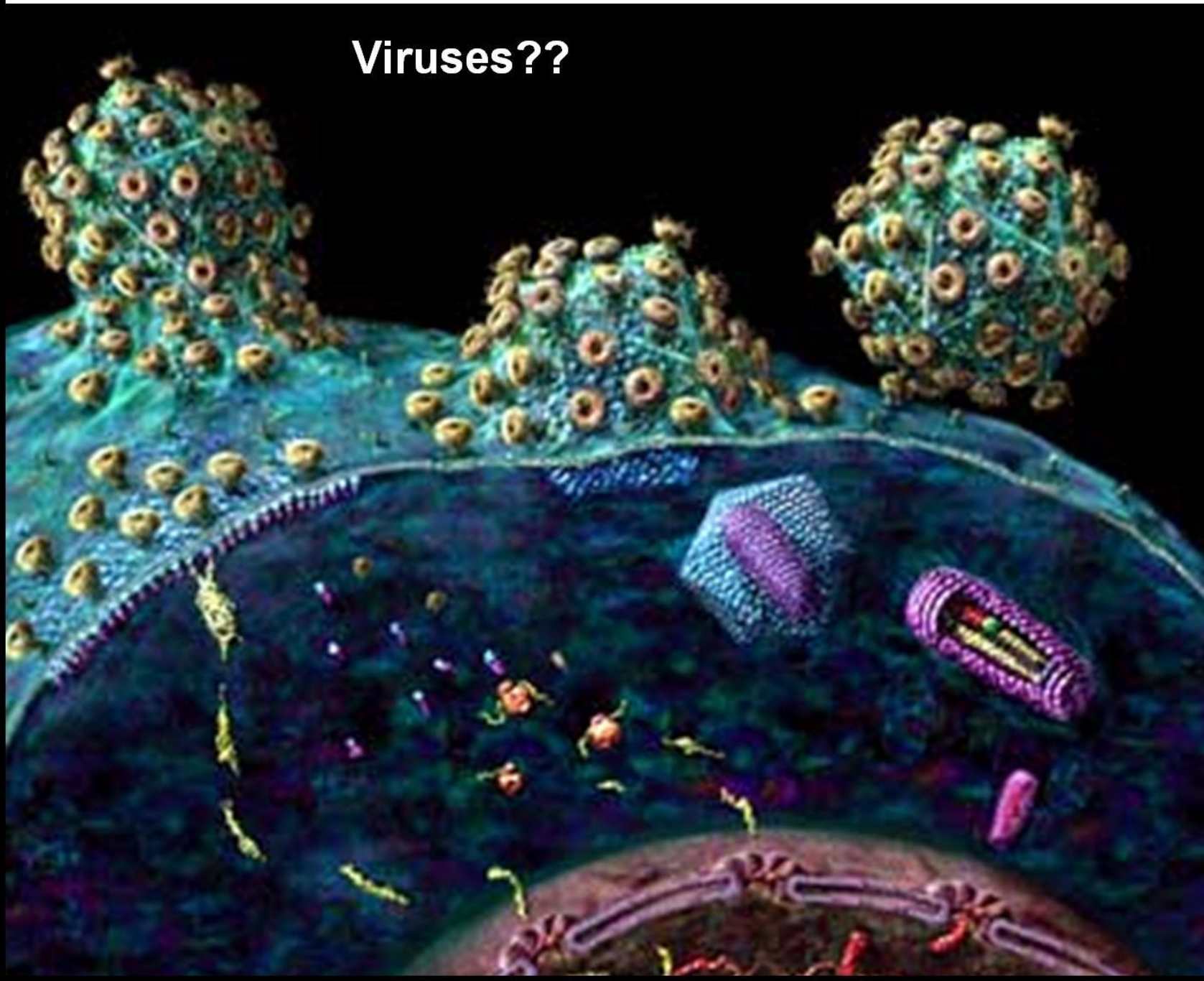
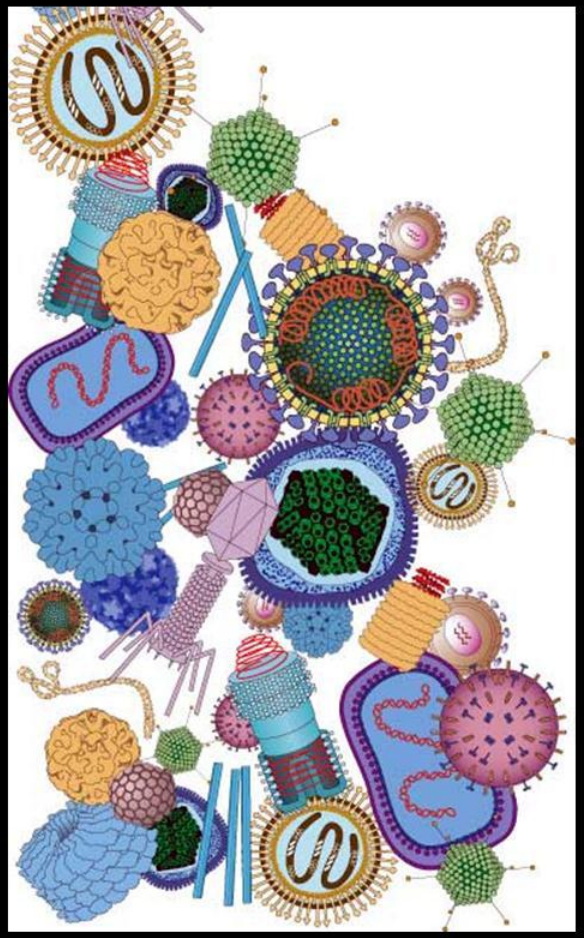
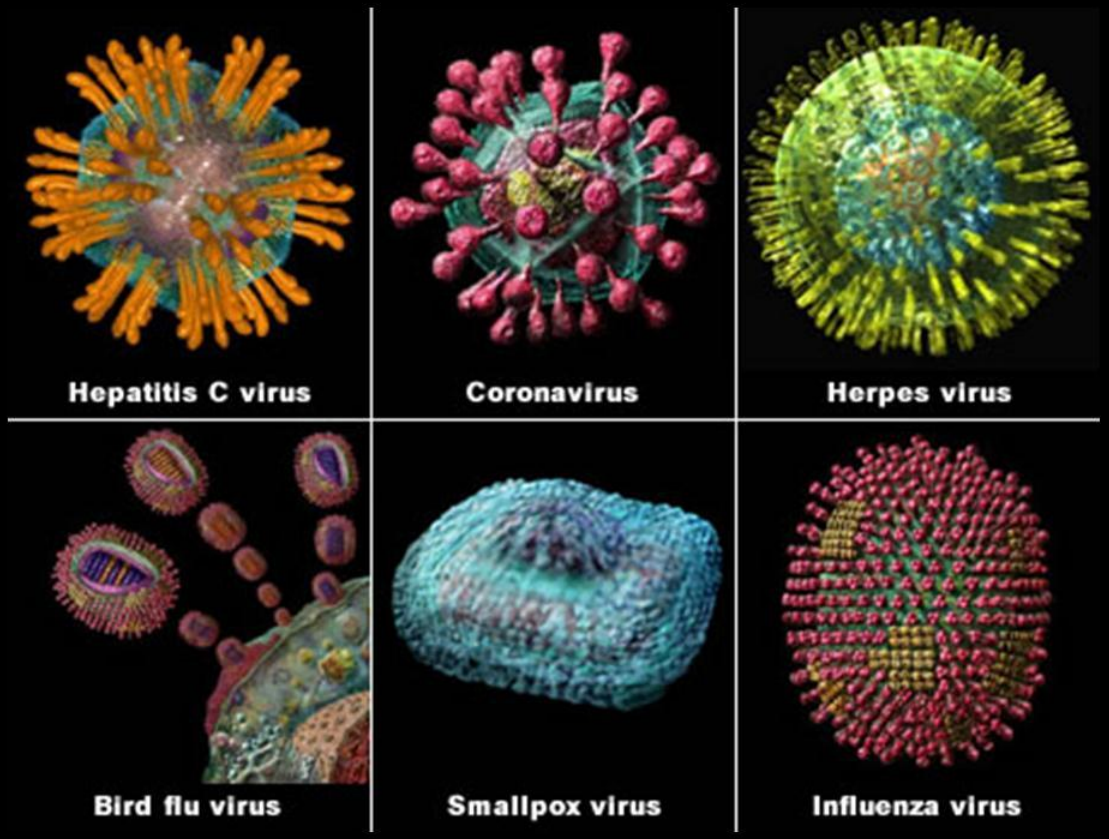
Viruses??



Viruses

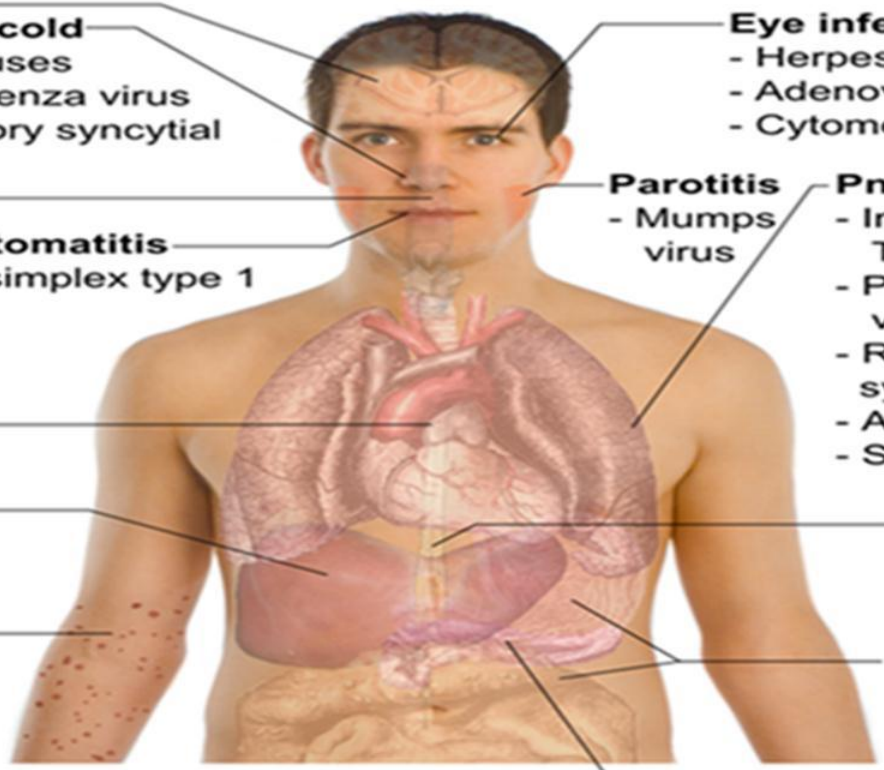



Hepatitis C virus
Coronavirus
Herpes virus
Bird flu virus
Smallpox virus
Influenza virus

Viruses

- Obligate intercellular organisms
- Affect virtually all life forms, including humans
- Antibiotics have no effect on viruses, but antiviral drugs have been developed to treat life-threatening infections
- Vaccines that produce lifelong immunity can prevent viral infections

Viral infections



Encephalitis/ meningitis
- JC virus
- Measles
- LCM virus
- Arbovirus
- Rabies

Common cold
- Rhinoviruses
- Parainfluenza virus
- Respiratory syncytial virus

Eye infections
- Herpes simplex virus
- Adenovirus
- Cytomegalovirus

Parotitis
- Mumps virus

Pneumonia
- Influenza virus, Types A and B
- Parainfluenza virus
- Respiratory syncytial virus
- Adenovirus
- SARS coronavirus

Pharyngitis
- Adenovirus
- Epstein-Barr virus
- Cytomegalovirus

Gingivostomatitis
- Herpes simplex type 1

Cardiovascular
- Coxsackie B virus

Hepatitis
- Hepatitis virus types A, B, C, D, E

Myelitis
- Poliovirus
- HTLV-I

Skin infections
- Varicella zoster virus
- Human herpesvirus 6
- Smallpox
- Molluscum contagiosum
- Human papillomavirus
- Parvovirus B19
- Rubella
- Measles
- Coxsackie A virus

Gastroenteritis
- Adenovirus
- Rotavirus
- Norovirus
- Astrovirus
- Coronavirus

Sexually transmitted diseases
- Herpes simplex type 2
- Human papillomavirus
- HIV

Pancreatitis
- Coxsackie B virus

Source: Wikipedia

Viral Infections

- Viruses in which the immune response eliminates them from the body (e.g. influenza and polio viruses). or

- Viruses can persist despite the host immune response.

