VIRUSES
Pathogenesis and Classification

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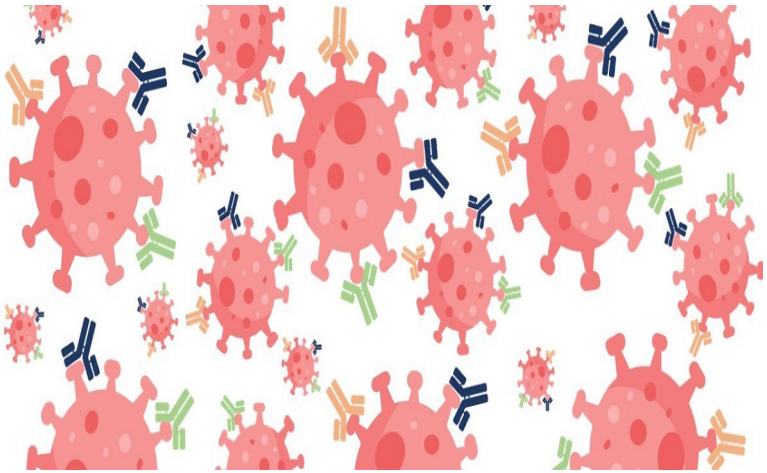
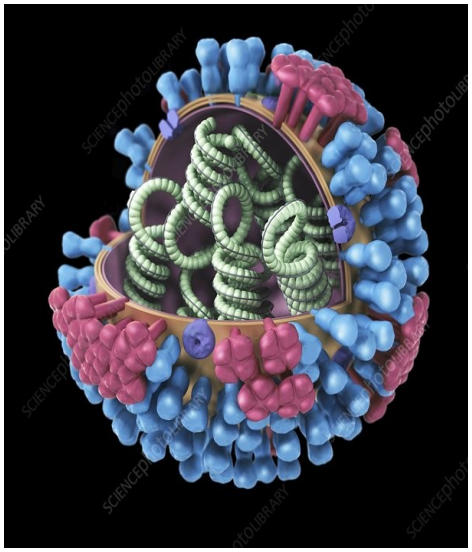
Viruses - Basics

An infective agent that typically consists of a nucleic acid molecule in a protein coat, is too small to be seen by light microscopy, and is able to multiply only within the living cells of a host



Viruses - Basics

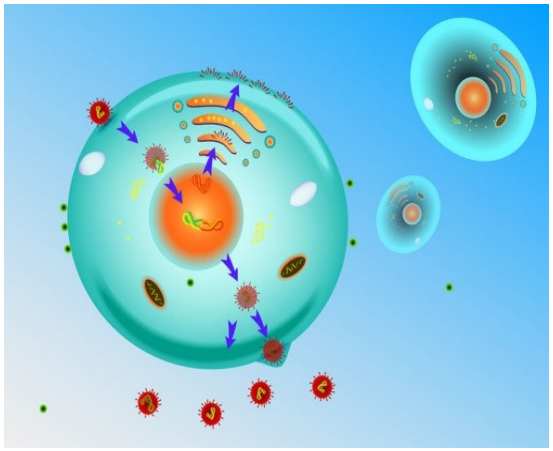
- Internal core containing *either* DNA *or* RNA
- Protective protein coat
- Outer lipoprotein membrane (envelope)

