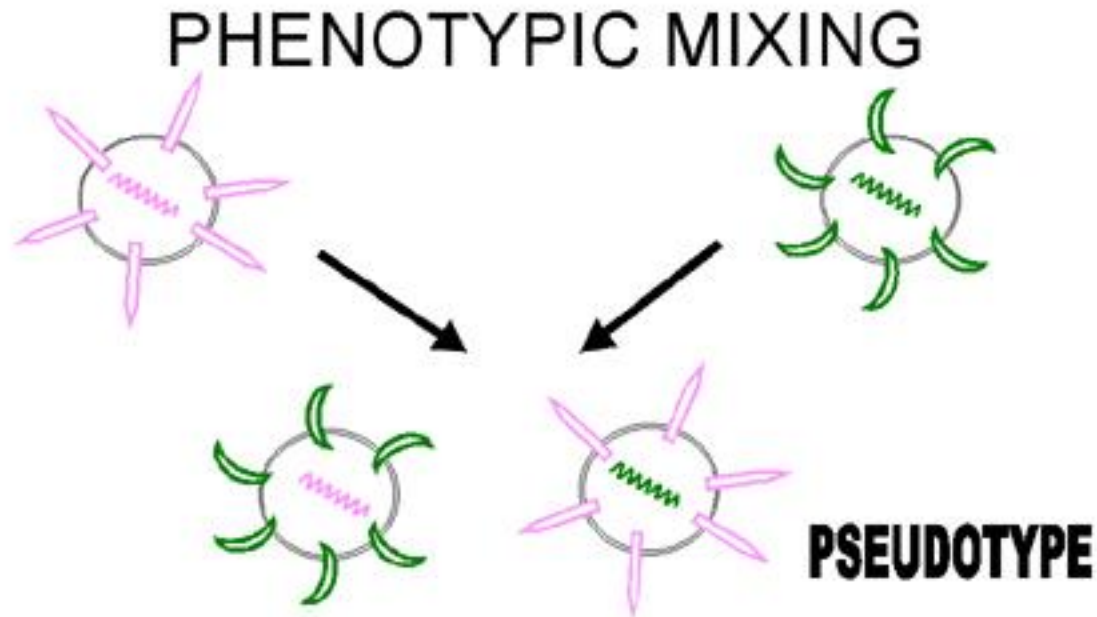




# Non-genetic interactions between viruses

- Non-genetic changes between viruses refer to changes in post-translational viral products. Such changes do not affect the genetics of viruses, but can be expected to affect the phenotype and antigenic properties of the virus.

- **Complementation:** The exchange of gene products such as structural proteins and enzymes without gene exchange between viruses that infect the same cell is called complementation.
- In this way, defective or inactive virions that are not capable of reproduction can become active or multiply at a higher titer.
  - Complementation can occur between two viruses of the same species or between viruses that are not closely related. The best example in this regard is between adenoviruses and adeno-associated viruses (Parvoviridae).



- **Phenotypic mixing (pseudotype):** In dual infections, it is the packaging of the nucleic acid of one virus with the capsid or envelope containing the proteins of the other virus.
- Packaging of the entire nucleic acid of the first virus with a capsid consisting of proteins of the second virus is called **transcapsidation**.
  - As a result of such phenotypic changes, viruses may gain the ability to enter host cell types that they cannot normally infect. Even this virus can reproduce in this new type of cell, it should be considered that the phenotypic mixture will not have significant consequences for the viruses, since the virions that will be formed in the next generation will contain the proteins encoded by the viral genome.

## ➤ Polyploidy:

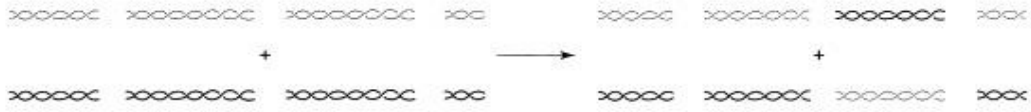
All animal viruses except retroviruses have haploid genomes. In other words, it carries a single copy of the chromosome.

Especially in enveloped viruses, although rare, it may be possible for more than one genome or nucleocapsid of the same virus to be packaged in a virion. This situation is defined as polyploidy.