Persistent Viral Infections

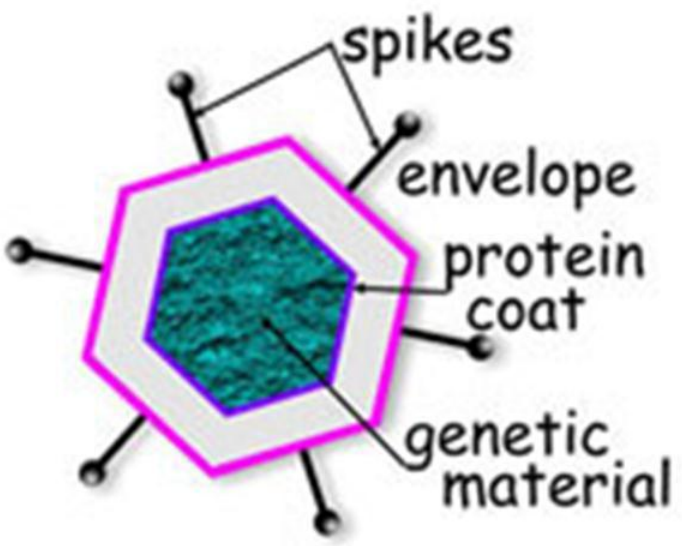
Chronic carrier infections refer to people who produce virus long periods of time and can serve as a source of infection for others (HCV).

Latent infections are those infections can be reactivated at a subsequent time (Herpes).

Slow virus infections are those infections with a long incubation period.

Virus Structure

Viruses are particles composed of an internal core containing either DNA or RNA (but not both) covered by a protective protein coat. Some viruses have an outer lipoprotein membrane, called an envelope, external to the coat.



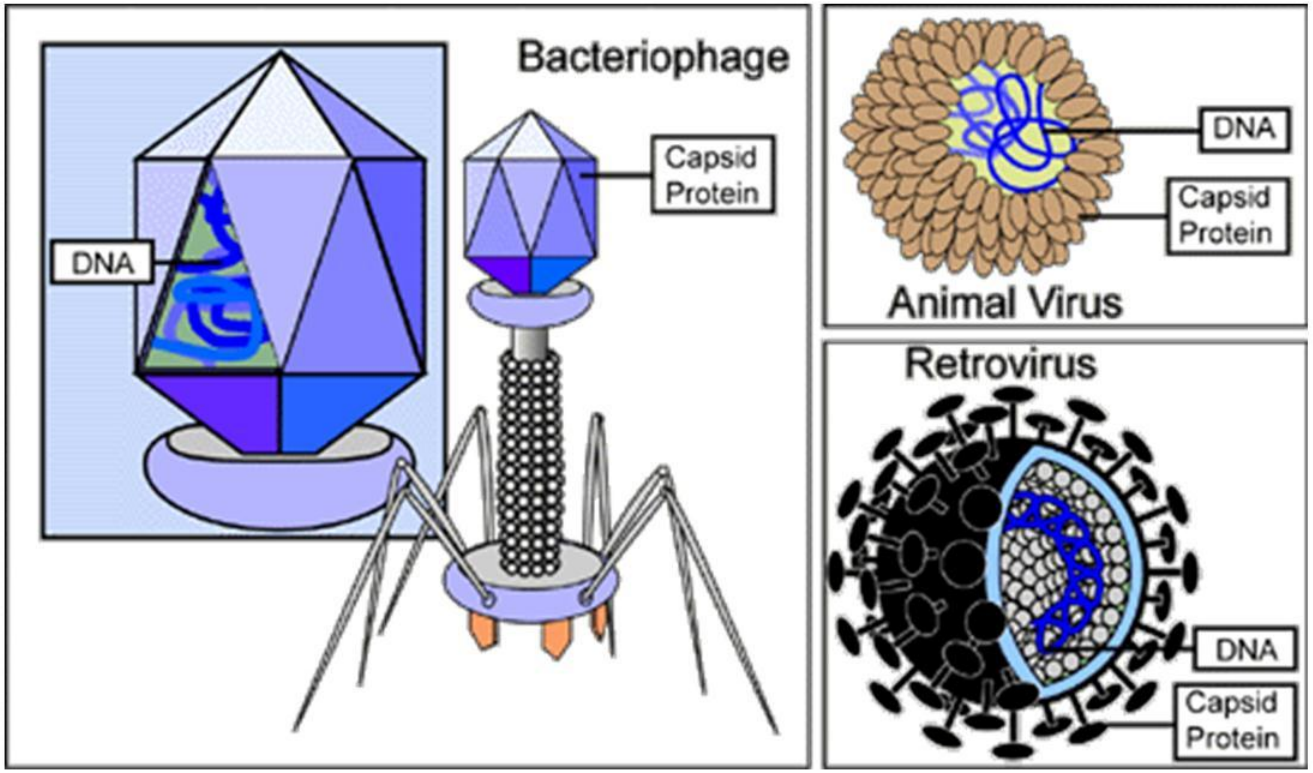
VIRUS STRUCTURE

Genetic Material
Viruses can have one of two kinds of genetic material, DNA or RNA. The latter are named retroviruses.

Membrane Envelope and Capsid
a layer of fatty acids coats many viruses. It is usually derived from the membrane of the host cell.

Ligands
proteins that stick out of the surface of the virus. They act as a key to recognize the cell to be infected and invade it.

Types of Viruses



Virus Structure

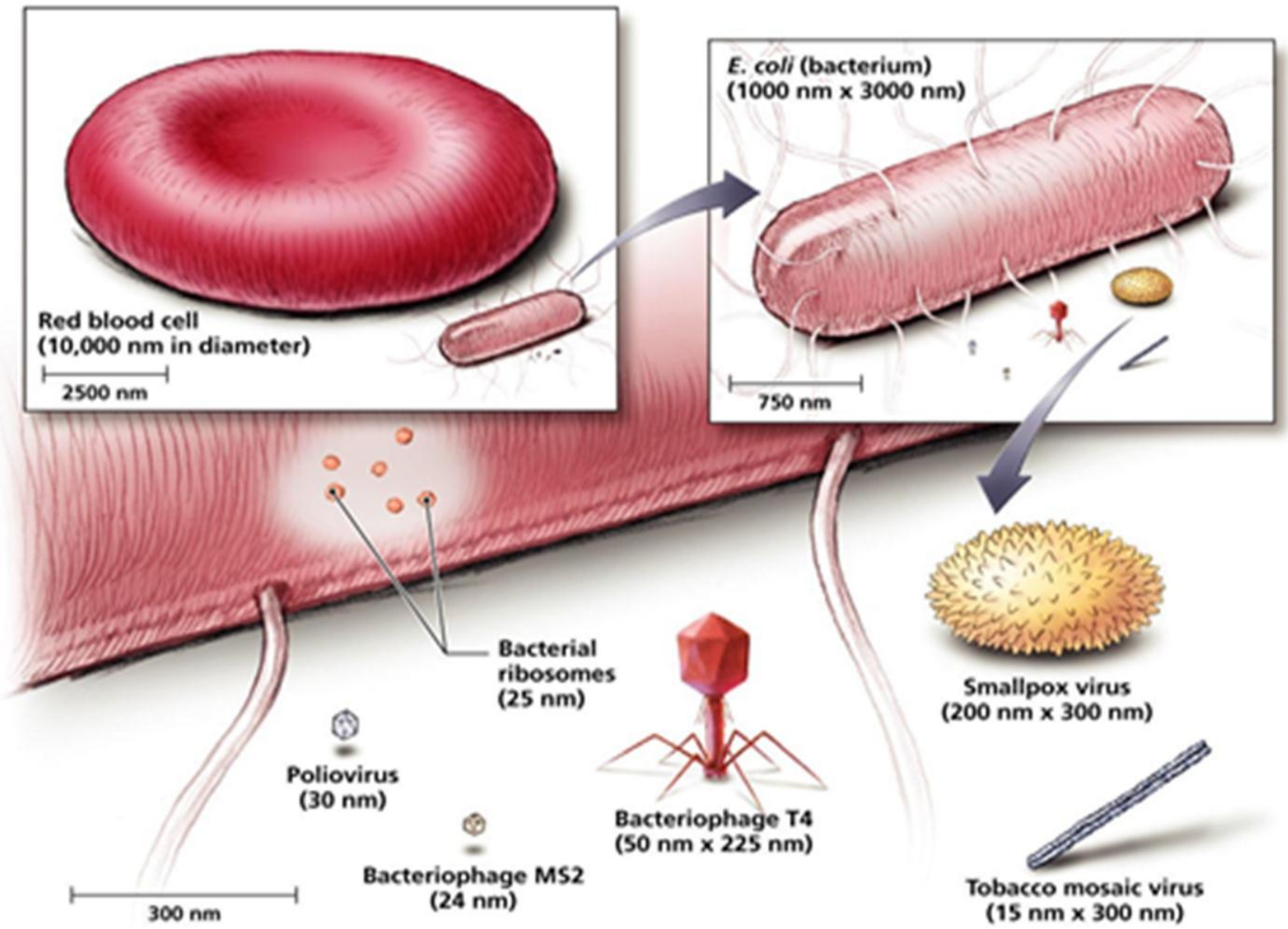
- Size & Shape
- Viral Nucleic Acids
- Viral Capsid and Symmetry
- Viral Proteins

Size and Shape

Viruses vary in size 20 to 300 nm in diameter.