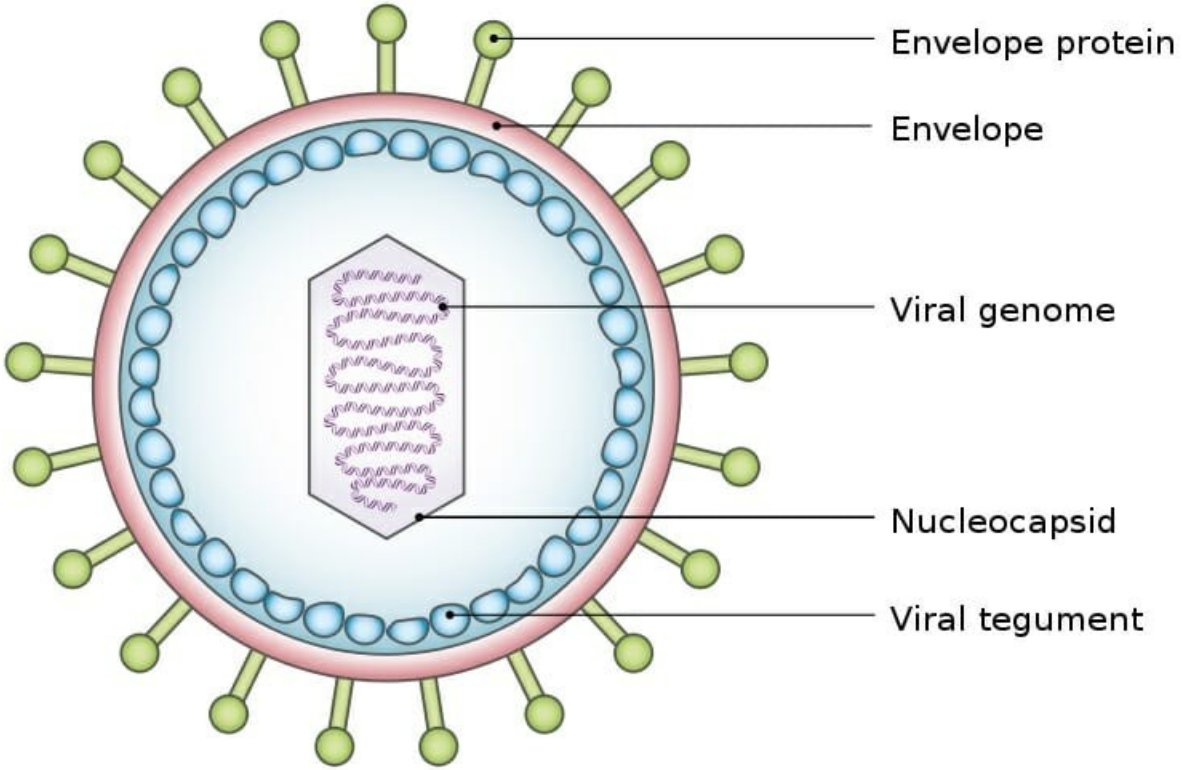


Viruses - Basics

- Reproduce (replicate) within cells – obligate intracellular parasites

- One virus can replicate to produce hundreds of progeny viruses

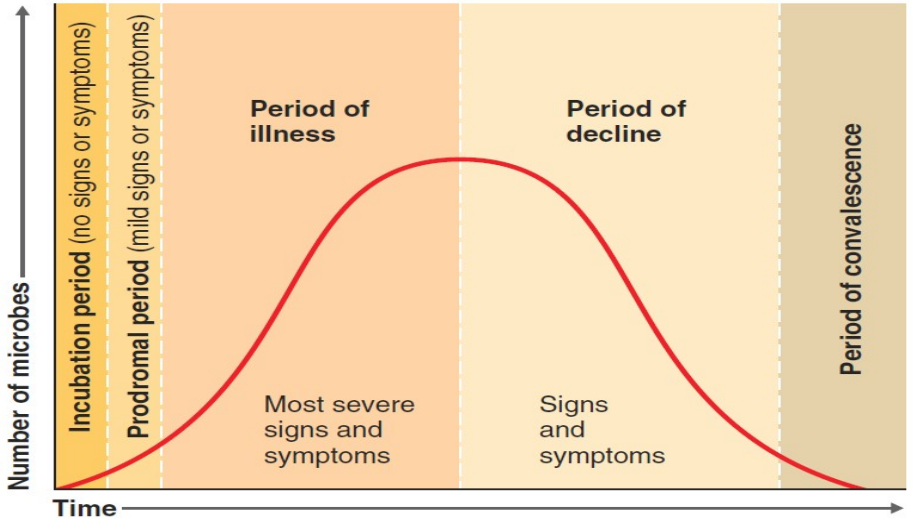



Envelope protein
Envelope
Viral genome
Nucleocapsid
Viral tegument

Viruses – Pathogenesis

Stages of typical viral infection:

- Incubation period
- Prodromal period
- Illness-specific period
- Recovery period



Viruses – Pathogenesis

- Process in the infected patient

- Changes within individual infected cell

Viruses – Pathogenesis

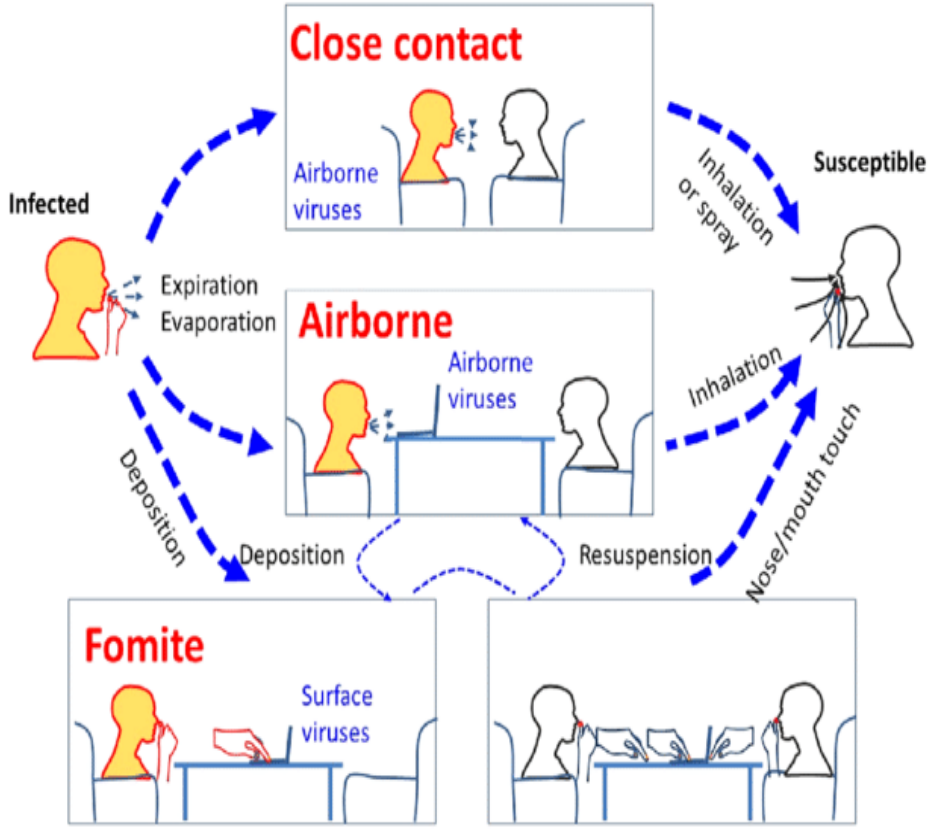
Process in the infected patient:

- Entry and transmission
- Replication and spread
- Immune response
- Persistence of virus

Viruses – Pathogenesis

Transmission of virus and Its entry:

