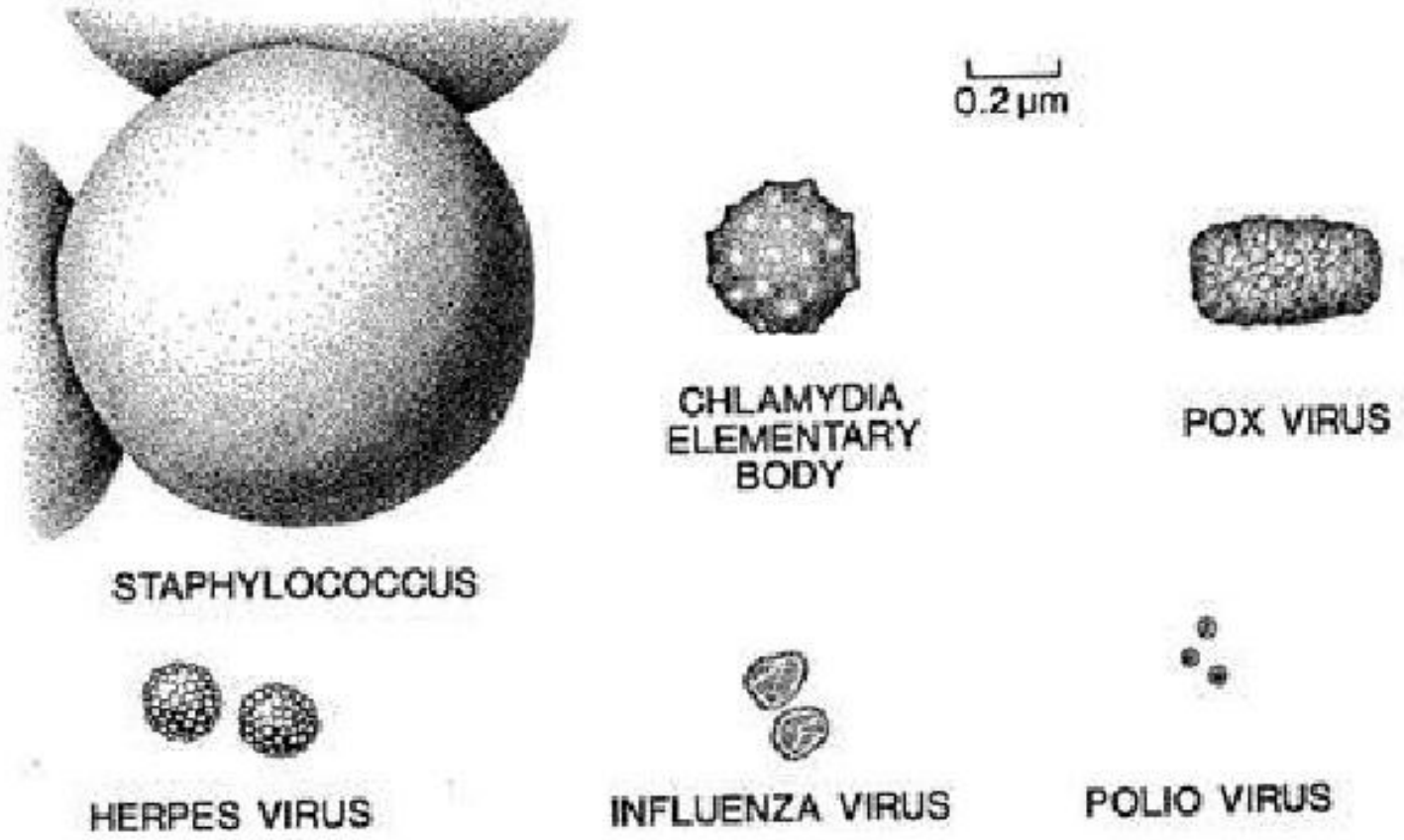
LECTURE VII

The causative agents of dental virus infections

Viral Properties

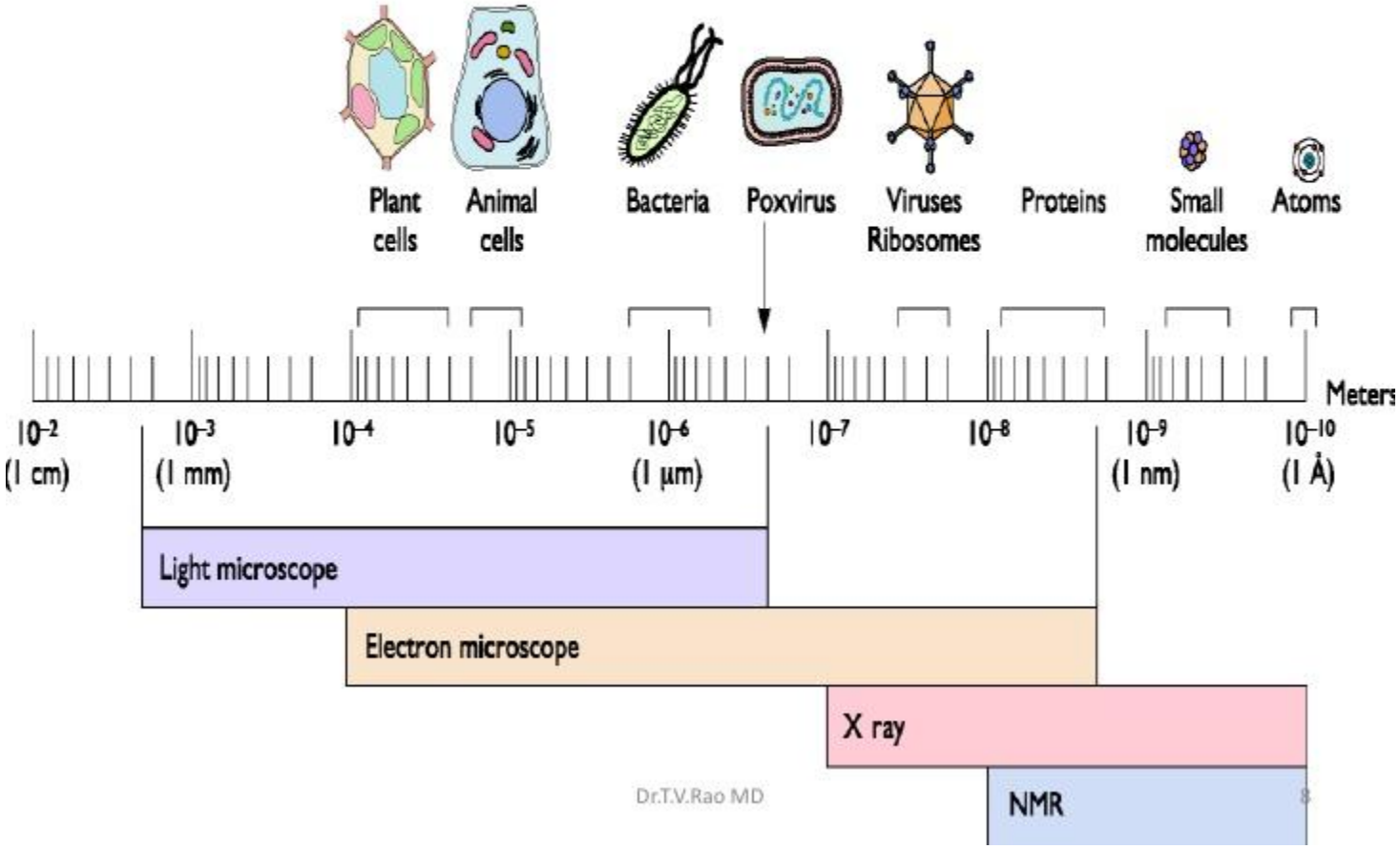
- Viruses are inert (nucleoprotein) filterable Agents
- Viruses are obligate intracellular parasites
- Viruses cannot make energy or proteins independent of a host cell
- Viral genome are RNA or DNA but not both.
- Viruses have a naked capsid or envelope with attached proteins
- Viruses do not have the genetic capability to multiply by division.
- Viruses are non-living entities

Viruses are Ultramicroscopic



Koneman et al. Color Atlas and Textbook of Microbiology 5th Ed. 1997

The size of viruses

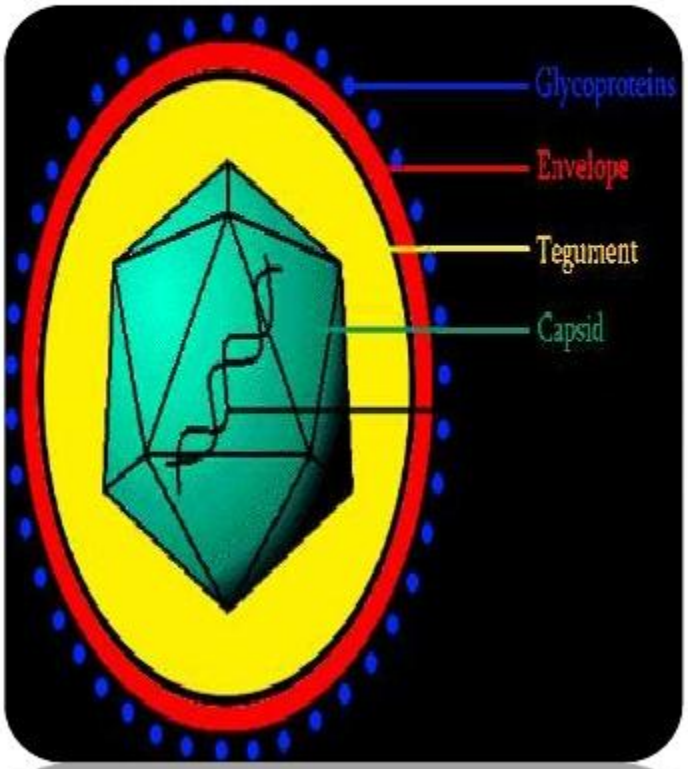


VIRAL STRUCTURE – SOME TERMINOLOGY

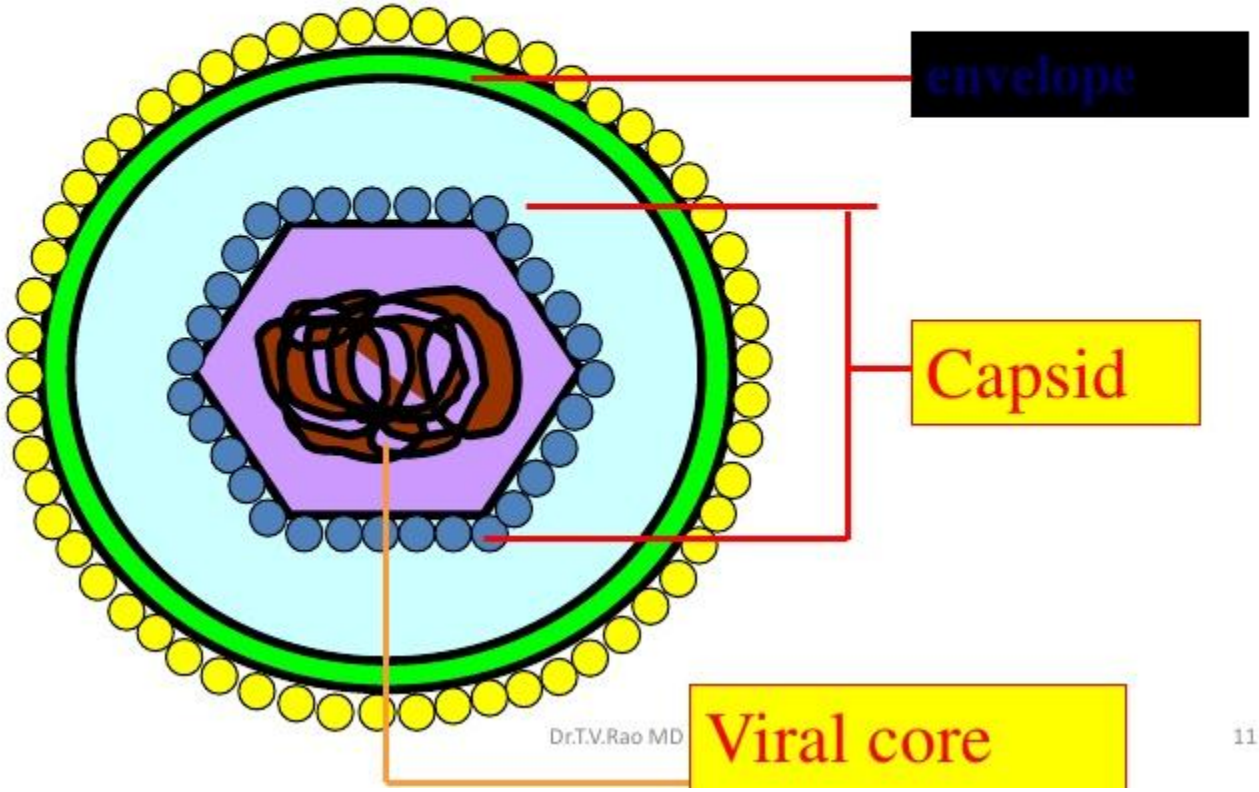
- virus particle = virion
- protein which coats the genome = capsid
- capsid usually symmetrical
- capsid + genome = nucleocapsid
- may have an envelope

Virion

- **The complete infectious unit of virus particle**
- **Structurally mature, extracellular virus particles.**



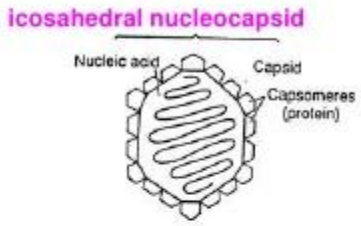
Virion



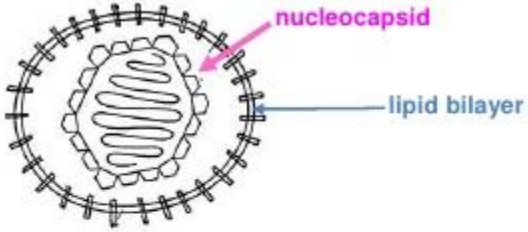
Distinguishing characteristics of viruses

- Obligate intracellular parasites
- Extreme genetic simplicity
- Contain DNA or RNA
- Replication involves disassembly and reassembly
- Replicate by "one-step growth”

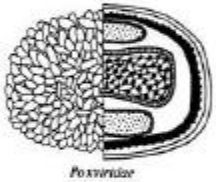
5 BASIC TYPES OF VIRAL STRUCTURE



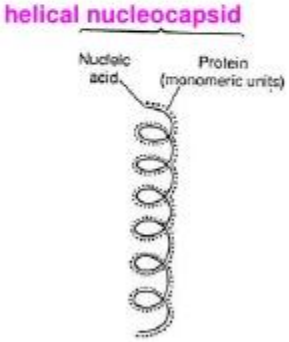
ICOSAHEDRAL



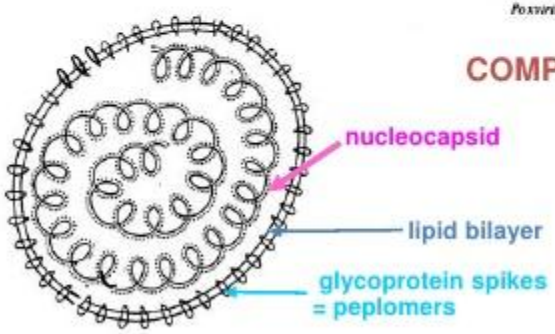
ENVELOPED ICOSAHEDRAL



COMPLEX



HELICAL



ENVELOPED HELICAL

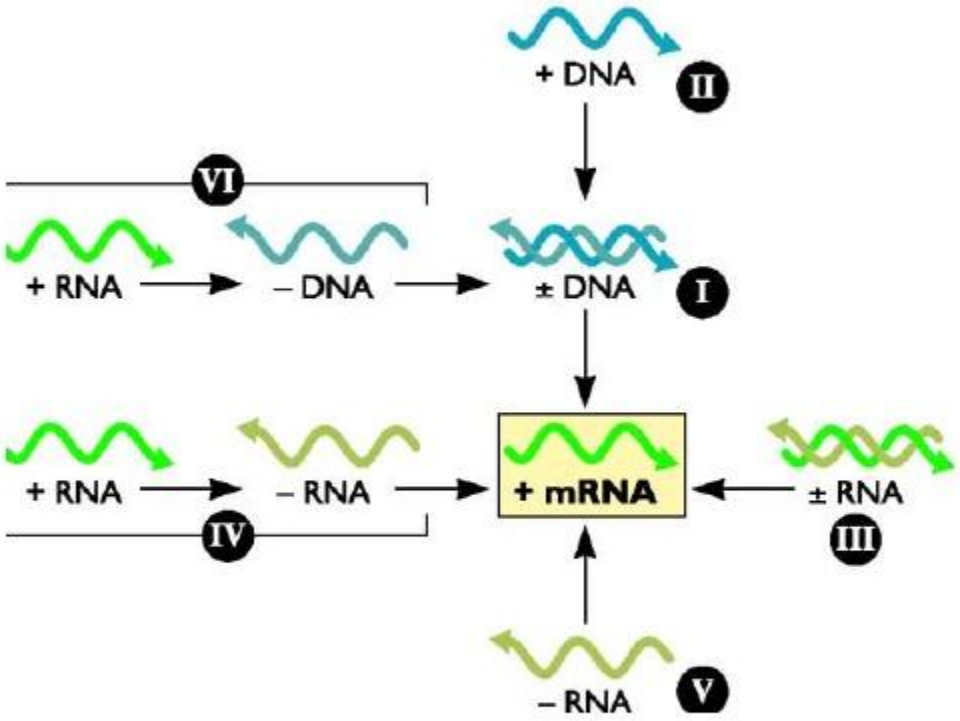
Adapted from Schaechter et al., Mechanisms of Microbial Disease

Virus Classification I
- the Baltimore classification

- All viruses must produce mRNA, or (+) sense RNA
- A complementary strand of nucleic acid is (–) sense

- The Baltimore classification has + RNA as its central point

- Its principles are fundamental to an understanding of virus classification and genome replication, but it is rarely used as a classification system in its own right



From Principles of Virology Flint et al ASM Press

Virus classification II - the Classical system

- This is a based on three principles -
  - 1) that we are classifying the virus itself, not the host
  - 2) the nucleic acid genome
  - 3) the shared physical properties of the infectious agent (e.g capsid symmetry, dimensions, lipid envelope)

Virus classification III - the genomic system

- More recently a precise ordering of viruses within and between families is possible based on DNA/RNA **sequence**

- By the year 2000 there were over 4000 viruses of plants, animals and bacteria - in 71 families, 9 subfamilies and 164 genera

Viral Structure - Overview

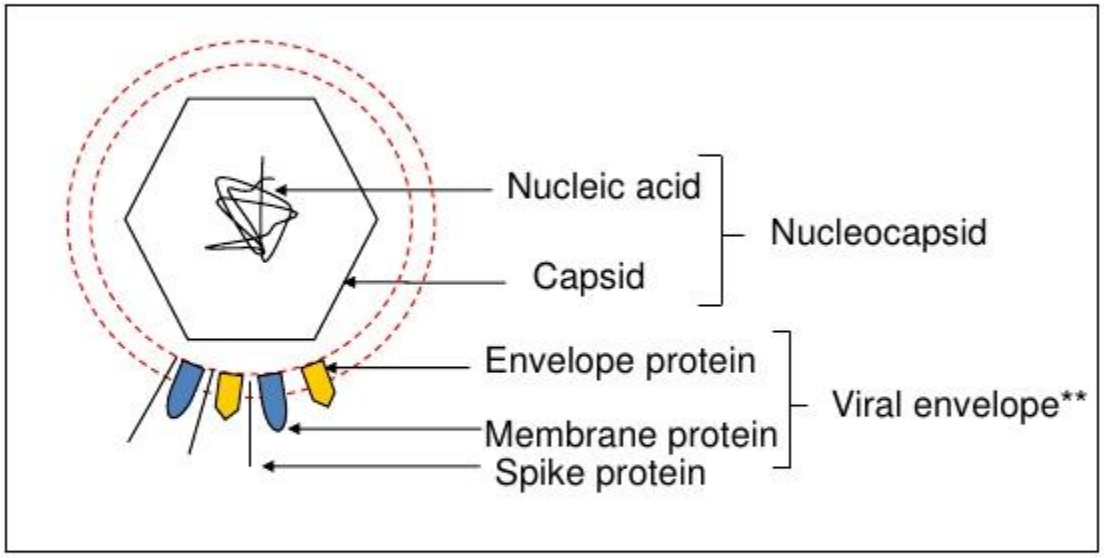
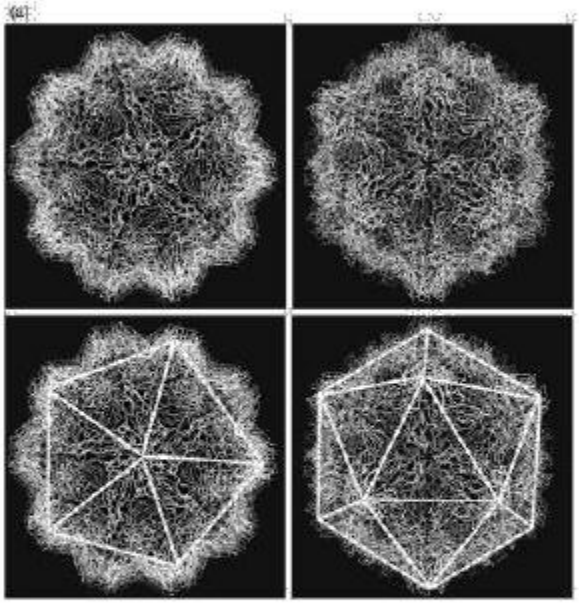


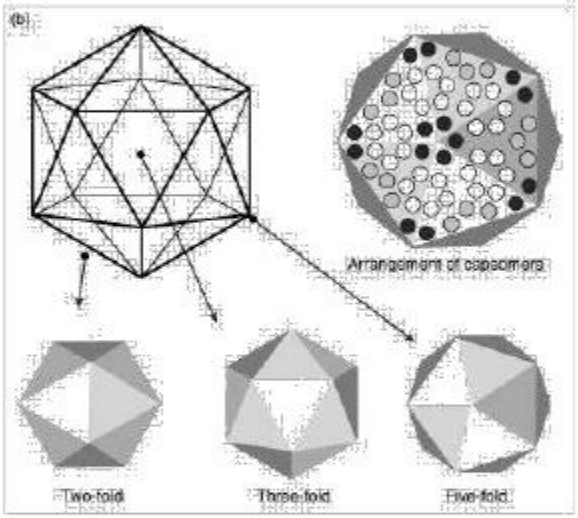
Fig 1. Schematic overview of the structure of animal viruses

** does not exist in all viruses

Icosahedral capsids

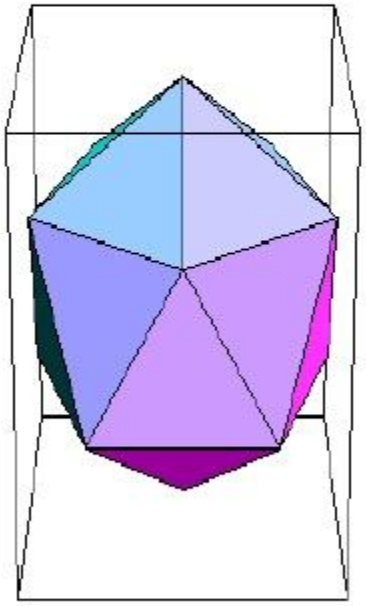


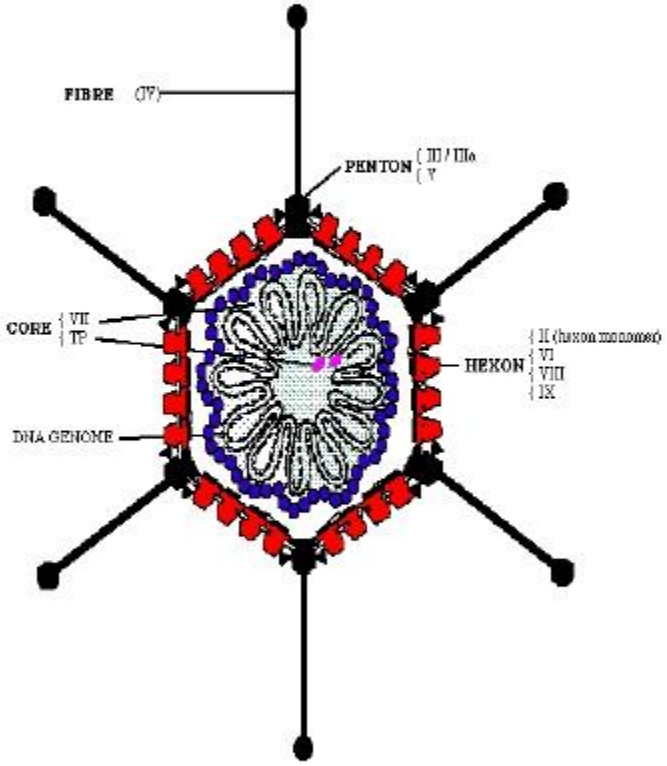
a) Crystallographic structure of a simple icosahedral virus.



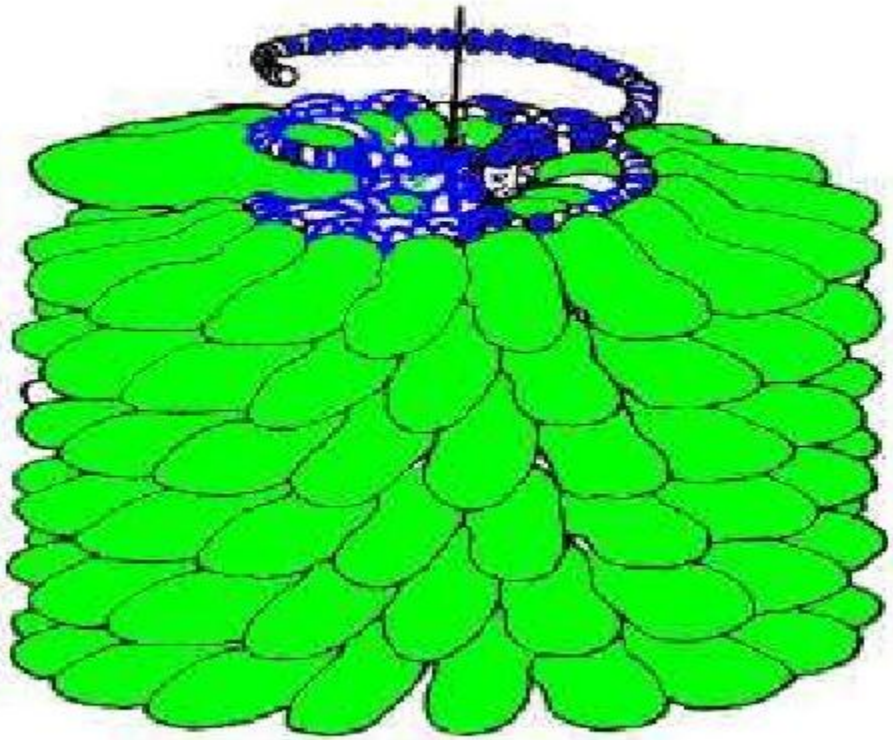
b) The axes of symmetry

Cubic or icosahedral symmetry





Helical symmetry



Helical

- California Encephalitis Virus
  Coronavirus
  Hantavirus
  Influenza Virus (Flu Virus)
  Measles Virus (Rubeola)
  Mumps Virus
  Para influenza Virus
  Rabies Virus
  Respiratory Syncytial Virus(RSV)

Genome

- The genome of a virus can be either DNA or RNA

- DNA-double stranded (ds): linear or circular

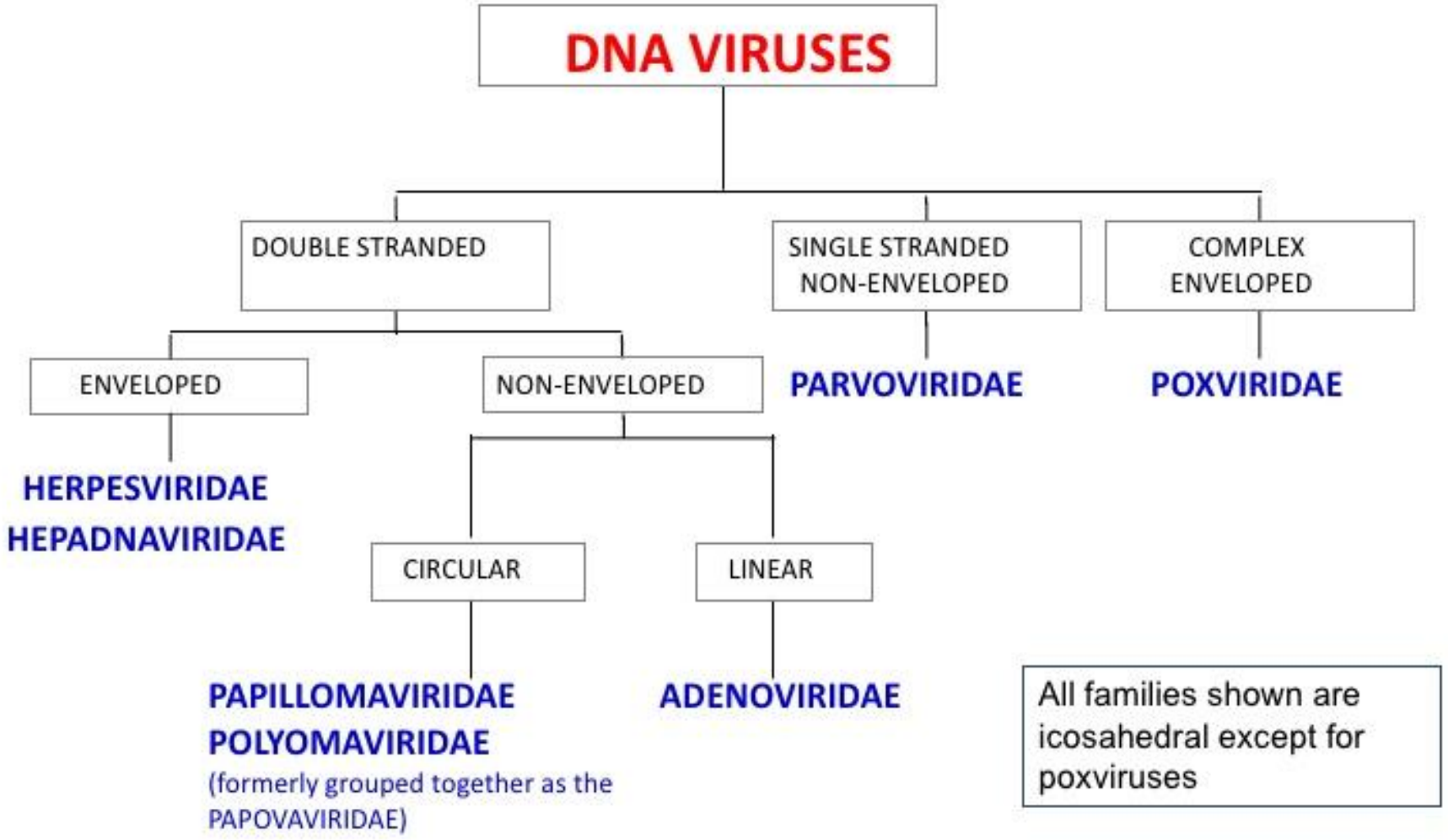
  Single stranded (ss) : linear or circular
- RNA- ss:segmented or non-segmented

  ss:polarity+(sense) or polarity –(non-sense)

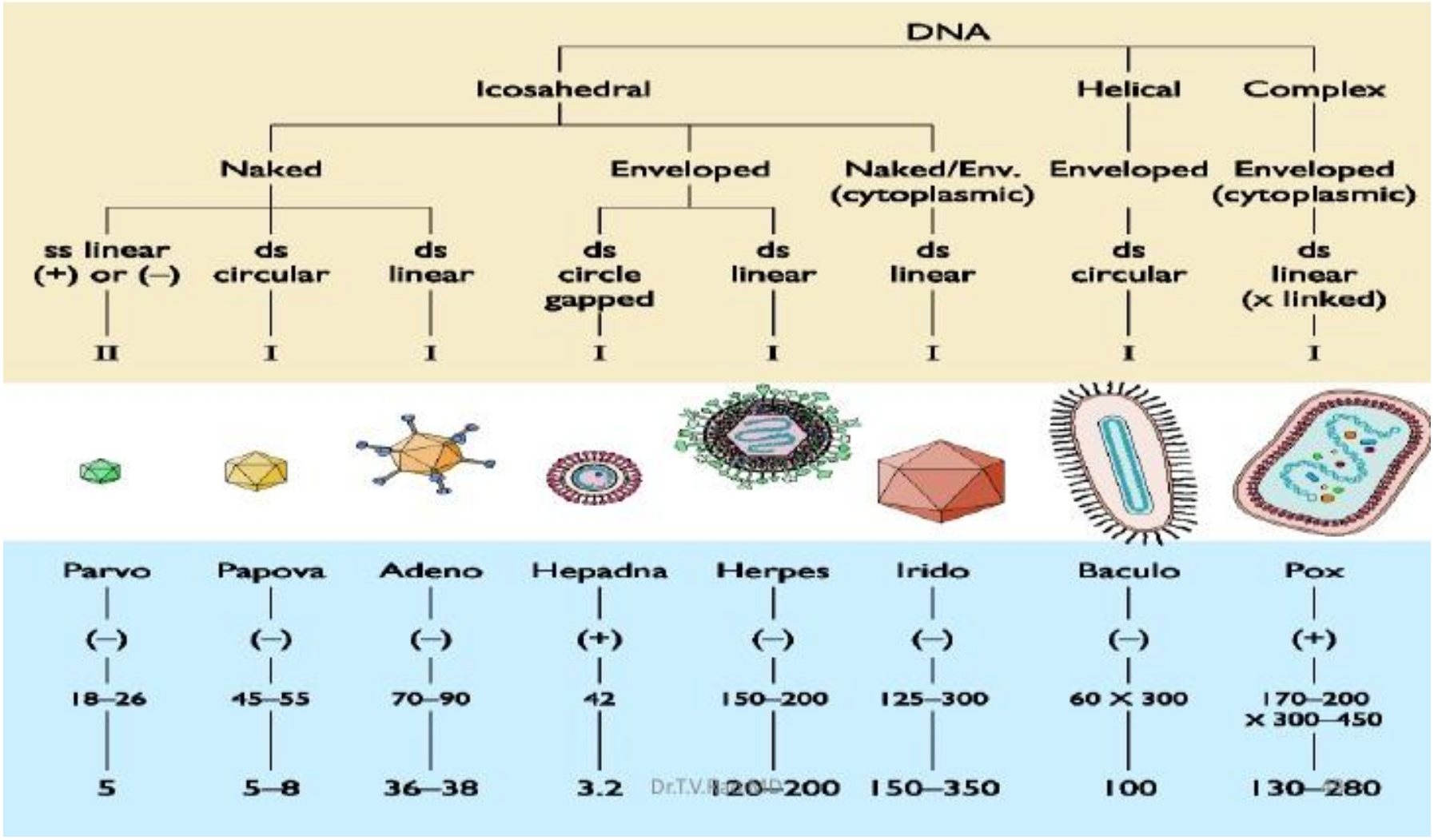
  ds: linear (only reovirus family)