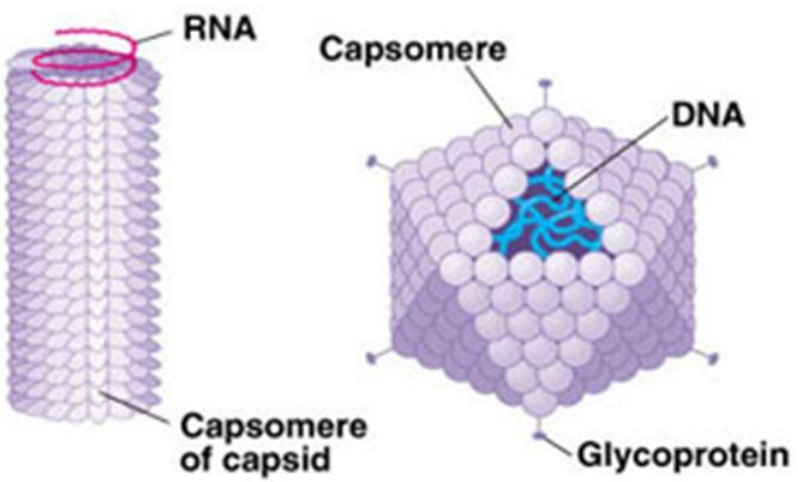
The shape of virus particles is determined by the arrangement of the repeating subunits that form the protein coat (capsid) of the virus.

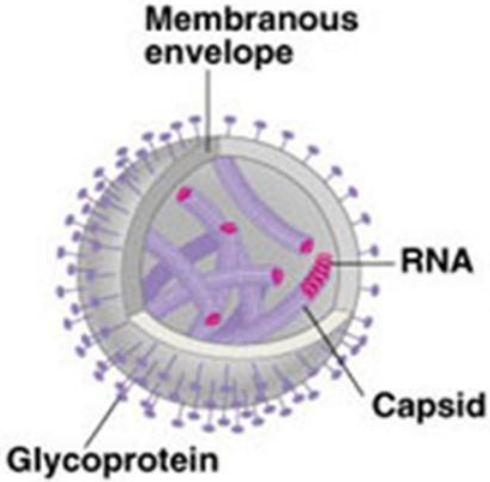
Most viruses appear as spheres or rods in the electron microscope. In addition to these forms, bacterial viruses can have very complex shapes.

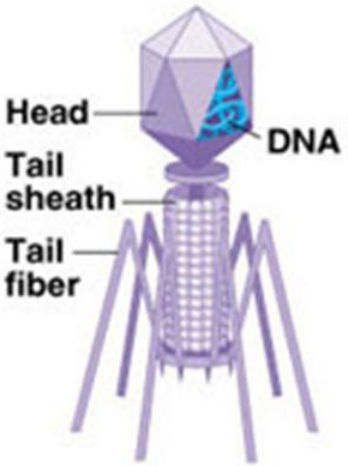

Red blood cell
(10,000 nm in diameter)
2500 nm
E. coli (bacterium)
(1000 nm x 3000 nm)
750 nm
Bacterial ribosomes
(25 nm)
Poliovirus
(30 nm)
Bacteriophage MS2
(24 nm)
300 nm
Bacteriophage T4
(50 nm x 225 nm)
Smallpox virus
(200 nm x 300 nm)
Tobacco mosaic virus
(15 nm x 300 nm)

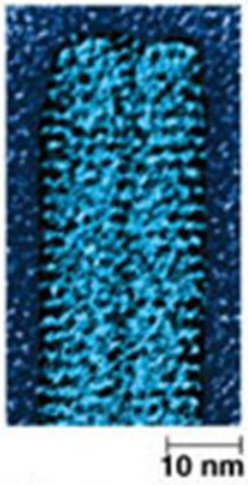
Viral Capsid and Symmetry

- The protein coat (capsid), made up of subunits called capsomers.
- The structure of the nucleic acid genome and the capsid protein is called the nucleocapsid.
- The arrangement of capsomers gives the virus structure its geometric symmetry.
- Three forms of symmetry either helical, icosahedral or complex.

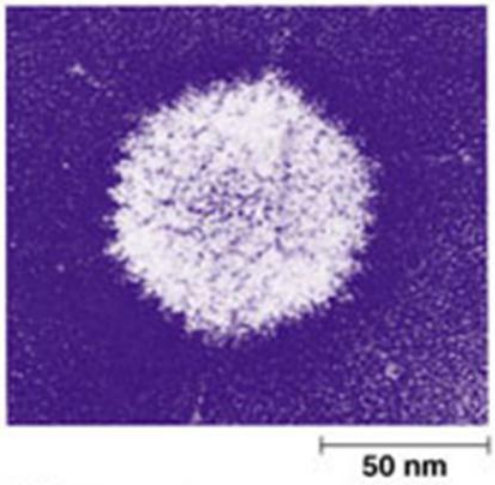






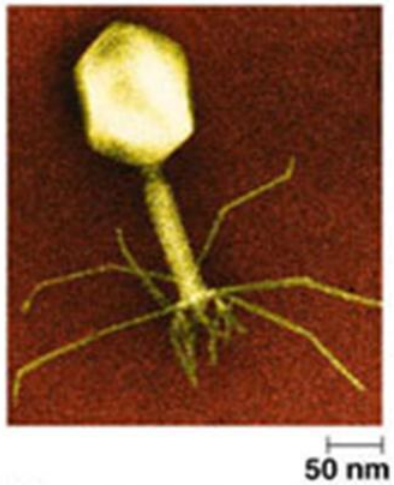


(a) Tobacco mosaic virus



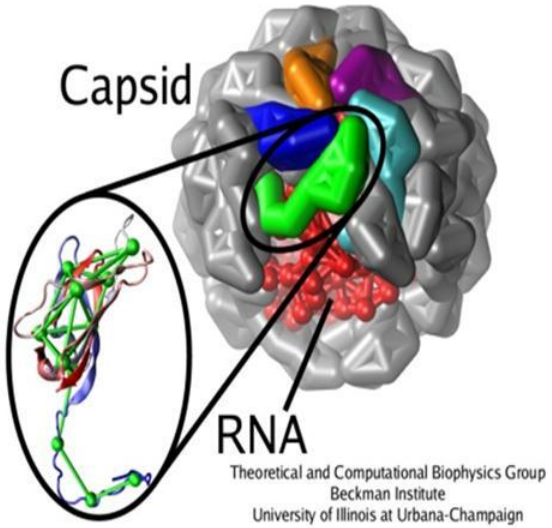
(b) Adenoviruses

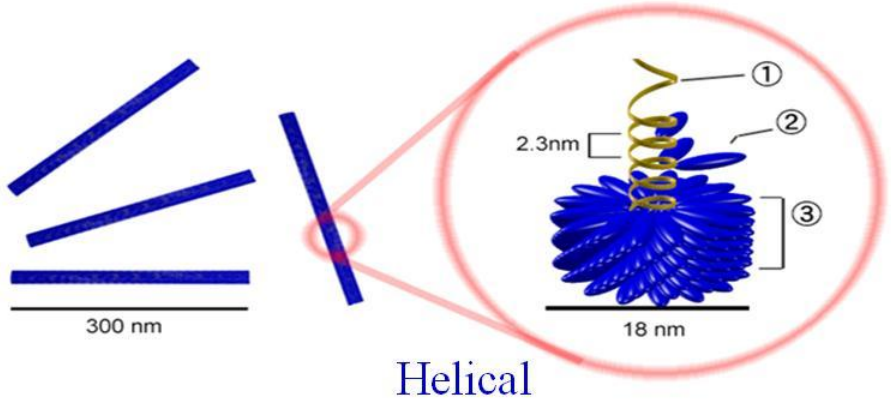
(c) Influenza viruses



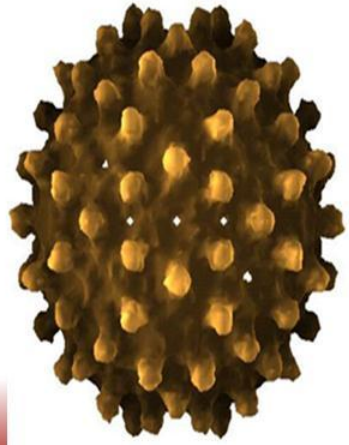
(d) Bacteriophage T4

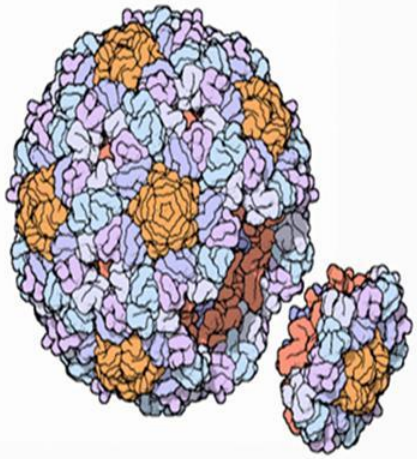
Viral Capsid and Symmetry

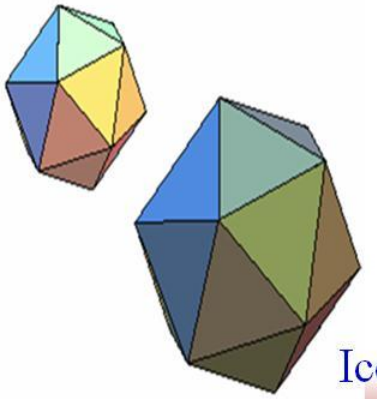




Helical







Icosahedral

Viral Nucleic Acids

- Single or double- stranded DNA or single or double- stranded RNA.
- The nucleic acid can be either linear or circular.

The Outer Capsid Proteins

- Protect the genetic material,
- Mediate the attachment of the virus to specific receptors on the host cell surface,
- The major determinant of the species and organ specificity of the virus,
- Important antigens that induce neutralizing antibody and activate cytotoxic T cells to kill virus- infected cells.

The Internal Viral Proteins

- Structural (e.g. the capsid proteins of the enveloped viruses),
- Enzymes. (e.g. the polymerases that synthesize the viral mRNA).