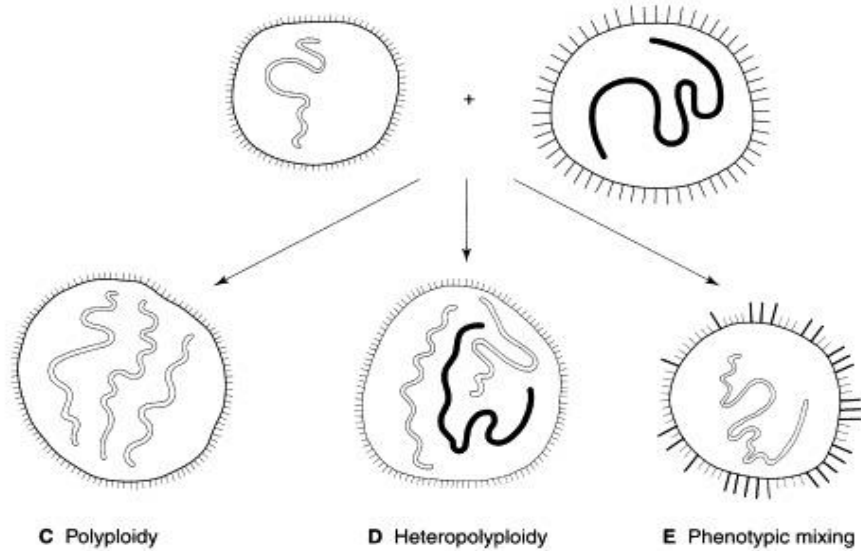
In paramyxoviruses, it can be seen that the nucleocapsid of more than one virus species is packaged together. This is called heteropolyploidy.



**A** Intramolecular recombination



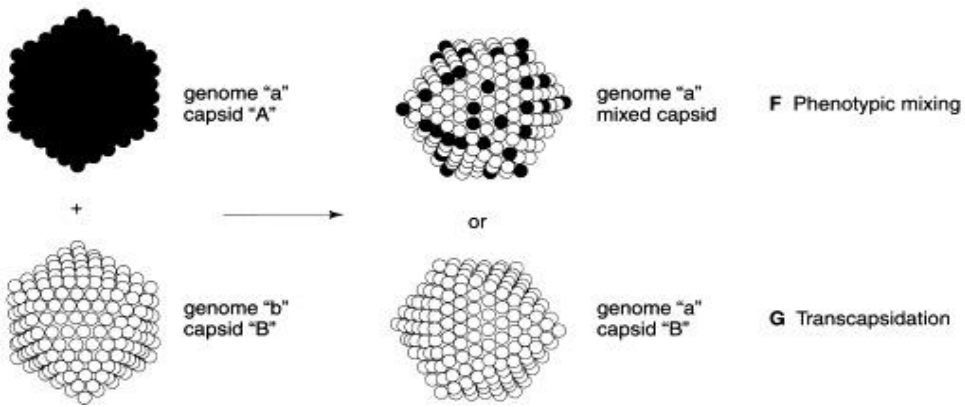
**B** Genetic reassortment



**C** Polyploidy

**D** Heteropolyploidy

**E** Phenotypic mixing



**F** Phenotypic mixing

**G** Transcapsidation

- Genetic recombination, polyploidy, phenotypic mixing and transcapsidation.
- (A) Intramolecular recombination.
- (B) Reassortment of genome fragments, as in reoviruses and orthomyxoviruses.
- (C) Polyploidy, as seen in unmixed infections with paramyxoviruses.
- (D) Heteropolyploidy, as may occur in mixed infections with paramyxo-viruses and other enveloped RNA viruses.
- (E–G) Phenotypic mixing: (E) with enveloped viruses; (F) viruses with icosahedral capsids; (G) extreme case of transcapsidation or genomic masking.

# EFFECTS OF GENETIC CHANGES ON VIRAL INFECTIONS

- **1. Emergence of new virus species:**

One of the most obvious examples of the emergence of new virus species due to genetic changes is the previously described relationship between FPV and CPV-2.

- **2. Effects on disease pathogenesis:**

Lentiviruses (Retroviridae), which cause infections such as HIV and Maedi-Visna, are subject to high rates of mutation while multiplying in the host organism after infection. Thus, the new generation virus particles formed are protected from previously formed neutralizing antibodies. In this way, the infection continues repeatedly.

- 3. Effects on disease epidemiology:

As a result of genetic changes, the course of viral diseases in the population, mortality/morbidity/lethality rates and host spectrum may change.

- 4. Virulence change:

Field strains with different virulence can be formed under the influence of mutations. Due to the high mutation rates, such changes are frequently encountered, especially in RNA viruses.

- **5. Effects on vaccination:**

As a result of the mutations that occur, antigenically different groups are formed among the field strains. Due to the variations in the surface proteins of viruses due to mutations, a decrease in the protective level of immunity obtained through vaccination and disease outbreaks in vaccinated animals can be observed.

- **6. Development of resistance to antiviral agents:**

It has been determined that resistance to antiviral agents has developed in many virus species due to genetic changes.