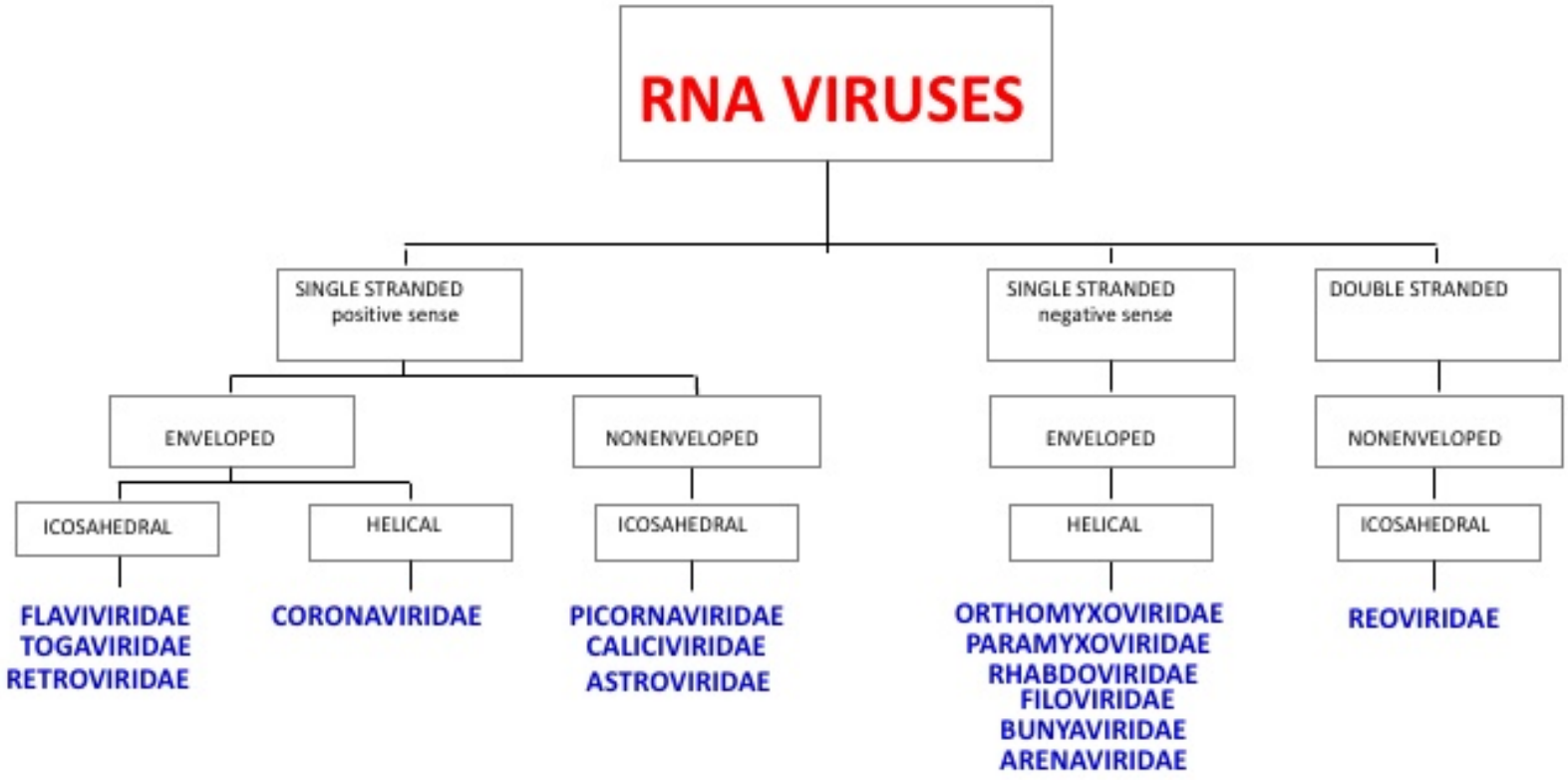
Viral genome strategies

- dsDNA (herpes, papova, adeno, pox)
- •ssDNA (parvo)
- •dsRNA (reo, rota)
- •ssRNA (+) (picorna, toga, flavi, corona)
- •ssRNA (-) (rhabdo, paramyxo, orthomyxo,
- bunya, filo)
- •ssRNA (+/-) (arena, bunya)
- •ssRNA (+RTase) (retro, lenti)


DNA VIRUSES
DOUBLE STRANDED
SINGLE STRANDED NON-ENVELOPED
COMPLEX ENVELOPED
ENVELOPED
NON-ENVELOPED
PARVOVIRIDAE
POXVIRIDAE
HERPESVIRIDAE
HEPADNAVIRIDAE
CIRCULAR
LINEAR
PAPILLOMAVIRIDAE
POLYOMAVIRIDAE
(formerly grouped together as the PAPOVAVIRIDAE)
ADENOVIRIDAE
All families shown are icosahedral except for poxviruses

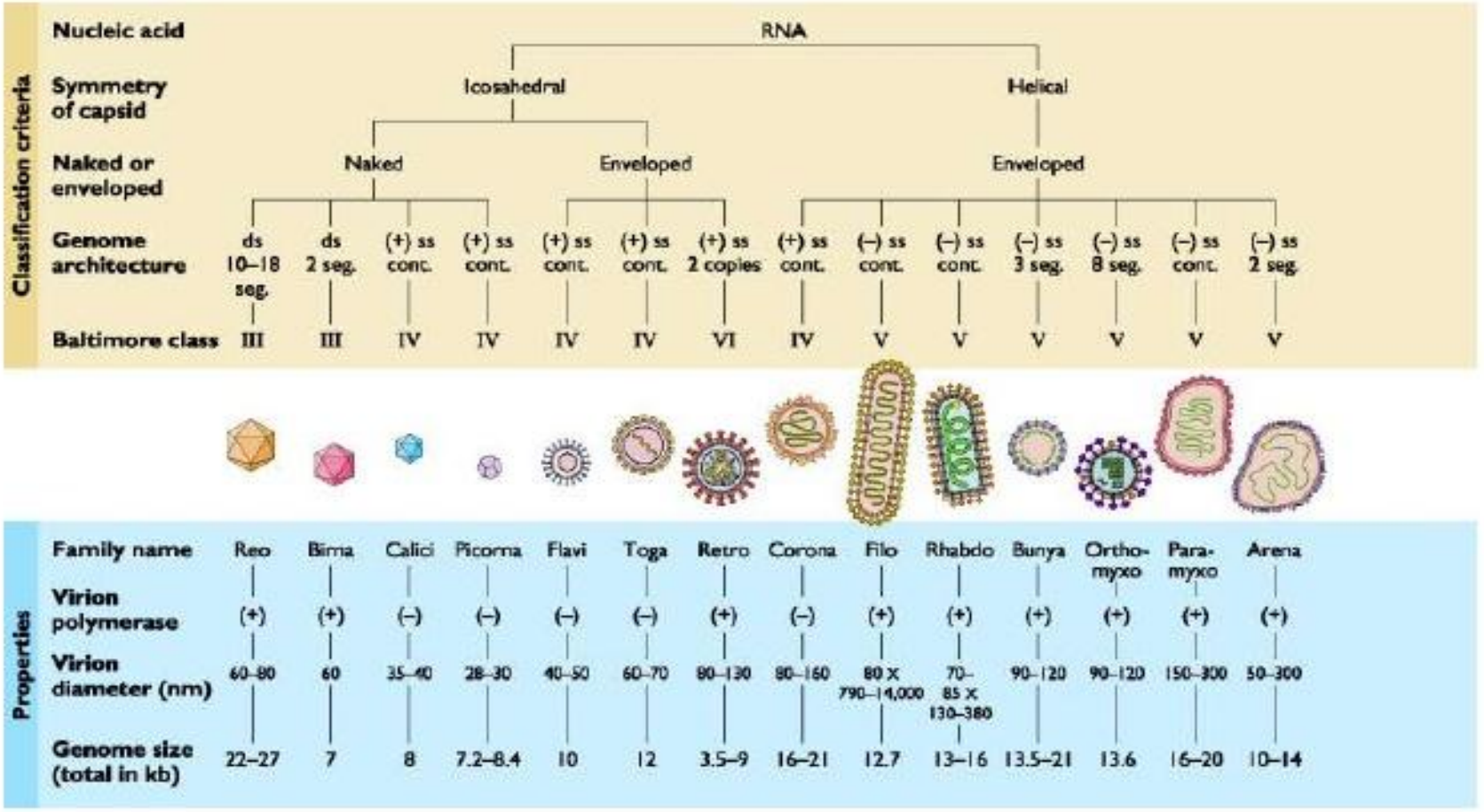
DNA viruses


DNA
Icosahedral
Helical
Complex
Naked
Enveloped
Naked/Env. (cytoplasmic)
Enveloped
Enveloped (cytoplasmic)
ss linear (+) or (–)
ds circular
ds linear
ds circle gapped
ds linear
ds linear
ds circular
ds linear (x linked)
II
I
I
I
I
I
I
I
Parvo
Papova
Adeno
Hepadna
Herpes
Irido
Baculo
Pox
(–)
(–)
(–)
(+)
(–)
(–)
(–)
(+)
18–26
45–55
70–90
42
150–200
125–300
60 X 300
170–200 X 300–450
5
5–8
36–38
3.2
120–200
150–350
100
130–280



Modified from Volk et al., Essentials of Medical Microbiology, 4th Ed. 1991

RNA viruses

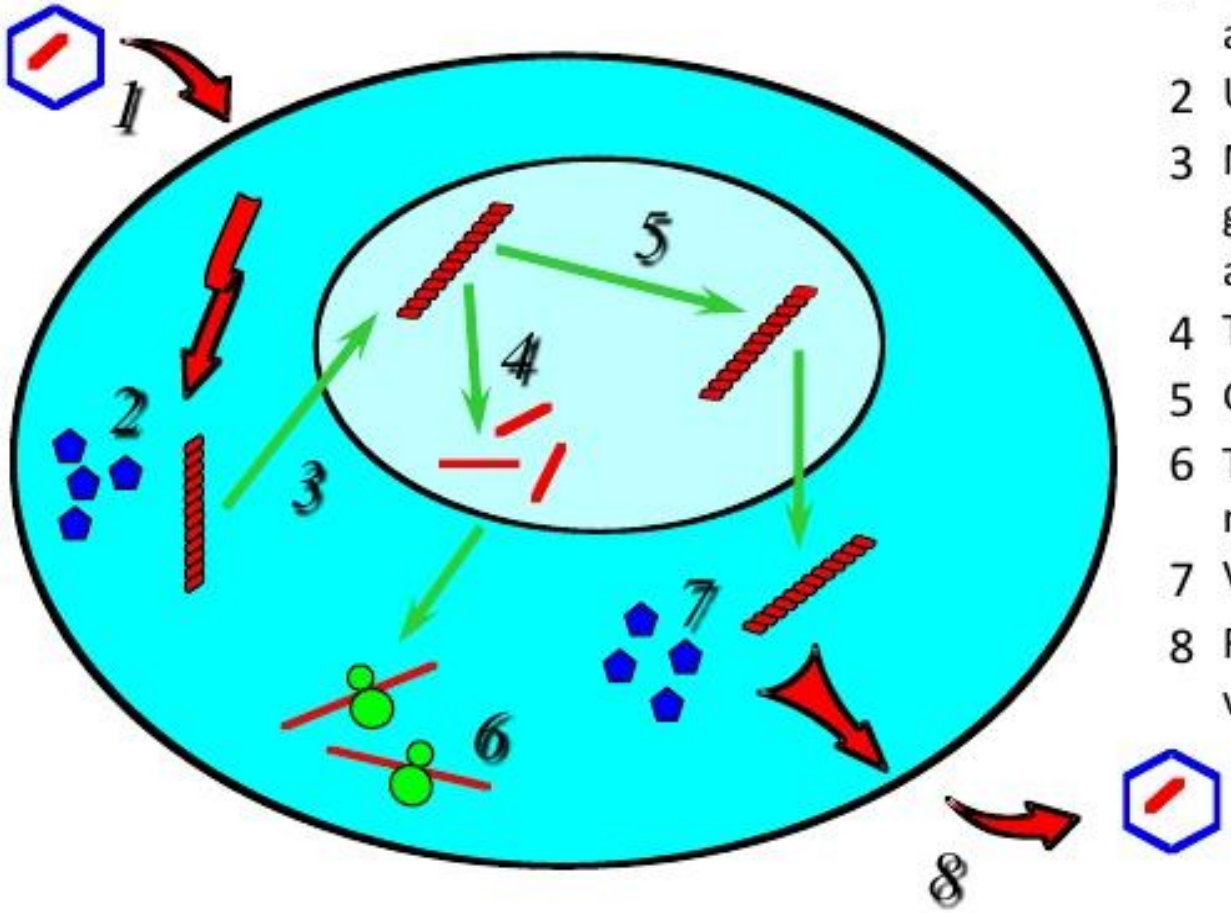


From Principles of Virology Flint et al ASM Press

BASIC STEPS IN VIRAL LIFE CYCLE

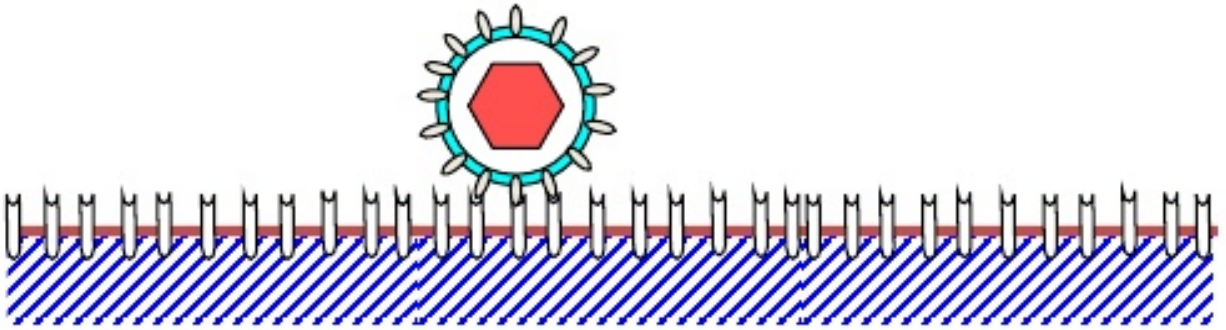
- ADSORPTION
- PENETRATION
- UNCOATING AND ECLIPSE
- SYNTHESIS OF VIRAL NUCLEIC ACID AND PROTEIN
- ASSEMBLY (maturation)
- RELEASE

Virus Replication



1 Virus attachment and entry
2 Uncoating of virion
3 Migration of genome nucleic acid to nucleus
4 Transcription
5 Genome replication
6 Translation of virus mRNAs
7 Virion assembly
8 Release of new virus particles

ADSORPTION

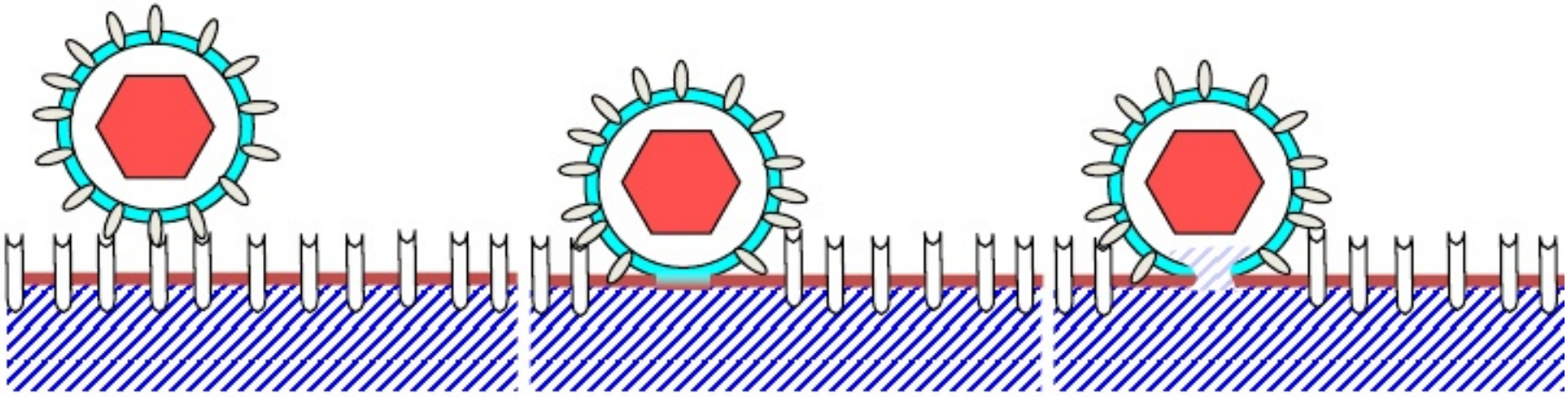


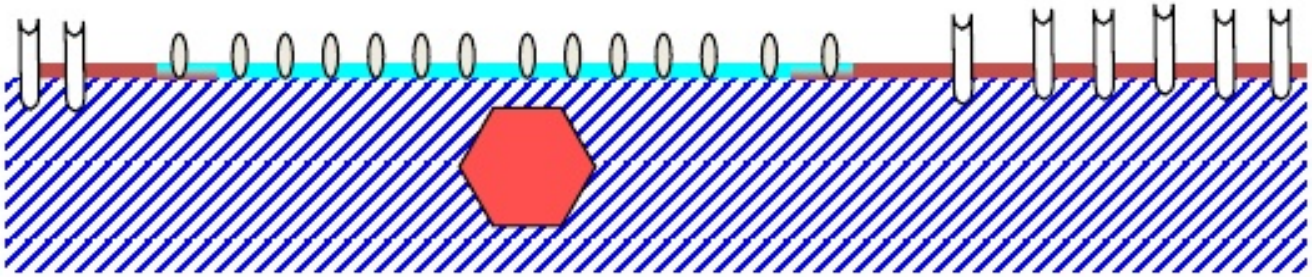
- TEMPERATURE INDEPENDENT
- REQUIRES VIRAL ATTACHMENT PROTEIN
- CELLULAR RECEPTORS

PENETRATION
- ENVELOPED VIRUSES

- FUSION WITH PLASMA MEMBRANE
- ENTRY VIA ENDOSOMES

PENETRATION





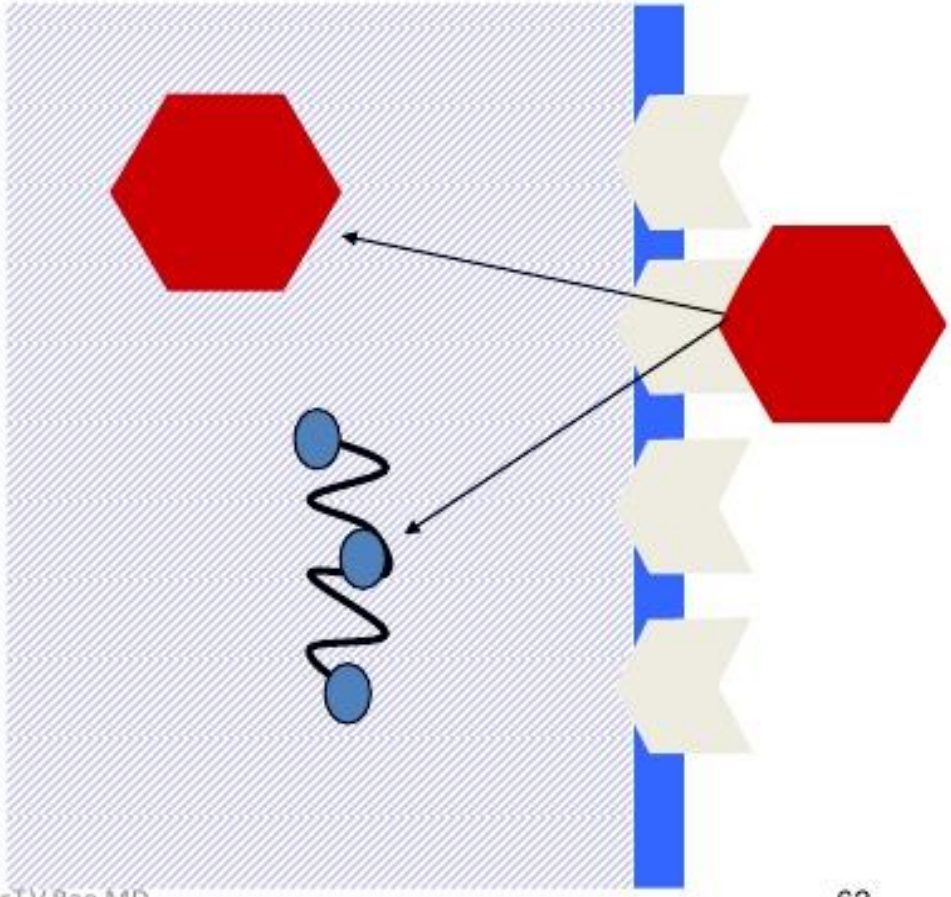
herpesviruses, paramyxoviruses, HIV

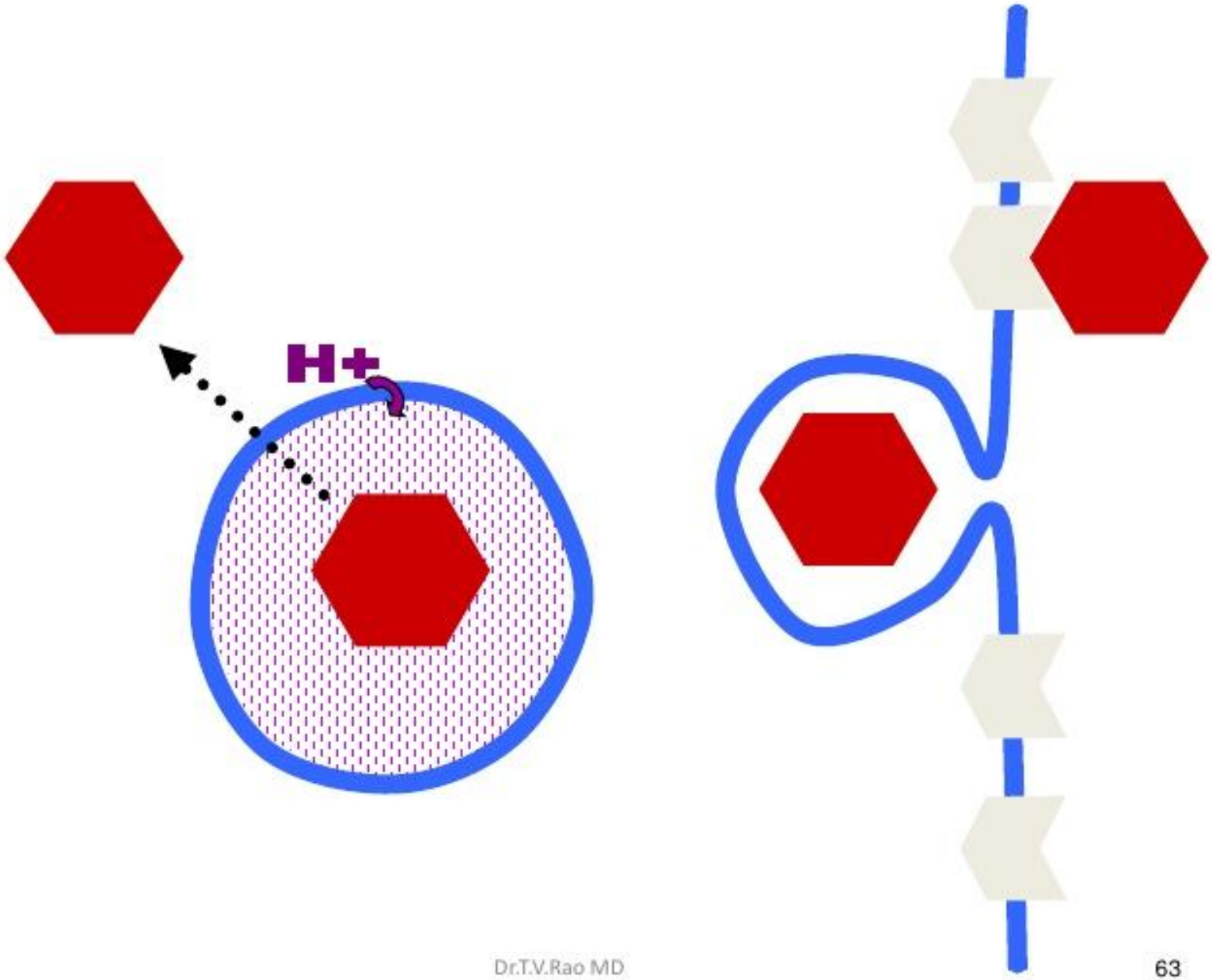
VIRUS UPTAKE VIA ENDOSOMES

- CALLED
  - –VIROPEXIS / ENDOCYTOSIS / PINOCYTOSIS

PENETRATION
NON-ENVELOPED VIRUSES

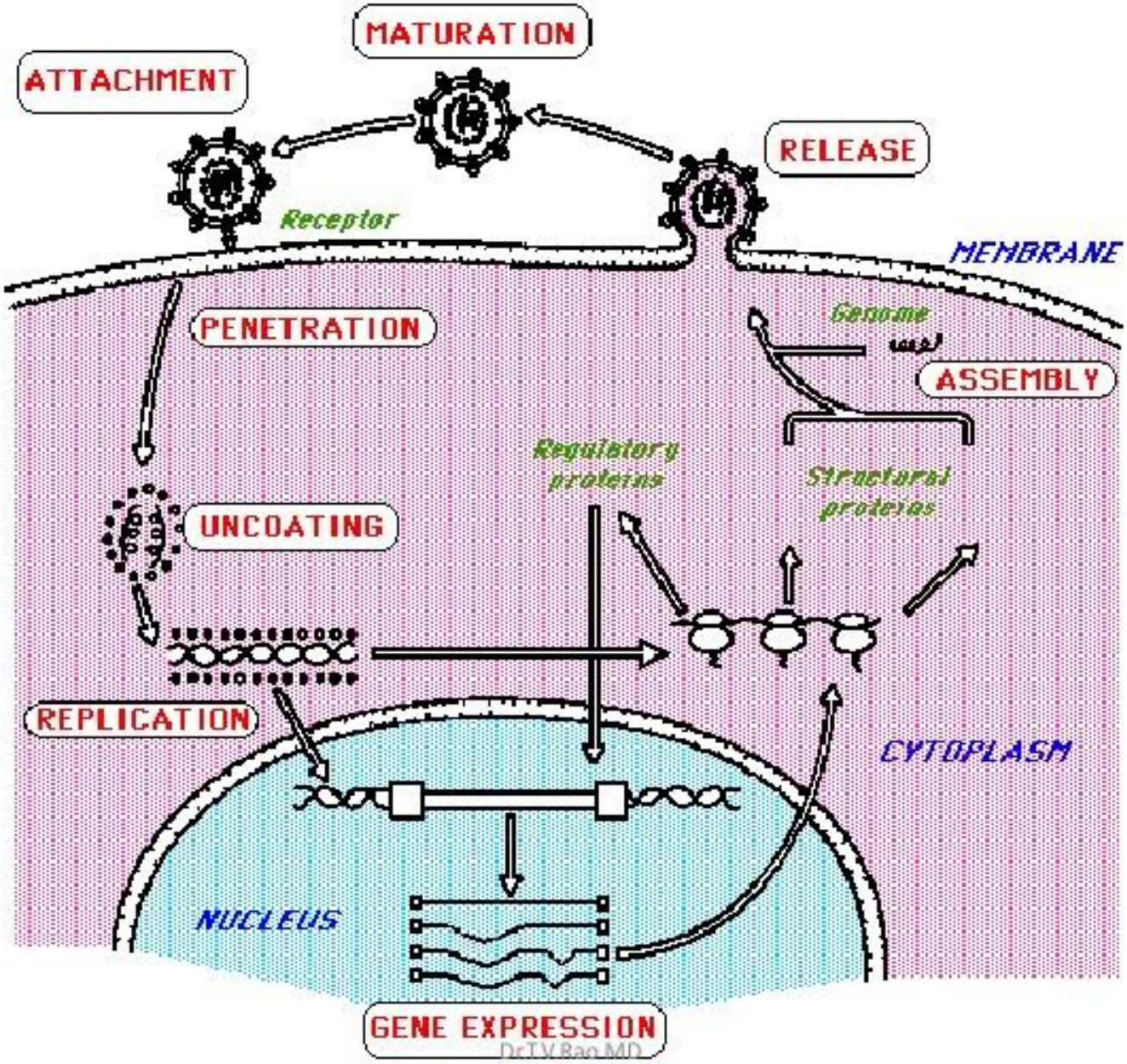
entry directly across plasma membrane:




H+

Replicative cycle

- As obligate intracellular parasites, Virus must enter and replicate in living cells in order to "reproduce" themselves. This "growth cycle" involves specific attachment of virus, penetration and uncoating, nucleic acid transcription, protein synthesis, maturation and assembly of the virions and their subsequent release from the cell by budding or lysis


MATURATION
ATTACHMENT
RELEASE
Receptor
MEMBRANE
PENETRATION
Genome
ASSEMBLY
Regulatory proteins
Structural proteins
UNCOATING
REPLICATION
CYTOPLASM
NUCLEUS
GENE EXPRESSION

UNCOATING

- NEED TO MAKE GENOME AVAILABLE
- ONCE UNCOATING OCCURS, ENTER ECLIPSE PHASE
- ECLIPSE PHASE LASTS UNTIL FIRST NEW VIRUS PARTICLE FORMED

SYNTHESIS OF VIRAL NUCLEIC ACID AND PROTEIN

- MANY STRATEGIES
- NUCLEIC ACID MAY BE MADE IN NUCLEUS OR CYTOPLASM
- PROTEIN SYNTHESIS IS ALWAYS IN THE CYTOPLASM

ASSEMBLY AND MATURATION

- NUCLEUS
- CYTOPLASM
- AT MEMBRANE

RELEASE

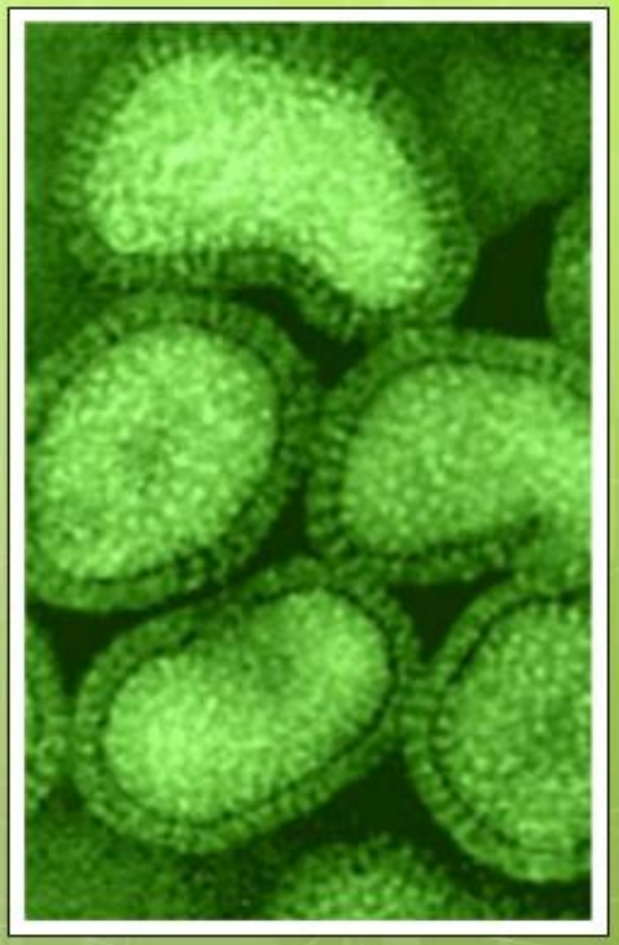
- LYSIS
- BUDDING THROUGH PLASMA MEMBRANE
- NOT EVERY RELEASED VIRION IS INFECTIOUS

Transmission of Viruses

- Respiratory transmission
  - Influenza A virus
- Faecal-oral transmission
  - Enterovirus
- Blood-borne transmission
  - Hepatitis B virus
- Sexual Transmission
  - HIV
- Animal or insect vectors
  - Rabies virus

Orthomyxoviridae

- The Orthomyxoviridae are a family of RNA viruses that includes five genera: Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus and Thogotovirus.
- The Influenzaviruses cause influenza in vertebrates, including birds , humans, and other mammals.
- Isaviruses infect salmon; thogotoviruses infect vertebrates and invertebrates, such as mosquitoes and sea lice.