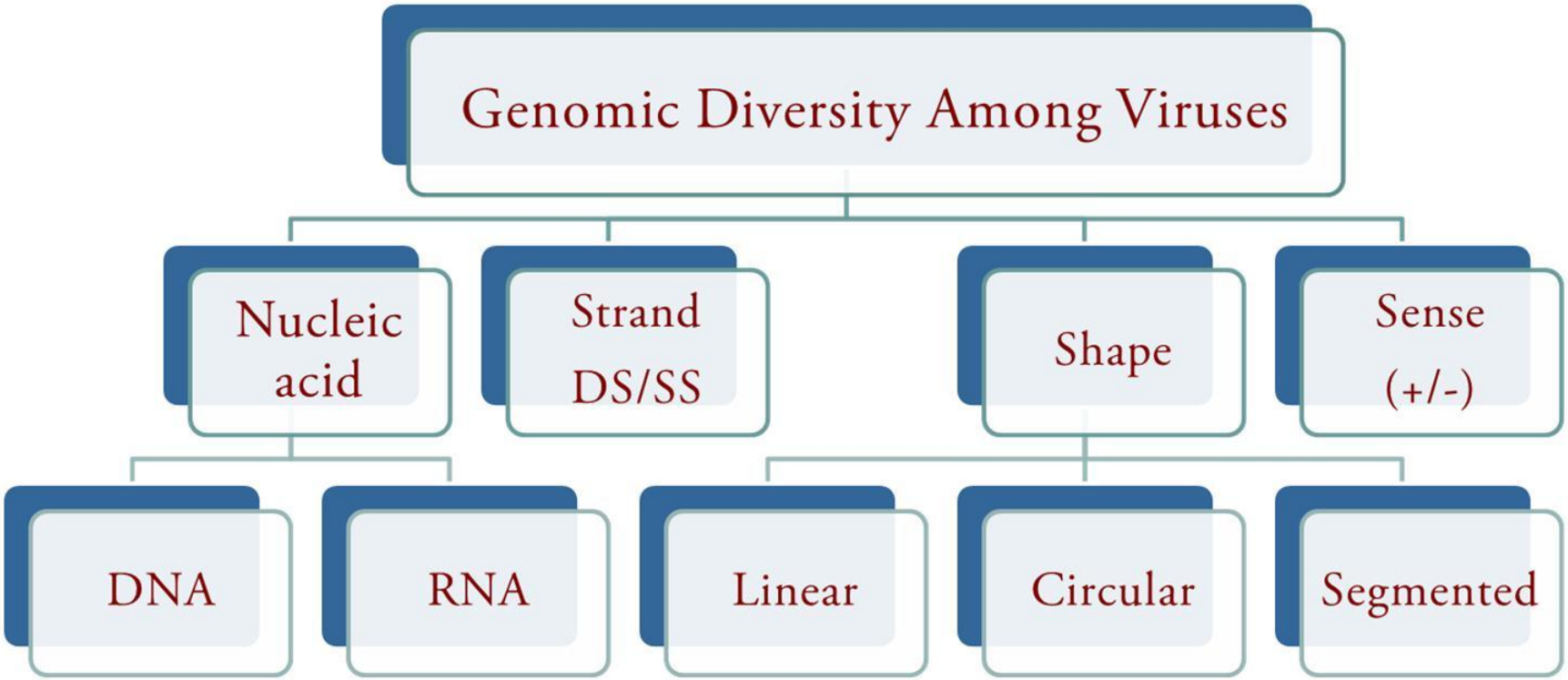
Viral Envelope

- Some virus has an outer envelope.
- Lipoprotein membrane composed of lipid derived from host cell membrane and protein that is virus specific.
- Acquired as the virus exits from the cell in a process called budding.
- Derived from the cell's outer membrane, except for herpes viruses acquired from the cell's nuclear membrane.

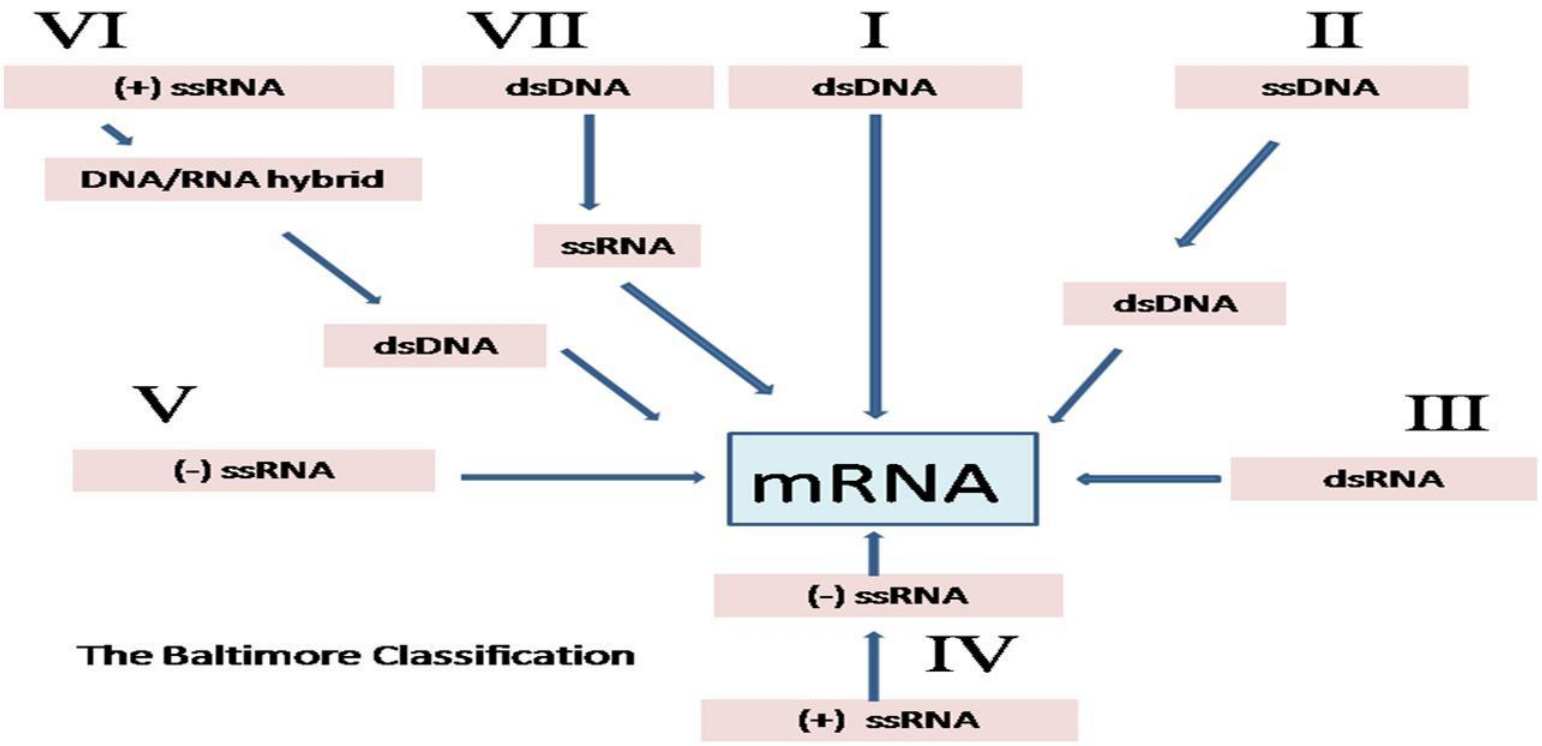
Enveloped Virus/ Non Enveloped Virus

Enveloped Virus more sensitive to heat, drying, detergents and lipid solvents such as alcohol and ether than non enveloped virus.

Most often enveloped viruses transmitted by direct contact via blood and body fluids; others transmitted by respiratory droplet. Most often non enveloped viruses transmitted by indirect means such as feco-oral route.

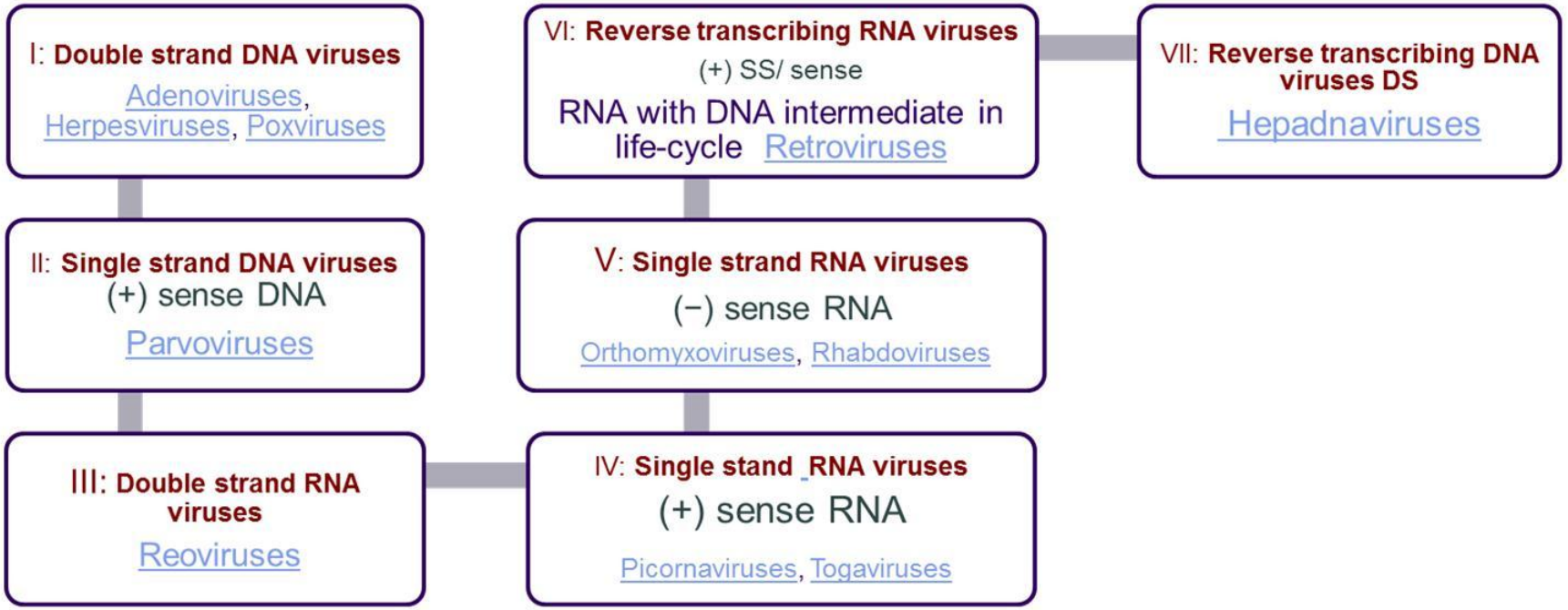

Genomic Diversity Among Viruses
Nucleic acid
Strand DS/SS
Shape
Sense (+/-)
DNA
RNA
Linear
Circular
Segmented