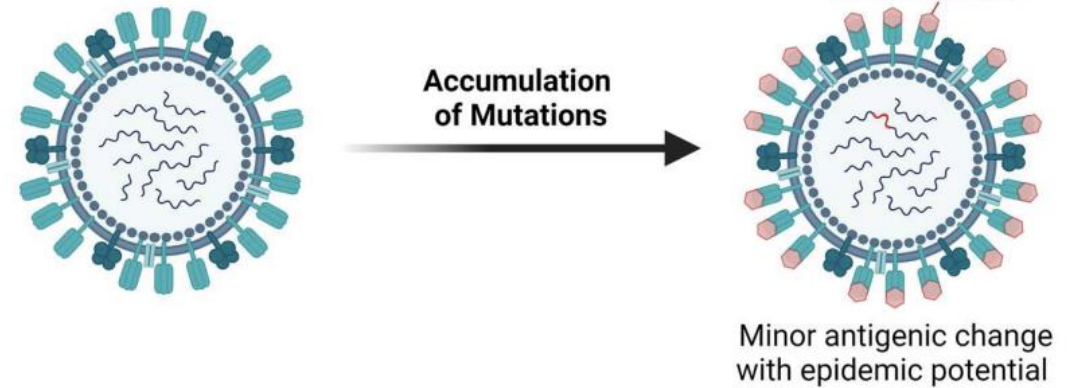
An example:

- The most striking effects of recombination type genetic changes occur in **influenza viruses**.
- Two types of genetic changes are observed in this virus group:
  - **Antigenic drift**
  - **Antigenic shift**

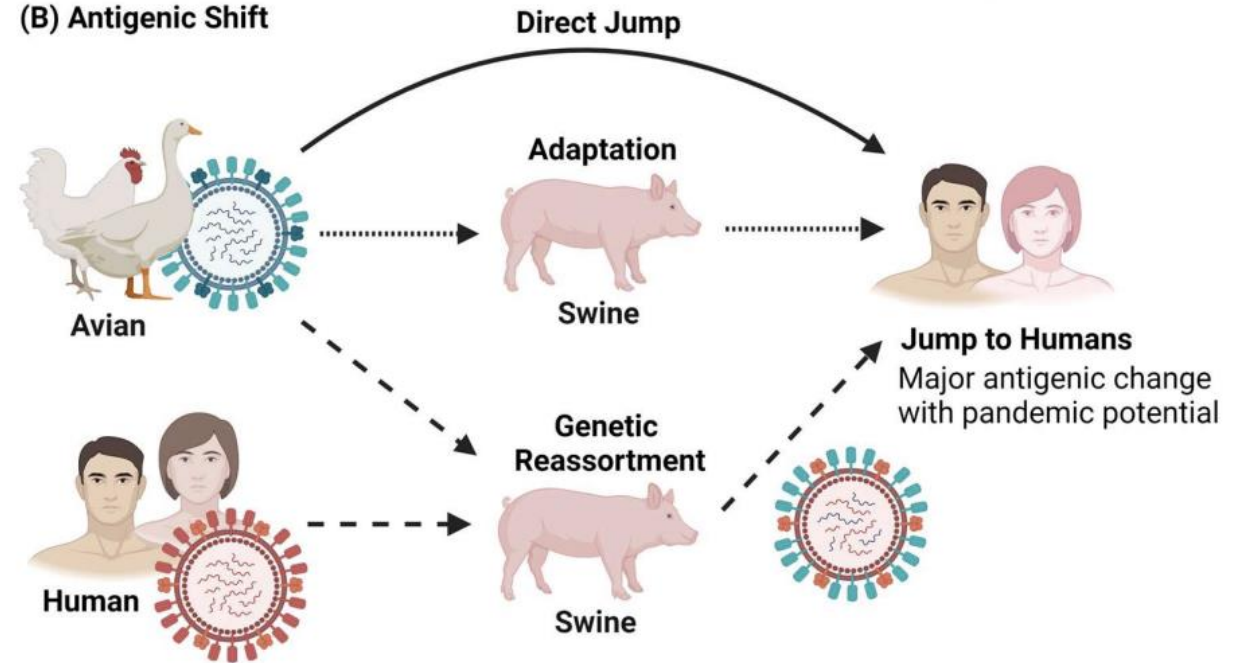


- **Antigenic drift** occurs when mutations accumulate over time, resulting in small-scale differences in the virus's antigens.
- **Antigenic shift** occurs when the genome segment of another influenza virus is transferred by reassortment to the viral genome, which has a segmented structure. As a result, a large-scale genetic change occurs and causes major changes in the antigenic structure of the virus.