Characteristics

RNA virus (negative-sense)

Pleomorphic virus

Spheric or tubular shape

80-120 nm

Structure

Envelope :

2 glycoproteins – hemagglutinin (HA)
neuraminidase (NA)

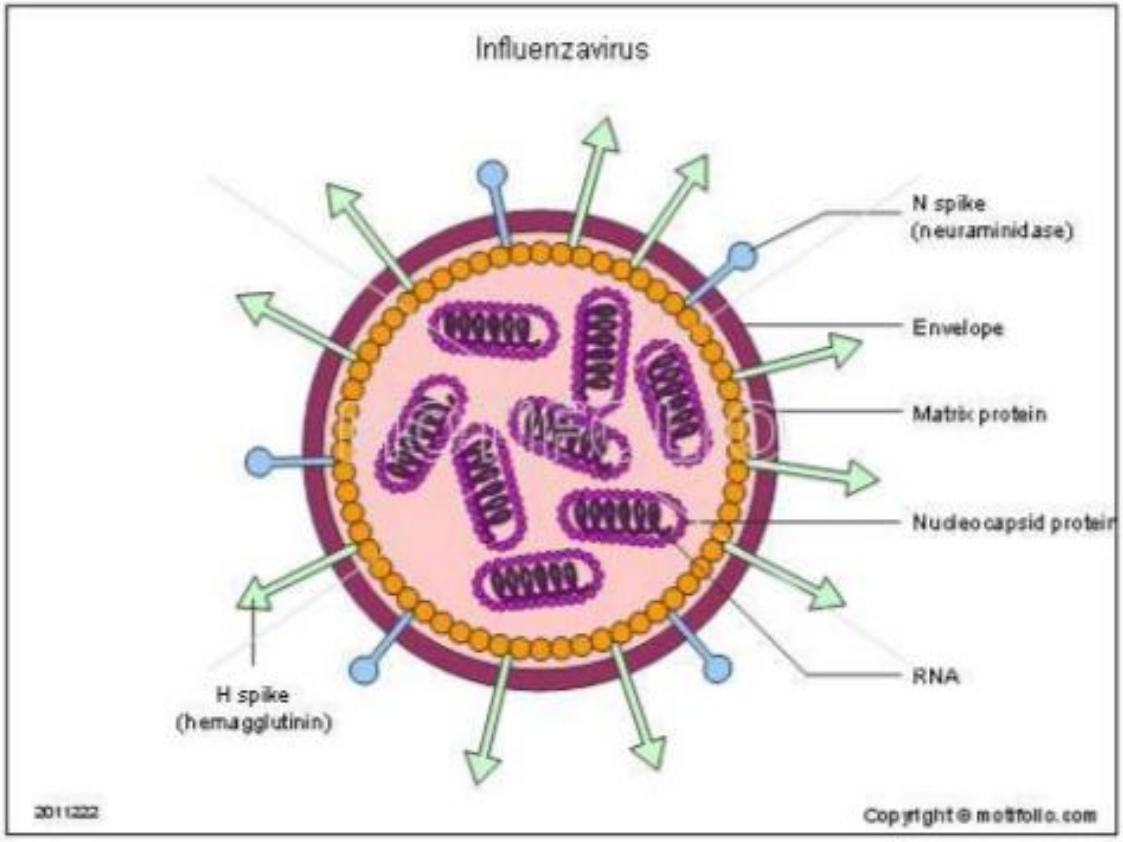
Membrane protein M2

Matrix protein M1

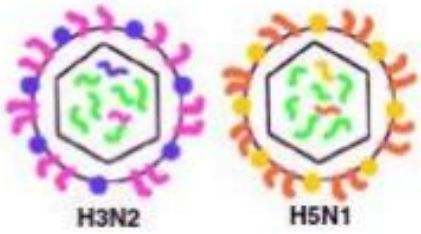
A + B viruses – 8 different hellical nucleocaspid segments of RNA

C – 7 genomic segments

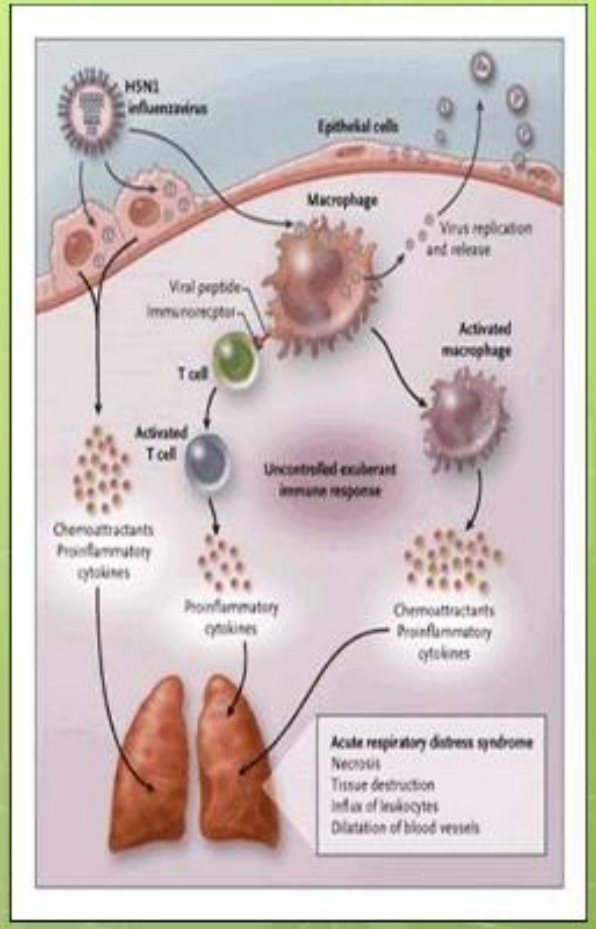
Characteristics



Ag Shifts



- The HA and NA of influenza A virus can undergo major and minor Ag changes to ensure the presence of immunologically naïve , susceptible people.
- Shifts occur only with influenza A virus , and the different HAs are designated H1, H2…H16.
- The NA of influenza A also undergoes antigenic shifts.
- Mutation-derived changes in HA are responsible for the changes in antigenicity (shifts).
- Influenza B virus undergoes only minor antigenic changes .
- This process occurs every 2 to 3 years causing local outbreaks of influenza A and B infection.



Pathogenesis

Transmission

Replication

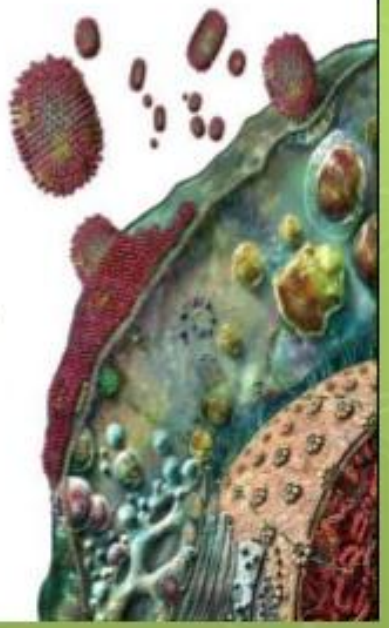
Mechanism of disease

Transmission

- Transmission mainly person to person by sneezing , coughing , or simply talking .
- Virus likes a cool , less humid atmosphere (winter heating season).
- Extensively spread by school children .
- The respiratory tract is the gate opening of the virus .
- Influenza can also be transmitted by saliva, nasal secretions, feces and blood.

Replication

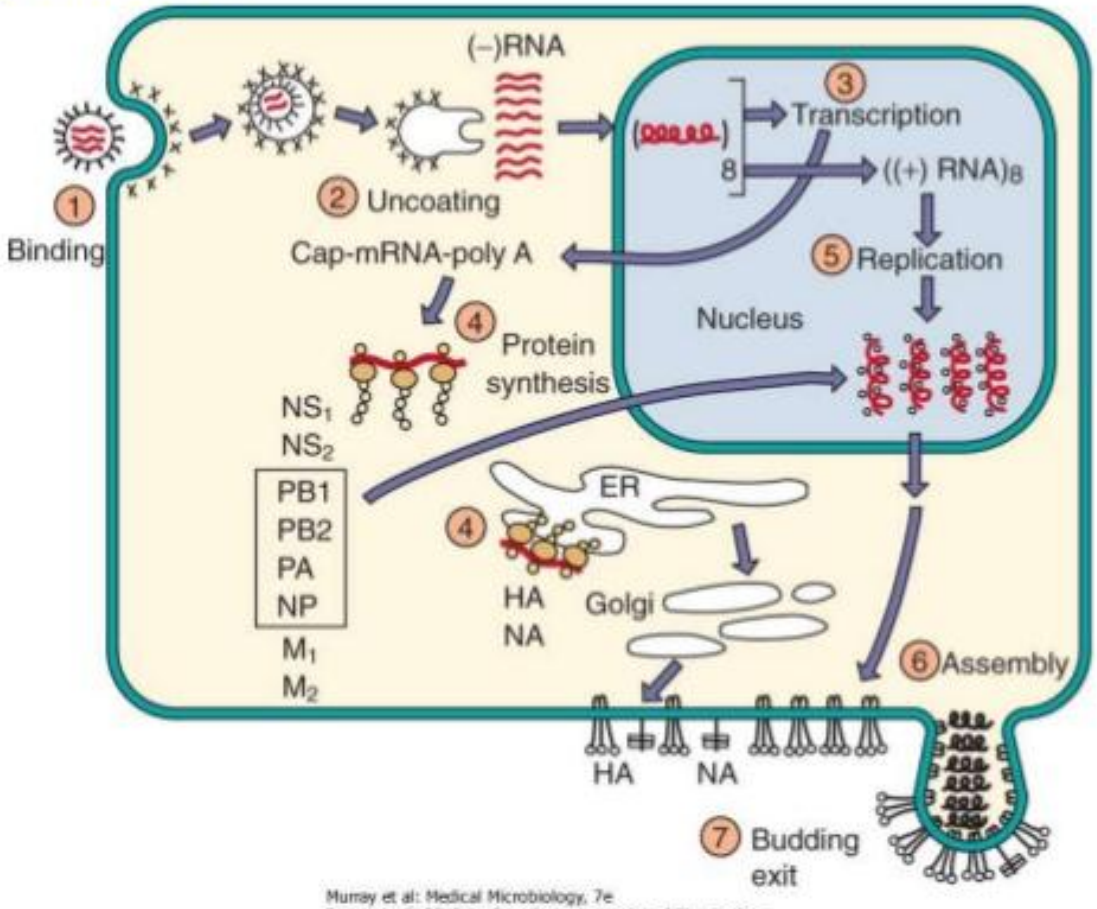
- Begins with the binding of HA to sialic acid on cell surface glycoproteins .
- The virus is then transferred to an endosome through vesicles .
- The nucleocapsid travels to the nucleus , where it is transcribed into messenger RNA.
- The transcriptase uses host cell mRNA as a primer for viral mRNA synthesis



Replication

- The mRNAs are translated into protein in the cytoplasm.
- The HA and NA glycoproteins are processed by the endoplasmic reticulum and Golgi apparatus.
- The HA and NA are then transported to the cell surface.
- The virus buds selectively from the apical (airway) surface of the cell as a result of the preferential insertion of the HA in this membrane.
- Virus is released approximately 8 hours after infection.

Replication



The important Products of Influenza Gene Segments

Segment	Protein	Function
4	HA	Hemagglutinin, viral attachment protein, fusion protein, target of neutralizing antibody
5	NP	Nucleocapsid
6	NA	Neuraminidase (cleaves sialic acid and promotes virus release)
7	M1	Matrix protein: viral structural protein (interacts with nucleocapsid and envelope, promotes assembly)
	M2	Membrane protein (forms membrane channel and target for amantadine, facilitates uncoating and HA production)

Pathogenesis

- Incubation period : 1-4 days (average of 2 days) .
- Adults can be infectious from 1 day before start of symptoms to 5-7 days after illness starts .
- More infectious in children .
- The main cause of hospitalization is flu .
- The symptoms and time course of the disease are determined by the extent of viral and immune killing of epithelial tissue and cytokine action .
- Influenza is normally a self-limited disease that rarely involves organs other than the lung .
- Repair of the compromised tissue is initiated within 3 to 5 days of the start of symptoms but may take as long as a month or more , especially in elderly people .

Pathogenesis

- Influenza initially establishes a local upper respiratory tract infection . To do so, the virus first targets and kills mucus-secreting, ciliated, and other epithelial cells, causing the loss of this primary defense system. NA facilitates the development of the infection by cleaving sialic acid (neuraminic acid) residues of the mucus, thereby providing access to tissue.
- Preferential release of the virus at the apical surface of epithelial cells and into the lung promotes cell-to-cell spread and transmission to other hosts. If the virus spreads to the lower respiratory tract, the infection can cause severe desquamation (shedding) of bronchial or alveolar epithelium down to a single-cell basal layer or to the basement membrane.

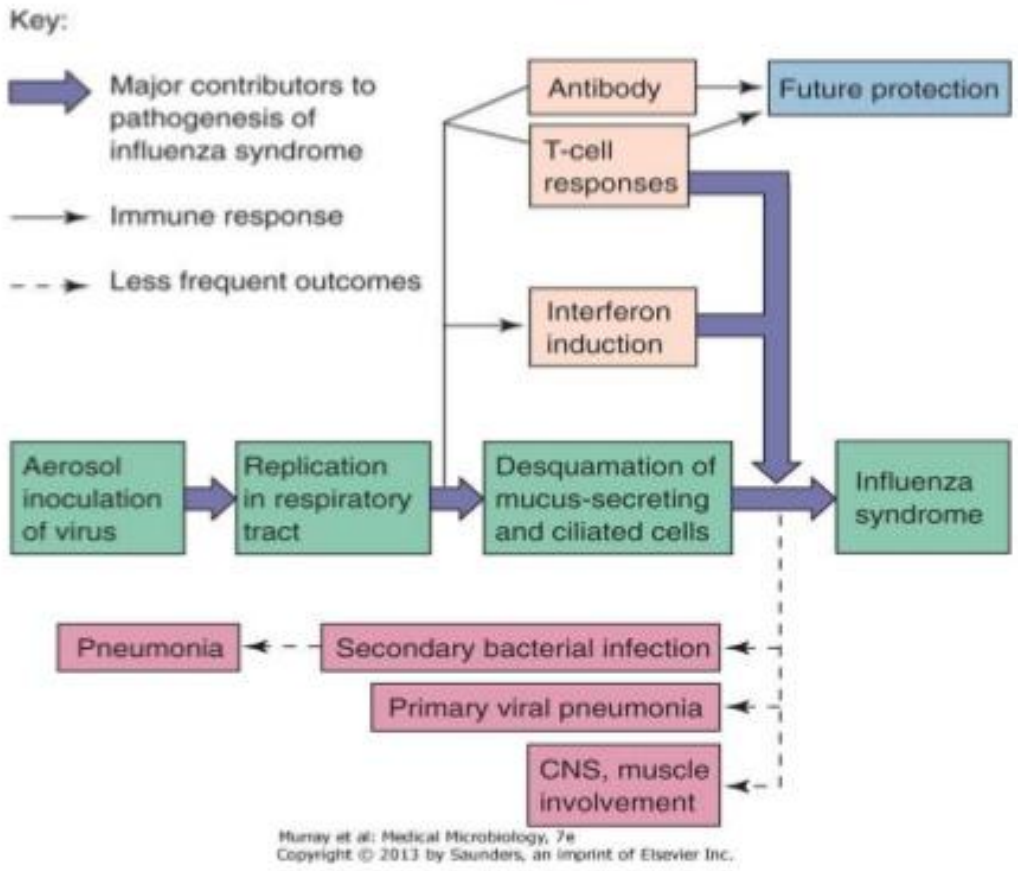
Pathogenesis (what else does influenza harm)

- Influenza infection promotes bacterial adhesion to the epithelial cells .
- Pneumonia may result from a viral pathogenesis or from a secondary bacterial infection .
- Inflammatory cell response of the mucosal membrane (monocytes, lymphocytes and few neutrophils) .
- Submucosal edema .
- Hyaline membrane disease .
- Alveolar emphysema .
- Necrosis of alveolar walls .

Pathogenesis and immunology

- Interferon and cytokine responses may be sufficient to control the infection and are responsible for the systemic **"flulike"** symptoms.
- T-cell responses are important for effecting recovery and immunopathogenesis , but Ab including vaccine induced Ab , can prevent disease .
- Influenza infection depresses macrophage and T-cell function .

Pathogenesis



Symptoms

F	Fever
A	Aches
C	Chills
T	Tiredness
S	Sudden Onset

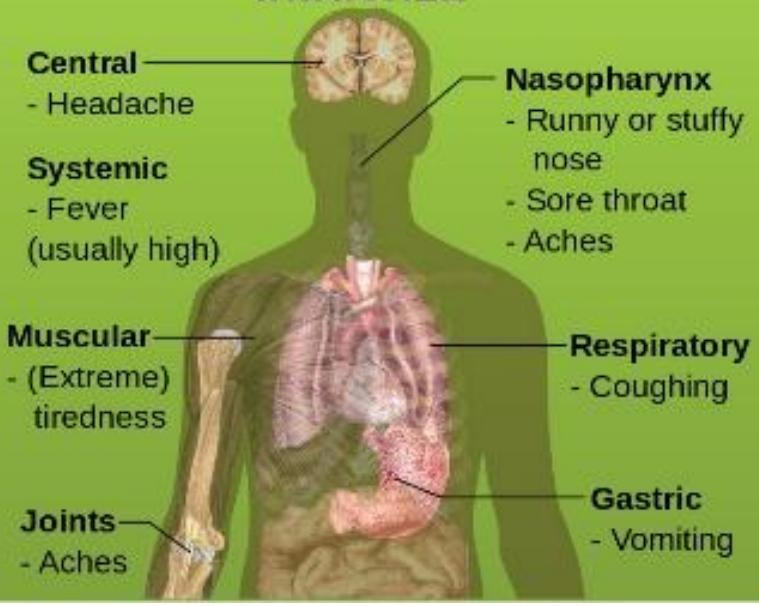
A brief prodrome of malaise and headache lasting a few hours

Onset fever , chills , severe myalgias , loss of apetite , weakness and fatigue , sore throat , nonproductive cough .

Recovery within 7 to 10 days

Pneumonia , myositis , and Rye syndrome .

Symptoms of
Influenza



Diagnosis

- Based on the characteristic symptoms.
- The season , presence of the virus in community .
- Cell culture in monkey kidney .
- Hemagglutination .
- Ab inhibition of hemadsorption .

Prevention

Vaccine :

- A shot containing killed virus (inactivated) given in the arm normally .
- Can be also given as nasal spray .

Other :

- Keeping good hygiene habits
- Covering coughs and sneezes
- Staying away of sick people

Paramyxoviridiae

- Looks similar to Orthomyxoviruses,
- Larger in size, More pleomorphic.
- Spherical in shape 100 to 300 nm
- Some times appear as filamentous,Gaint forms are present.
- But contains only single stranded RNA.
- **Do not contain** segmented RNA like Orthomyxoviruses, **Antigenic variation absent**.
- Reassrtment like Influenzae viruses – ABSENT.

Paramyxoviridae

RNA viruses

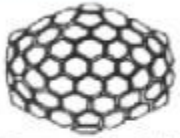
Paramyxoviridae

Orthomyxoviridae

Coronaviridae

Retrovirida

Reoviridae



Birnaviridae

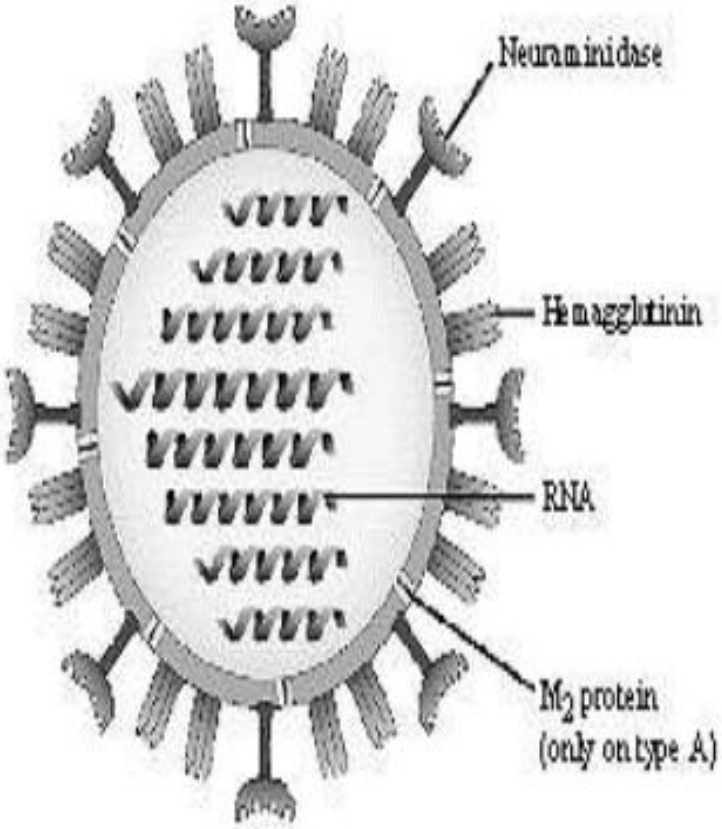
100 nm

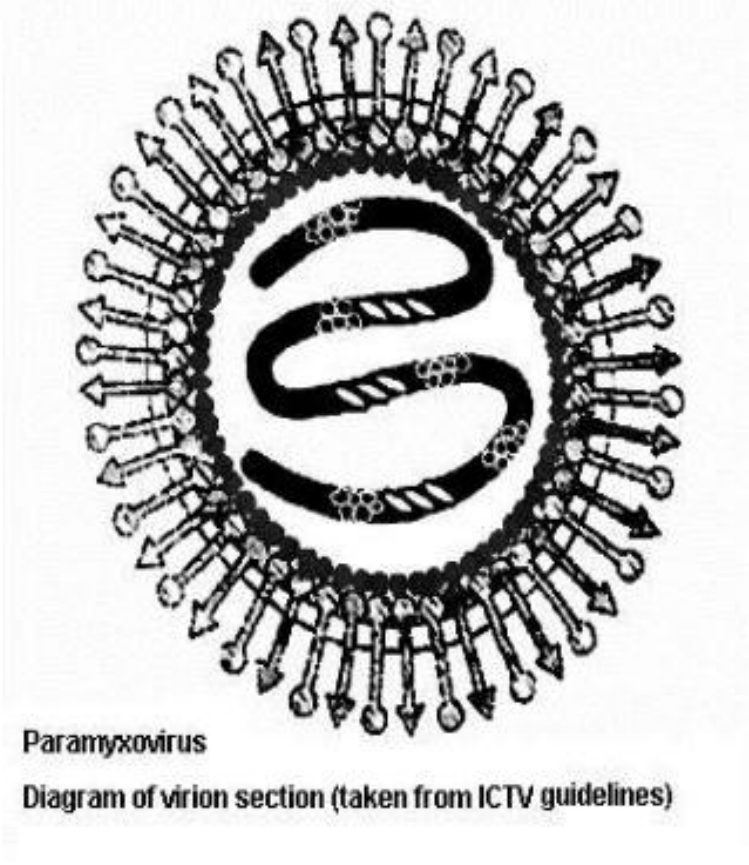
Picornaviridae

Caliciviridae

Togaviridae
Flaviviridae
Arterivirus

ORTHOMYXO / PARAMYXO Viruses





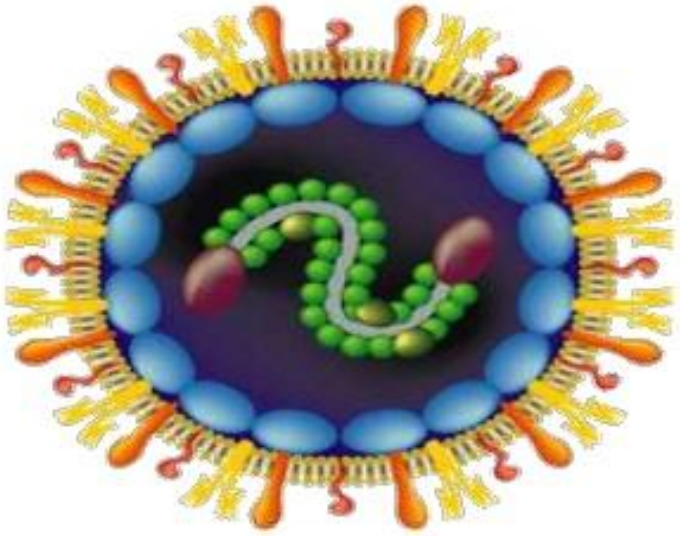
Paramyxovirus

Diagram of virion section (taken from ICTV guidelines)

Paramyxovirus

Paramyxovirus

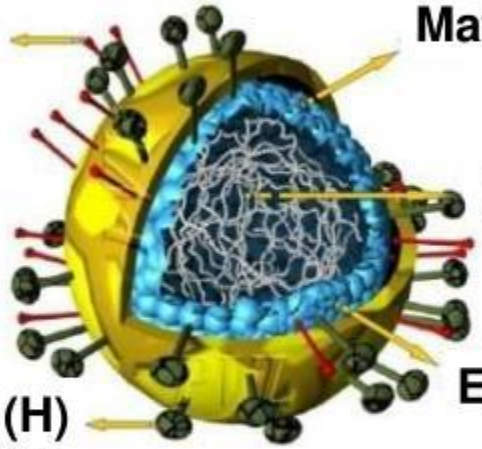
Diagram of virion section (taken from ICTV guidelines)



Family *Paramyxoviridae*

Enveloped, helical nucleocapsid, 220 nm

Single strand, non-segmented, negative sense RNA



Fusion (F) protein

Matrix (M) protein

Nucleocapsid
Nucleoprotein (NP)
RNA

HN or G protein

Haemagglutinin (H)
Neuraminidase (N)

Envelope
Lipid membrane

Not all *Paramyxoviridae* have haemagglutinin or neuraminidase properties

Family *Paramyxoviridae*

Subfamily *Paramyxovirinae*

- Genus *Morbillivirus*
- Genus *Rubulavirus*
- Genus *Avulavirus*
- Genus *Respirovirus*
- Genus *Henipavirus*

Subfamily *Pneumovirinae*

- Genus *Pneumovirus*
- Genus *Metapneumovirus*

Incubation Period

- The incubation period is 14-21 days and is communicable from 6 days before to 9 days after facial swelling is apparent. It can lead to brain inflammation, deafness or sterility

Paramyxoviridae

Pathogenesis

- Epitheliotropic and neurotropic
- Replicate in cytoplasm
  - Eosinophilic inclusion bodies in cytoplasm and nucleus
- Respiratory disease
- Neurological disease
- Alimentary tract disease
- Persistent infection (e.g. old dog encephalitis)

Paramyxoviridae

Immunity

- Effective immune response in most animals
  - Antibodies are neutralising
  - Vaccination is protective
- Some paramyxoviruses establish persistent infections in the central nervous system

CORONAVIRUS

- Single stranded RNA
- Pleomorphic, 80 to 160 nm in diameter
- subfamilies *Coronavirinae* and *Torovirinae* in the family *Coronaviridae*, in the order Nidovirales.[1][2]
- Coronaviruses are enveloped viruses with a positive-sense RNA genome and with a nucleocapsid of helical symmetry

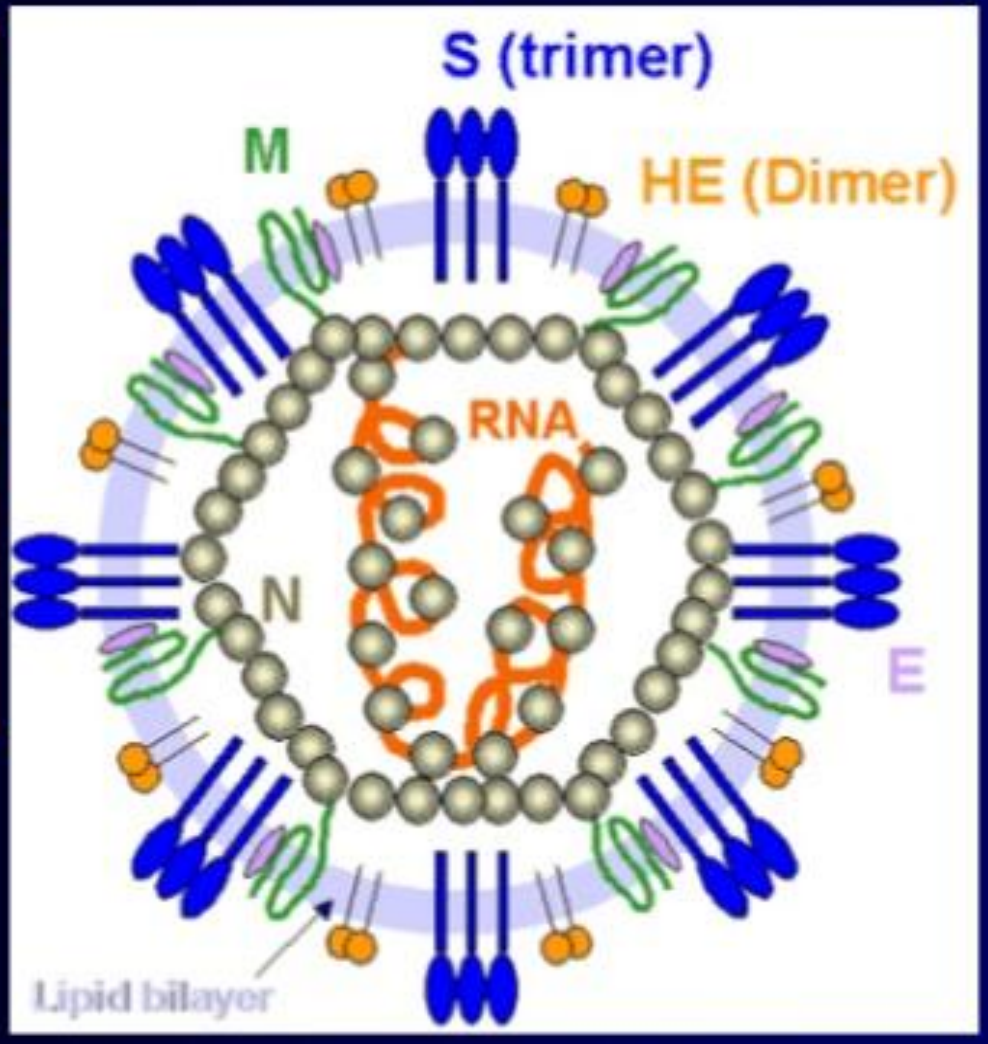
By Sachitanand Prasad Chaudhary

CORONAVIRUSES

The genome

- SS linear non segmented +ve sense RNA

- the largest among RNA viruses.

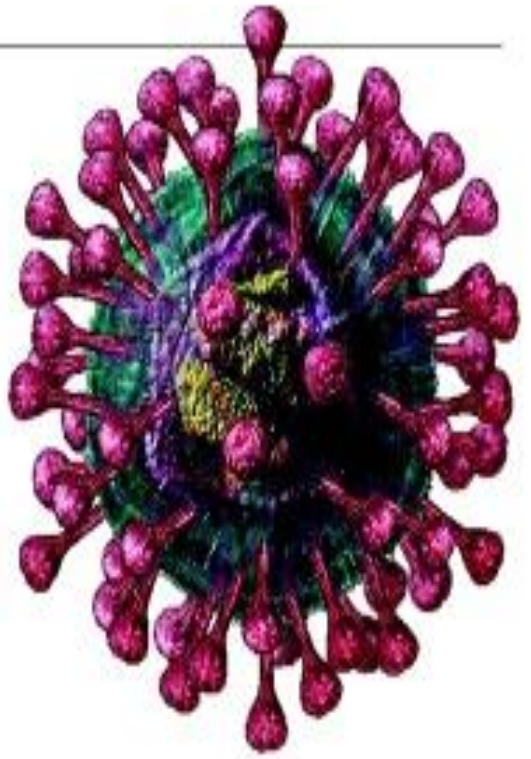


HUMAN CORONAVIRUS

- Human coronavirus were first identified in the mid-1960s
- Six coronavirus that can infect people are
- Alpha coronaviruses 229E
- Beta coronaviruses NL63
- Beta coronaviruses OC43
- Beta coronaviruses HKUI
- Beta coronaviruses SARS-CoV(causes severe acute respiratory syndrome)
- Beta coronaviruses MERS-CoV(Middle east respiratory syndrome)

Classification :

- Family: Coronaviridae
- • Gender: Coronavirus
- • Genome: linear single-stranded RNA +
- • pleomorphic, Wrapped
- • 80 to 220 nm
- • 30 serotypes



Characteristics:

- Protein S. Form projected responsible for stimulating neutralizing antibody and interaction with cellular receptors.
- Bind to cells via specific receptors.
- Enter through membrane fusion.
- In the cytoplasm, the viral RNA is translated by the host machinery.
- Viral proteins are synthesized, assembled, are fused to the cell membrane and the virus out.