The Baltimore Classification

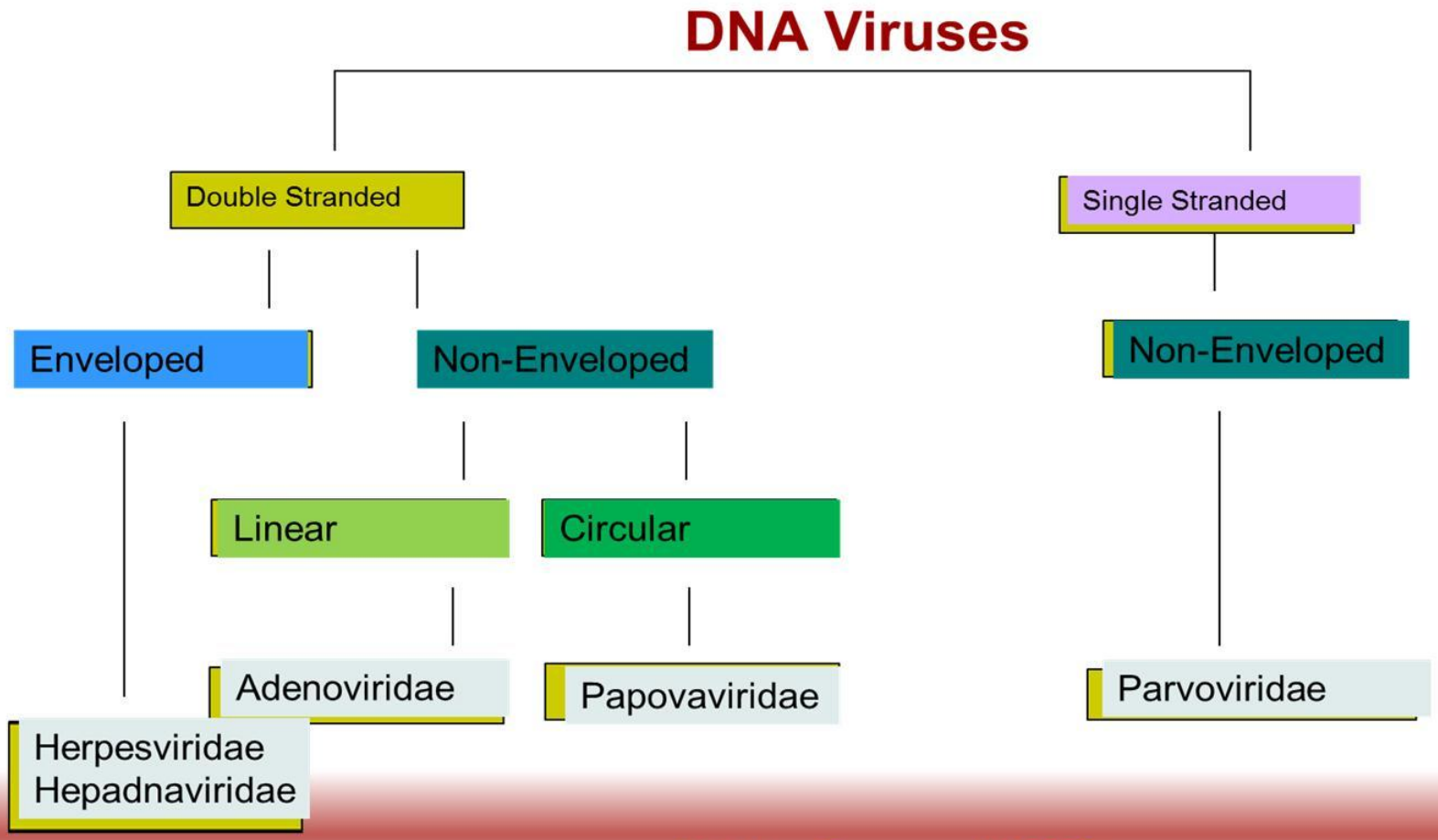


Source: Wikipedia

The Baltimore Classification



DNA Viruses


DNA Viruses
Double Stranded
Single Stranded
Enveloped
Non-Enveloped
Non-Enveloped
Linear
Circular
Adenoviridae
Papovaviridae
Parvoviridae
Herpesviridae
Hepadnaviridae

RNA Viruses

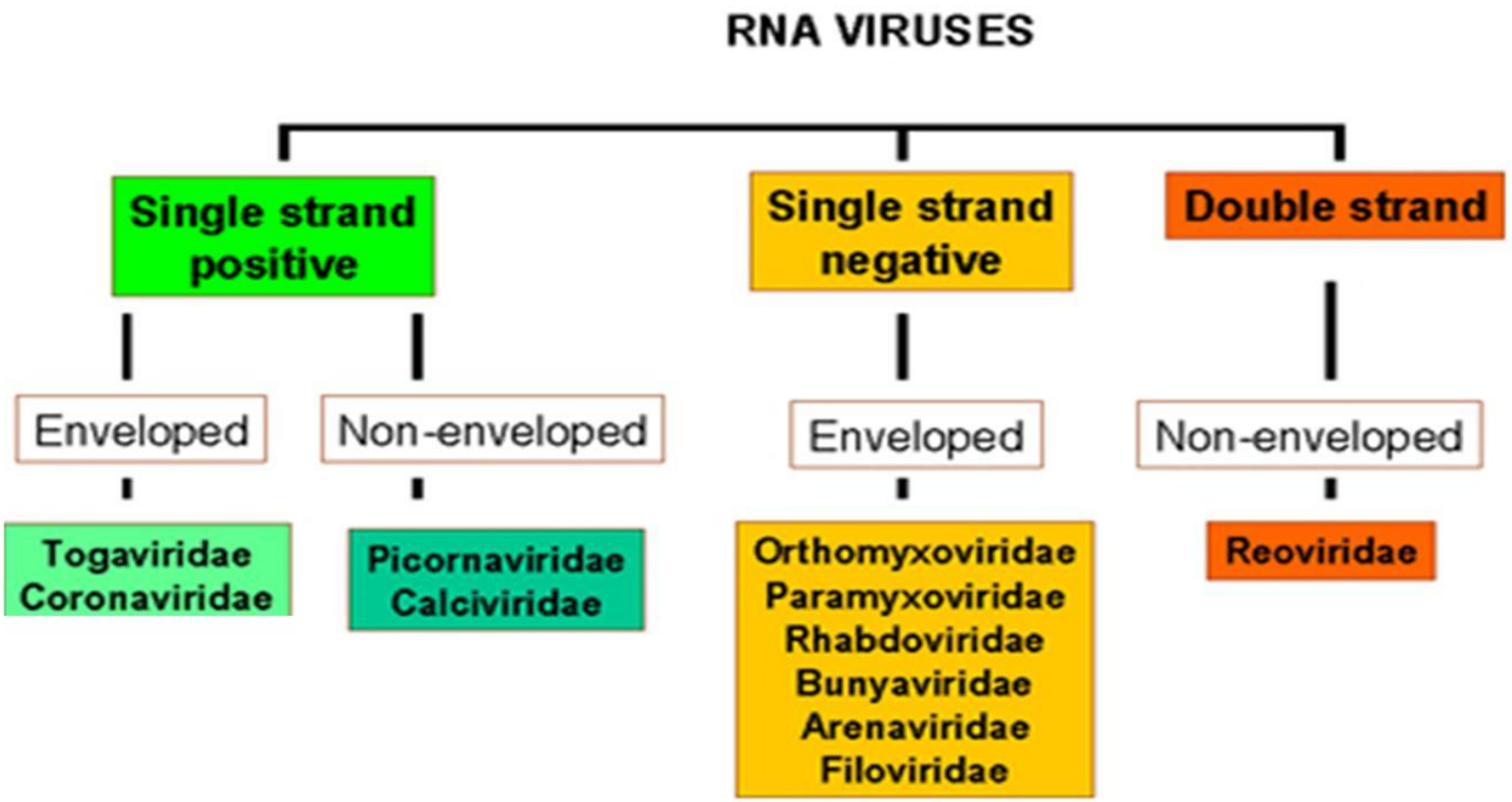
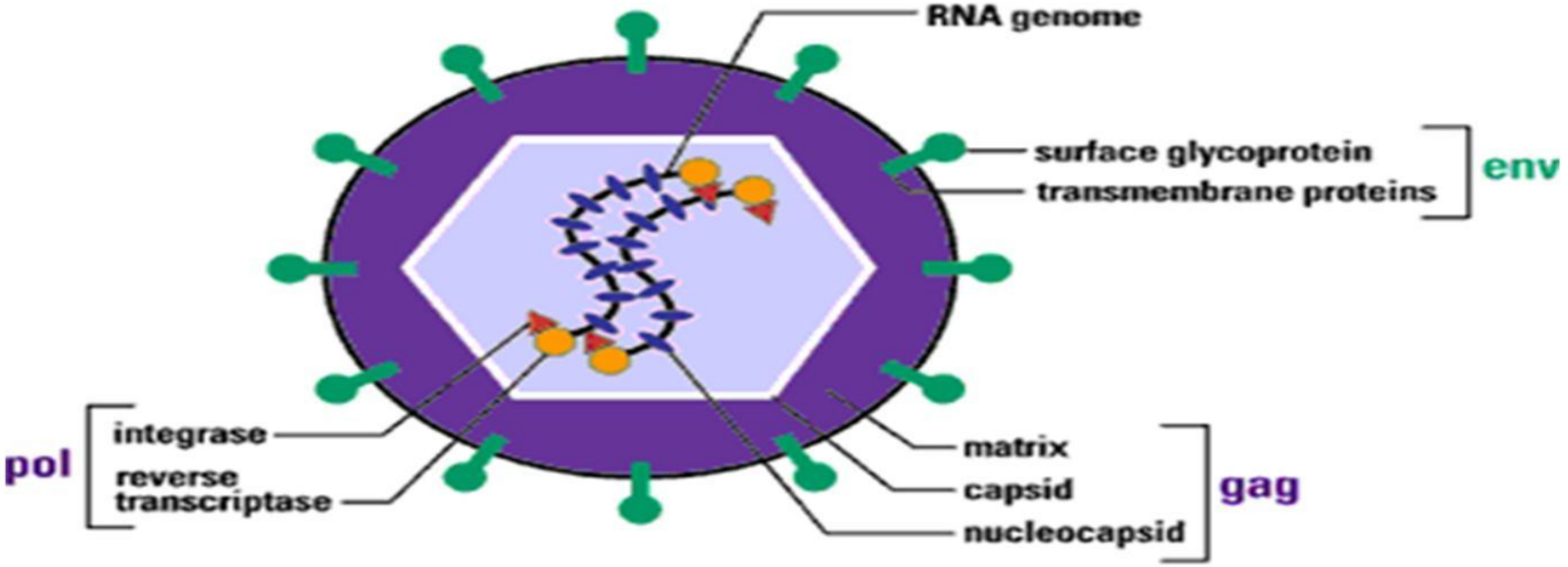
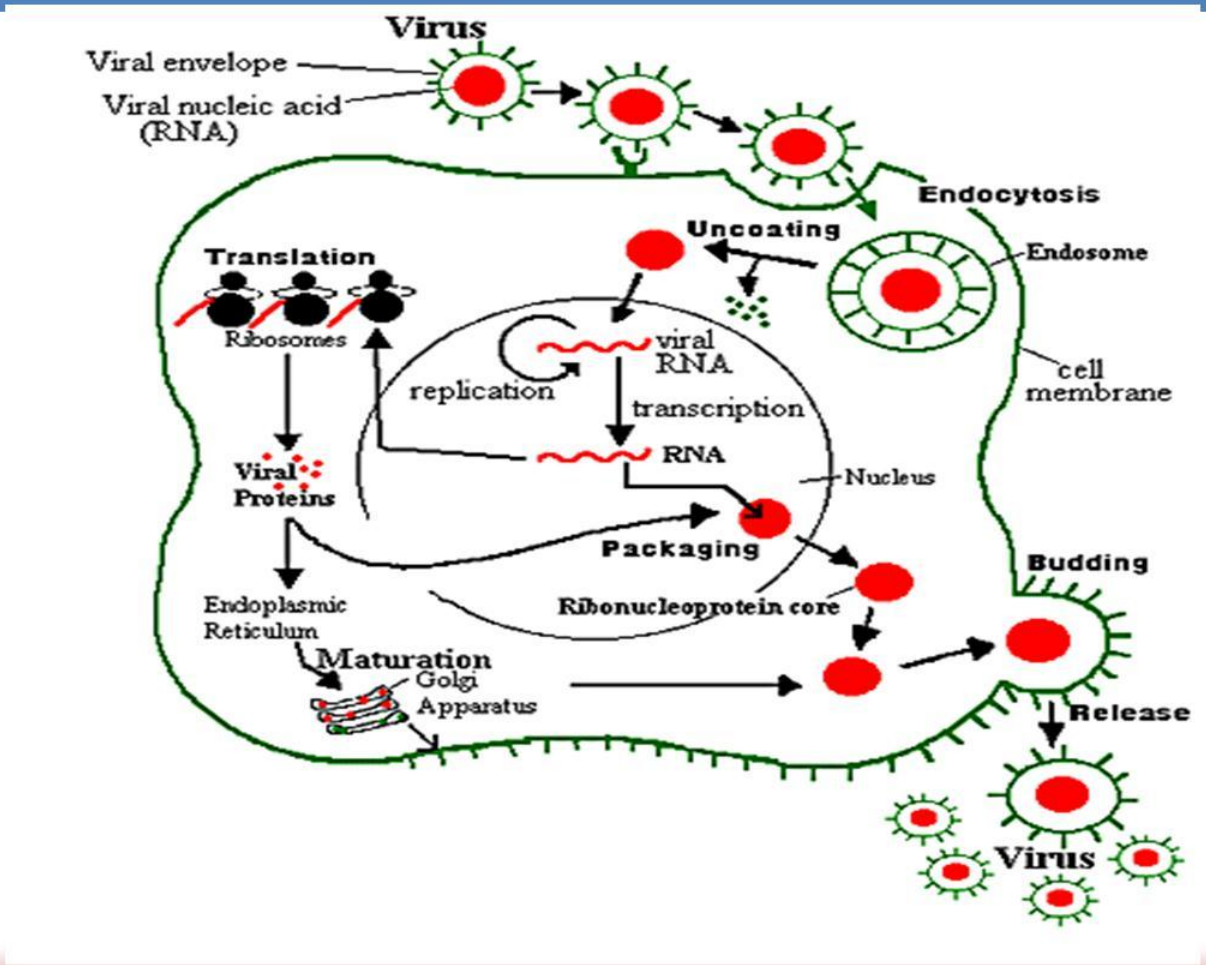