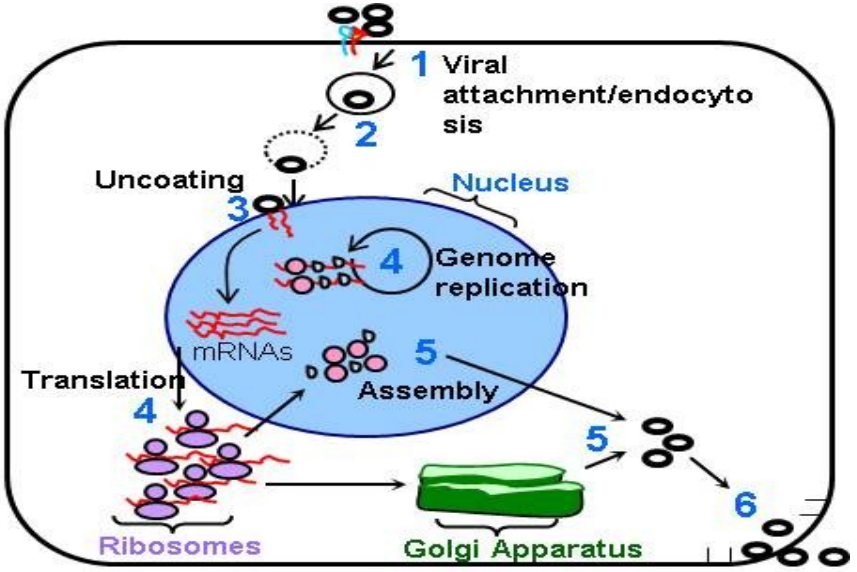
- Direct contact transmission
- Fomite transmission
- Airborne
- Oral
- Vector borne



Viruses – Pathogenesis

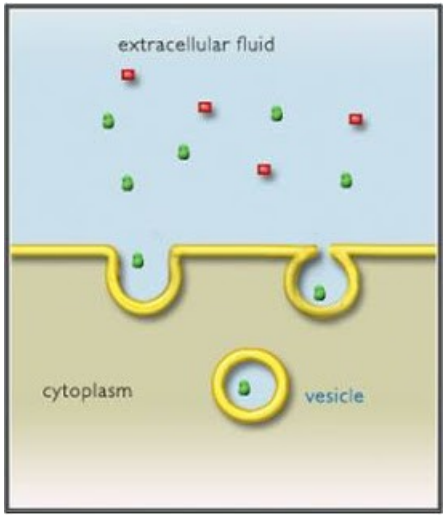
Replication and damage to cells:

- Early events
- Middle events
- Late events



Viruses – Pathogenesis

- Attachment: Specific receptor proteins on cell surface
- Penetration: Engulfed in a pinocytotic vesicle
- Uncoating: Begins in the vesicle



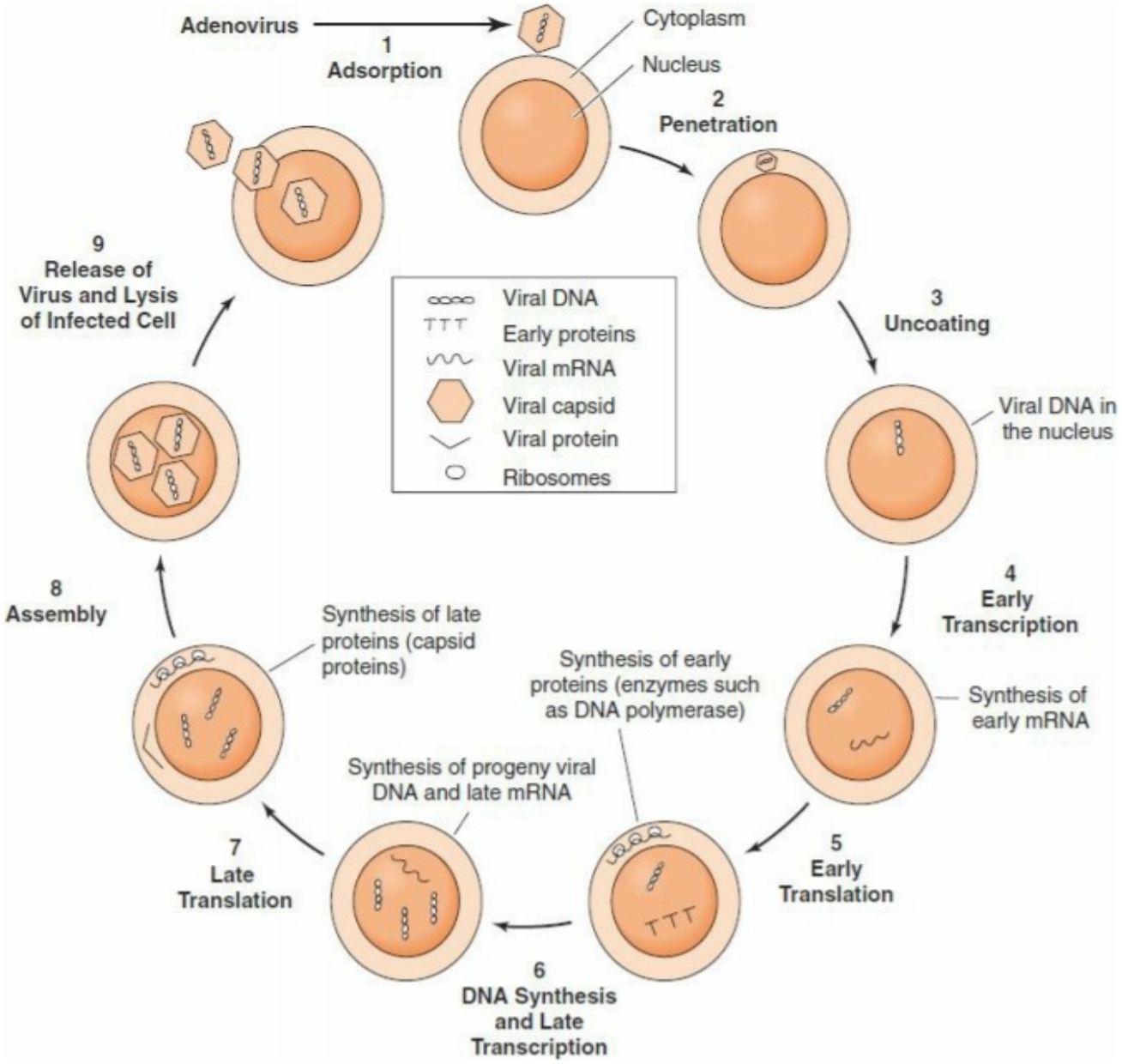
Viruses – Pathogenesis

- Gene expression: mRNA synthesis
- Translation into viral proteins
  - Early proteins (Enzymes), late proteins (structural proteins)
- Genome replication: Principle of complementarity
  - Structural capsid proteins are also synthesized