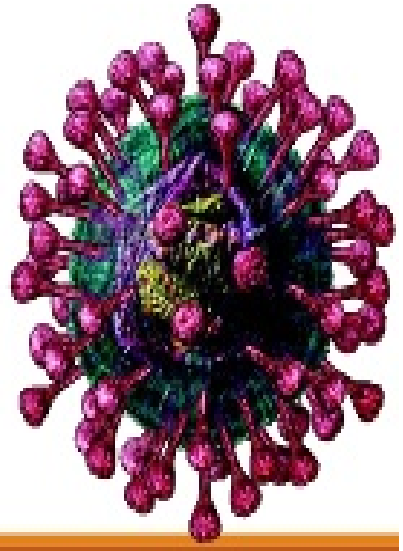
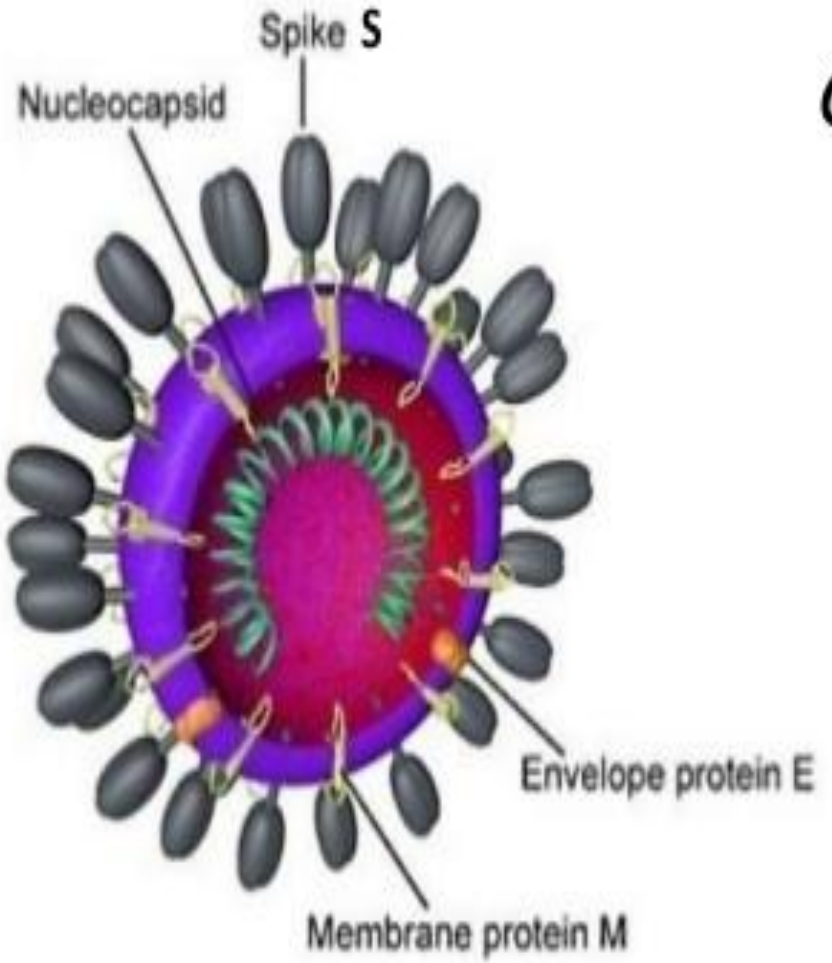
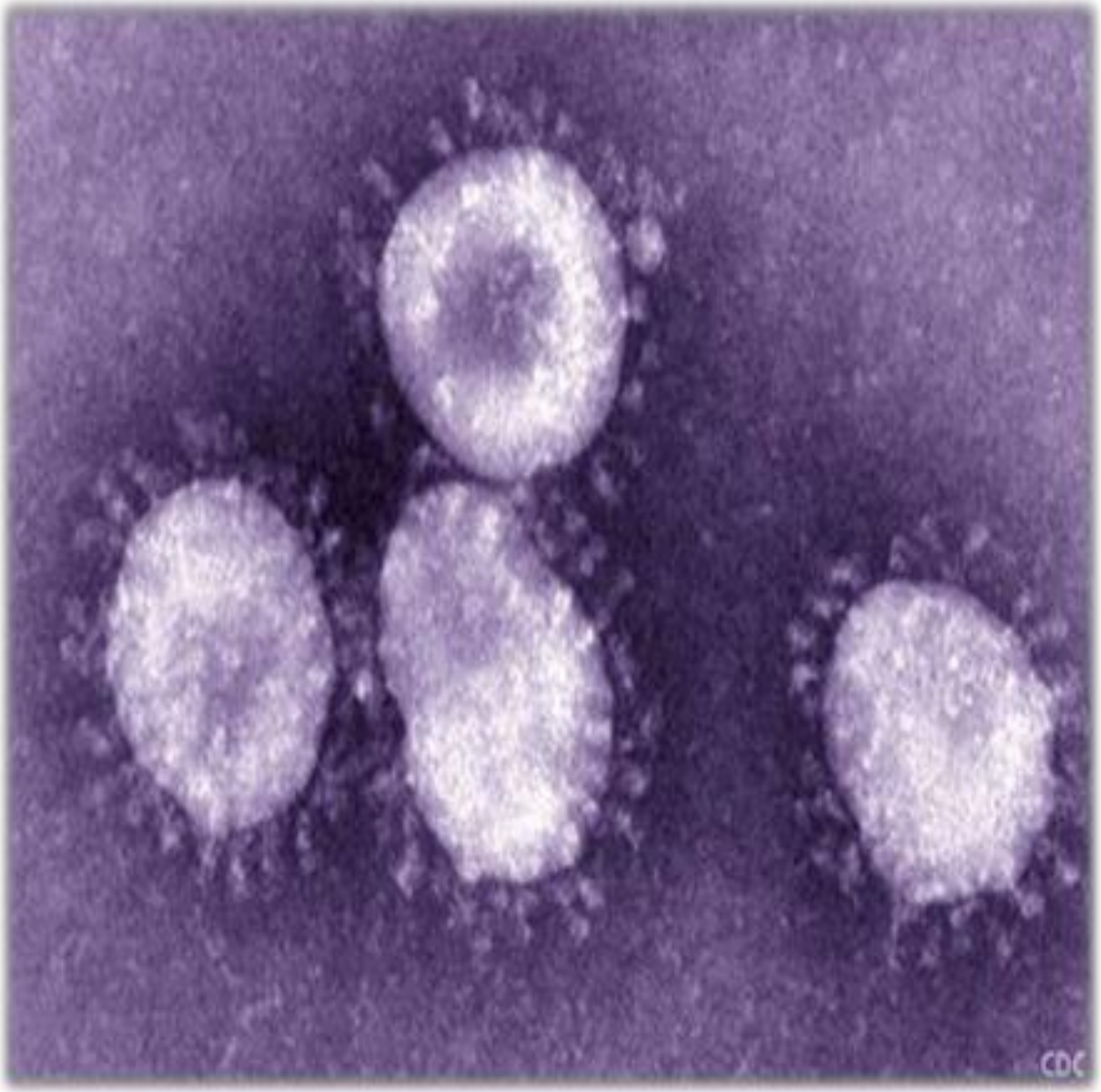


Diagram of **Coronavirus Virion**

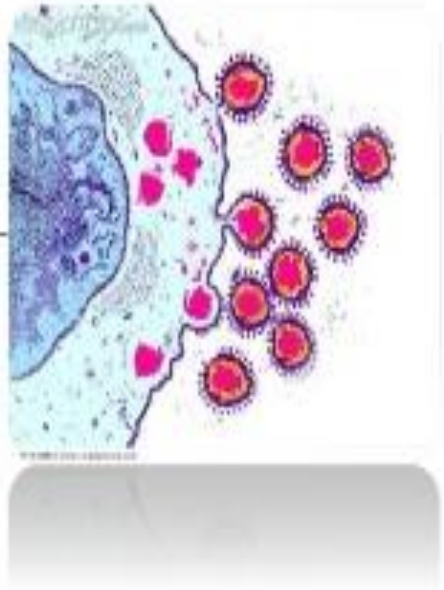




❖ A **picture** of a coronavirus as seen through an "electron microscope"

Infection:

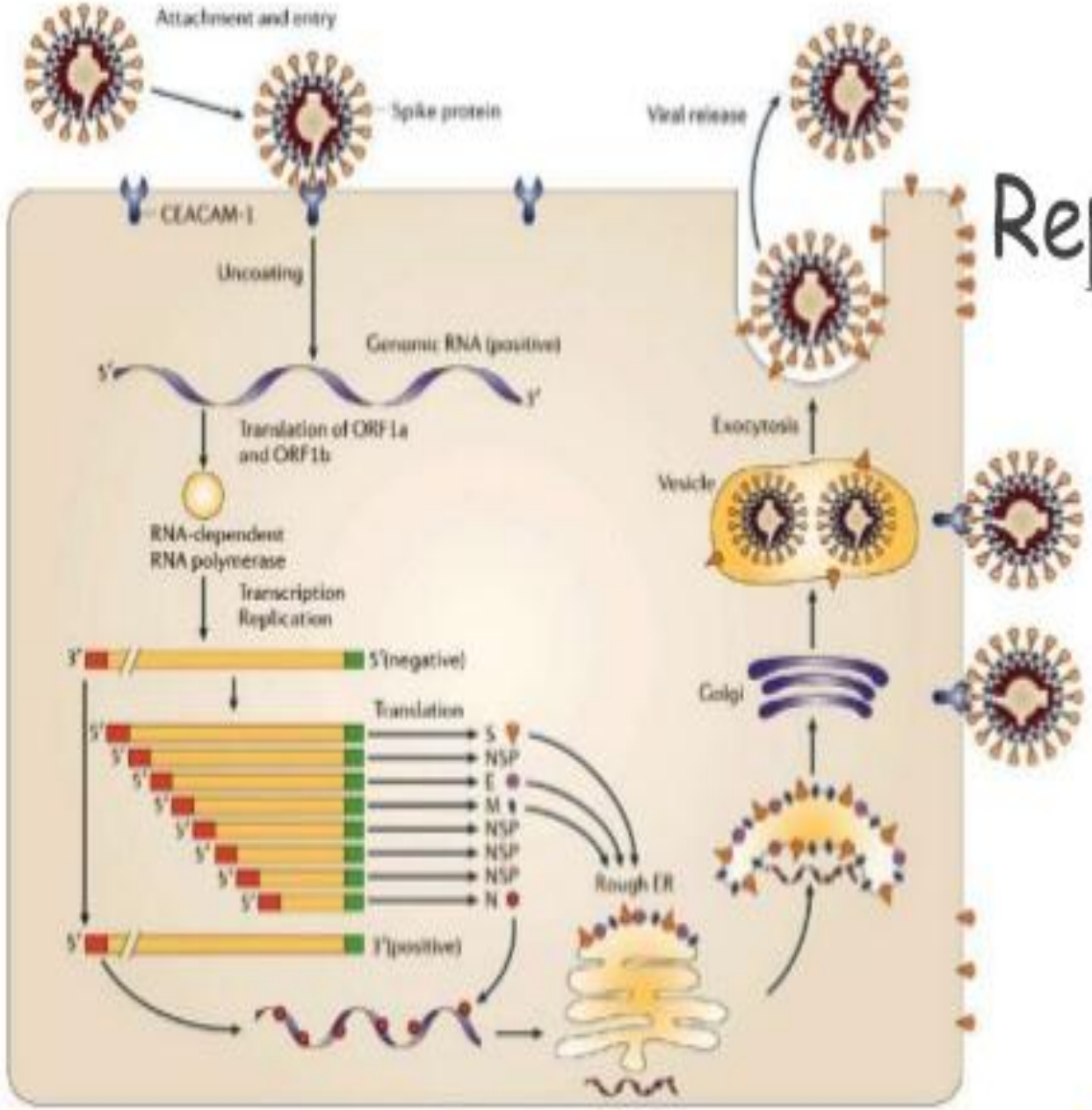
- They are transmitted by aerosols secretions respiratory.
- It has an incubation period of 2 days to a week, eliminating virus for one week.



Infection:

- The virus replicates in the cytoplasm of the cell host, mend in the endoplasmic reticulum and pass the Golgi cisternae until they are finally released by exocytose.
- Are responsible for up to 15% of colds, taking more often in the winter and beginning of the spring with a characteristic periodicity of 2-4 years

Replication:



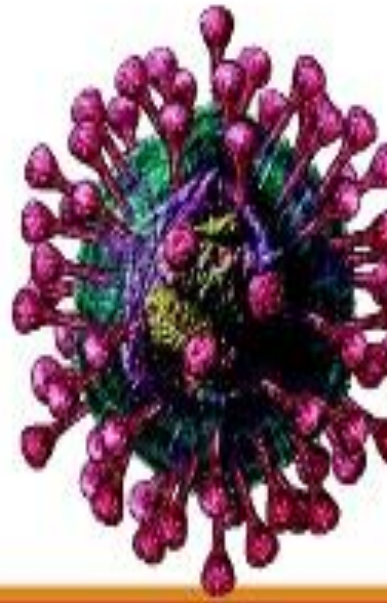
PATHOGENESIS/SYMPTOM

- It causes mild to moderate upper-respiratory tract illnesses of short duration
- It shows severe symtoms in people with cardiopulmonary disease or compromised immune system, or the elderly
- Symtoms
- Runny nose
- Cough
- Sore throat
- Fever
- Lower respiratory tract illness, such as pneumonia
- MERS-CoV and SARS-CoV causes severe illness

Laboratory Diagnosis

ELISA

PCR



PICORNAVIRUSES

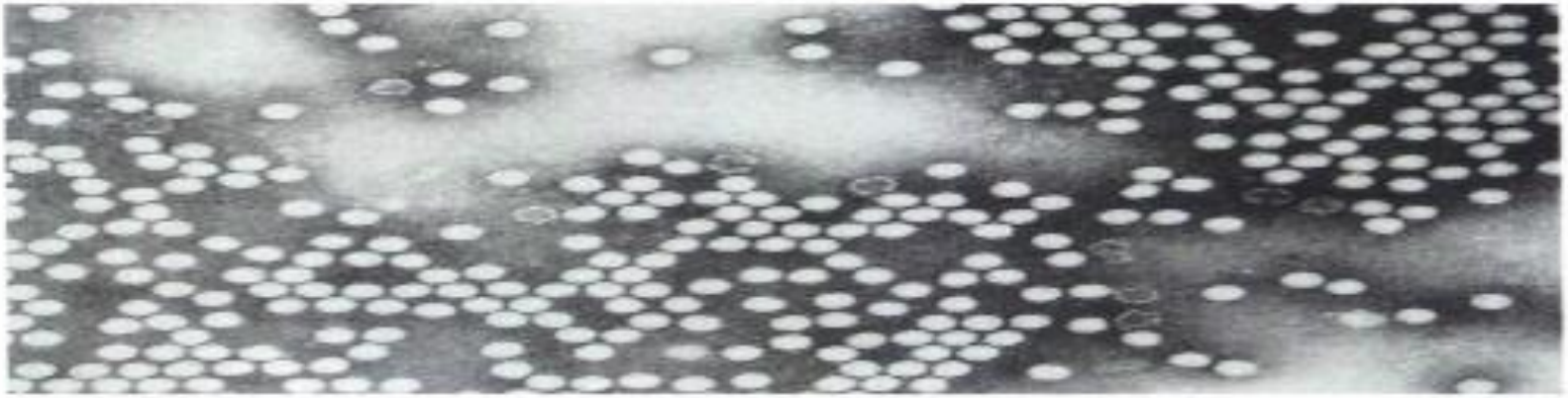


FIGURE 57–1. Electron micrograph of poliovirus. (Courtesy Centers for Disease Control and Prevention, Atlanta.)

PROPERTIES

Structure and composition

30 nm, icosahedral

plus-strand RNA, 7.2-8.4 kb

RNA is poly adenylated

VP1, VP2, VP3, VP4 structural proteins

VP4 interacts with viral RNA

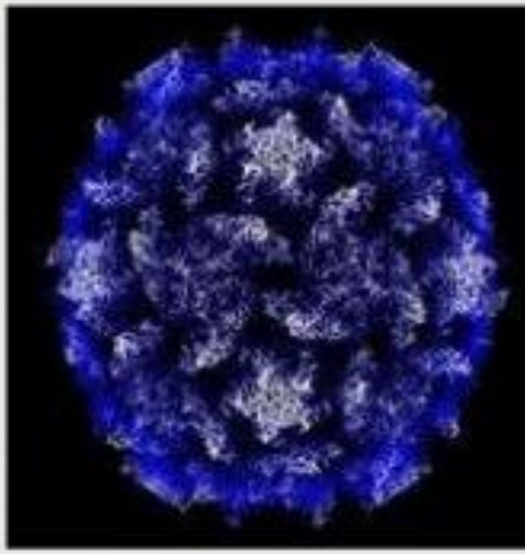
2A, 2B, 2C proteases

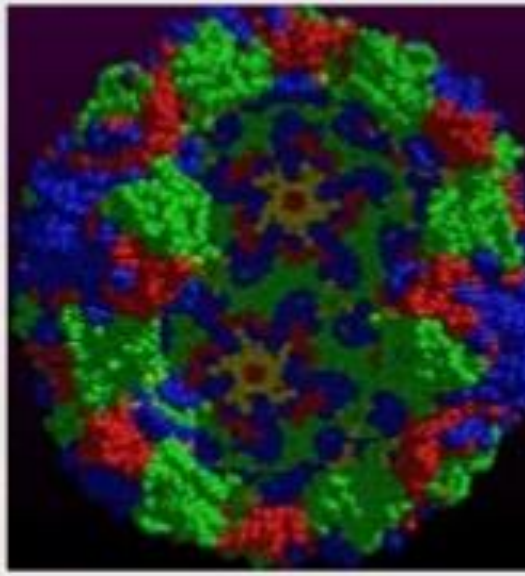
3A, 3B, 3C, 3D RNA replication

Nonenveloped

Cytoplasmic replication

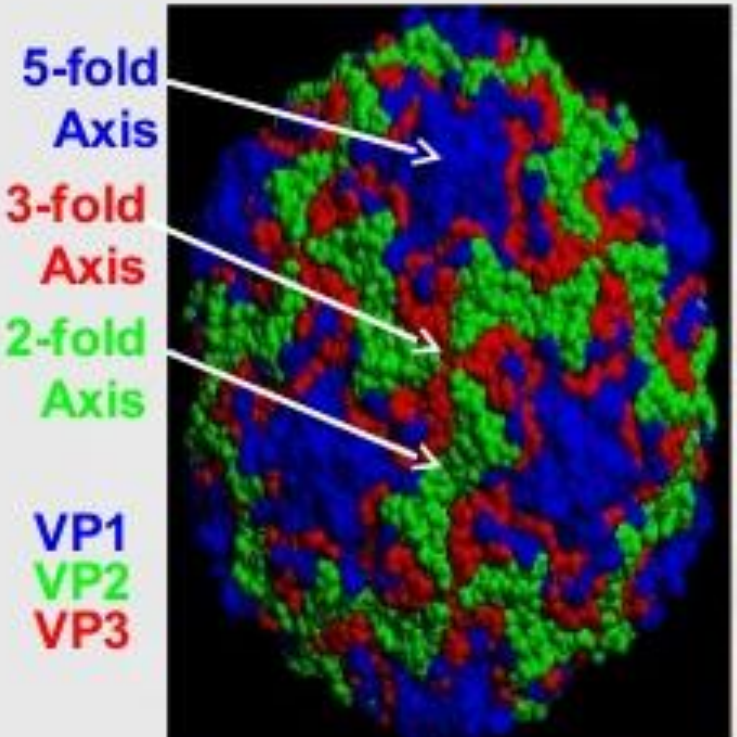
Resistant to pH 3 to 9 (except for Rhinoviruses).

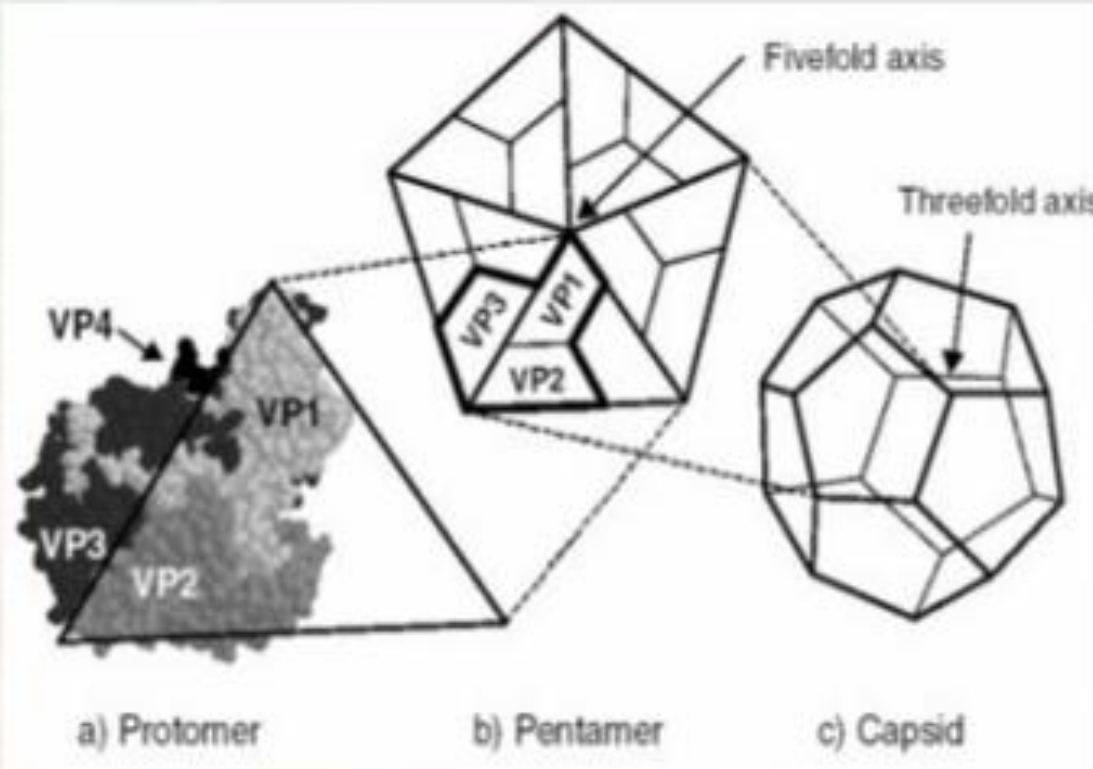




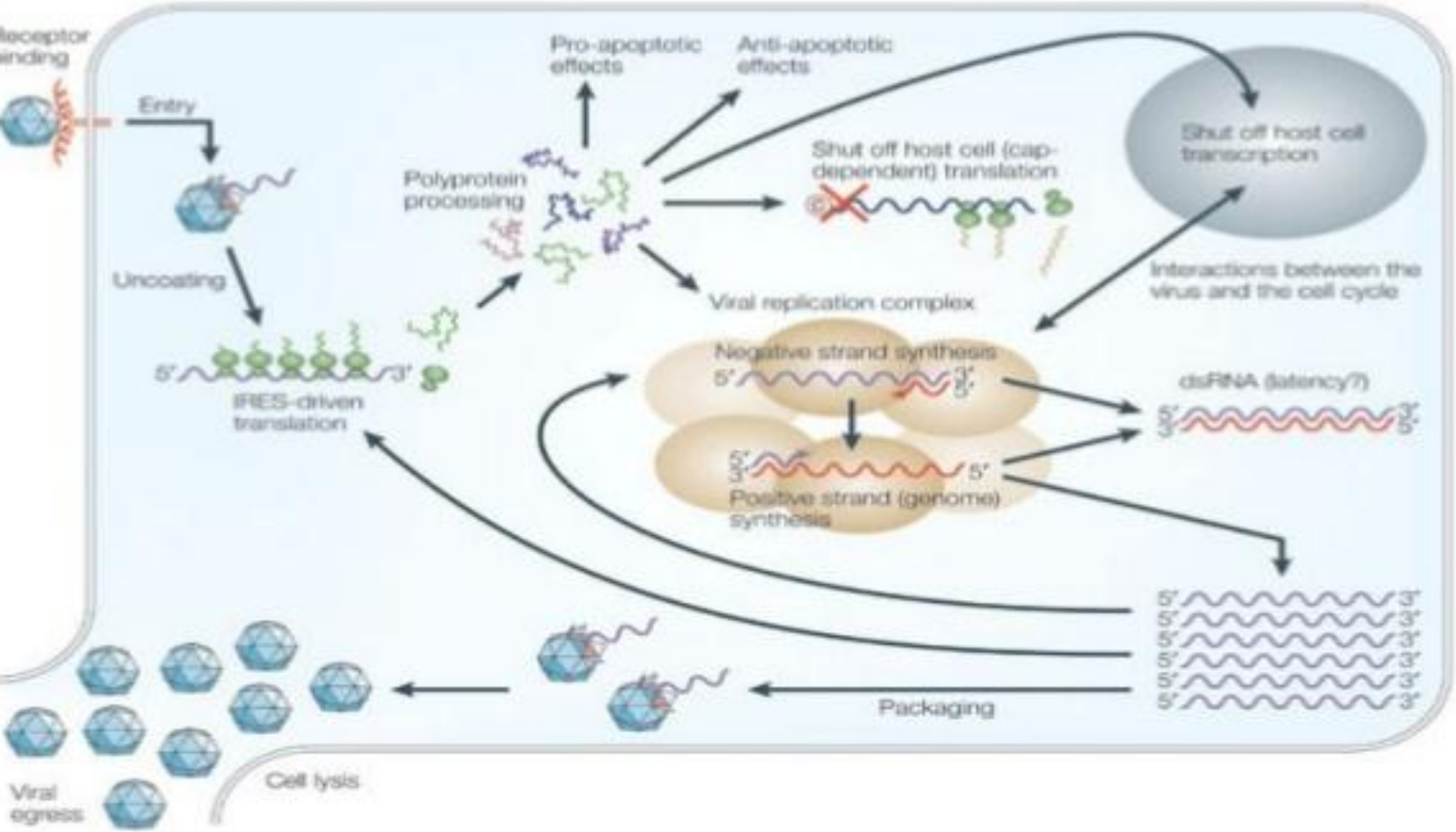
PICORNAVIRUS STRUCTURE

- The Basic capsid building block is a protomer that consists of one copy each of VP1, VP2, VP3 & VP4. VP1, VP2 & VP3 are on the virion surface, with VP4 being internal. VP1, VP2 & VP3 have no sequence homology, but have the same topology.



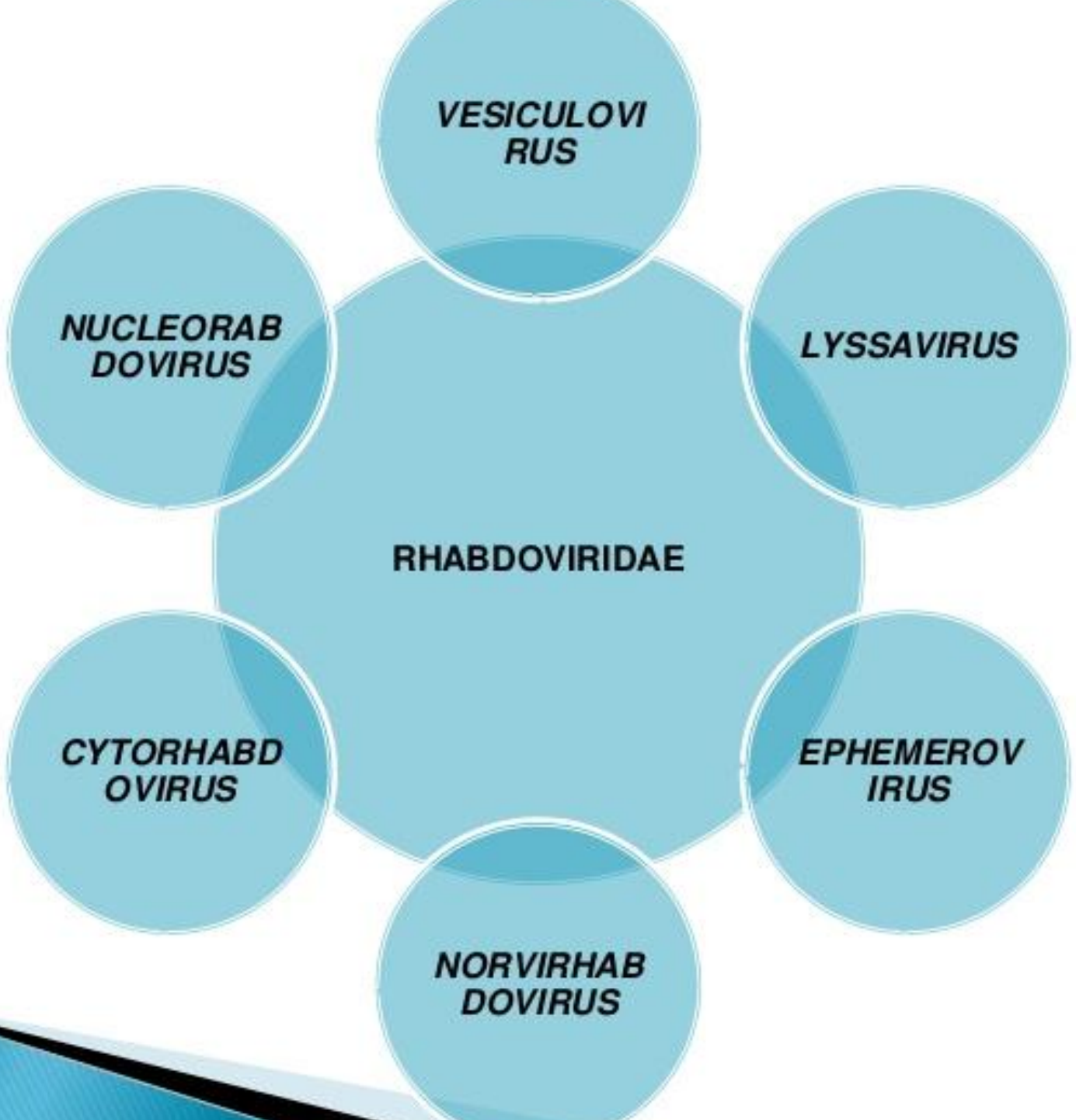


PICORNAVIRUS REPLICATION CYCLE



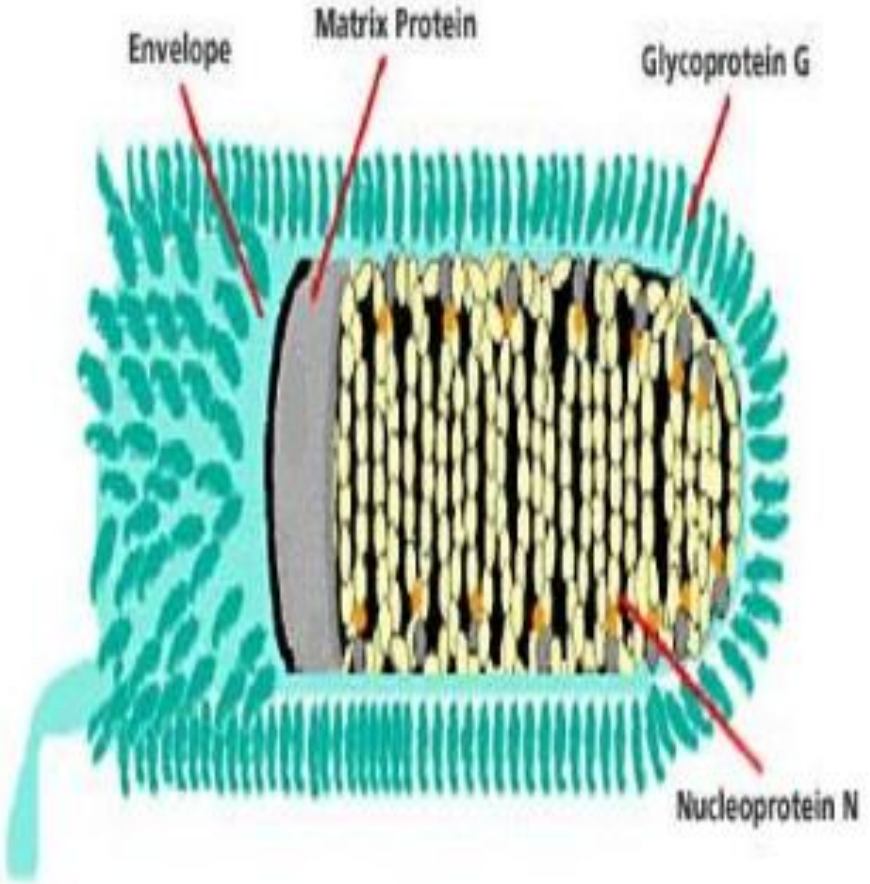
RHABDOVIRUSES:

- ***Mononegavirales order***
- **are *negative, single stranded, monopartite RNA viruses***
- **capsid is roughly bullet shaped**
- **genome, about 11-15 kb in size**
- **Encodes for 5 to six proteins.**
- **SIX genera**

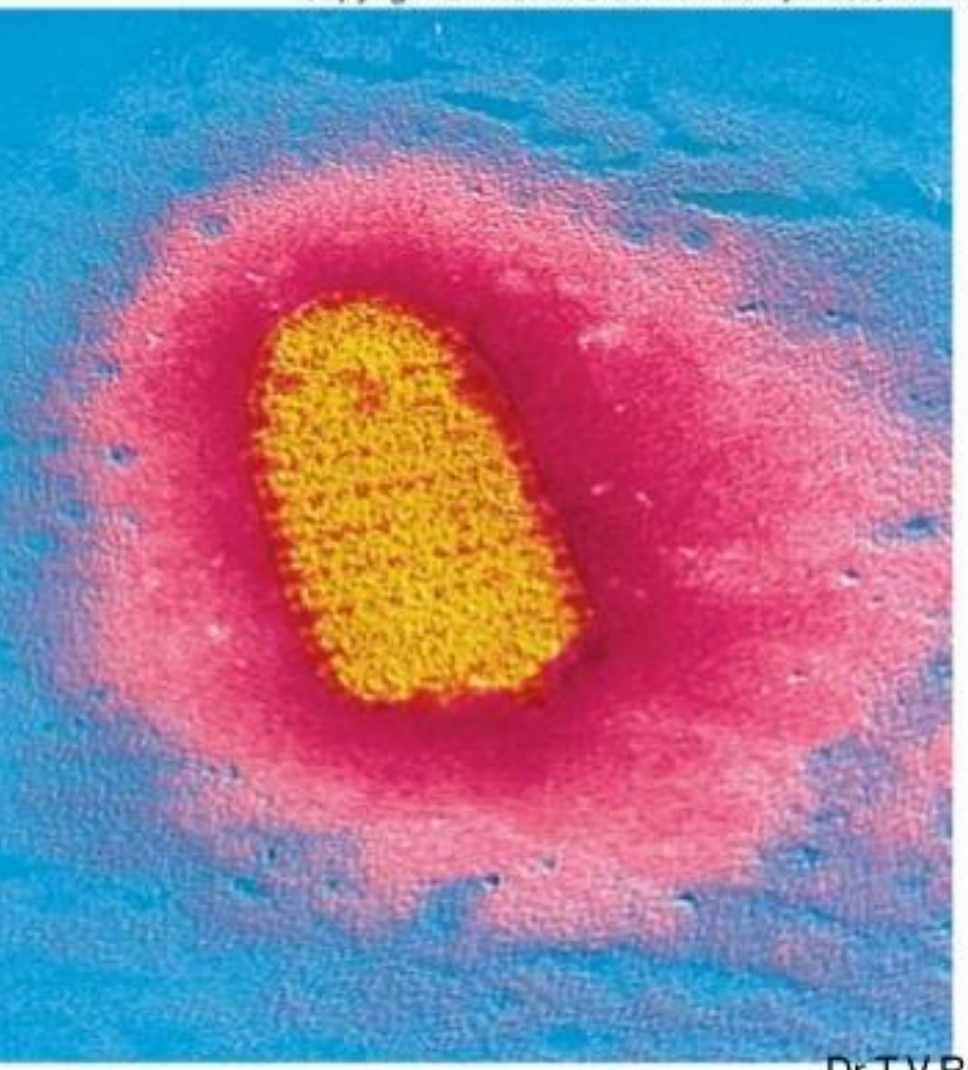

VESICULOVI RUS
NUCLEORAB DOVIRUS
LYSSAVIRUS
RHABDOVIRIDAE
CYTORHABD OVIRUS
EPHEMEROV IRUS
NORVIRHAB DOVIRUS

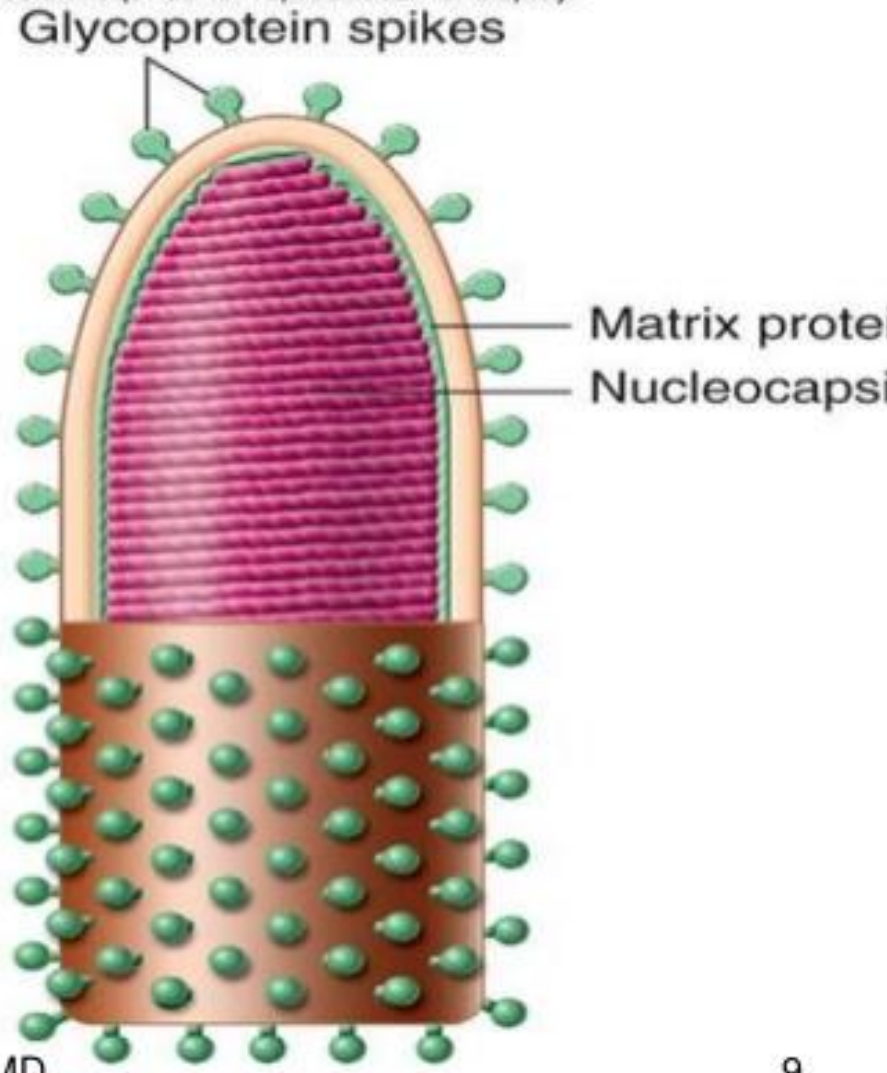
Rabies virus

- Bullet shaped virus
- Size is 180 x 75 nm
- Has Lipoprotein envelop
- Knob like spikes /Glycoprotein S
- Genome un segmented
- Linear negative sense RNA