RNA VIRUSES
Single strand positive
Single strand negative
Double strand
Enveloped
Non-enveloped
Enveloped
Non-enveloped
Togaviridae
Coronaviridae
Picornaviridae
Calciviridae
Orthomyxoviridae
Paramyxoviridae
Rhabdoviridae
Bunyaviridae
Arenaviridae
Filoviridae
Reoviridae

Diagram of a Generalized Retrovirus



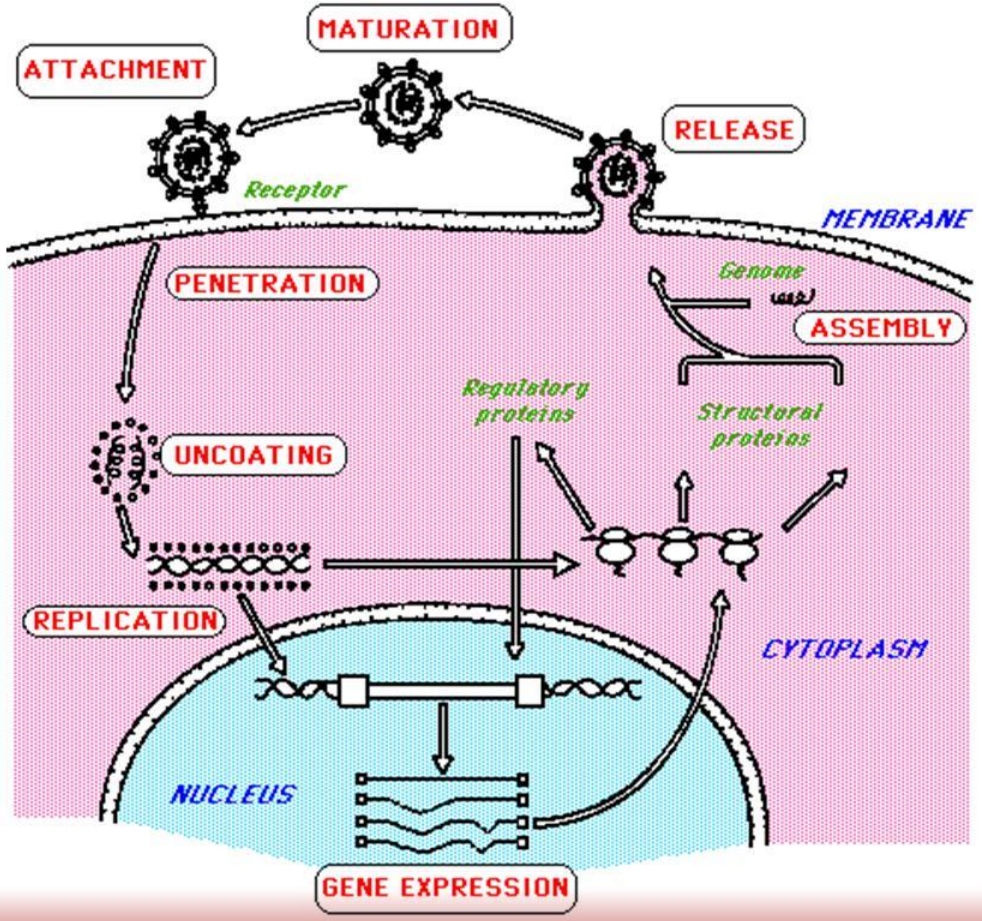
Virus Replication



Virus Life Cycle

Virus Life Cycle

The life cycle of viruses differs greatly between species but there are six basic stages:



Virus Life Cycle

Attachment is a specific binding between viral capsid proteins and specific receptors on the host cellular surface,

Penetration; viruses enter the host cell through receptor- mediated endocytosis or membrane fusion,

Uncoating; the viral capsid is degraded by viral enzymes or host enzymes thus releasing the viral genomic nucleic acid,

Replication involves the synthesis of viral messenger RNA (mRNA) for viruses except positive sense RNA viruses,

Assembly; viral protein synthesis and assembly of viral proteins and viral genome replication,

Release viruses are released from the host cell by lysis. Enveloped viruses (e.g., HIV) typically are released from the host cell by budding.

Virus Replication

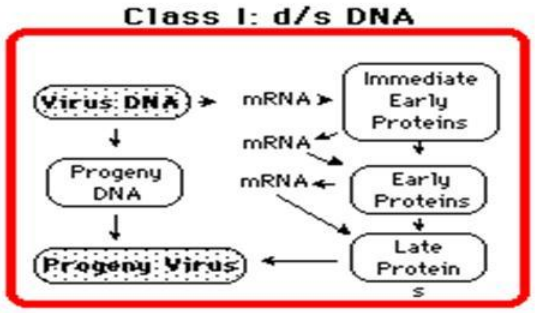
DNA viruses

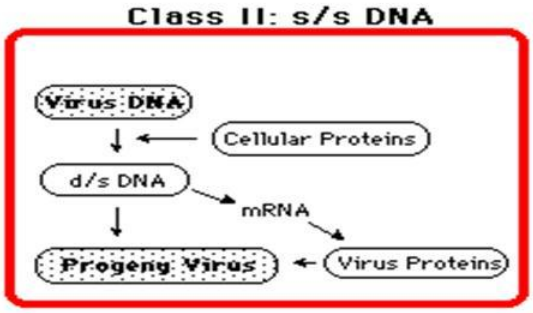
The genome replication of most DNA viruses takes place in the cell's nucleus.

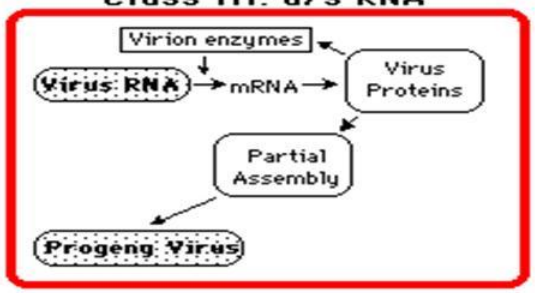
RNA viruses

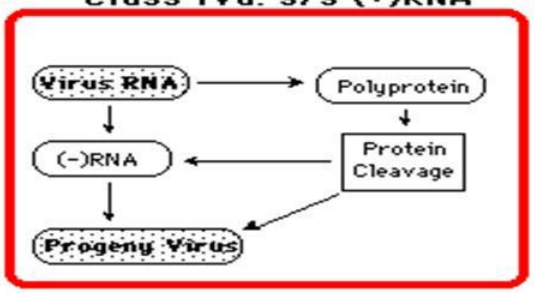
Replication usually takes place in the cytoplasm. RNA viruses can be placed into about four different groups depending on their modes of replication. RNA viruses use their own RNA replicase enzymes to create copies of their genomes.

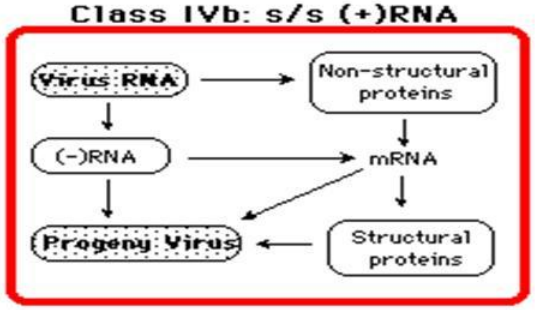
Reverse transcribing viruses replicate using reverse transcription.