Viruses – Pathogenesis

- Assembly: packaging viral nucleic acid within capsid proteins

- Release: Rupture of cell membrane and release of mature virions


Adenovirus
1
Adsorption
Cytoplasm
Nucleus
2
Penetration
3
Uncoating
Viral DNA in the nucleus
4
Early
Transcription
Synthesis of early mRNA
5
Early
Translation
Synthesis of early proteins (enzymes such as DNA polymerase)
6
DNA Synthesis and Late Transcription
Synthesis of progeny viral DNA and late mRNA
7
Late
Translation
Synthesis of late proteins (capsid proteins)
8
Assembly
9
Release of Virus and Lysis of Infected Cell
Viral DNA
Early proteins
Viral mRNA
Viral capsid
Viral protein
Ribosomes

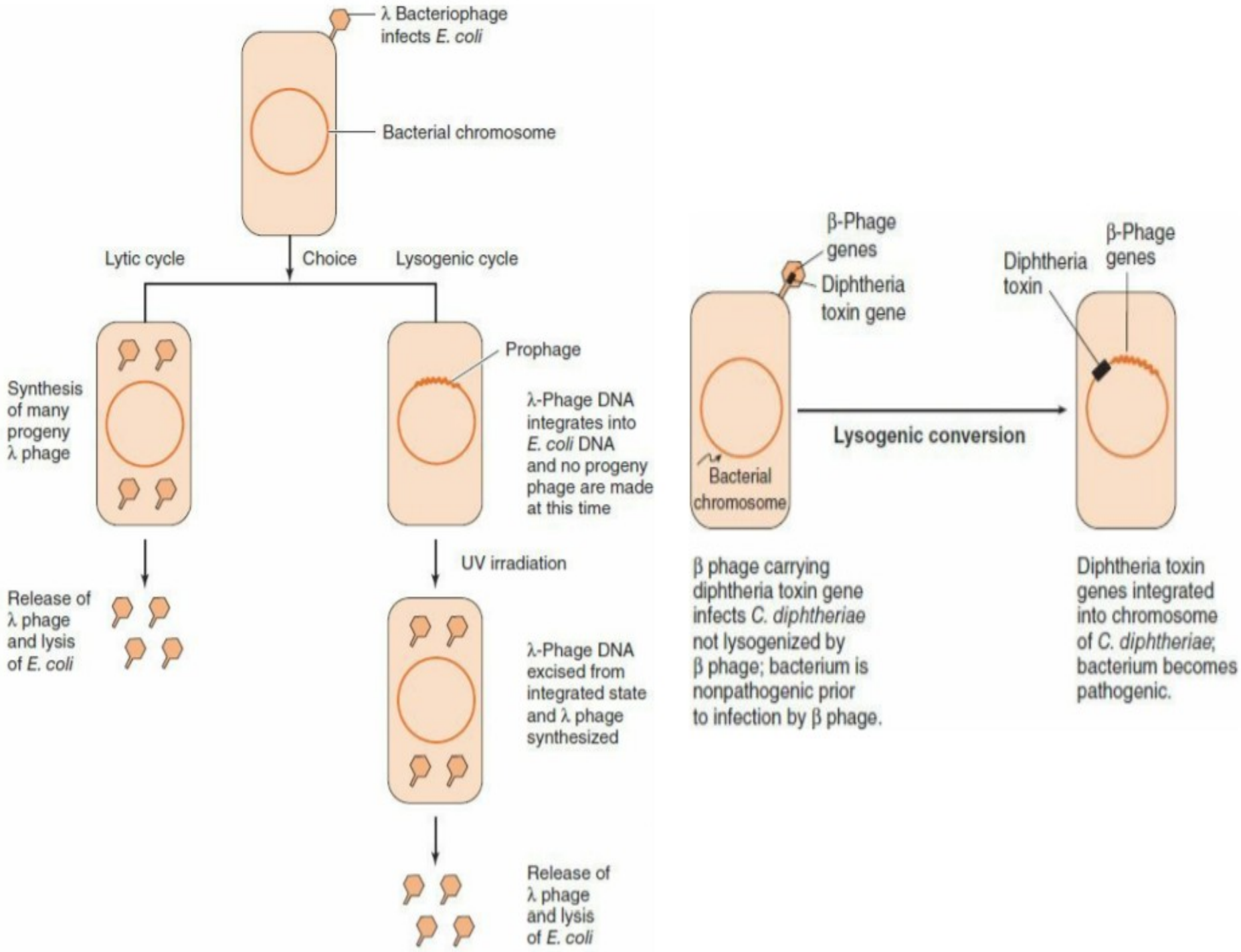
Viruses – Pathogenesis

Lysogeny:

- Viral DNA integrated into host cell chromosome
- No progeny virus produced
- Viral nucleic acid continues to function in other ways

Viruses – Pathogenesis

- Synthesis of several exotoxins in bacteria
- Encoded by genes of the integrated bacteriophage
- Lysogenic conversion.


λ Bacteriophage infects *E. coli*
Bacterial chromosome
Lytic cycle
Choice
Lysogenic cycle
Synthesis of many progeny λ phage
Release of λ phage and lysis of *E. coli*
Prophage
λ-Phage DNA integrates into *E. coli* DNA and no progeny phage are made at this time
UV irradiation
λ-Phage DNA excised from integrated state and λ phage synthesized
Release of λ phage and lysis of *E. coli*
β-Phage genes
Diphtheria toxin gene
Bacterial chromosome
Lysogenic conversion
Diphtheria toxin
β-Phage genes
β phage carrying diphtheria toxin gene infects *C. diphtheriae* not lysogenized by β phage; bacterium is nonpathogenic prior to infection by β phage.
Diphtheria toxin genes integrated into chromosome of *C. diphtheriae*; bacterium becomes pathogenic.