Structure of the rabies virus



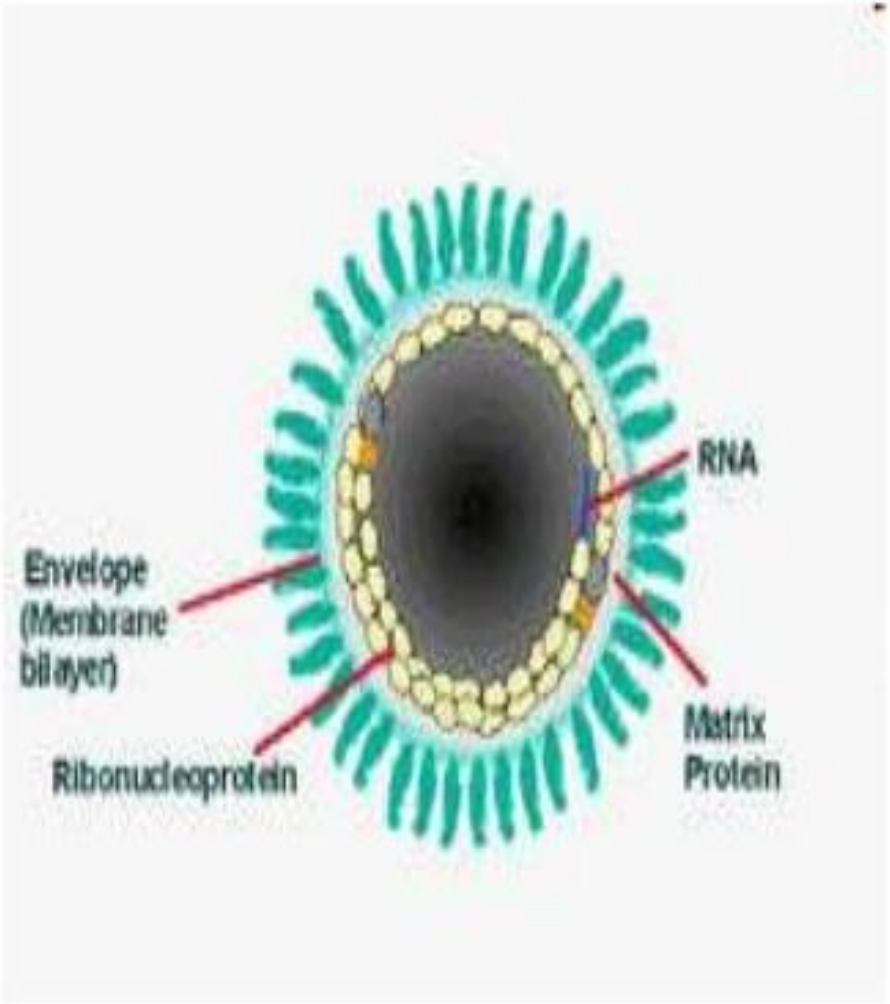


)

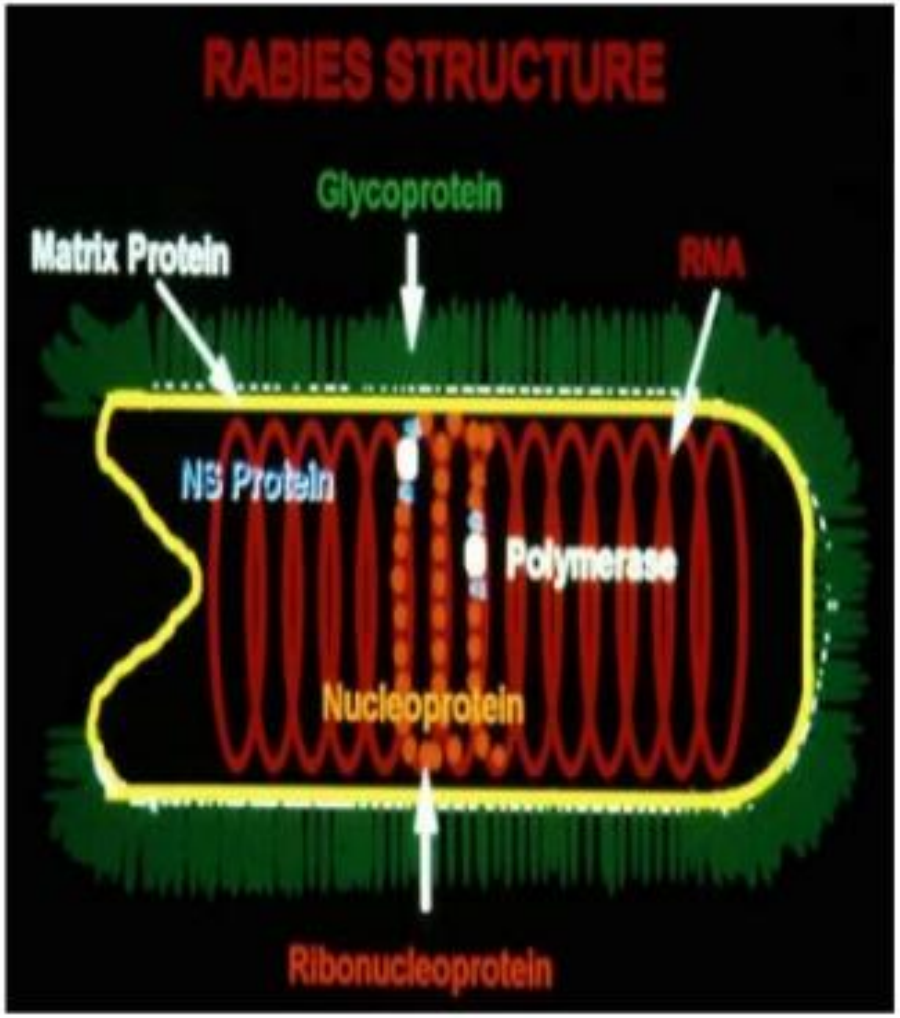
(b)

Fixed Virus

- One whose virulence and incubation period have been stabilized by serial passage and remained fixed during further transmission.
- Rabies virus that has undergone serial passage through rabbits, thus stabilizing its virulence and incubation period



Street Virus

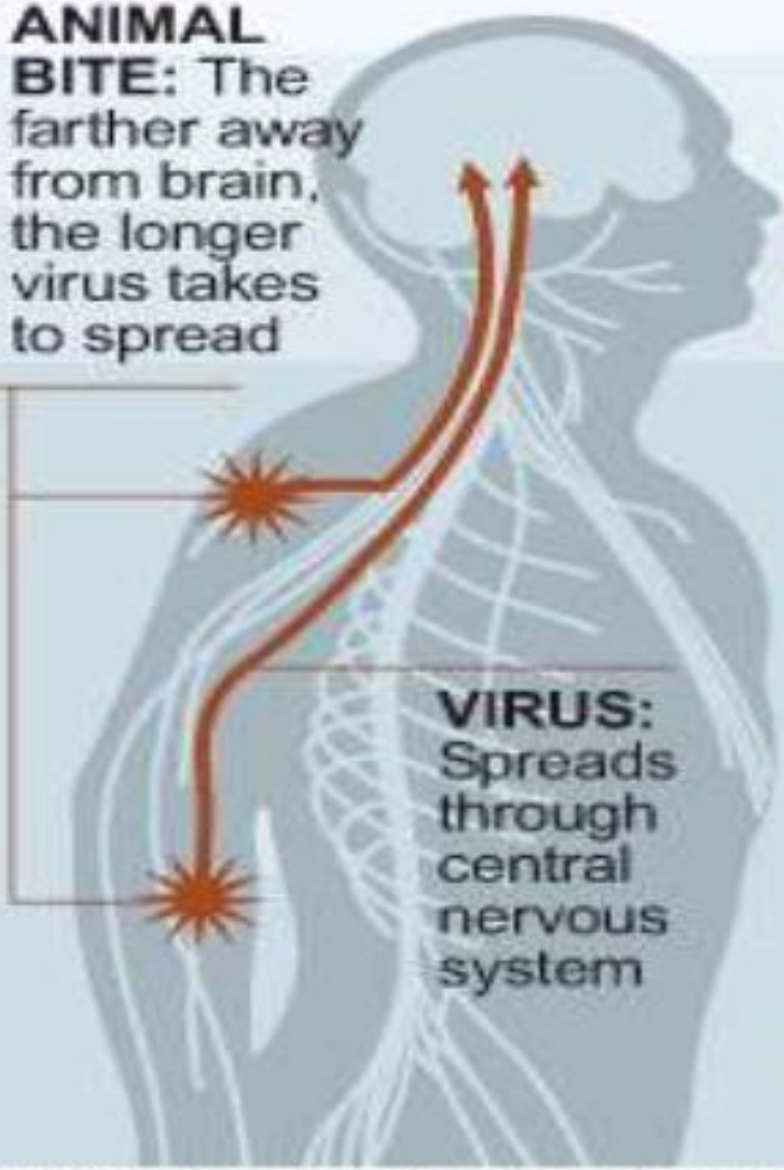


- Virus from a naturally infected animal, as opposed to a laboratory-adapted strain of the virus
- The virulent rabies virus from a rabid domestic animal that has contracted the disease from a bite or scratch of another animal.

Rabies

How it spreads

ANIMAL BITE: The farther away from brain, the longer virus takes to spread



VIRUS: Spreads through central nervous system

Common carriers of rabies

Infected animals: Show no fear for humans; act very agitated

Dog: Another common rabies source

Symptoms in humans

- Fever, depression
- Agitation
- Painful spasms followed by excessive saliva
- Death within a week without vaccine

Treatment: Hospitalization, immune globulin injections, anti-rabies vaccine

Foaming at mouth after drinking: Produced by spasms in throat

Pathogenesis of Rabies

- Bite by Rabid dog or other animals
- Virus are carried in saliva virus deposited on the wound site.
- If untreated 50% will Develop rabies.
- Rabies can be produced by licks and corneal transplantation.
- Virus multiply in the muscle ,connective tissue, nerves after 48 – 72 hours.
- Penetrated nerve endings.

PATHOGENESIS

Live virus → Epidermis, Mucus membrane

↓

Peripheral nerve

↓

centripetally

↓

CNS (gray matter)

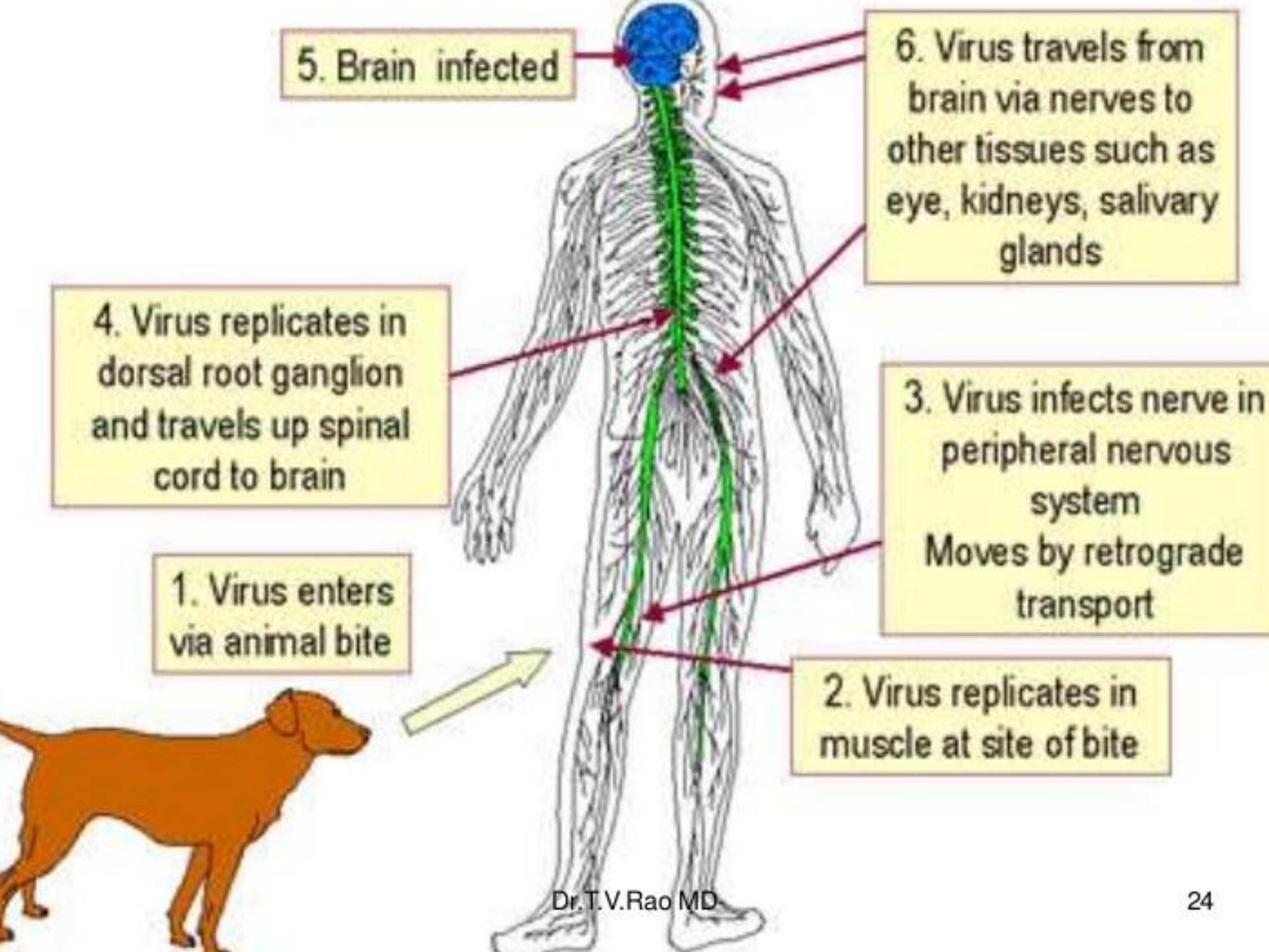
↓

centrifugally

↓

Other tissue (salivary glands,…)


Brain inflammation
Virus transmitted by infected saliva through bite or wound


5. Brain infected
6. Virus travels from brain via nerves to other tissues such as eye, kidneys, salivary glands
4. Virus replicates in dorsal root ganglion and travels up spinal cord to brain
3. Virus infects nerve in peripheral nervous system
Moves by retrograde transport
1. Virus enters via animal bite
2. Virus replicates in muscle at site of bite

Spread of Virus

- From Brain virus spread to

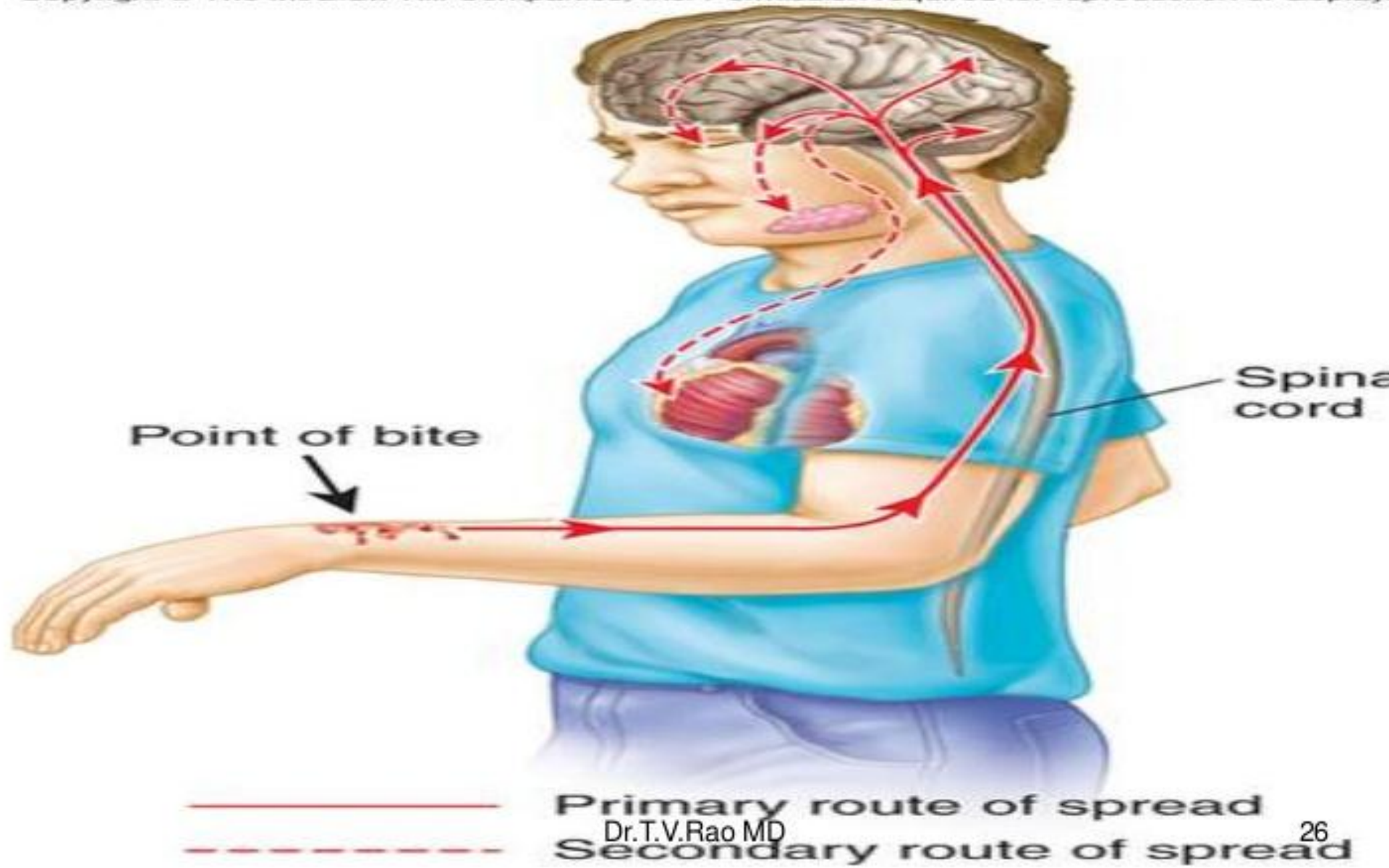
  Salivary glands,

  Conjunctival cell released into tears

  Kidney

  Lactating glands and Milk after pregnancy

Pathologic pictures of Rabies



Pathogenesis

- Incubation 1 – 3 months.
- **May be average from 7 days to 3 years.**
- Stages of the disease.

  Prodrome

  Acute encephalitis.

  Coma / Death.

Category as per WHO

- **Category I:** touching or feeding suspect animals, but skin is intact
- **Category II:** minor scratches without bleeding from contact, or licks on broken skin
- **Category III**: one or more bites, scratches, licks on broken skin, or other contact that breaks the skin; or exposure to bats

Symptoms

- Headache, fever, sore throat
- Nervousness, confusion
- Pain or tingling at the site of the bite
- **Hallucinations**
  - Seeing things that are not really there
- **Hydrophobia**
  - "Fear of water" due to spasms in the throat
- **Paralysis**
  - Unable to move parts of the body
- Coma and death

CLINICAL MANIFESTATIONS

1 – Non specific prodrome

2 – Acute neurologic encephalitis

Acute encephalitis

Profound dysfunction of brainstem

3 – Coma

4 - Death (Rare cases → recovery)

Post exposure Prophylaxis

- The vaccination is given on

  0, 3, 7, 14, 30, and 90th day

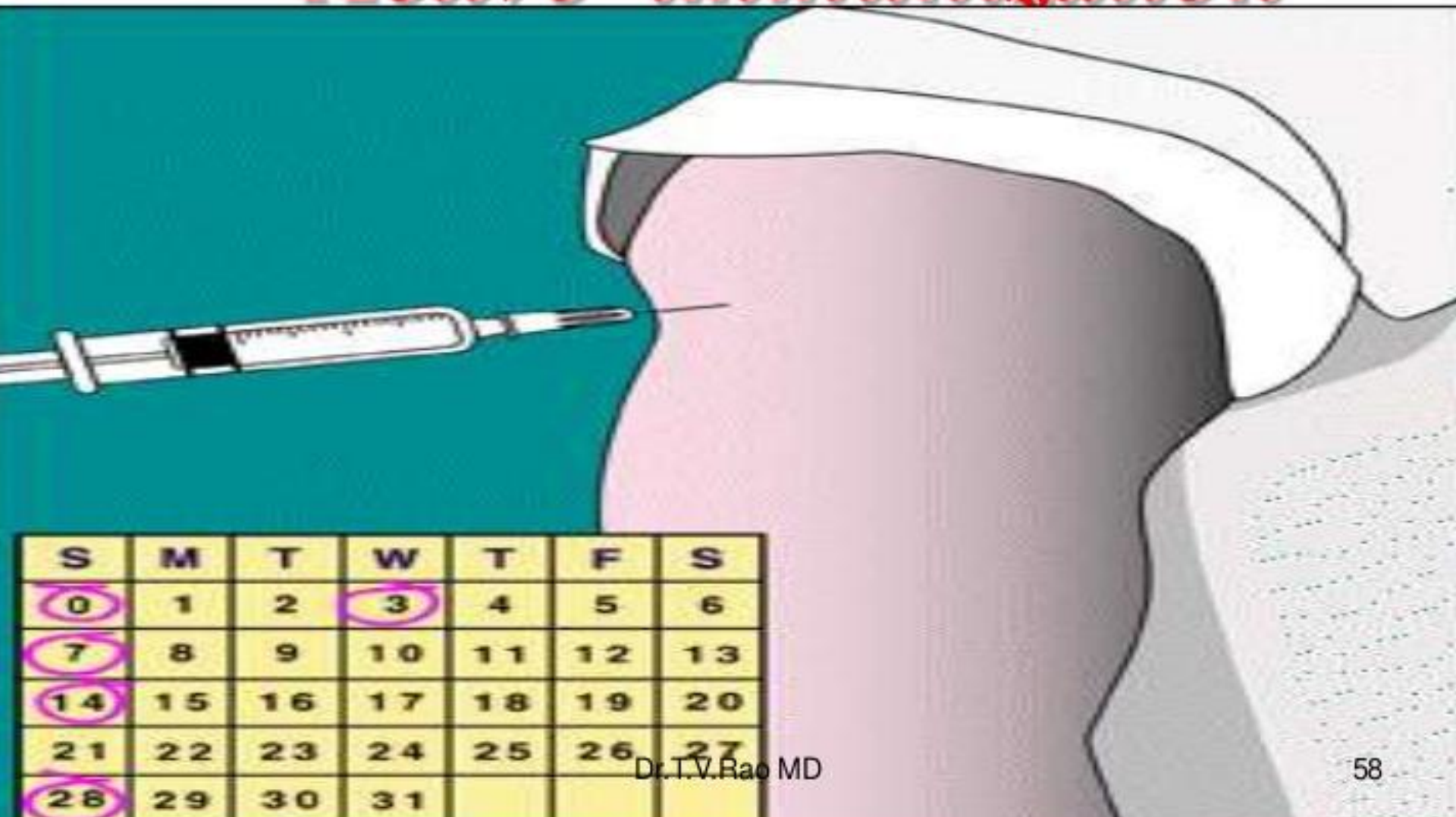
  Immunity lasts for 5 years

  Injected on deltoid region IM/SC

  Not to be given in the gluteal region

POSTEXPOSURE PROPHYLAXIS

– Active immunization



S	M	T	W	T	F	S
0	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

What are Adenoviruses

- Adenoviruses are a group of medium sized, nonenvelopedd, double stranded DNA viruses that share a common complement fixing antigen
- They infect humans and animals

Chaterstics of Adenovirus

- **Adenoviruses** are medium-sized (90–100 nm, nonenveloped (naked) **icosahedral** viruses composed of a nucleocapsid and a double-stranded linear DNA genome. There are over 52 different serotypes in humans, which are responsible for 5–10% of upper respiratory infections in children, and many infections in adults as well.

CLASSIFICATION

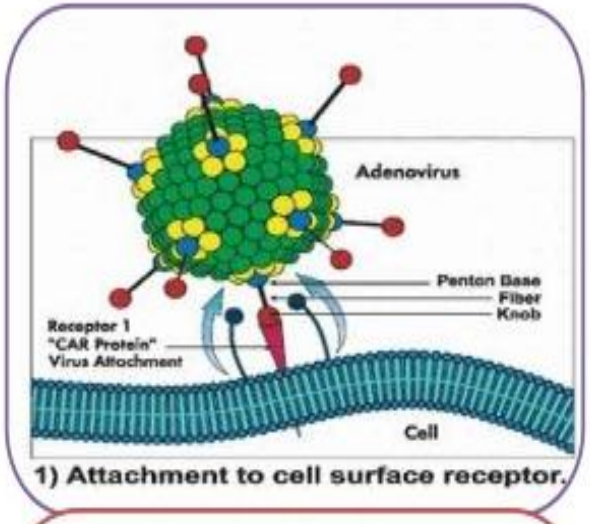
- Family Adenoviridae : 2 genera
  - Aviadenovirus : adenoviruses of birds;
  - Mastadenovirus : infect mammals;
    - **47 serotypes** of human origin;
    - **6 subgroups (A-F)** based on genome homology;
    - **Subgroup A : serotypes 12,18 and 31 : highly oncogenic;**

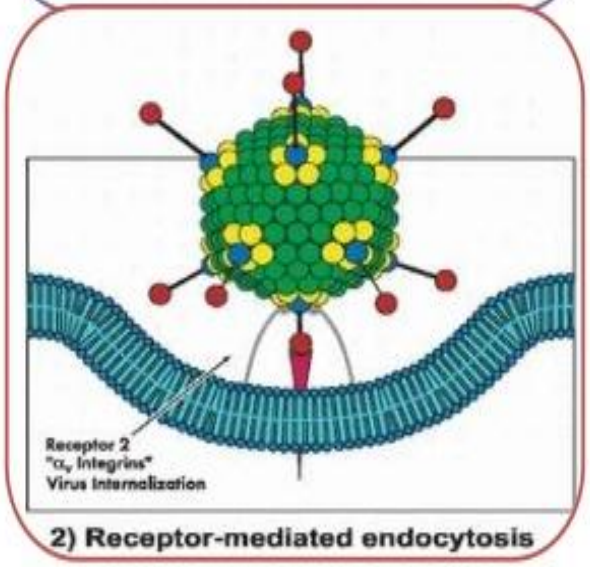
DISEASE ASSOCIATIONS

Serotype	Disease	At risk
1-7	Acute febrile pharyngitis	Children
3,7,14	Pharyngoconjunctival fever	Older children
8,9,37	Epidemic keratoconjunctivitis (shipyard eye)	Adults
3,4,11	Acute follicular conjunctivitis	Any age
40,41	Diarrhoea	Infants, young children
11,21	Hemorrhagic cystitis	Children

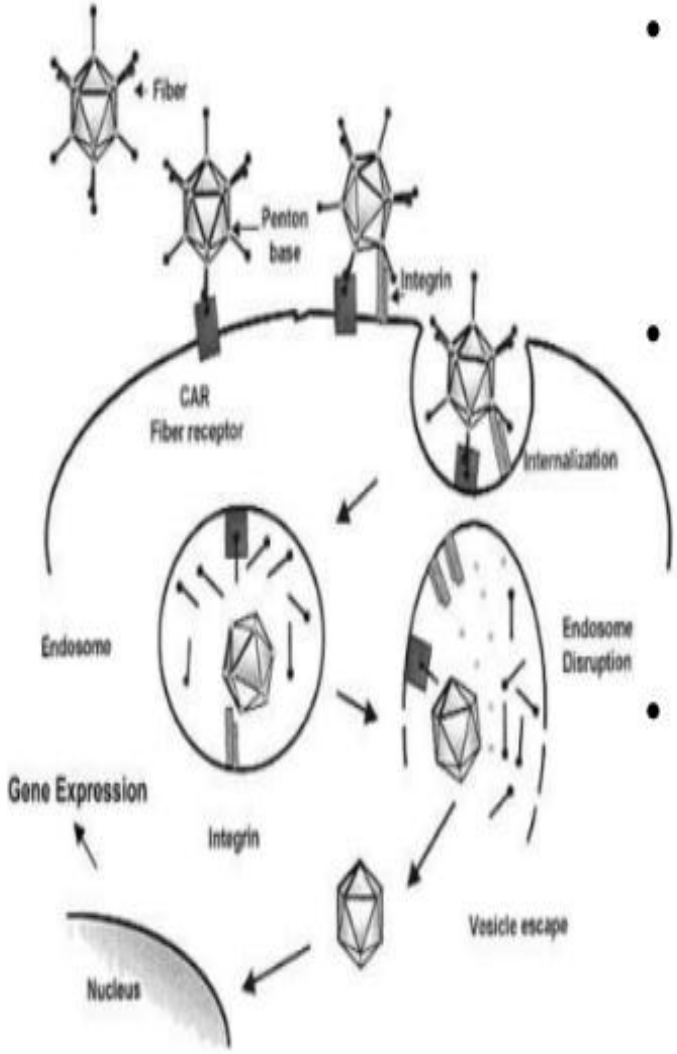
VIRAL REPLICATION

- Adenoviruses attach to surface of the cells by their fibers, then penetrate the cell, and once inside the cell, uncoat the viral DNA.
- The viral DNA is then transported into the nucleus of the cell and initiates replication cycle.
- Host cell DNA-dependent RNA polymerase transcribes the early genes leading to formation of functional mRNA.





VIRAL REPLICATION



- Then in the cytoplasm, the early mRNA is translated into nonstructural proteins.
- In the nucleus, after viral DNA replication, late mRNA is transcribed and then translated into structural virion proteins.
- This is followed by assembly of virions in the nucleus and release of virions by lysis of the cells, but not by budding.

PATHOGENESIS

- Adenoviruses are transmitted mainly by respiratory or feco-oral contact from humans.
- They infect the conjunctiva or the nasal mucosa.
- They may multiply in conjunctiva, pharynx, or small intestine, and then spread to preauricular, cervical and mesenteric lymph nodes, where epithelial cells are infected.

respiratory transmission

fomite transmission

water-borne transmission

fecal-oral transmission

PATHOGENESIS

- Adenoviruses may cause three different types of interaction with the infected cells.
- These are (a) lytic infection, (b) latent infection, and (c) transforming infection.
- lytic infection: Adenoviruses infect mucoepithelial cells in the respiratory tract, gastrointestinal tract, and conjunctiva or cornea, causing damage of these cells directly.
- After local replication of the virus, viremia follows with subsequent spread to visceral organs.
- Dissemination occurs more commonly in immunocompromised patients than in the immunocompetent individuals.

PATHOGENESIS

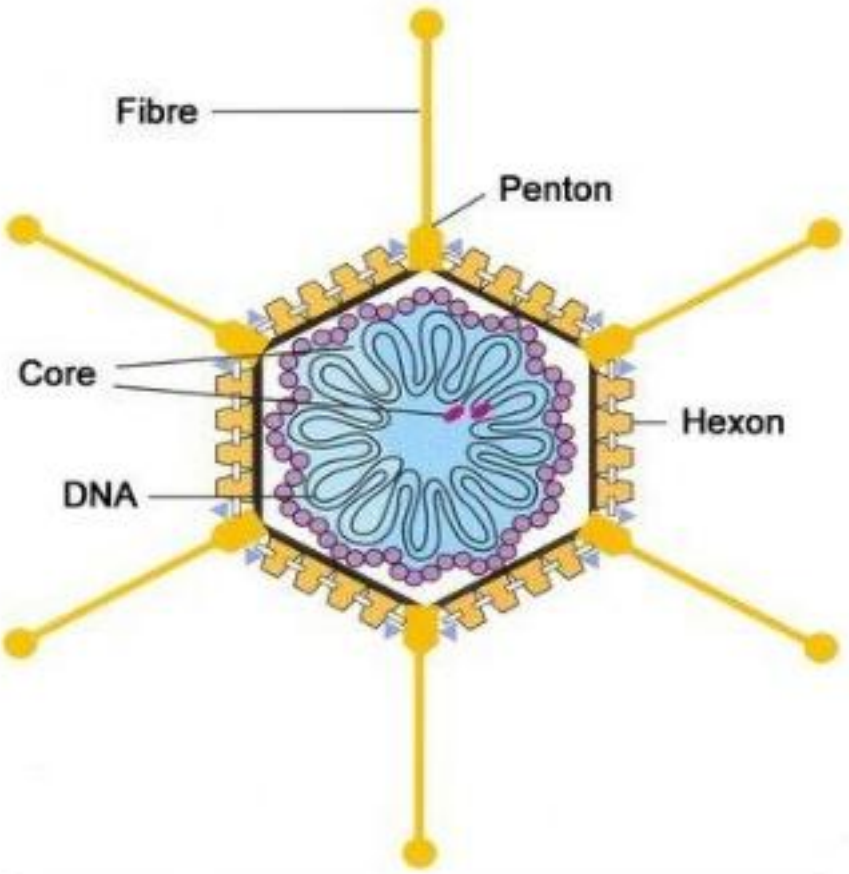
- latent infection: The adenovirus has a unique ability to become latent in lymphoid and other tissues such as adenoids, tonsils, and Payer's patches.
- The exact mechanism of latency of adenoviruses in these tissues is not known.
- These latent infections can be reactivated in patients infected with other agents or in the patients who are immunocompromised.

PATHOGENESIS

- Oncogenic transformation: Some adenoviruses belonging to groups A and B have the property for oncogenic transformation in rodent cells.
- During oncogenesis the multiplication of adenovirus is inhibited followed by integration of viral DNA into the host DNA.
- After integration adenoviruses produce E1A proteins which target rodent cells by altering cellular transcription, finally leading to transformation of rodent cells.
- However, oncogenesis of human cells has not been demonstrated.

Morphology of Adenovirus

- Adenovirus are 70-75 nm in size
- The capsid contains 252 capsomers arranged as icosahedrons with 20 triangular facets and 12 vertices
- 240 are called as hexons
- 12 are called as pentons



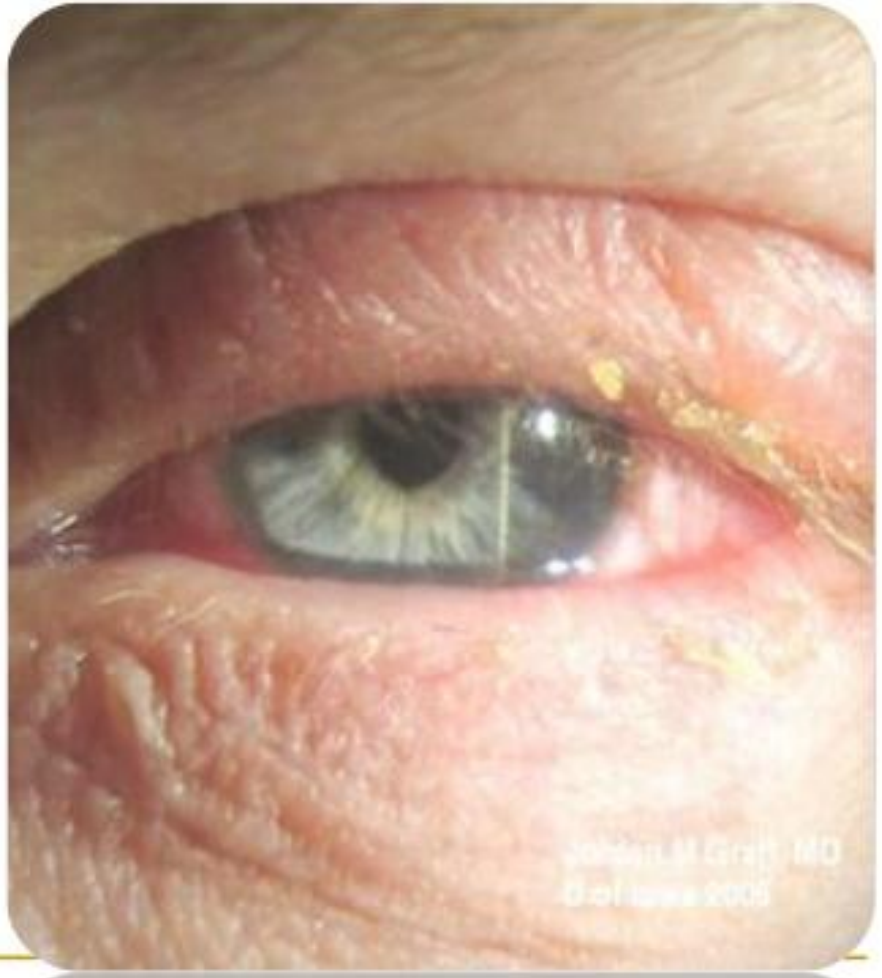
Pathogenesis:

- Adenoviruses infect and replicate in the epithelial cells of the:
  - pharynx,
  - conjunctiva,
  - urinary bladder
  - small intestine.