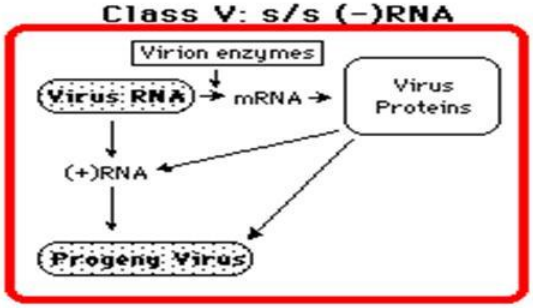

Class I: d/s DNA
Virus DNA
mRNA
Immediate Early Proteins
mRNA
Progeny DNA
mRNA
Early Proteins
Late Proteins
Progeny Virus

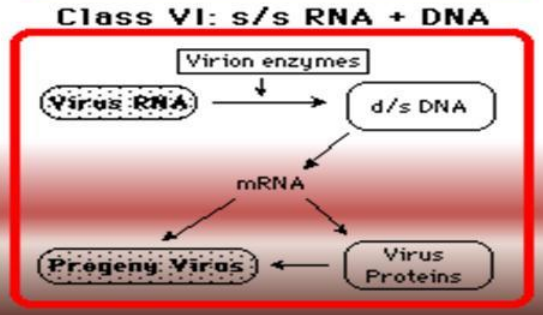

Class II: s/s DNA
Virus DNA
Cellular Proteins
d/s DNA
mRNA
Progeny Virus
Virus Proteins

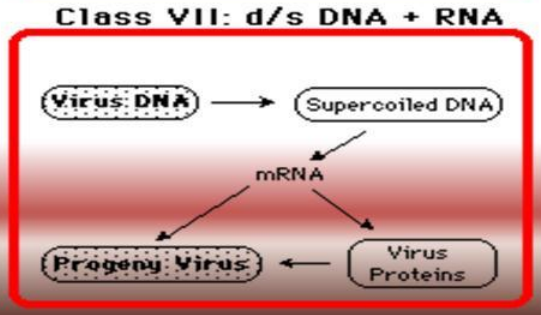

Class III: d/s RNA
Virion enzymes
Virus RNA
mRNA
Virus Proteins
Partial Assembly
Progeny Virus

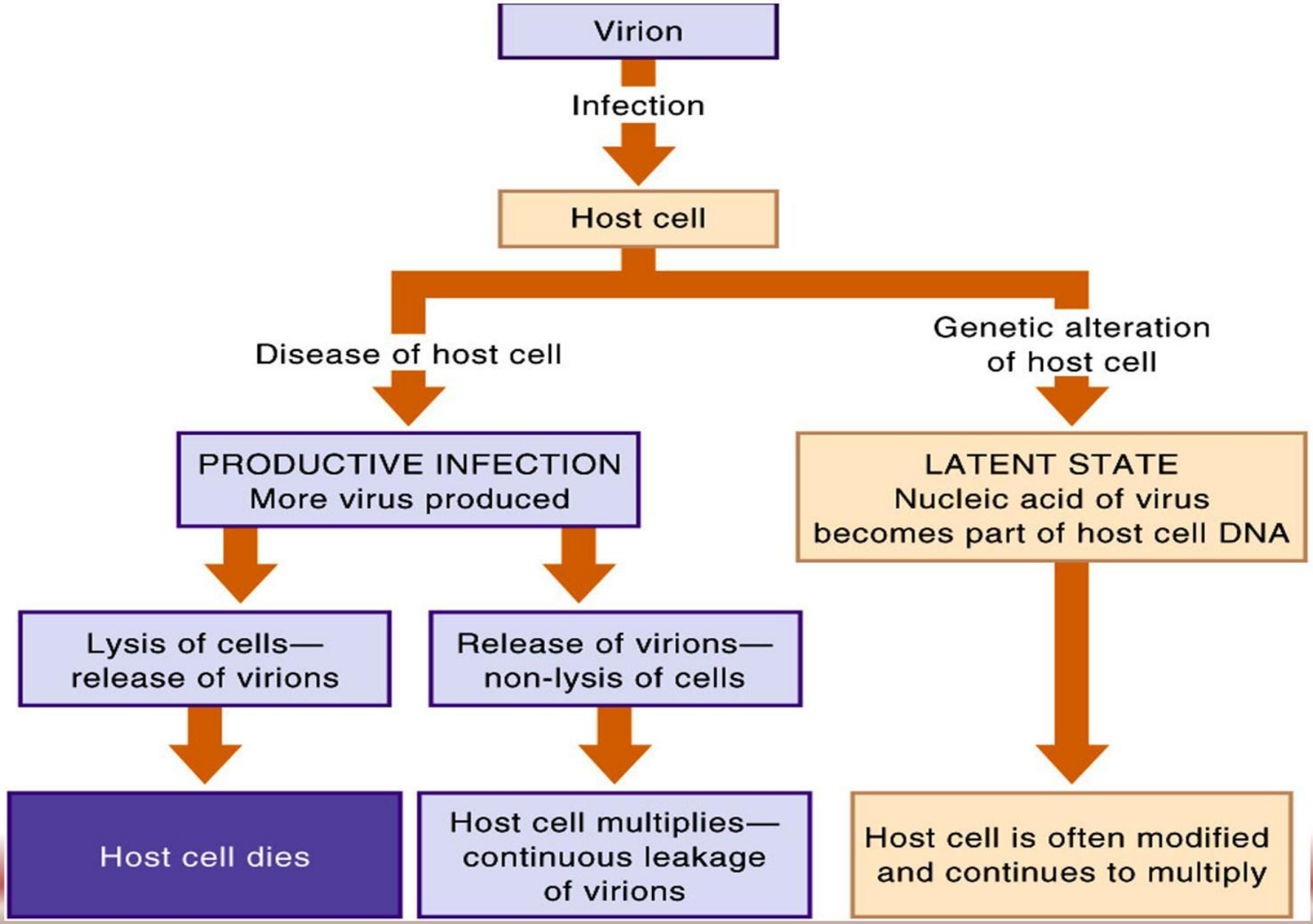

Class IVa: s/s (+)RNA
Virus RNA
Polyprotein
(-)RNA
Protein Cleavage
Progeny Virus


Class IVb: s/s (+)RNA
Virus RNA
Non-structural proteins
(-)RNA
mRNA
Progeny Virus
Structural proteins


Class V: s/s (-)RNA
Virion enzymes
Virus RNA
mRNA
Virus Proteins
(+)RNA
Progeny Virus

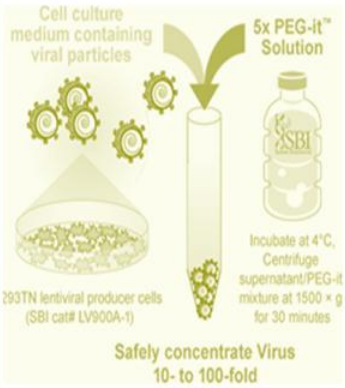

Class VI: s/s RNA + DNA
Virion enzymes
Virus RNA
d/s DNA
mRNA
Progeny Virus
Virus Proteins


Class VII: d/s DNA + RNA
Virus DNA
Supercoiled DNA
mRNA
Progeny Virus
Virus Proteins


Virion
Infection
Host cell
Disease of host cell
Genetic alteration of host cell
PRODUCTIVE INFECTION
More virus produced
LATENT STATE
Nucleic acid of virus becomes part of host cell DNA
Lysis of cells—release of virions
Release of virions—non-lysis of cells
Host cell dies
Host cell multiplies—continuous leakage of virions
Host cell is often modified and continues to multiply

Laboratory Diagnosis

- Identification of the virus in cell culture
- Microscopic identification directly in the specimen
- Serologic procedures to detect a rise in antibody titer or the presence of IgM antibody
- Detection of viral antigen in blood or body fluids
- Detection of viral nucleic acids in blood or patient's cells



Identification of the virus in cell culture;

Microscopic identification directly in the specimen;

Serologic procedures to detect a rise in antibody titer or the presence of Ig M antibody;

Detection of viral antigen in blood or body fluids;

Detection of viral nucleic acids in blood or patients cells.

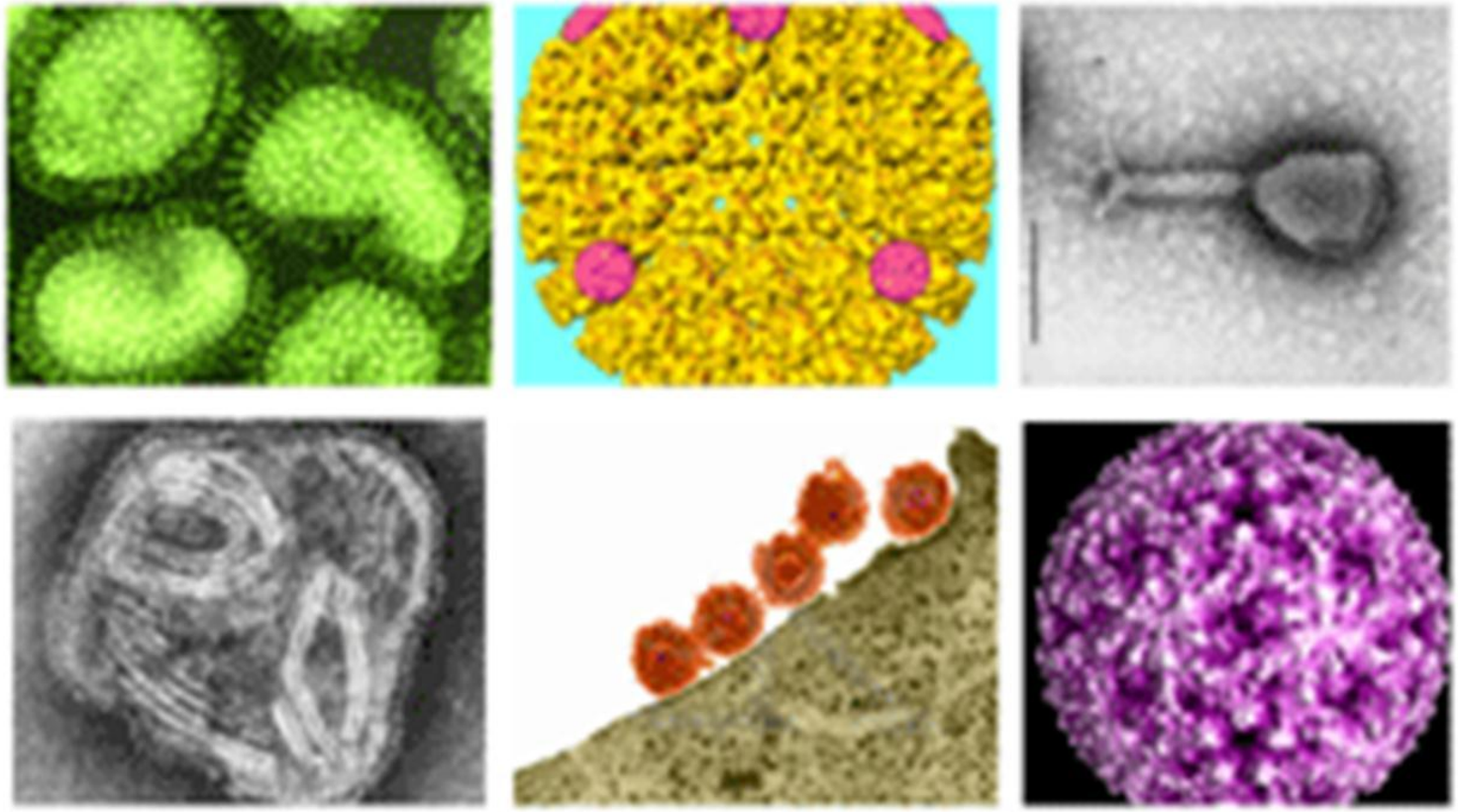
Virus identification in cell culture

- Cytopathic (CPE) effect
- Hemadsorption/ Interference
- Complement fixation
- Hemagglutination inhibition
- Neutralization, Other procedure
- Fluorescent antibody assay
- ELISA
- RIA,……

Microscopic Identification

- Electron Microscopy/ Immune electron microscopy; it detects virus particles, which can be characterized by their size and morphology.
- Light microscopy; reveal characteristic inclusion bodies or multinucleated giant cell.
- UV microscopy is used for fluorescent antibody staining of the virus in infected cells.