Viruses – Pathogenesis

Spread to other cells/organs:

- Some viruses remain localized

- Some viruses have tendency to spread systemically through the body.

Viruses – Pathogenesis

Immune response

- Immunologic attack by cytotoxic T cells
- Virus–antibody-complement complexes form and are deposited in various tissues
- Some viruses encode the receptors for various mediators of immunity

Viruses – Pathogenesis

Persistence of virus

- Integration of a DNA provirus into host cell DNA
- Immune tolerance/suppression
- Virus–antibody complexes
- Immunologically sheltered “sanctuary”
- Rapid antigenic variation
- Spread from cell to cell without an extracellular phase

Viruses – Pathogenesis

Chronic-Carrier Infections: Continue to produce significant amounts of the virus for long periods

- Can follow an asymptomatic infection/actual disease

Latent Infections: The patient recovers from the initial infection and virus production stops. The symptoms may recur, accompanied by the production of virus

Viruses – Pathogenesis

Slow Virus Infections: Prolonged period (years) between the initial infection and the onset of disease

- The incubation period and progression of the disease are prolonged

Viruses – Pathogenesis

Changes within individual infected cell

- Death
- Fusion of the cell to multinucleate giant cell
- Malignant transformation
- No apparent morphologic or functional change

- Cytopathic effect

Viruses - Classification

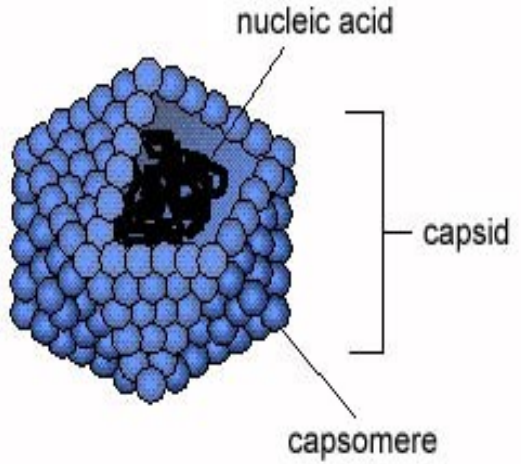
Capsid: Protein coat surrounding nucleic acid.

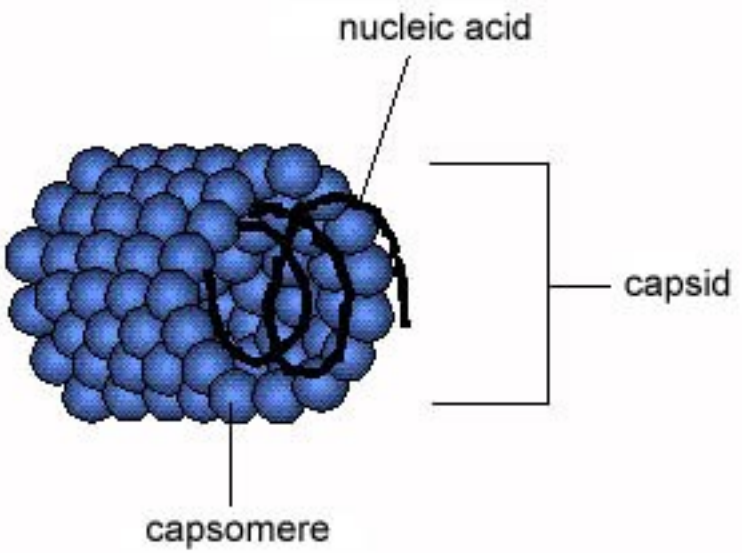
Nucleocapsid:

Nucleic acid genome + capsid protien.

Icosahedral or Helical

Envelope: Lipoprotien membrane





Viruses - Classification

- The nucleic acid – DNA or RNA.
- Capsid – size, symmetry, envelope/non-enveloped.

DNA viruses:

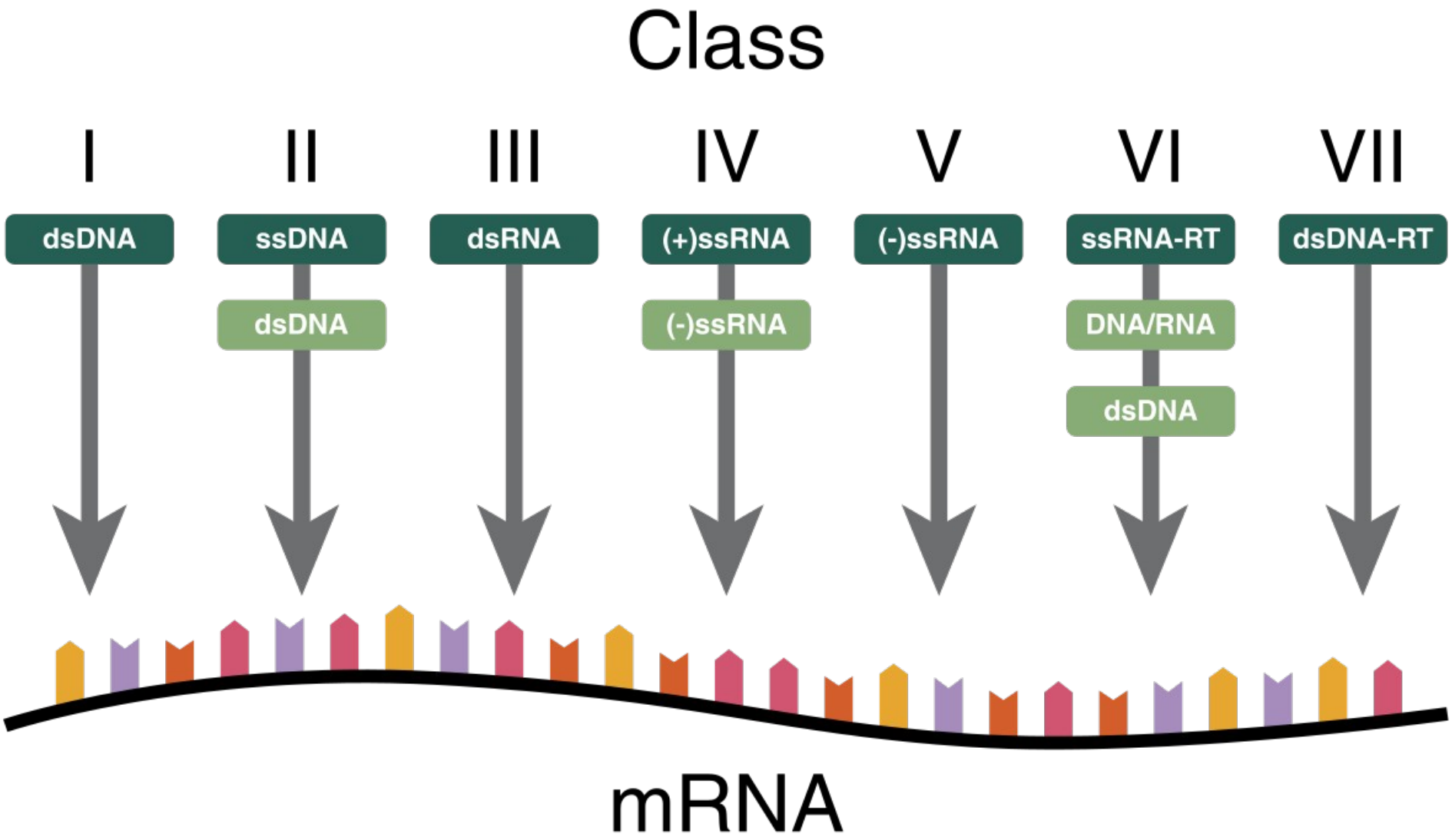
Virus Family	Envelope Present	Capsid Symmetry	Virion Size (nm)	DNA MW ($\times 10^6$)	DNA Structure[1]	Medically Important Viruses
Parvovirus	No	Icosahedral	22	2	SS, linear	B19 virus
Polyomavirus	No	Icosahedral	45	3	DS, circular, supercoiled	JC virus, BK virus
Papillomavirus	No	Icosahedral	55	5	DS, circular, supercoiled	Human papillomavirus
Adenovirus	No	Icosahedral	75	23	DS, linear	Adenovirus
Hepadnavirus	Yes	Icosahedral	42	1.5	DS, incomplete circular	Hepatitis B virus
Herpesvirus	Yes	Icosahedral	100[2]	100–150	DS, linear	Herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein–Barr virus
Poxvirus	Yes	Complex	250 × 400	125–185	DS, linear	Smallpox virus, molluscum contagiosum virus

RNA viruses

Virus Family	Envelope Present	Capsid Symmetry	Particle Size (nm)	RNA MW ($\times 10^6$)	RNA Structure[1]	Medically Important Viruses
Picornavirus	No	Icosahedral	28	2.5	SS linear, nonsegmented, positive polarity	Poliovirus, rhinovirus, hepatitis A virus
Hepevirus	No	Icosahedral	30	2.5	SS, linear, nonsegmented, positive polarity	Hepatitis E virus
Calicivirus	No	Icosahedral	38	2.7	SS linear, nonsegmented, positive polarity	Norovirus
Reovirus	No	Icosahedral	75	15	DS linear, 10 or 11 segments	Rotavirus
Flavivirus	Yes	Icosahedral	45	4	SS linear, nonsegmented, positive polarity	Yellow fever virus, dengue virus, West Nile virus, hepatitis C virus
Togavirus	Yes	Icosahedral	60	4	SS linear, nonsegmented, positive polarity	Rubella virus
Retrovirus	Yes	Icosahedral	100	7^2	SS linear, 2 identical strands (diploid), positive polarity	HIV, human T-cell leukemia virus

Orthomyxovirus	Yes	Helical	80–120	4	SS linear, 8 segments, negative polarity	Influenza virus
Paramyxovirus	Yes	Helical	150	6	SS linear, nonsegmented, negative polarity	Measles virus, mumps virus, respiratory syncytial virus
Rhabdovirus	Yes	Helical	75 × 180	4	SS linear, nonsegmented, negative polarity	Rabies virus
Filovirus	Yes	Helical	80[3]	4	SS linear, nonsegmented, negative polarity	Ebola virus, Marburg virus
Coronavirus	Yes	Helical	100	10	SS linear, nonsegmented, positive polarity	Coronavirus
Arenavirus	Yes	Helical	80–130	5	SS circular, 2 segments with cohesive ends, negative polarity	Lymphocytic choriomeningitis virus
Bunyavirus	Yes	Helical	100	5	SS circular, 3 segments with cohesive ends, negative polarity	California encephalitis virus, hantavirus
Deltavirus	Yes	Uncertain[4]	37	0.5	SS circular, closed circle, negative polarity	Hepatitis delta virus

Baltimore Classification



Viruses – DNA Viruses

Parvoviruses:

- 22nm, naked, icosahedral
- SS linear DNA

Eg: Parvovirus B19 (Hydrops fetalis, aplastic anemia, erythema infectiosum)

Polyomaviruses:

- 45 nm, naked, icosahedral
- DS circular DNA

Eg: JC virus (Progressive multifocal leukoencephalopathy)

BK virus (Immunosupressed patients)

Viruses – DNA Viruses

Papillomaviruses:

- 55 nm, naked, icosahedral
- DS supercoiled DNA

Eg: HPV (Warts, carcinoma of cervix)

Adenoviruses:

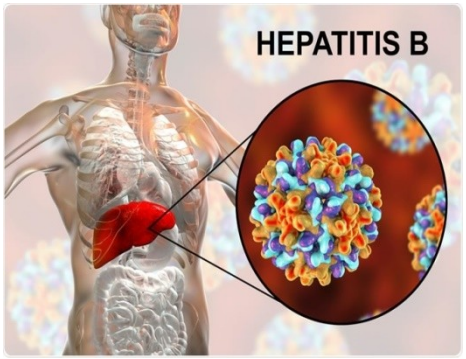
- 75 nm, naked, icosahedral
- DS linear DNA
- Pharyngitis, URTD and LRTD.