  They usually do not spread beyond the regional lymph nodes **EXCEPT IN THE IMMUNE COMPROMIZED HOST.**

Pathogenesis

- Adenovirus cause infections in
- Respiratory tract
- Eye, Urinary bladder, and Intestines
- More than one type of virus may cause clinically different diseases



CLINICAL SYNDROMES

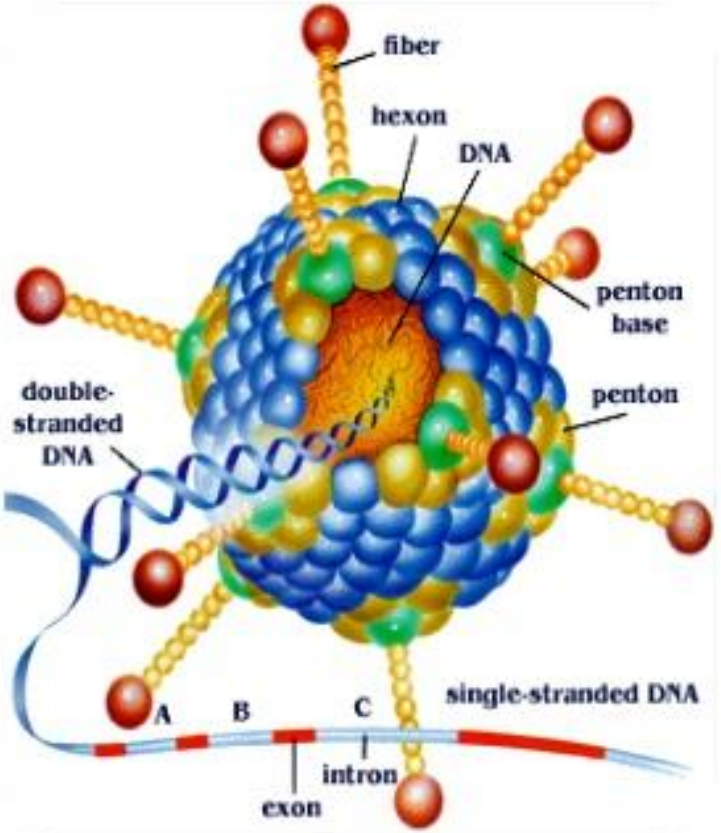
A. Respiratory diseases:

B. Eye infections:

C. Gastrointestinal disease

D. Other diseases:

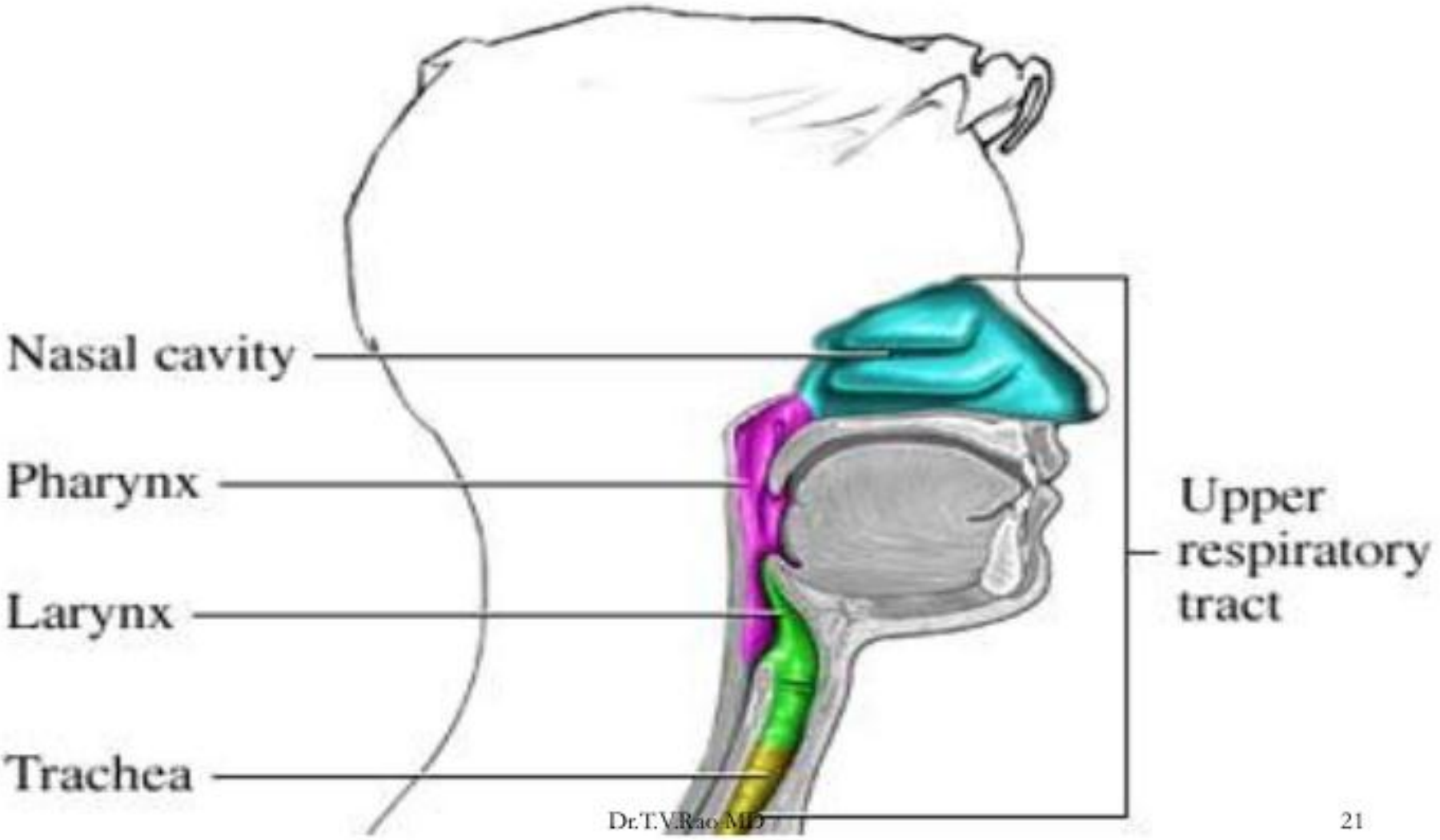
E. Adenoviral infections of the immune compromised host



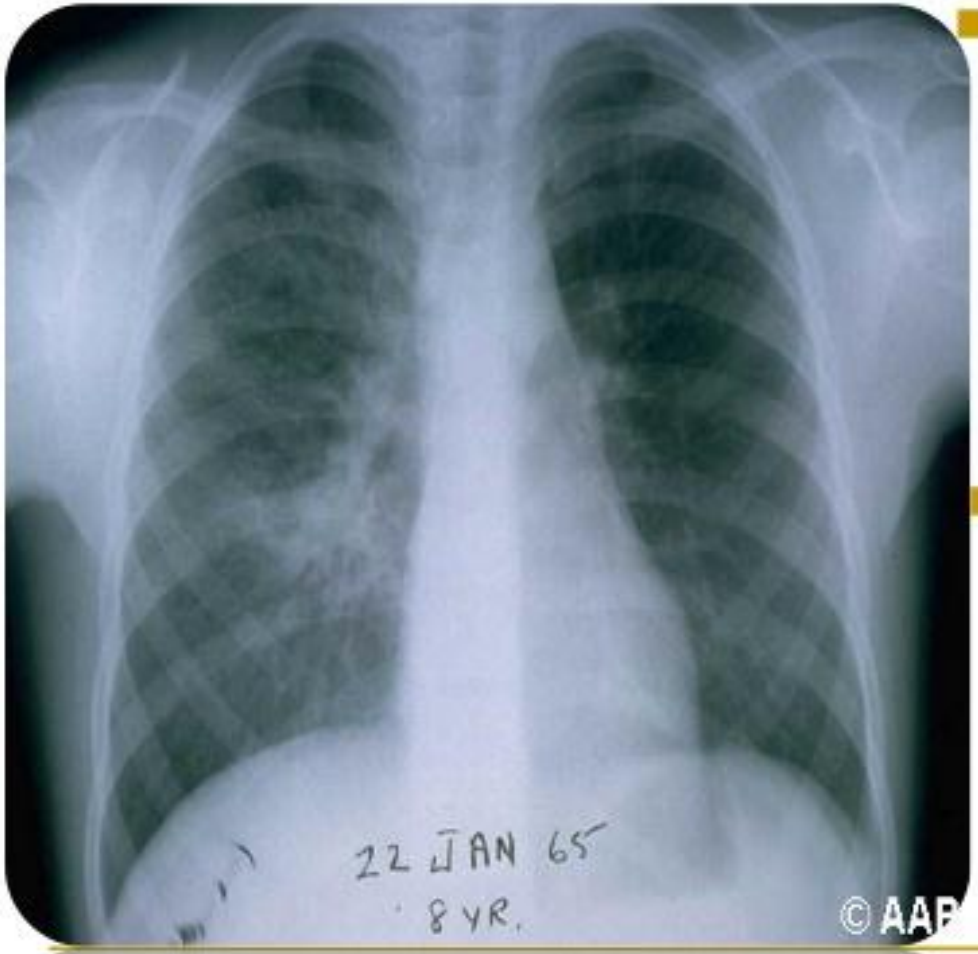
Adenovirus - Pharyngitis

- Major cause of infections associated with nonbacterial pharyngitis and tonsillitis
- Causes febrile common cold
- Types 1 – 7 are common types

Adenovirus Common cause of Respiratory infections



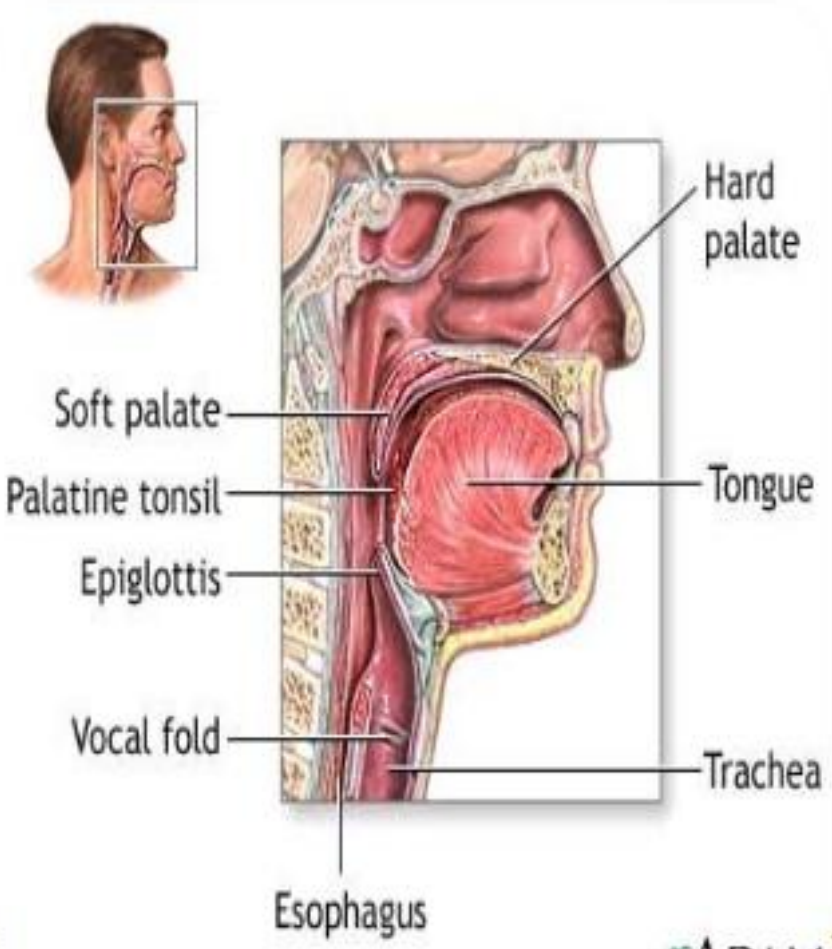
Pneumonia - Adenovirus



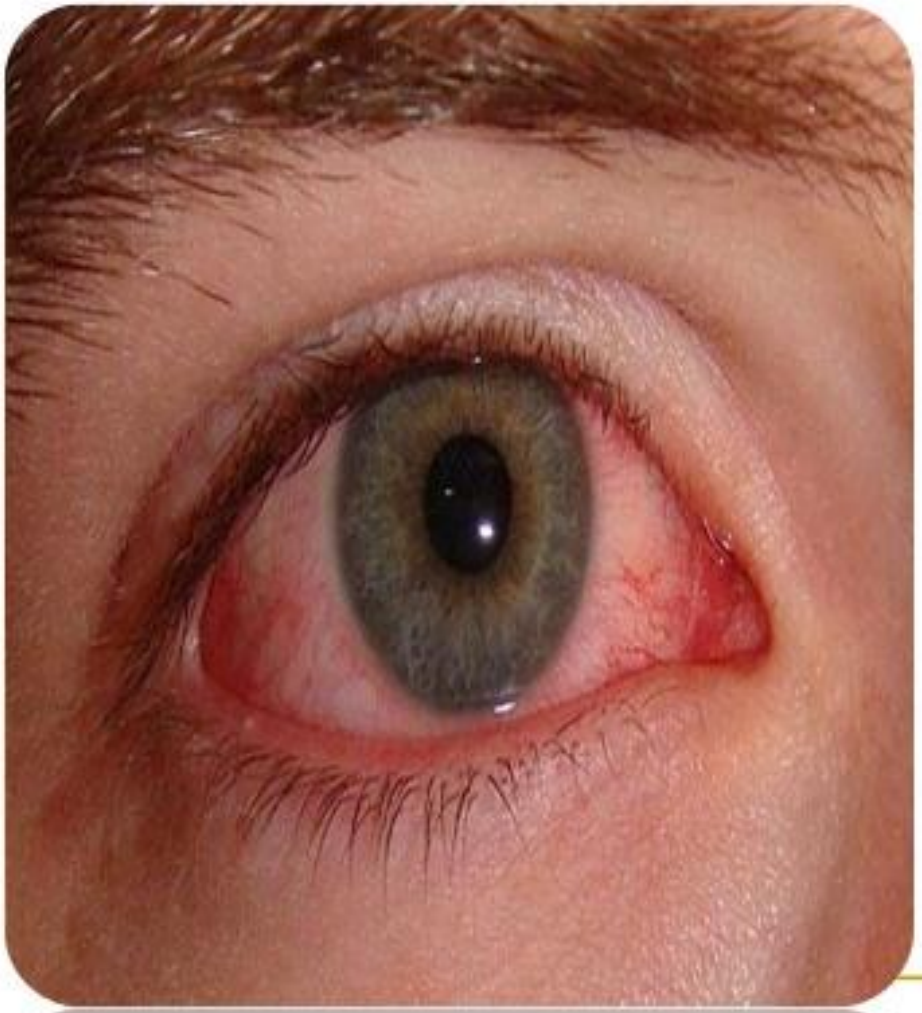
- Adenovirus types 3 and 7 are associated with pneumonia resembles like atypical pneumonia in adults.
- Type 7 causes serious and even fatal pneumonia in infants and young children

ARD – Acute respiratory disease with Adenovirus

- Occurs usually in military recruits
- Serotypes 4,7,and 21 are agents commonly associated.

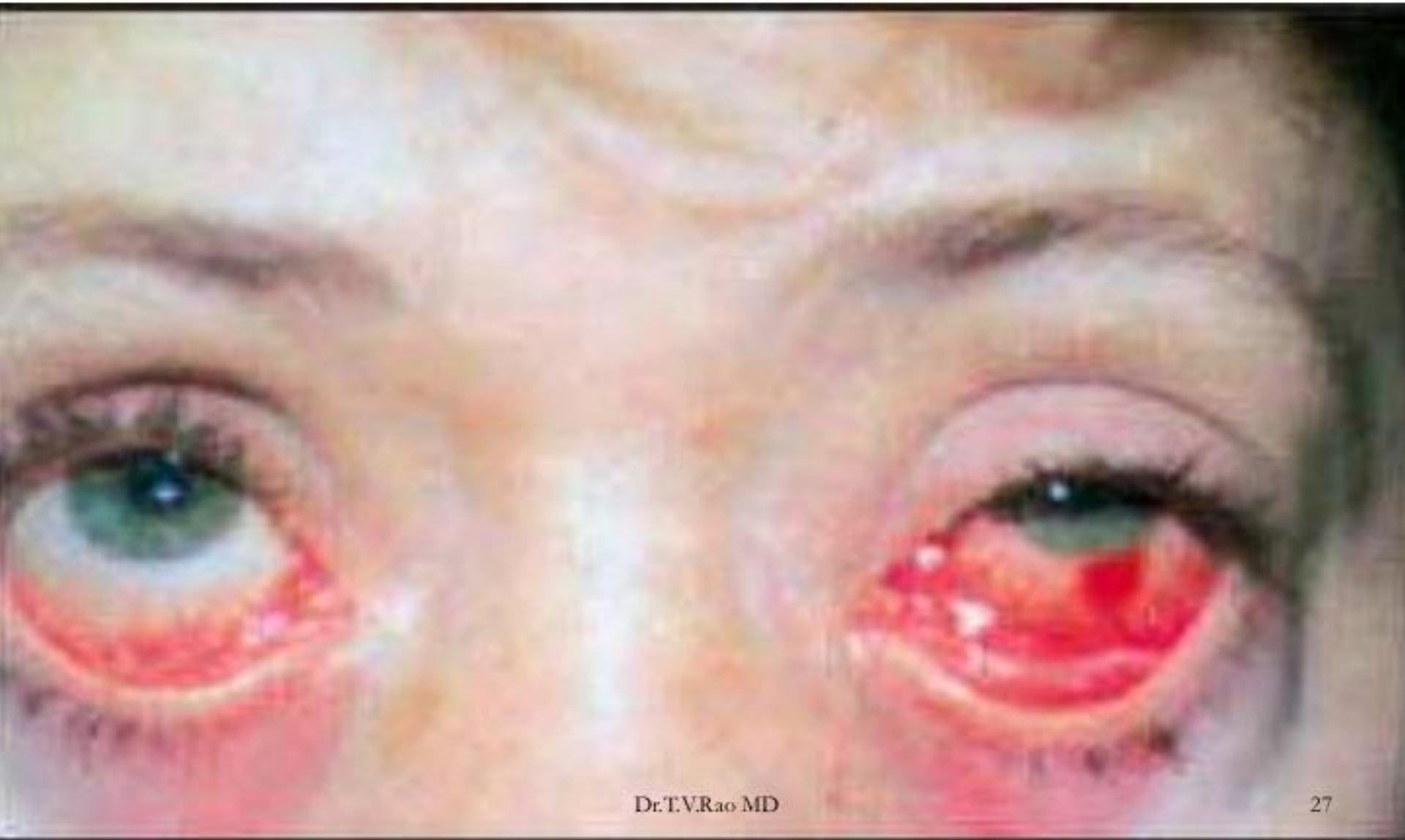


Epidemic keratoconjunctivitis



- Occurs with serious epidemic
- Caused by serotypes 8, and less frequently with 19, and 37.

A severe Adenoviral Infection



C. Gastrointestinal disease:

No disease association

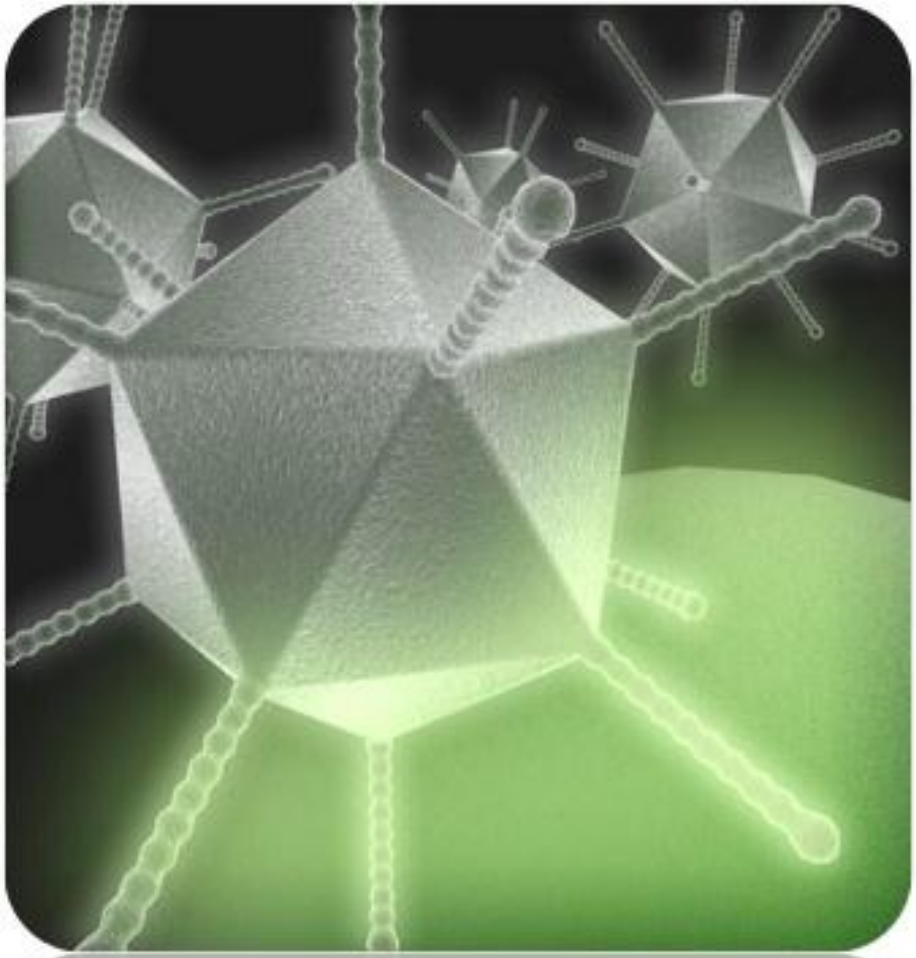
- Many Adenoviruses replicate in intestinal cells and are **present in the stools withou being associated with GIT disease**.

Infantile gastroenteritis

- **Two serotypes (40, 41)** have been etiologically associated with infantile gastroenteritis.

Laboratory Diagnosis

- Direct detection:
- Isolation
- Serology



Laboratory Diagnosis

Direct detection:

- **Virus particle by EM** can be detected by direct examination of fecal extracts

- **Detection of adenoviral antigens by ELISA.**

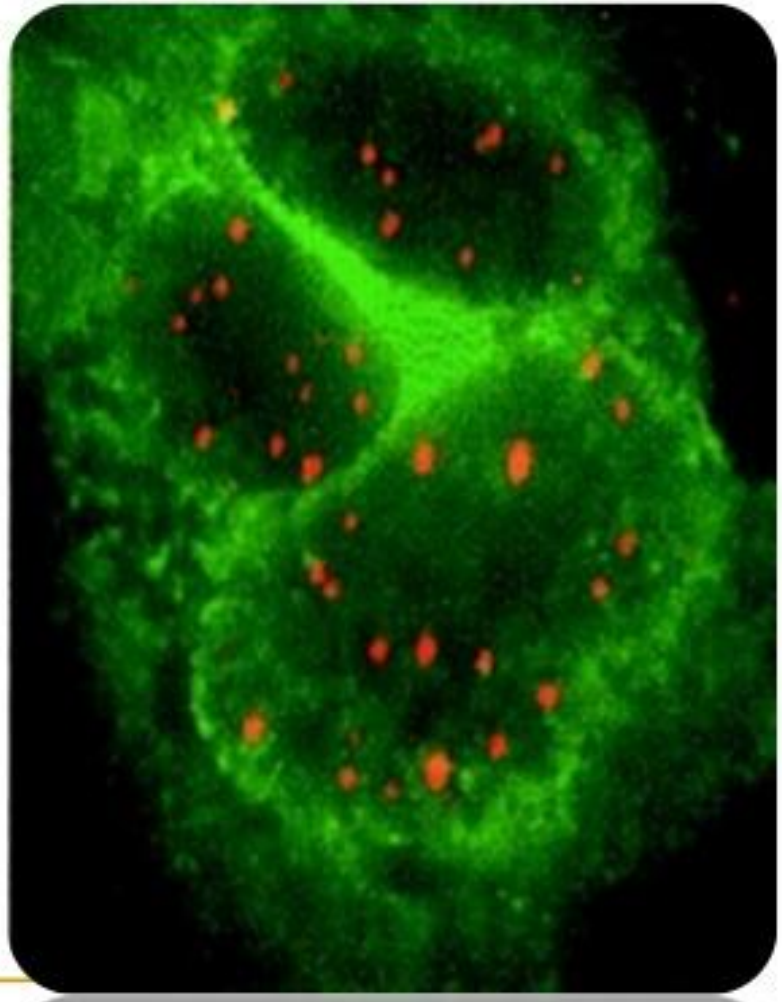
  Enteric Adenoviruses

- **Detection of adenoviral NA by Polymerase chain reaction:** can be used for diagnosis of Adenovirus infections in tissue samples or body fluids.

Laboratory Diagnosis

Isolation

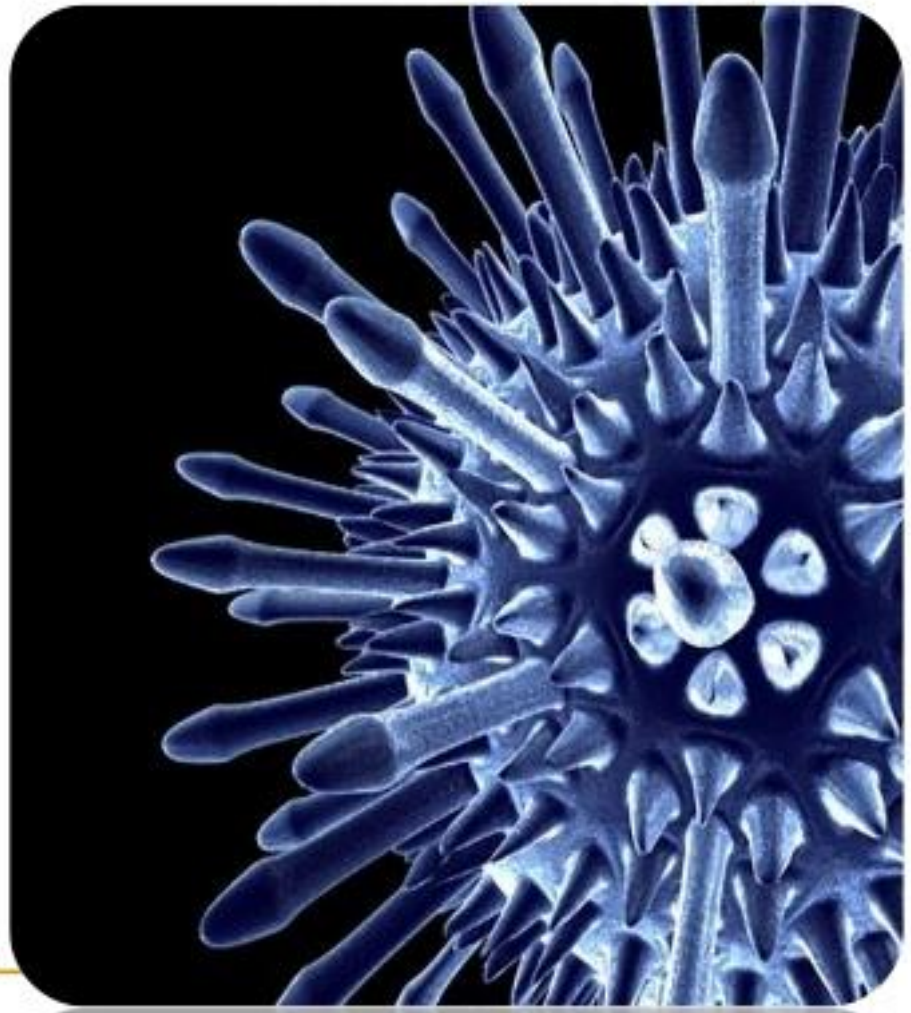
- Isolation depending on the clinical disease, the virus may be recovered from **throat, or conjunctival swabs or and urine.**
- **Isolation is much more difficult from the stool or rectal swabs**



Laboratory Diagnosis

Serology

- Haemagglutination inhibition
- Neutralization tests can be used to detect specific antibodies following Adenovirus infection.

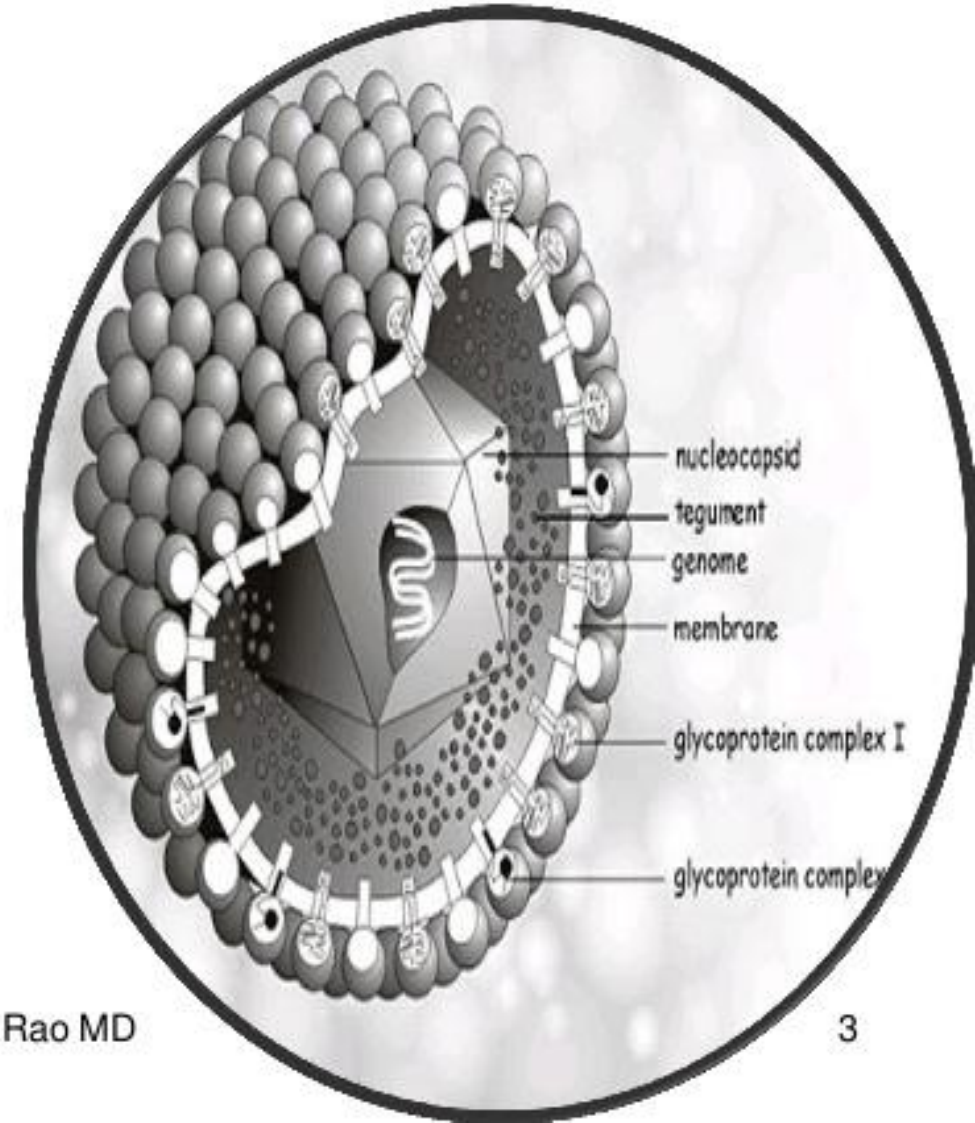


Herpesviridae

- The *Herpesviridae* are a large family of DNA viruses that cause diseases in animals, including humans The family name is derived from the Greek word *herpein* ("to creep"), referring to the latent, re-occurring infections typical of this group of viruses. *Herpesviridae* can cause latent or lytic infections.

Herpes Viruses DNA group

- Most important Human Pathogens
- Wide Host cell range
- Life Long Infection – Periodic reactivation
- Immunocompromised
- Large number of genes,
- Some viruses susceptible to treatment.



Infecting Humans.

Herpes Simplex virus 1 and 2

Varicella Zoster Viruses

Cytomegalovirus virus

Epstein Barr virus

Human Herpes viruses 6, 7.

Kaposi's Sarcoma associated Viruses

Properties of Herpes Viruses.