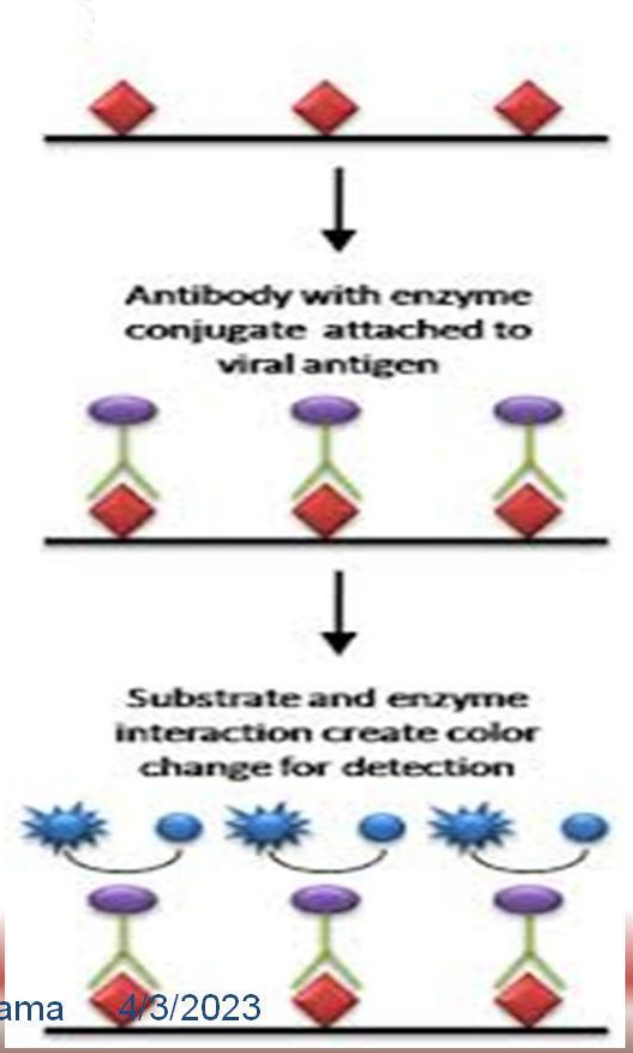
Microscopic Identification



Detection of Viral Antigen

Antigen detection

- Immunofluorescence
- ELISA
- etc……



Serology

- Antibody is detected in patient's serum by reaction with known virus preparation (antigen); ELISA, RIA,..
- The presence of IgM antibody can be used to diagnose current infection.
- The presence of Ig G antibody cannot be used to diagnose current infection. Rise in antibody titer that is 4 fold or greater in the convalescent serum sample compared to the acute sample can be used to make a diagnosis.

Molecular Diagnostic Methods

- Detect non culturable agents such as human papilloma virus, human parvovirus or difficult to culture, including enteric adenovirus, some coxsackie viruses.
- Viruses that are present in low numbers, CMV in transplanted organs.
- Detect infections when a viable virus cannot be obtained (latent viral infection or viruses that are present in immune complexes).
- Predict antiviral drug susceptibilities.

Laboratory Tests/ Sensitivity range

Test	% Sensitivity Range
Rapid antigen	
Immunofluorescence assay	9-23%
Enzyme immunoassay	0-20%
Viral culture	20-45%
RT-PCR	60-90%
Serology	
Immunoglobulin M	58-81%
Complement fixation> four fold rise	50%
Enzyme immunoassay>four fold rise	85-95%

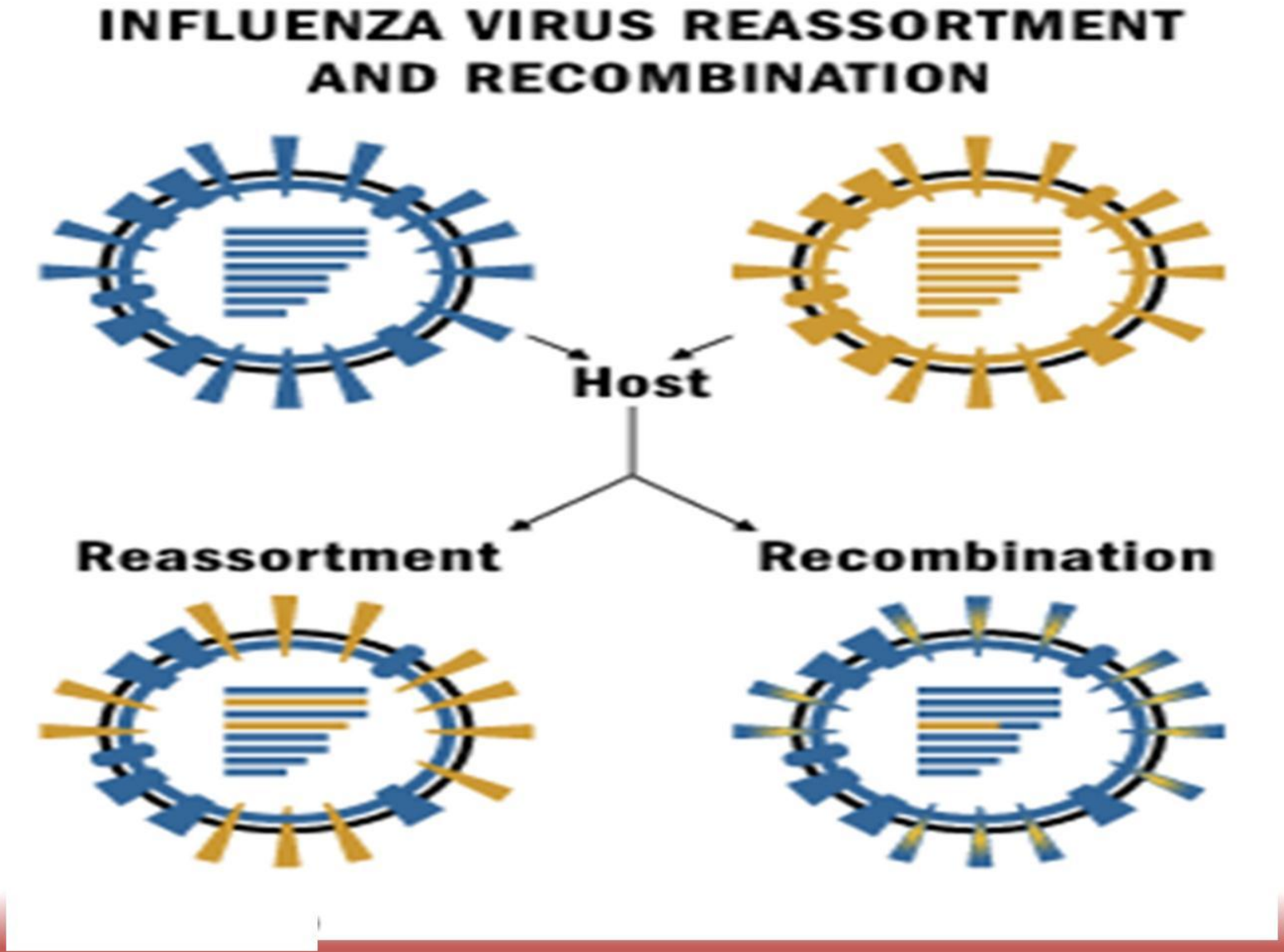
Viral Genetics

- Viruses grow rapidly
- Large number of progeny virions per cell
- More chances of mutations occurring over a short time period
- The nature of the viral genome (RNA/DNA; segmented/ non-segmented) plays an important role in the genetics of the virus
- DNA viruses tend to be more genetically stable than RNA viruses
- Error correction mechanisms in the host cell for DNA repair, but probably not for RNA

Viruses undergo genetic change by several mechanisms:

Genetic drift where an individual bases in the DNA or RNA mutate to other bases.

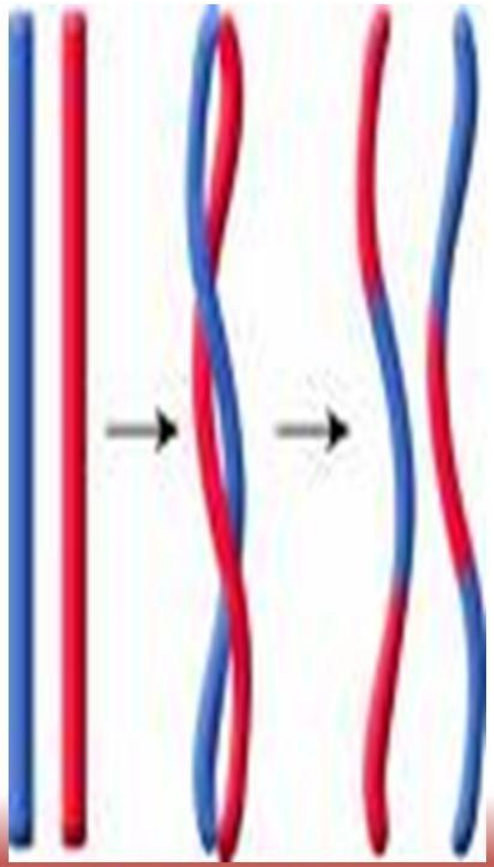
Antigenic shift is where there is a major change in the genome of the virus. This occurs as a result of recombination or reassortment


INFLUENZA VIRUS REASSORTMENT
AND RECOMBINATION
Host
Reassortment
Recombination

Recombination

Process of exchange of genes between two chromosomes within regions of significant base sequence homology.

This kind of break/join recombination is common in DNA viruses or those RNA viruses which have a DNA phase (retroviruses).



Reassortment

- The mixing of the genetic material of a species into new combinations in different individuals.
- Virus has a segmented genome; RNA viruses e.g. orthomyxoviruses, reoviruses, arenaviruses,..
- Novel reassortants

Oncovirus

- A virus that can cause cancer

Viruses seem able to cause cancer in three ways

- Presence of the viral DNA may disrupt normal host DNA function.
- Viral proteins needed for virus replication may also affect normal host gene regulation.
- The virus may serve as a vector for oncogene insertion.

Virus with oncogenic potential

Virus	Human tumours	Non-malignant disease	Experimental tumours in animals
Papovaviridae			
• Human papillomavirus	Cervical cancer	Warts	Skin cancer
• BK	None	Cystitis in immunocompromised	Multiple tumours in rodents
• JC	None	Progressive multifocal leucoencephalopathy	Multiple tumours in rodents
Adenoviridae			
• Adenovirus	None	Gut and respiratory infections	Sarcomas, carcinomas in rodents
Herpesviridae			
• Epstein–Barr virus	Nasopharyngeal carcinoma, Burkitt's lymphoma, immunoblastic lymphoma, Hodgkin's lymphoma	Infectious mononucleosis	Lymphoma in monkeys
• Kaposi's sarcoma-associated herpesvirus	Kaposi's sarcoma, primary effusion lymphoma	Multicentric Castleman's disease	Not known
Retroviridae			
• Human T cell lymphotrophic virus-1	Adult T cell leukaemia	Tropical spastic paraparesis	Adult T cell leukaemia in rabbits
• Murine mammary tumour virus	Breast cancer?	Not known	Mammary tumours in mice
• HIV (indirect)		B cell lymphoma, Kaposi's sarcoma	AIDS
Hepadnaviridae			
• Hepatitis B virus	Liver cancer	Liver cancer	Hepatitis, cirrhosis
Flaviviridae			
• Hepatitis C virus	Liver cancer	Hepatitis, cirrhosis	Not known


THANK YOU