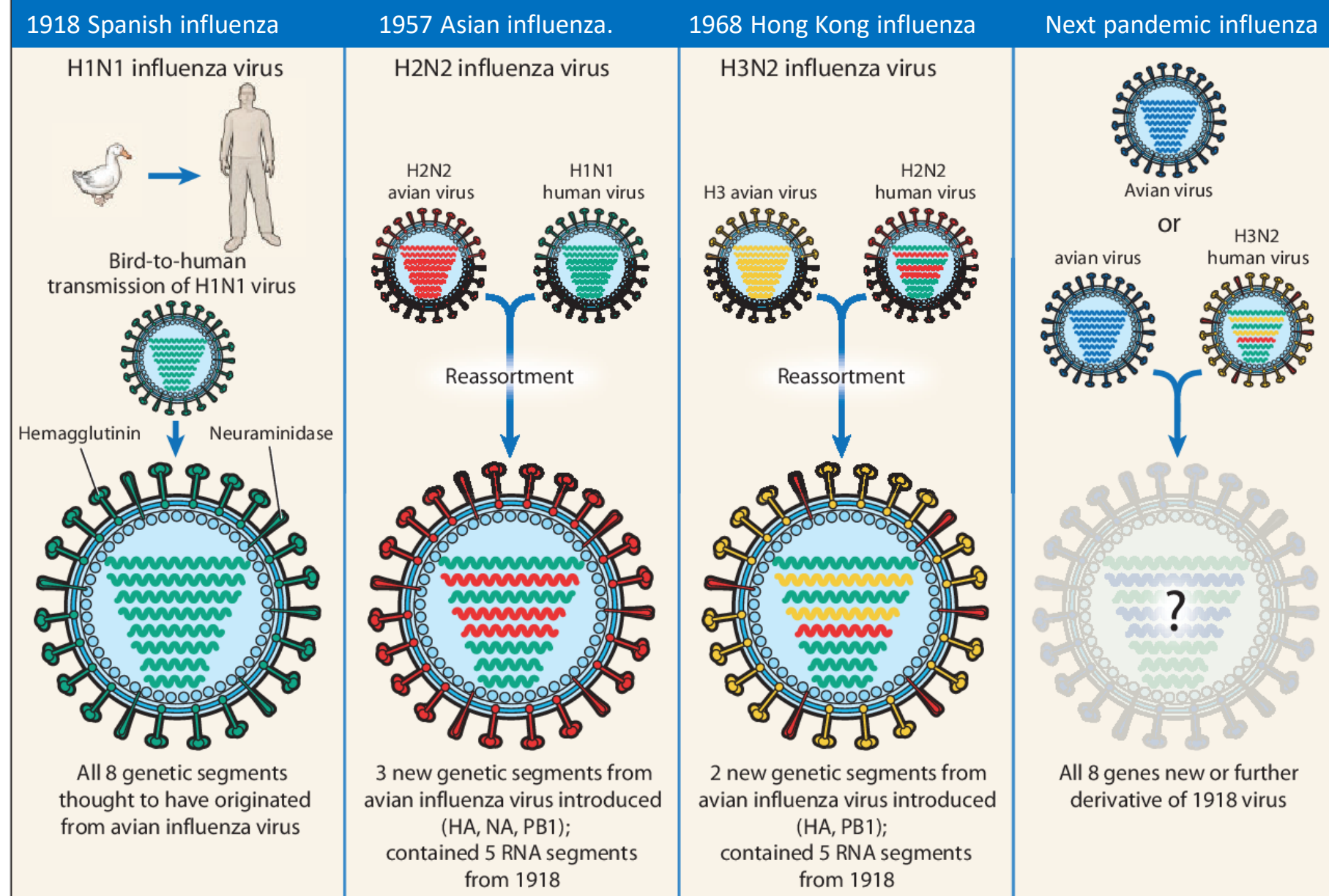
(A) Antigenic Drift



(B) Antigenic Shift



- Reassortant influenza viruses that emerge as a result of antigenic shift can cause major epidemics worldwide
- The most dramatic of such epidemics is the 1918 Spanish flu. It is known that more than 20 million people lost their lives due to the effect of the H1N1 (bird flu) virus, which was active in this epidemic.
- Later, the 1957 Asian flu and 1968 Hong Kong flu epidemics were caused by viruses containing similar genomic changes.
- It was determined that the Asian flu (1957) virus received 3 segments by reassortment from the H2N2 avian influenza virus circulating in wild ducks, while the Hong Kong flu (1968) virus received 2 segments from the avian influenza virus also found in ducks.



**FIGURE 1** Mechanism of genetic reassortment in influenza virus: origin of the 1957 and 1968 strains

Source: Belshe 2005

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