- Spherical in Shape
- Icosahedral 150 to 200 nm in size
- Genome – Double stranded DNA Linear
- Envelope contains Glycoprotein's

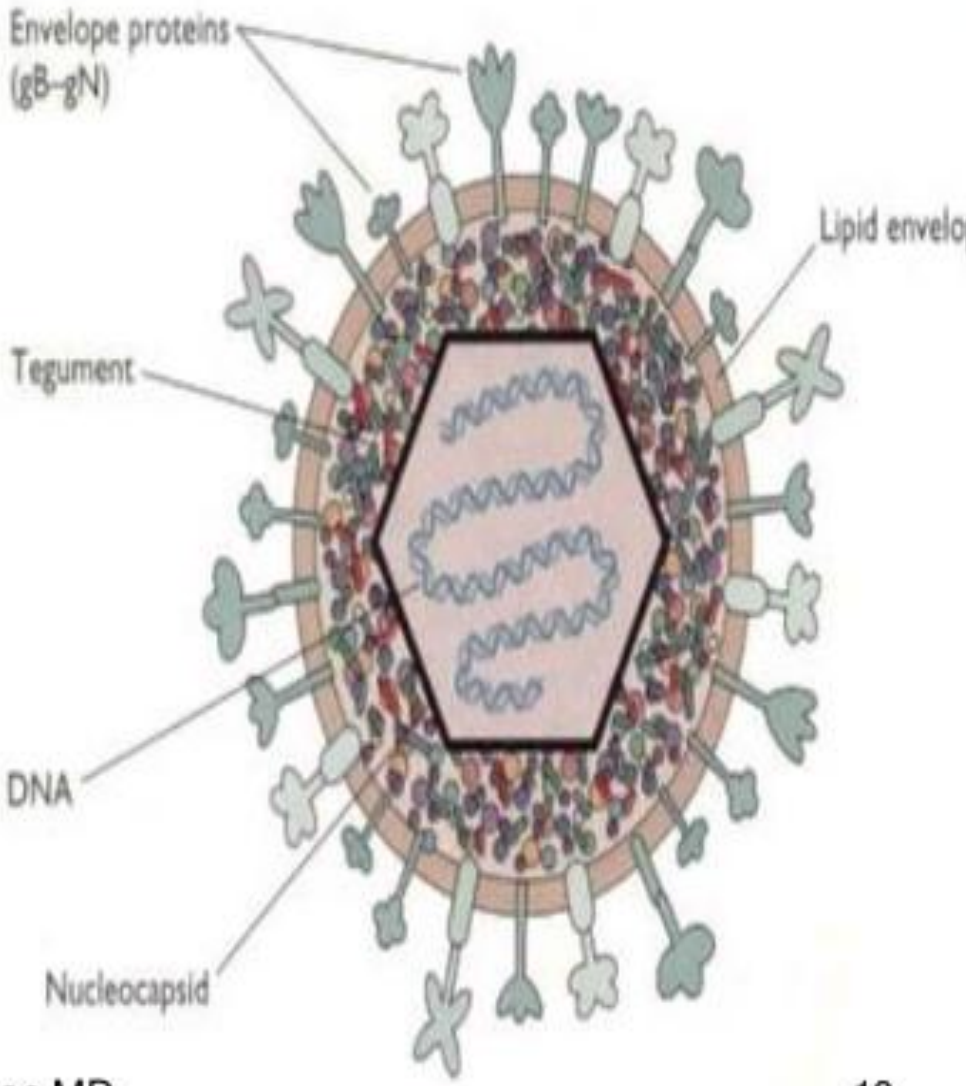
Herpes Virus Replication

- Replicates in Host Cell Nucleus
- Form Cow dry A Type inclusion bodies.
- More than 50 different types protein in infected cell.
- Large number of enzymes in DNA synthesis

Herpes Simplex 1 and 2

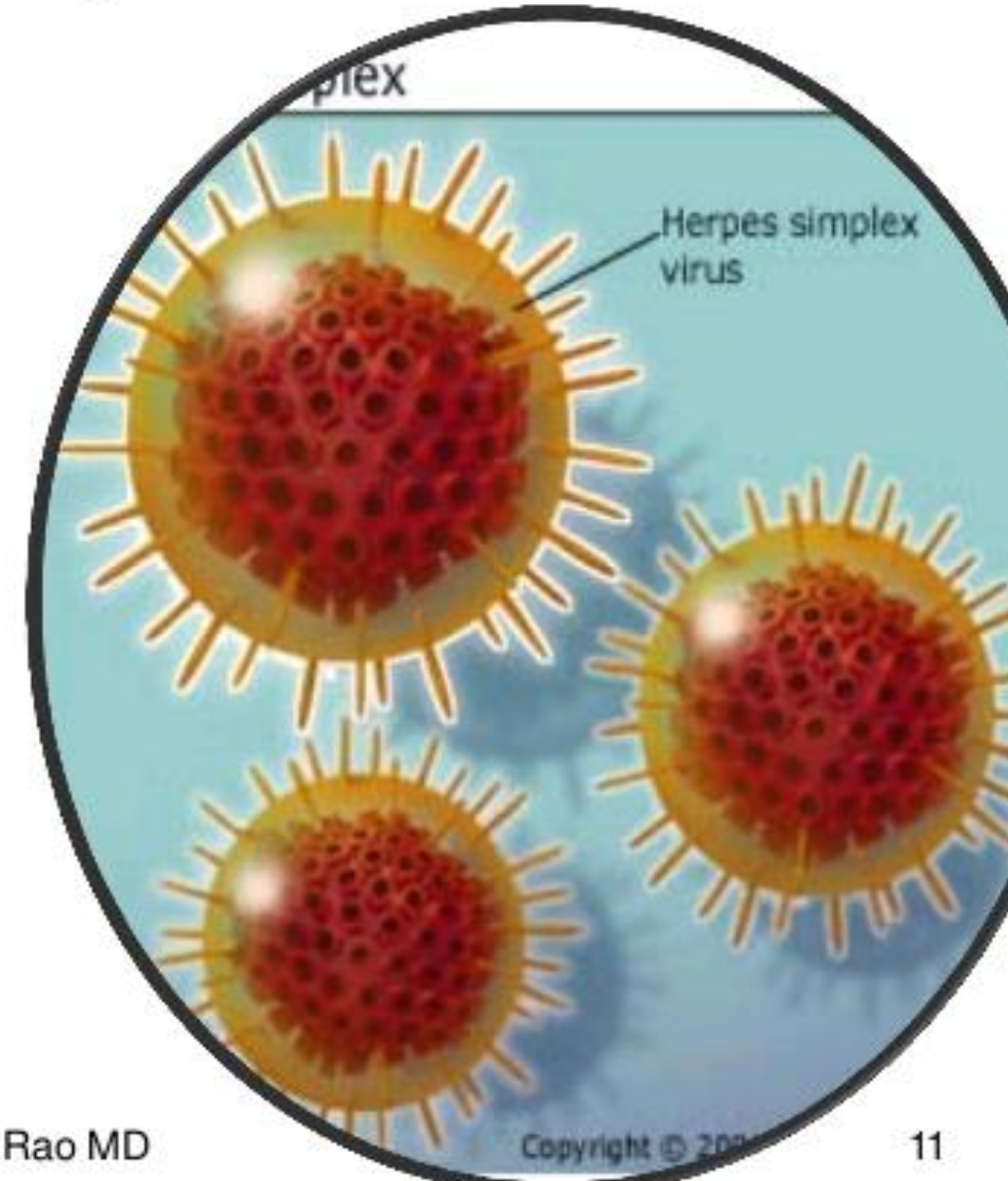
Herpesviridae

- Group:Group I
  Family:*Herpesviridae*
  Subfamily:Alphaherpesvirinae
  Genus:*Simplexvirus*
- ***Species***
- ***Herpes simplex virus 1*** *(HWJ-1)*
  Herpes simplex virus 2 *(HWJ-2)*

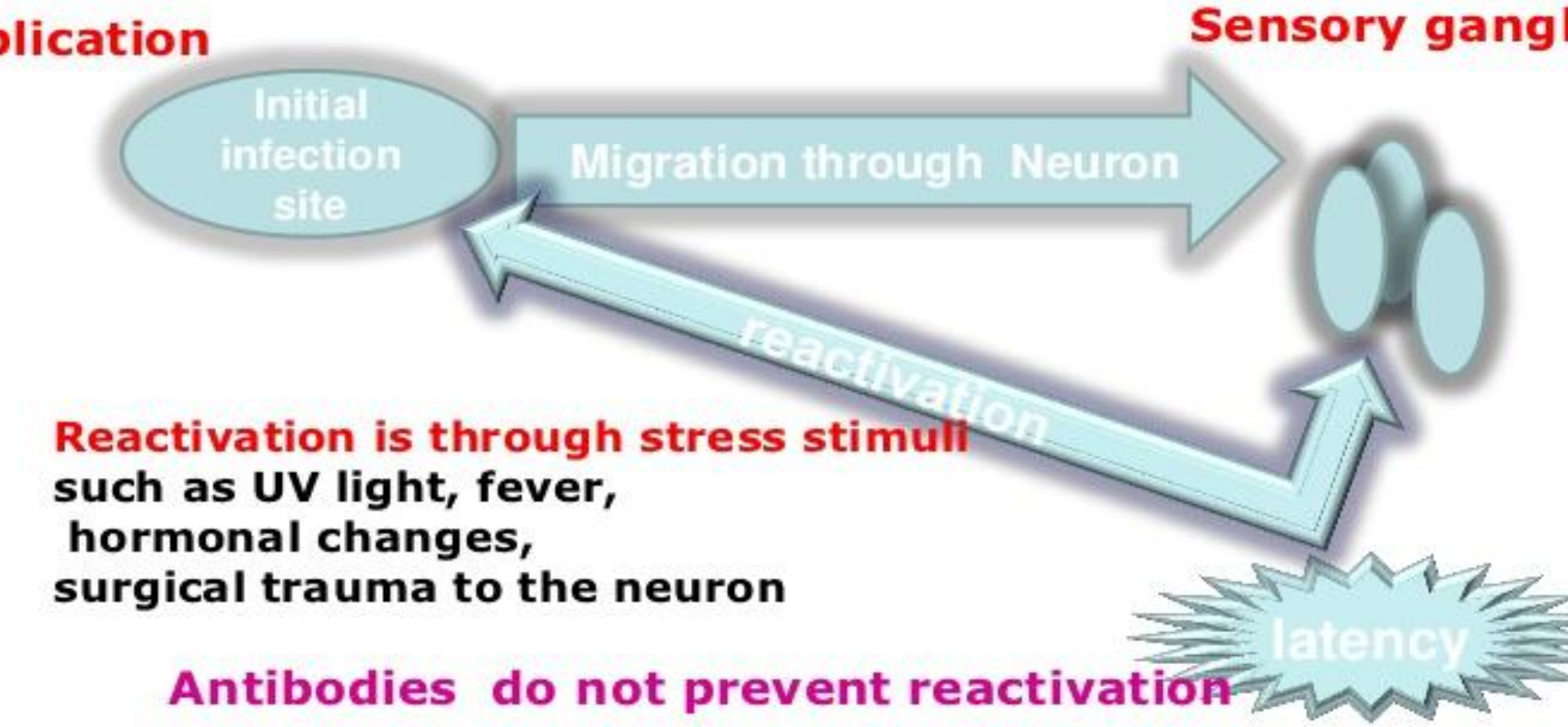


Herpes Simplex Virus

- HSV are spherical in shape
- Ds DNA
- 35 proteins



Pathogenesis of HSV 1 &2



Reactivation is through stress stimuli
such as UV light, fever,
hormonal changes,
surgical trauma to the neuron

Antibodies do not prevent reactivation

HSV-1: trigeminal ganglia
HSV-2: sacral ganglia

Infections in Humans.(Herpes Simplex 1 and 2)

- Wide spread in Humans
- Broad Host Ranges.
- Replicate in Many types of Cells.
- Produce cytolytic effects
- Most Common Diseases.
- Gingival stomatitis, Kerato conjunctivitis
- Encephalitis Genital diseases,
- New Born Infections, Latent Infections in Nerve Cells,
- Recurrence.

HERPES SIMPLEX VIRUS (HSV)

- HSV 1 infect the upper part of the body
  - mouth and the face
- HSV 2 infect the lower part of the body
  - genital infections
- There is little cross protection

- Therefore, one can get both the

Properties of Herpes Simplex Viruses Type 1 and 2

- Similar in Organization
- Restriction Enzyme Differentiates
- H S V 1 contact with Saliva.
- H S V 2 Sexual
- Maternal infection (Genital Infection spreads to New Born)
- Replicates in 8-16 hours.

Virus Grows in the following.

- Primary and Continues Cell lines.
- Monkey and Rabbit Kidney,
- Human Amnion
- Syncytial formation and Giant cell formations
- Multiplies in Chorio Allontoic membrane
- Monoclonal Antibodies differentiates Type 1 and 2 types.

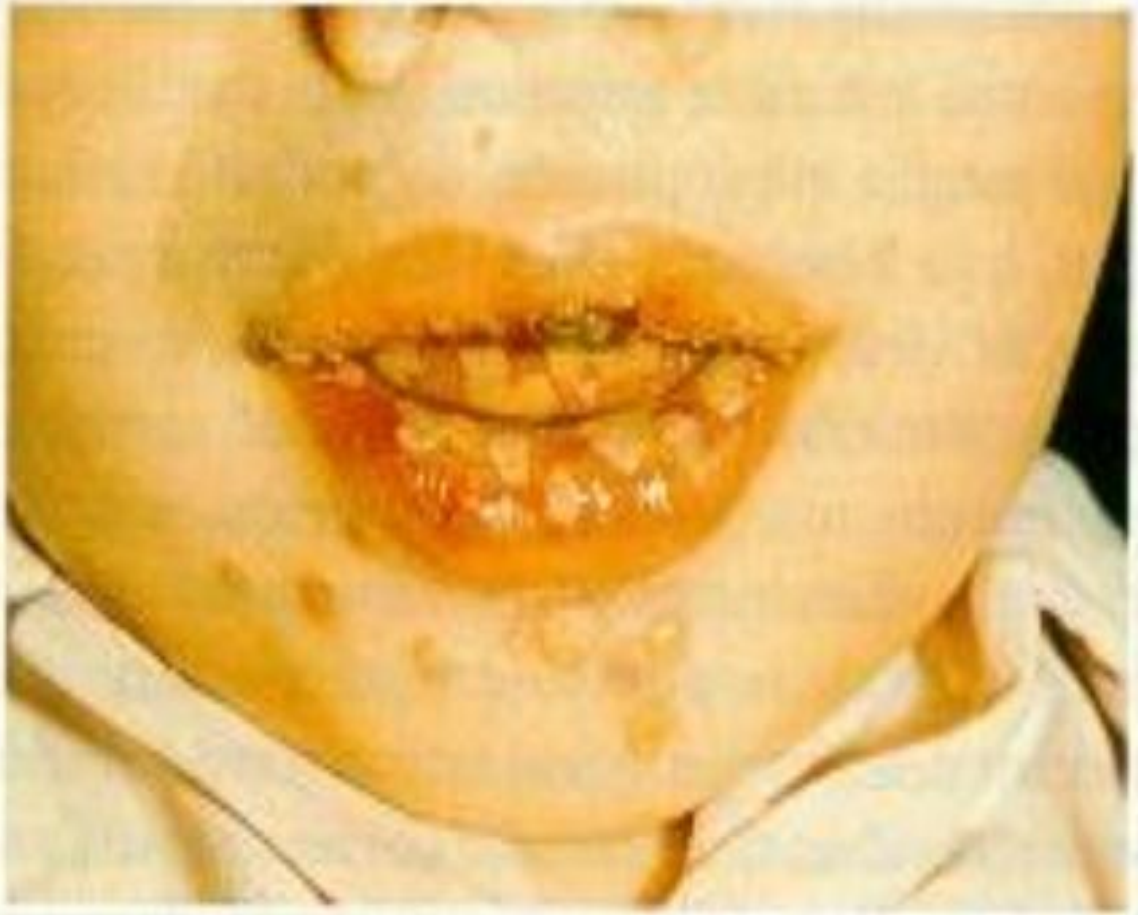
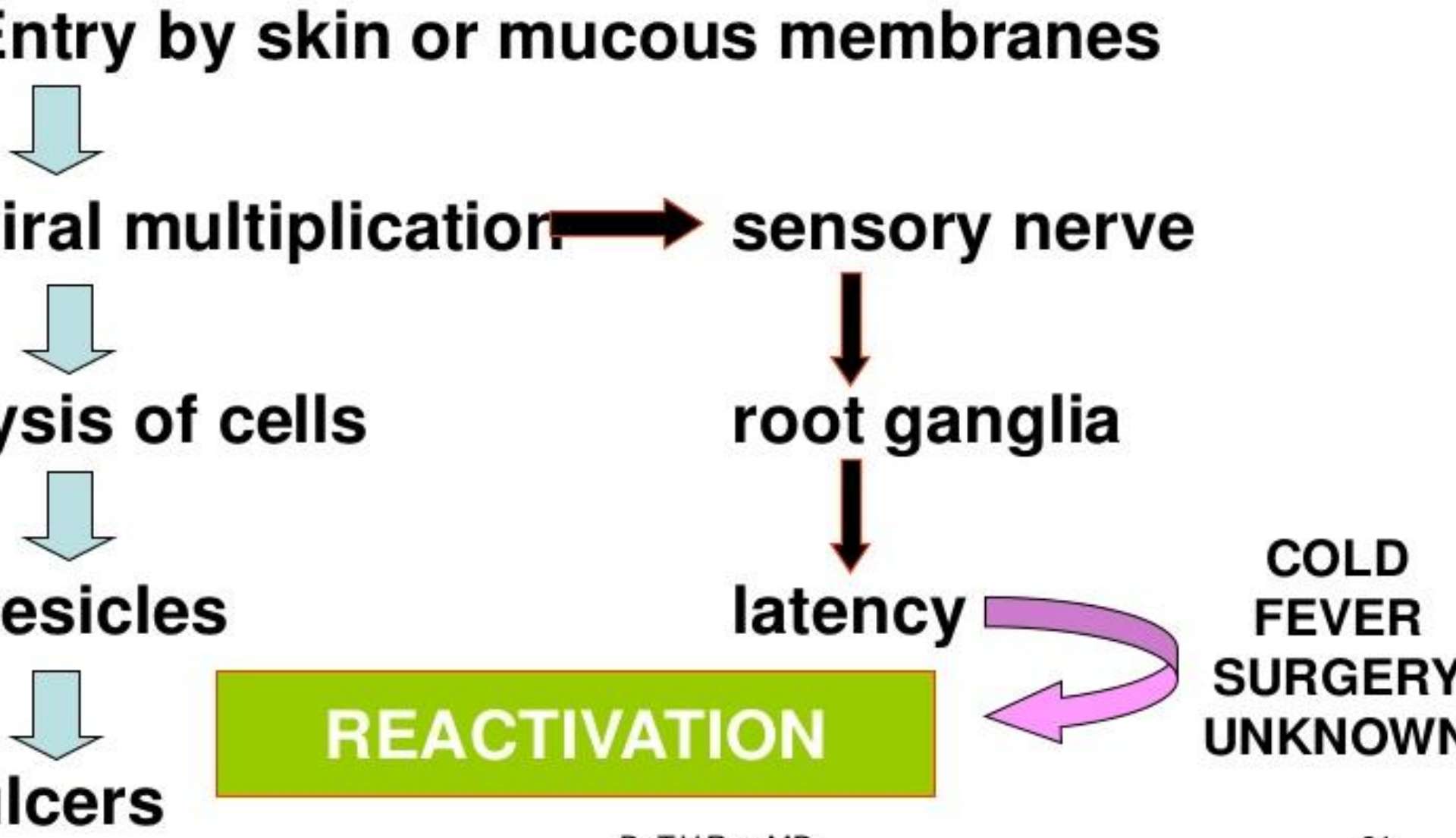
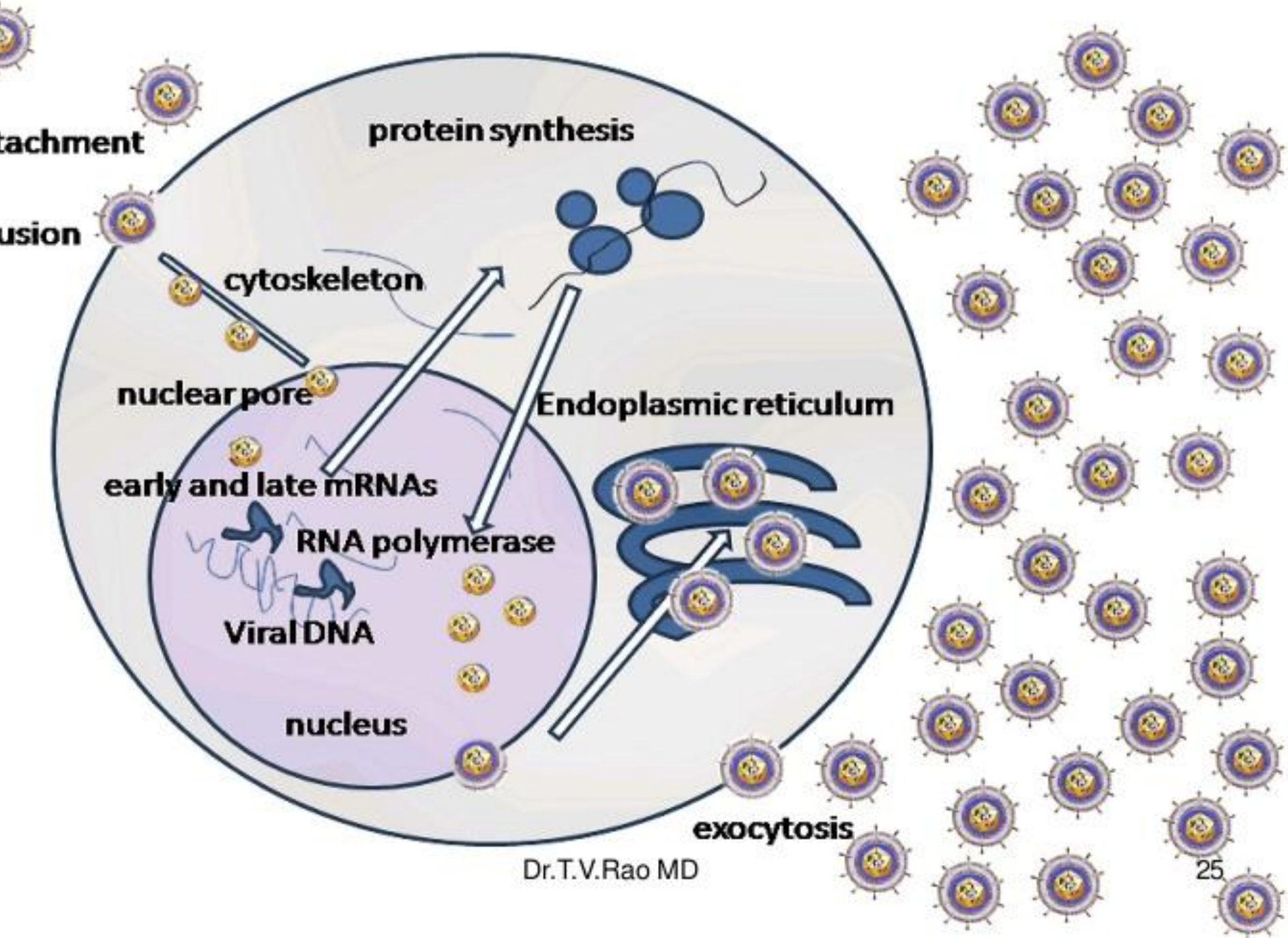


Fig. 11.1 Primary herpes simplex infection. Stomatitis with satellite vesicles over the chin. (Reproduced, with permission, from *Diseases of Infection* by N.R. Grist, D.O. Ho-Yen, E. Walker and G.R. Williams, 1988. Oxford University Press.)

Pathogenesis




tachment
usion
protein synthesis
cytoskeleton
nuclear pore
Endoplasmic reticulum
early and late mRNAs
RNA polymerase
Viral DNA
nucleus
exocytosis

Predisposition of Latent Infection in

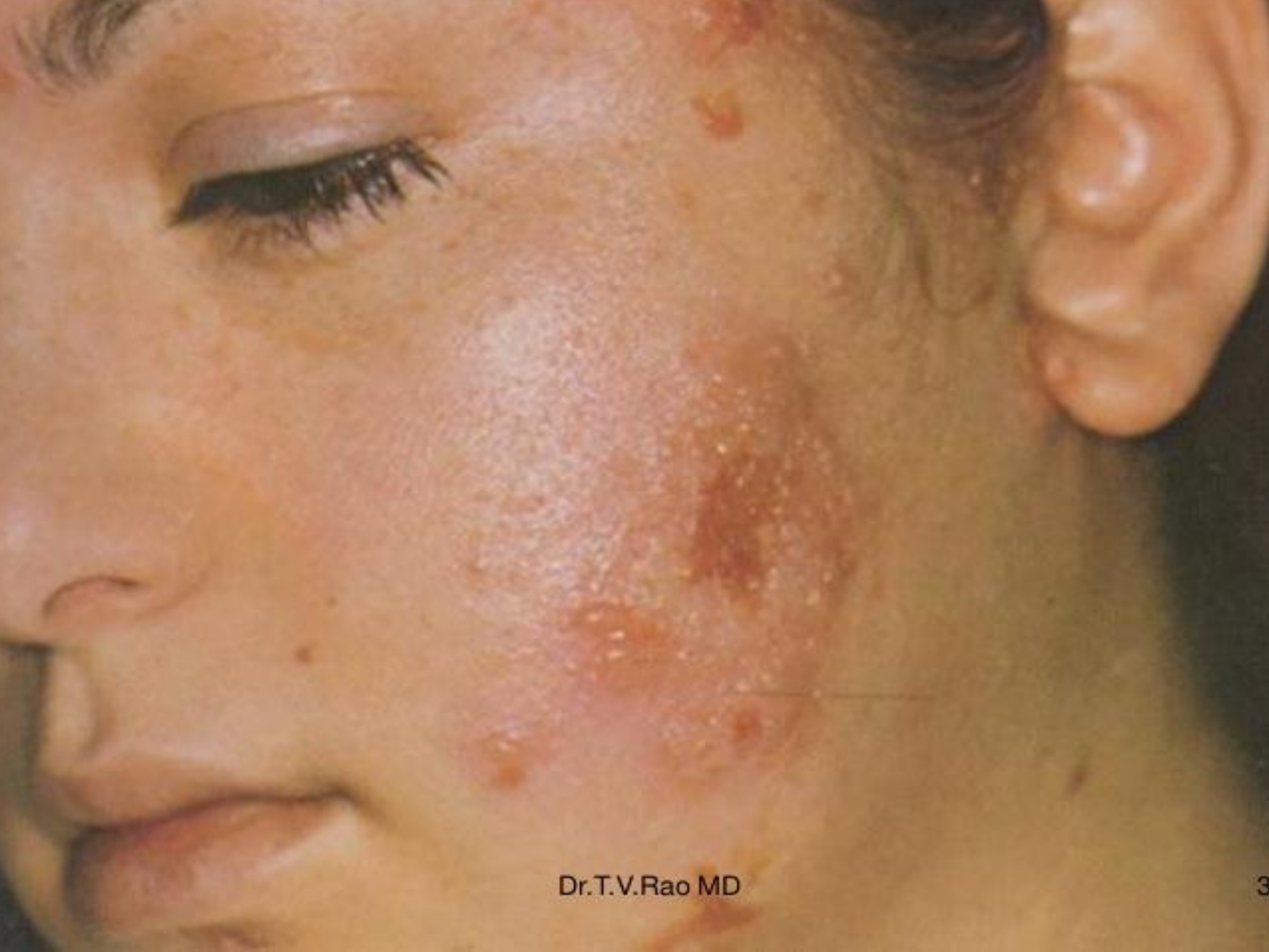
- Ganglion
- Trigeminal HSV 1
- Sacral HSV 2
- Immunity.
- Cell Mediated (CMI)
- Predisposing Factors

Axonal Injury

Physical and Emotional stress

U V light

80% Adults harbour Antibodies to HSV


Dr.T.V.Rao MD

Recurrent Blisters in Herpes simplex 1

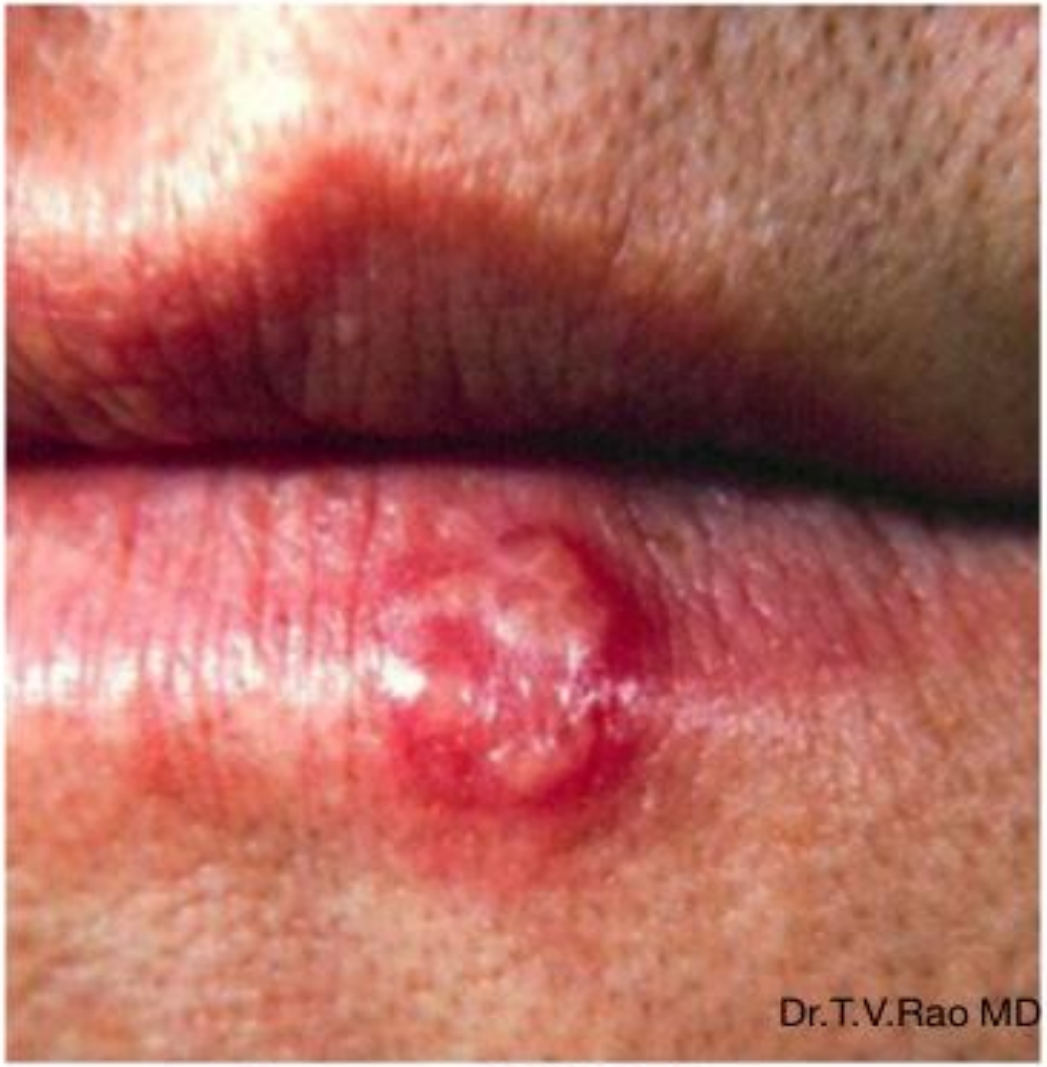
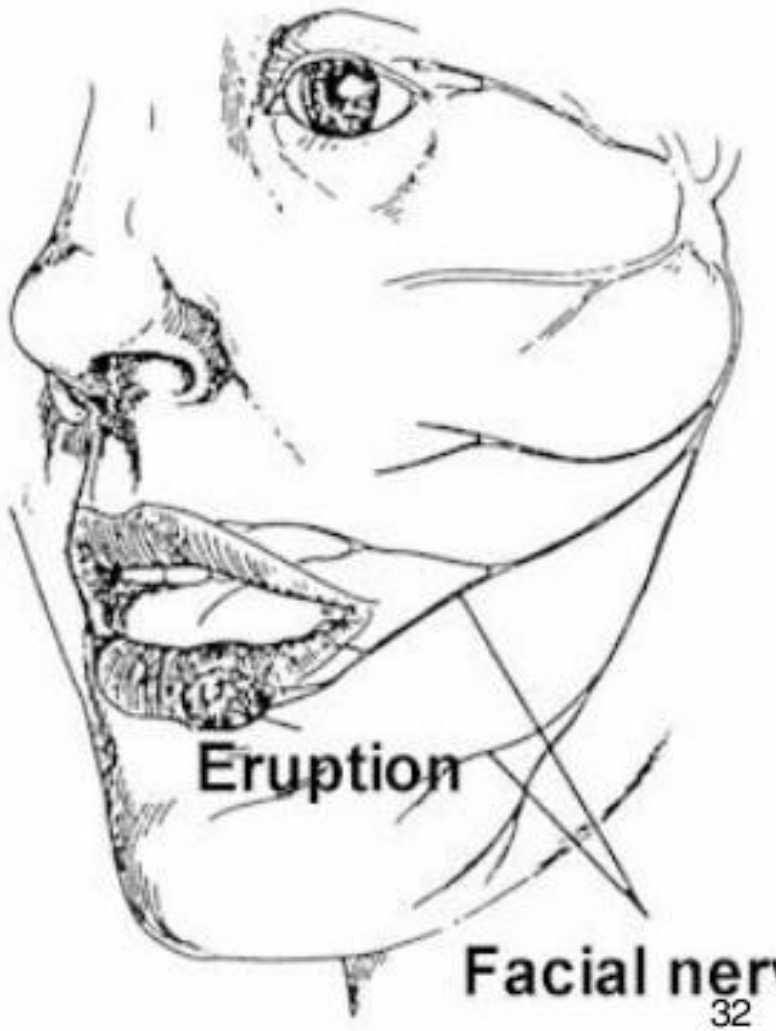
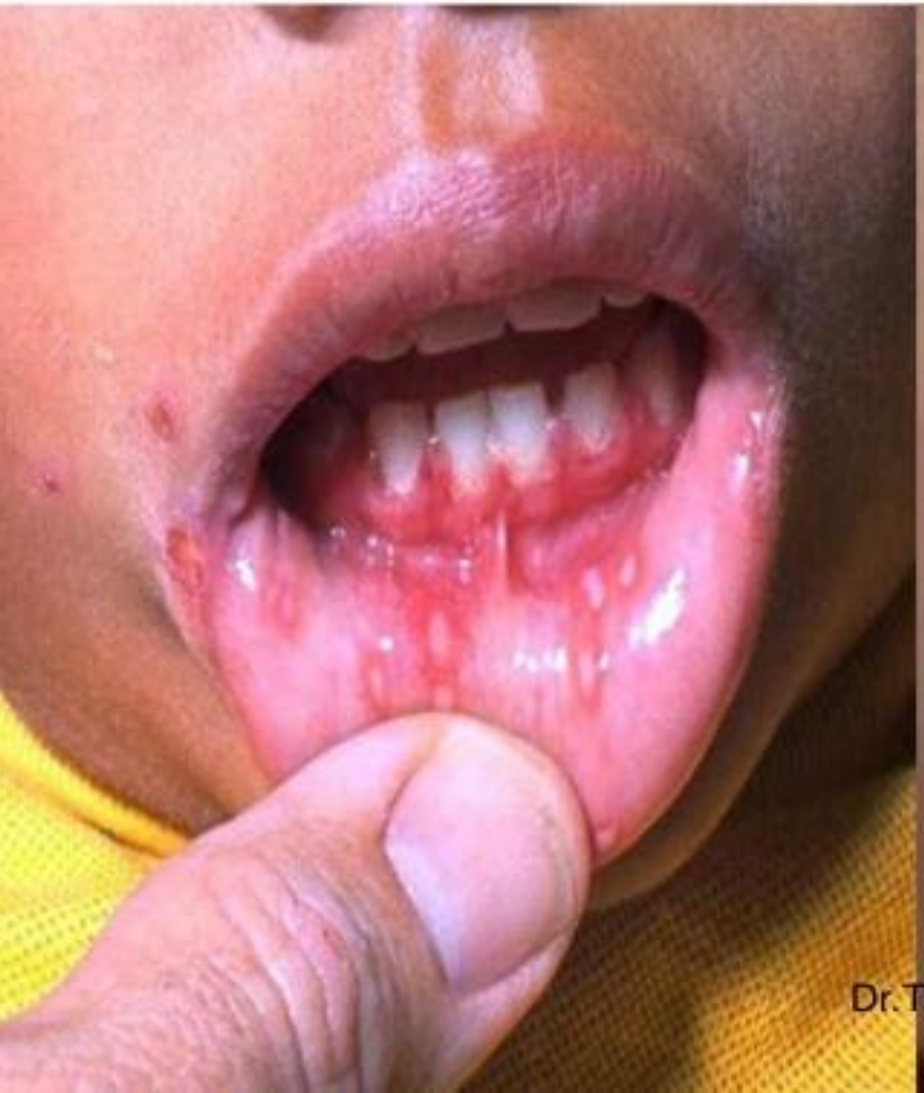
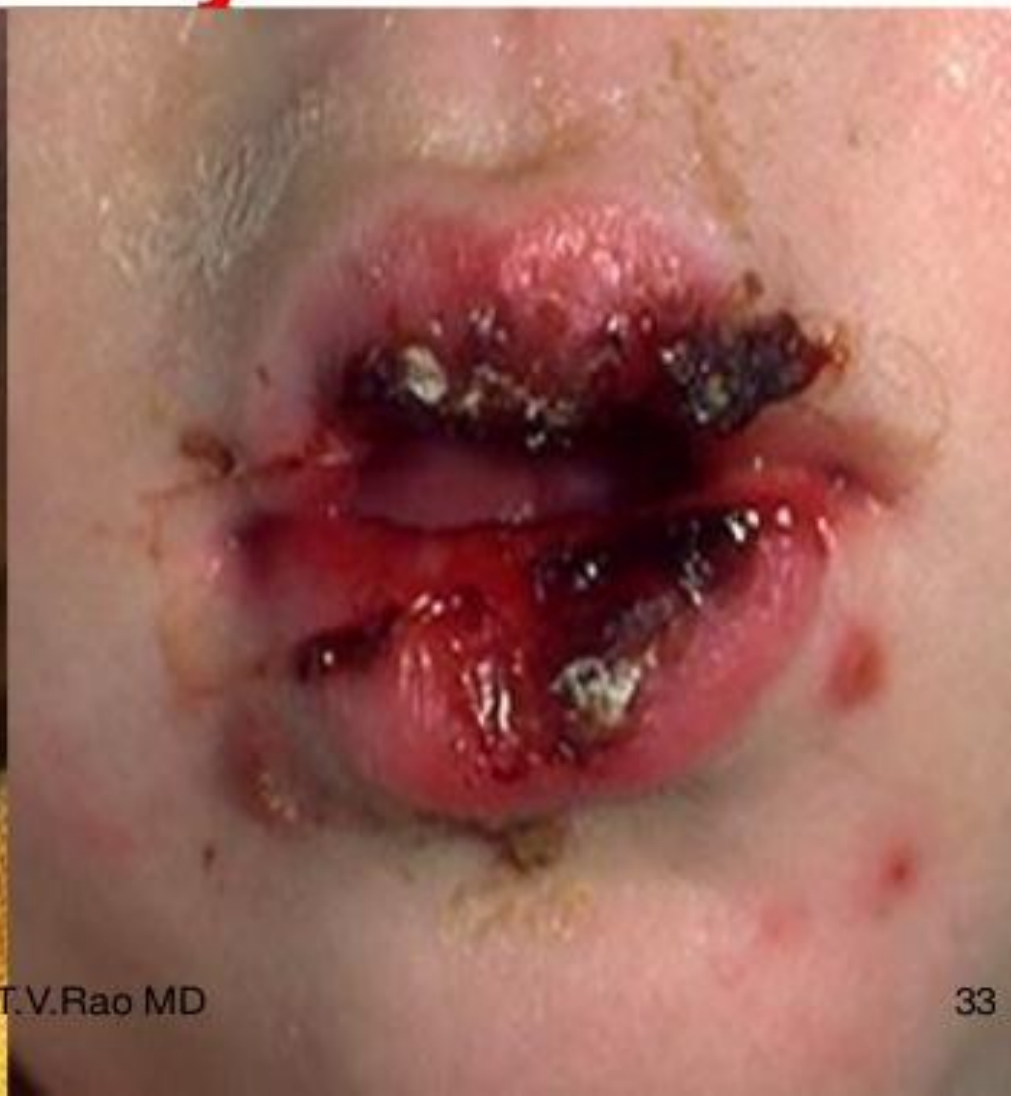


Photo courtesy of CDC - Dr. Herrmann



Herpes lesions in the oral cavity





Eye Infections and Genital Infections.