Viruses – DNA Viruses

Hepadnaviruses:

- 42 nm, enveloped, icosahedral
- DS circular DNA

Eg: Hep B virus



Herpesviruses:

- 100 nm, enveloped, icosahedral
- DS linear DNA

Eg: Herpes simplex 1 and 2, varicella-zoster virus, CMV and EBV

Viruses – DNA Viruses

Poxviruses:

- 400 nm, enveloped, complex capsid
- DS linear DNA

Eg: small pox virus,

molluscum contagiosum

Viruses – RNA Viruses

Picornaviruses:

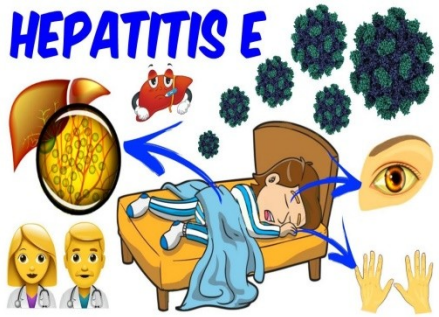
- 28 nm, naked, icosahedral
- SS linear non-segmented RNA

Eg: enteroviruses (polio virus, coxsackie virus, echo virus, Hep A virus), Rhinoviruses

Hepeviruses:

- 30 nm, naked, icosahedral
- SS linear non-segmented RNA

Eg: Hep E virus



Viruses – RNA Viruses

Caliciviruses:

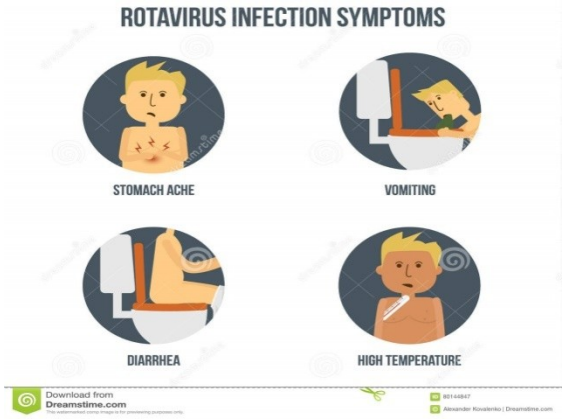
- 38 nm, naked, icosahedral
- SS linear non-segmented RNA

Eg: norovirus

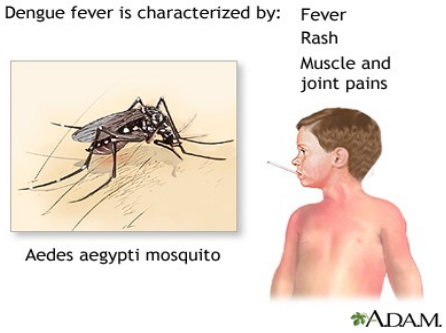
Reoviruses:

- 75 nm, naked, icosahedral
- DS linear segmented RNA

Eg: rotavirus.



Viruses – RNA Viruses



Flaviviruses:

- 45nm, enveloped, icosahedral
- SS linear non-segmented RNA

Eg: Hep C virus, Yellow fever virus, dengue virus, West Nile virus, Zika virus, Japanese encephalitis virus

Togaviruses:

- 60nm, enveloped, icosahedral
- SS linear non-segmneted RNA

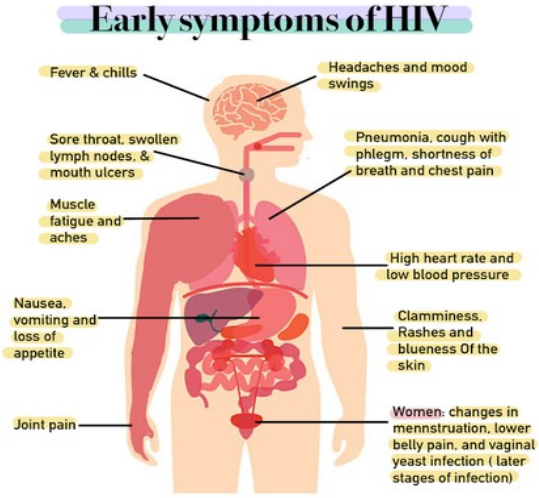
Eg: Alpha viruses (eastern and western encephalitis viruses), Rubi viruses (Rubella virus)

Viruses – RNA Viruses

Retroviruses:

- 100nm, enveloped, icosahedral
- SS linear RNA

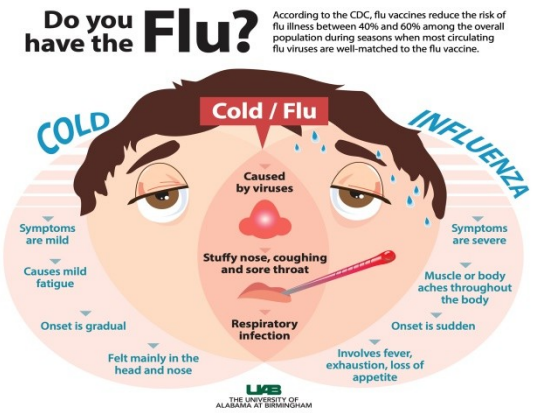
Eg: oncovirus (HTLV), lentivirus (HIV)



Orthomyxoviruses:

- 120nm, enveloped, helical
- SS linear segmented RNA

Eg: influenza virus

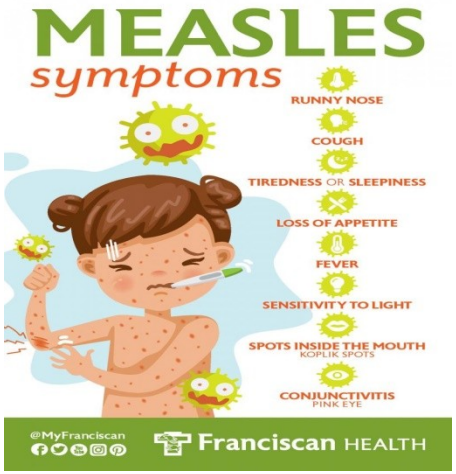


Viruses – RNA Viruses

Paramyxoviruses:

- 150nnm, enveloped, helical
- SS linear non-segmented RNA

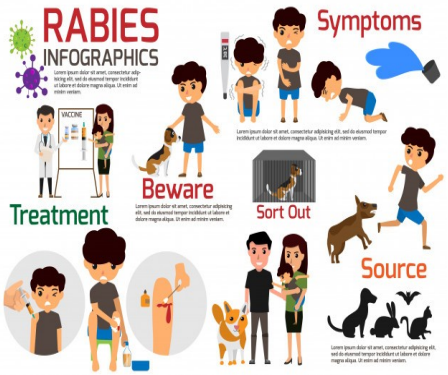
Eg: Measles, Mumps, Parainfluenza & respiratory syncytial viruses



Rhabdoviruses:

- 180nm, enveloped, helical
- SS linear non-segmented RNA

Eg: Rabies virus

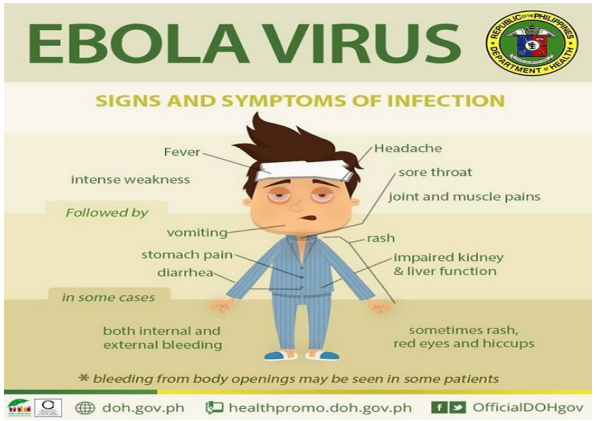


Viruses – RNA Viruses

Filoviruses:

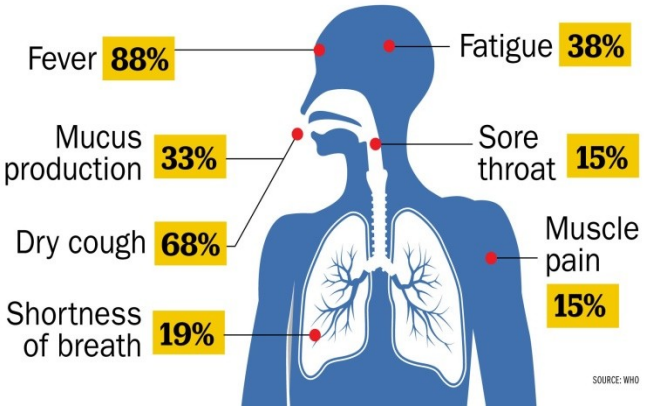
- 80nm, enveloped, helical
- SS linear non-segmented RNA

Eg: Ebola virus, Marburg virus



Coronaviruses:

- 100nm, enveloped, helical
- SS linear non-segmented RNA
- Respiratory tract infections



Viruses – RNA Viruses

Arenaviruses:

- 130 nm, enveloped, helical
- SS circular segmented RNA

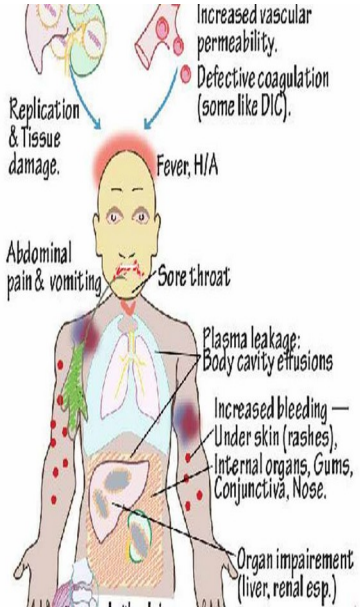
Eg: Lymphocytic choriomengitis virus, Lassa fever virus

Bunyaviruses:

- 100nm, enveloped, helical
- SS circular segmented RNA

Eg: Hantaviruses (Korean hemorrhagic fever),

CCHV (Crimean-congo hemorrhagic fever)



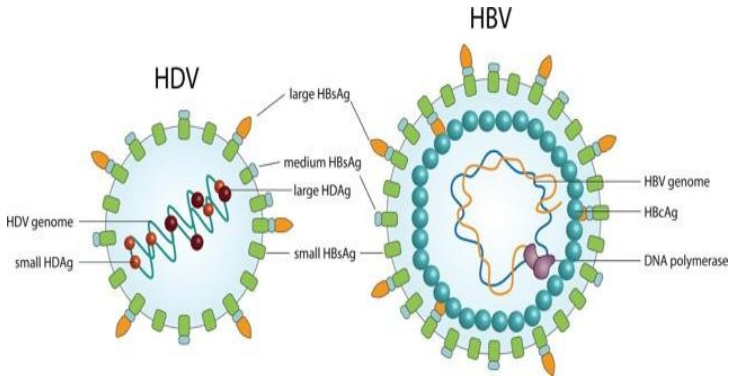
Viral Hemorrhagic Fevers

Viruses – RNA Viruses

Deltaviruses:

- 37nm, enveloped, uncertain
- SS circular RNA

Eg: Hep D virus (A defective virus)



- References:

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Thank you.