- Corneal ulcerations pacifications
- Blindness
- Vesiculo ulcerative Lesions

penis, Cervix, Vulva and Vagina.

Manifest with Painful lesions.

Herpes simplex 1 infecting eye

Skin Infections

- Infect abrasions
- Dentists, (Herpetic Whitlow) Health care workers,
- Eczema , Burns

Neonatal Herpes.

- In Uterus
- At Birth
- After Birth.
- Delivery By Caesarean Section

Reduces the Infection

Laboratory Diagnosis

- Microscopy,
- Antigen Detection
- DNA detection PCR.
- Viral Isolation.
- Serology

Laboratory Diagnosis

- Specimen: Vesicular fluid- Corneal scrapping

1- Direct Virus Demonstration:

a) L/M:

1. Tzanck smear – from the base of vesicles, 1% aq. soln. of toluidine blue 'O'
   shows multinucleated giant cells with faceted nuclei & homogenously stained 'ground glass' chromatin (Tzanck cells)

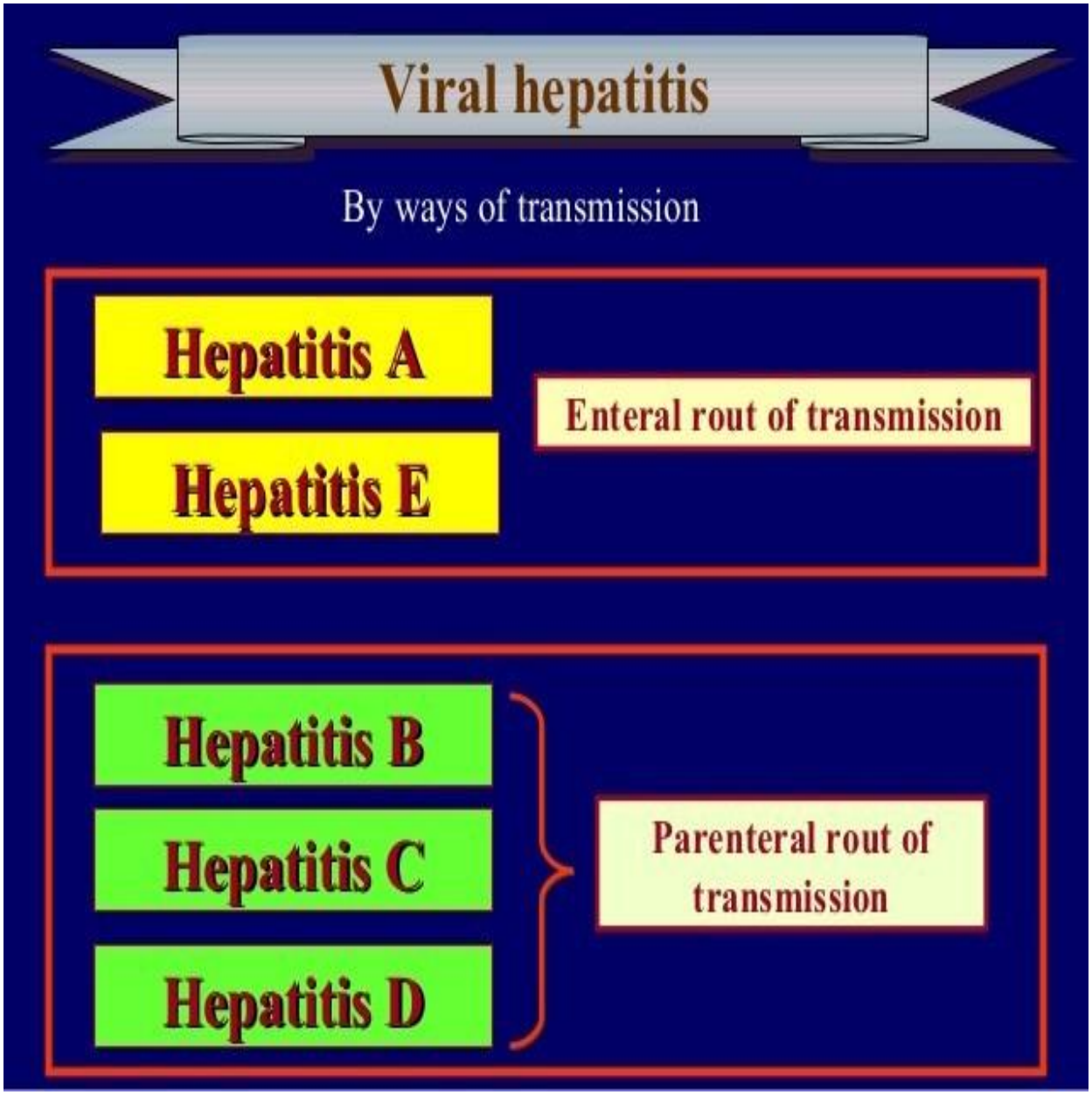
2. Giemsa stained smear – intranuclear Cowdry type A inclusion bodies

- 2- **Viral Isolation:** tissue culture: human diploid fibroblasts, human amnion, human embryonic kidney: CPC (syncytium formation) seen in 24-48 hrs.

- 3) **Serology**: useful in the diagnosis of primary infection, Ab (IgM) detection by ELISA, NT or CFT.

Types of Hepatitis

- Hepatitis A – Infectious hepatitis
- Hepatitis B – Serum hepatitis
- Hepatitis C – Non-A non-B or Post transfusion hepatitis
- Hepatitis D – with Hep B
- Hepatitis E - Epidemic hepatitis


Viral hepatitis
By ways of transmission
Hepatitis A
Hepatitis E
Enteral rout of transmission
Hepatitis B
Hepatitis C
Hepatitis D
Parenteral rout of transmission

HEPATITIS B

DNA virus

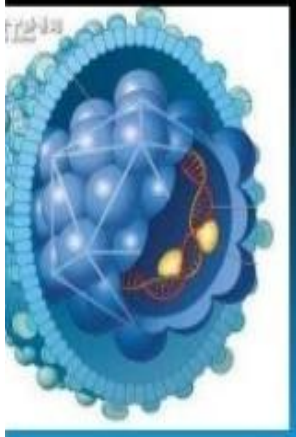
Family- Hepadnaviridae

Genus – Orthohepadnavirus

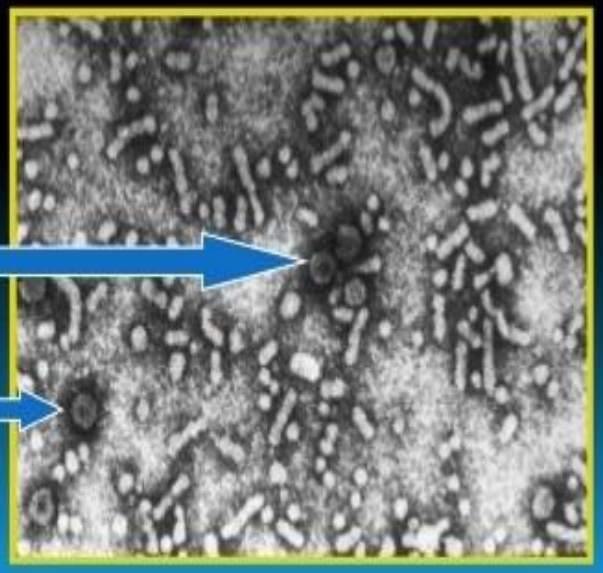
Hepatitis B virus is 30-42 nm in diameter.

Hepatitis B virus (HBV)

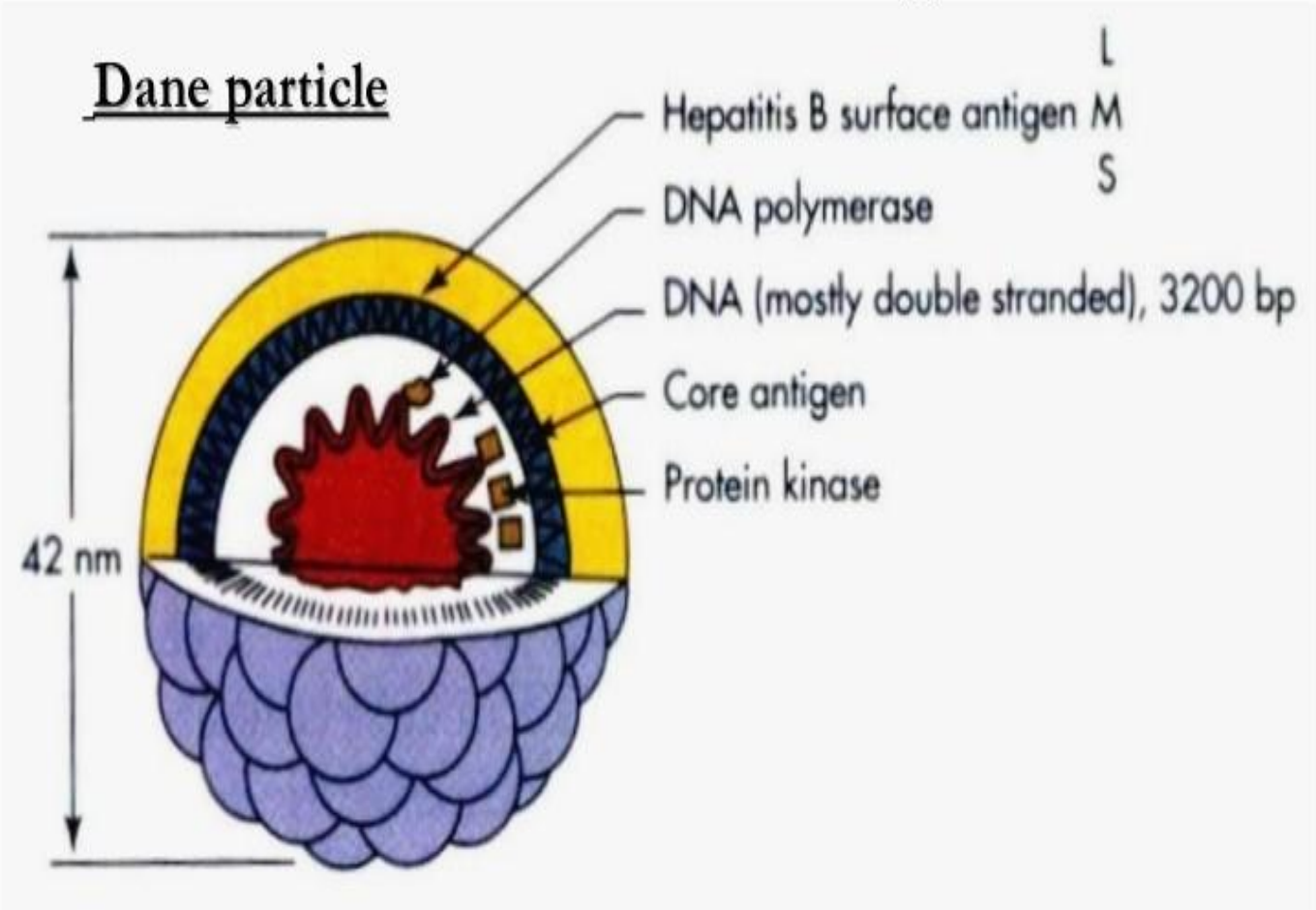
- DNA virus (hepadnavirus).
- Complete virus particle is named Dane-particle,
- Genome is composed of incomplete double-stranded DNA.



Dane's particle



HBV Structure & Antigens



HBsAg = surface (coat) protein (**4 phenotypes : adw, adr, ayw and ayr)**

HBcAg = inner core protein (**a single serotype)**

HBeAg = secreted protein; function unknown

Route of transmission

Body fluids contain viral particles

- Semen
- vaginal secretions
- Blood
- Saliva

Route of transmission

- HORIZONTAL TRANSMISSION
  - Parenteral: Blood & blood products

    Injections

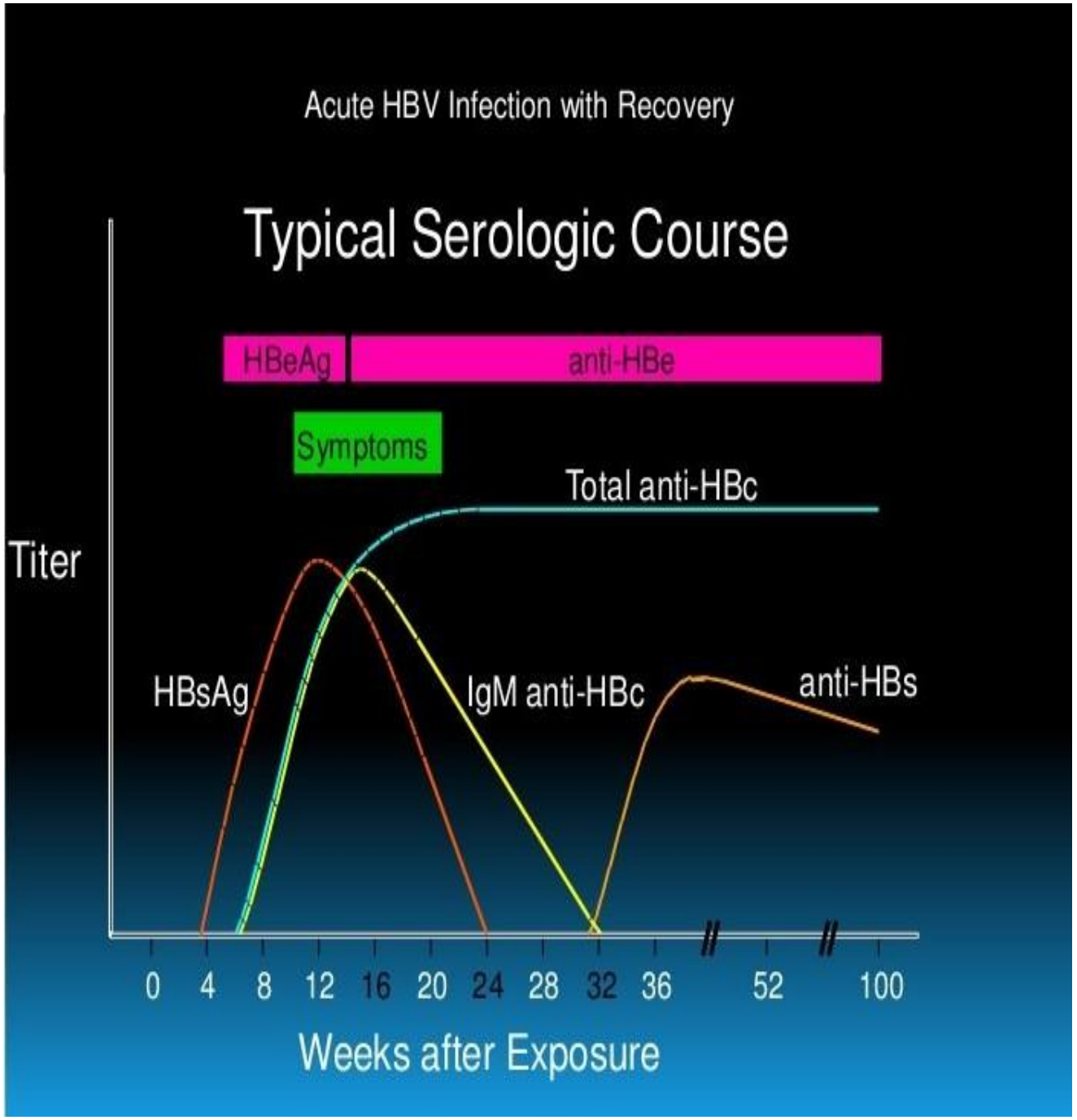
    Acupuncture needles
  - Sexual
- VERTICAL TRANSMISSION
  - Hbs Ag – positive mothers

Risk Groups

- Multiple sex partners
- IV drug abusers
- Hemodialysis patients
- Patients requiring repeated blood transfusions
  - Hemophilia
  - Thalassemia
- Health care workers

Serological Markers of HBV

- **HBsAg**: Marker of infectivity
- **Anti-HBs**: Marker of immunity
- **HBcAg**: No commercial test available.
- **Anti-HBc**: Marker of past or current infection.
  - **IgM anti-HBc:** Recent infection.
  - **IgG anti-HBc**: Older infection.
- **HBeAg**: Marker of high degree of infectivity.
- **Anti-HBe**: May be present in infected or immune person.


Acute HBV Infection with Recovery
Typical Serologic Course
HBeAg
anti-HBe
Symptoms
Total anti-HBc
Titer
HBsAg
IgM anti-HBc
anti-HBs
0
4
8
12
16
20
24
28
32
36
52
100
Weeks after Exposure

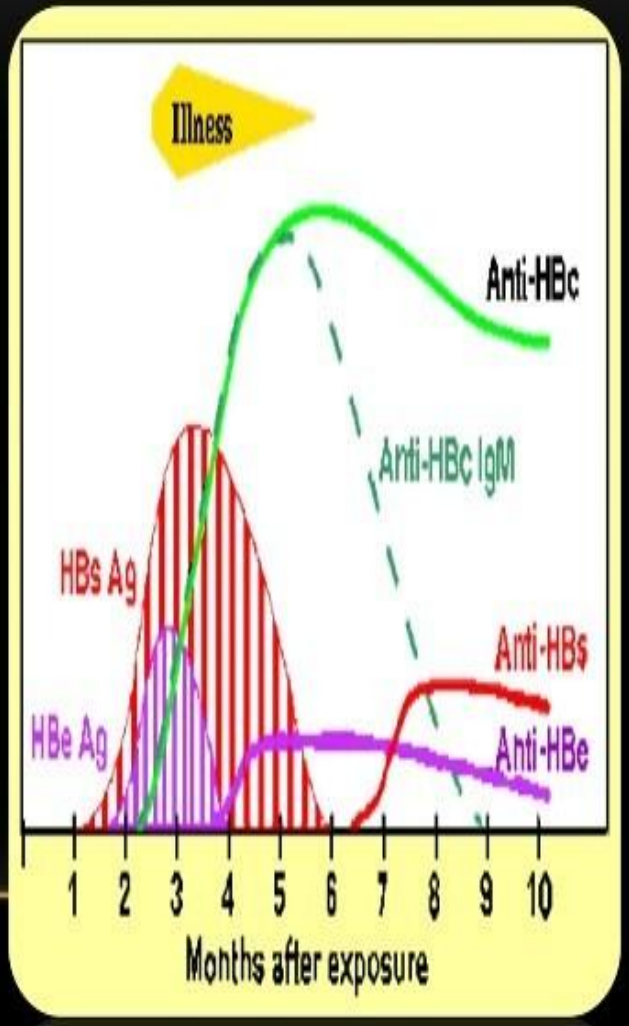
HBV Markers in different Stages:

Stage of infection	HBV DNA	HBsAg	HBeAg	Anti-HBc Ig M	Anti-HBc Total	Anti-HBe	Anti-HBs
Susceptible	–	–	–	–	–	–	–
Early incubation	+	–	–	–	–	–	–
Late incubation	+	+	+/–	–	–	–	–
Acute infection	+	+	+	+	–	–	–
Recent infection	–/+	–	–	+	+	+	+++

Stage of infection	HBV DNA	HBsAg	HBeAg	Anti-HBc Ig M	Anti-HBc Total	Anti-HBe	Anti-HBs
Remote infection	_ or very low	–	–	–	+	+/_	+
HBsAg-ve Acute infect	_	–	–	+	+	–	–
HBsAg variant infect.	_/+	–	_/+	+/_	+	–	–
Immune active carrier	++	+	_/+	_/+	+++	–	–
Healthy HBsAg carrier	_	+	–	–	+	+	–
Vaccination response	_	–	–	–	–	–	+

HBV – SEROLOGY INTERPRETATION

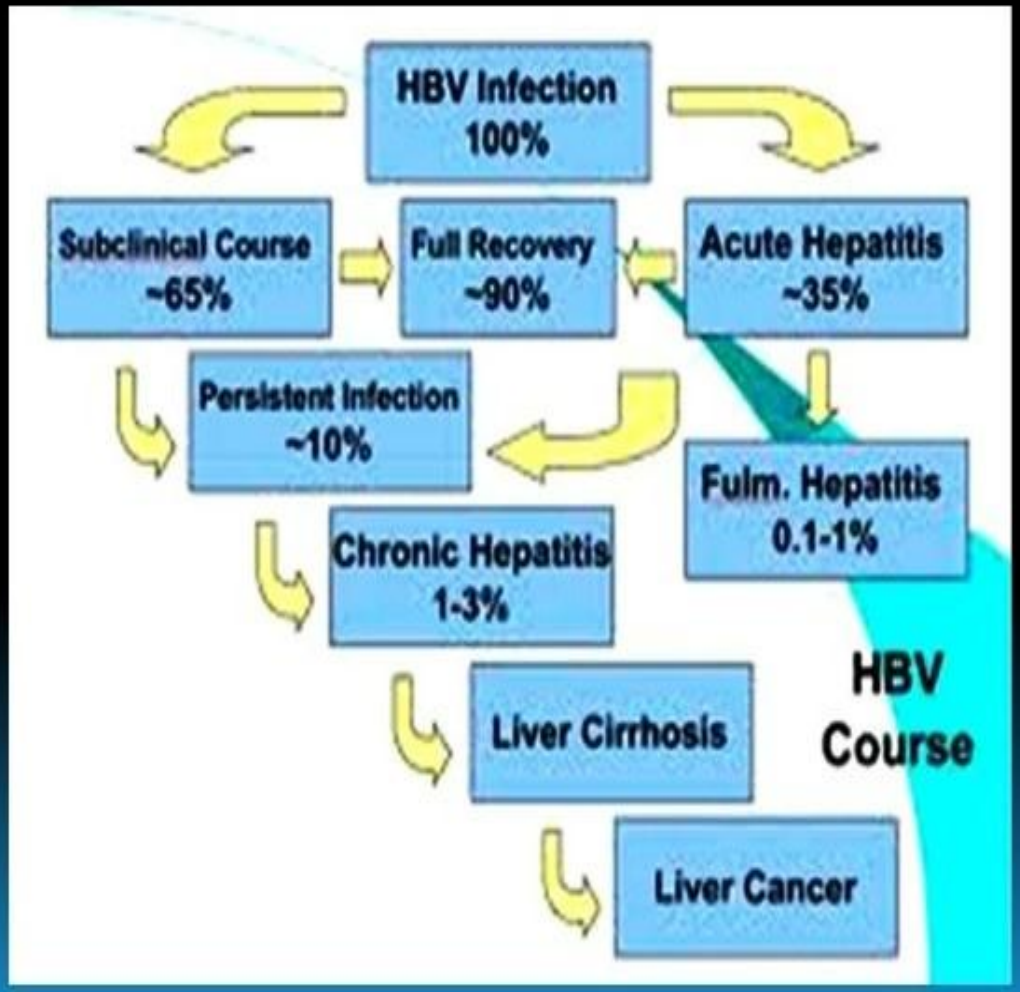
- **Acute infection**
  - HBsAg positive and anti-HBcAg IGM
  - Rarely, IgM anti-HBc only marker
    - Usually seen in acute fulminate Hep B
- **Chronic infection**
  - HBsAg positive and anti-HBcAg
- **Previous Infection**
  - HBsAg negative
  - anti-HBs positive
  - IgG anti-HBc positive



Factors associated with the severity of hepatitis

- Infecting dose
  - Higher the dose of HBV, shorter is incubation period and more severe hepatitis.
- Age
  - Young age: mild initial hepatitis & more chance of chronicity.
- Immunological status
  - Immunological impaired hosts: Milder initial disease.

CLINICAL COURSE



ACUTE ICTERIC HEPATITIS

- Incubation period - 70 days (30 - 180 days);

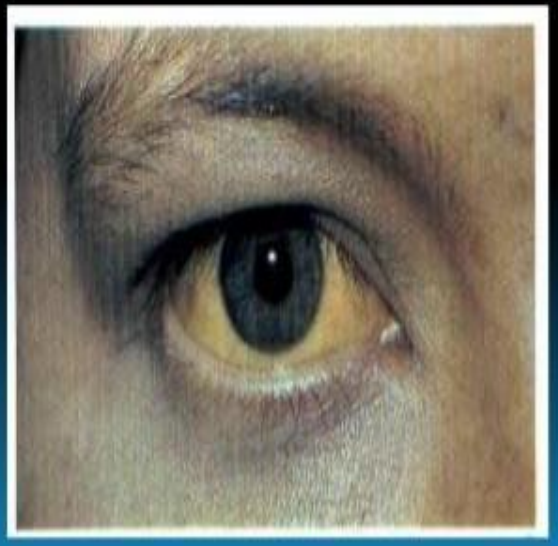
- Four clinical stages:
  - incubation period,
  - prodromal phase (pre-icteric phase),
  - icteric phase
  - convalescence.

Pre-icteric phase

- Symptoms are nonspecific;
  - Moderate fever
  - Headache
  - Malaise and weakness
  - Anorexia, nausea, vomiting
  - A vague, dull, right upper quadrant pain.

Icteric phase

- Clinical features of icteric phase:
  - Symptoms of pre-icteric phase being mild;
  - Jaundice (dark urine, skin and scleral icterus);
  - Stool light or clay colored;
  - Hepatomegaly
  - Liver function abnormalities
    - ALT and AST ⇧
    - Bilirubin (direct & indirect) ⇧



Acute anicteric hepatitis

---No jaundice otherwise similar to acute icteric hepatitis,.

---The symptoms are less severe than that in acute icteric hepatitis.

COMPLICATIONS

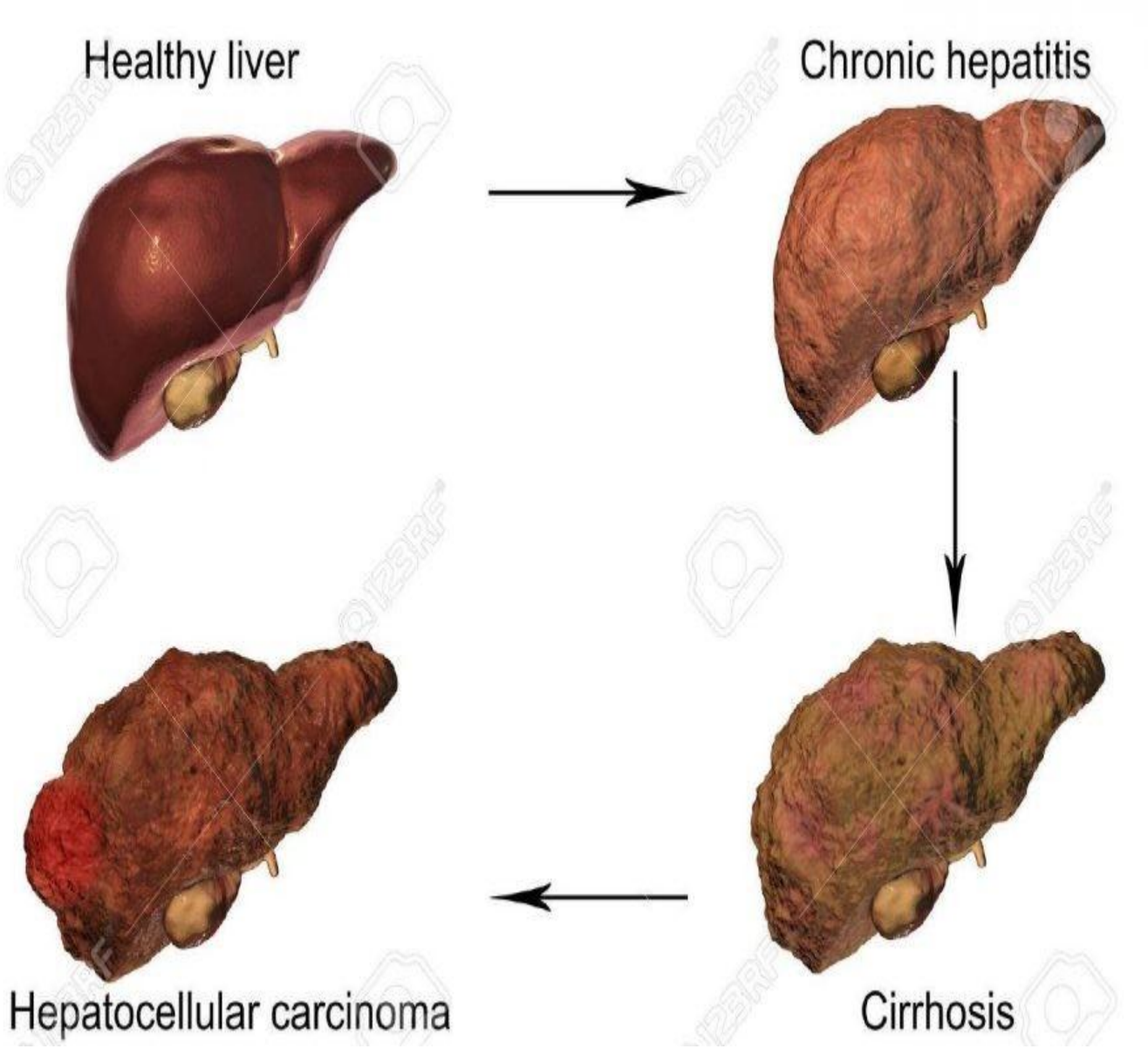
- Fulminant Hepatitis
- Chronic Hepatitis
- Rare complications:
  - Pancreatitis,
  - Myocarditis
  - Atypical pneumonia
  - Aplastic anemia
  - Transverse Myelitis

CHRONIC HEPATITIS

- Chronic viral hepatitis: Inflammatory disease of the liver > 6 months.

CLINICAL FEATURES

- Fatigue, anorexia, abdominal distension, diarrhea are common, but they are fluctuant.
- Hepatomegaly, splenomegaly, hepatic facies, liver palms, spider angioma can be seen.


Healthy liver
Chronic hepatitis
Cirrhosis
Hepatocellular carcinoma

DIAGNOSIS

SEROLOGY

- HBsAg
- Anti HBcAg IgM
- HBV DNA by PCR is most sensitive test

DIAGNOSIS

SEROLOGY

- HBsAg positive > 6 months
- Anti-HBc IgG in blood
- Serum HBV DNA > 10^5 copies/ml (20,000 IU/ml)
- HBeAg or Anti HBeAg may be present

Treatment of Chronic Hepatitis B

- **DRUGS :** No specific therapy available
  - Interferon-alfa
    - IFN α → 6 month in Hbe +ve
    - Peg IFN α → 12 months in Hbe - ve
  - Lamivudine :100mg OD 48 weeks
  - Adefovir : 10 mg OD 48 weeks
  - Entecavir
  - Telbivudine
- **Liver Transplantation**

PREVENTION

- HBV Vaccine
  - DNA Recombinant vaccine
  - IM (deltoid but not gluteal)
  - 3 doses 0, 1, 6
  - Duration of protection – 5 to 10 yrs

❖ POST-EXPOSURE PROPHYLAXIS

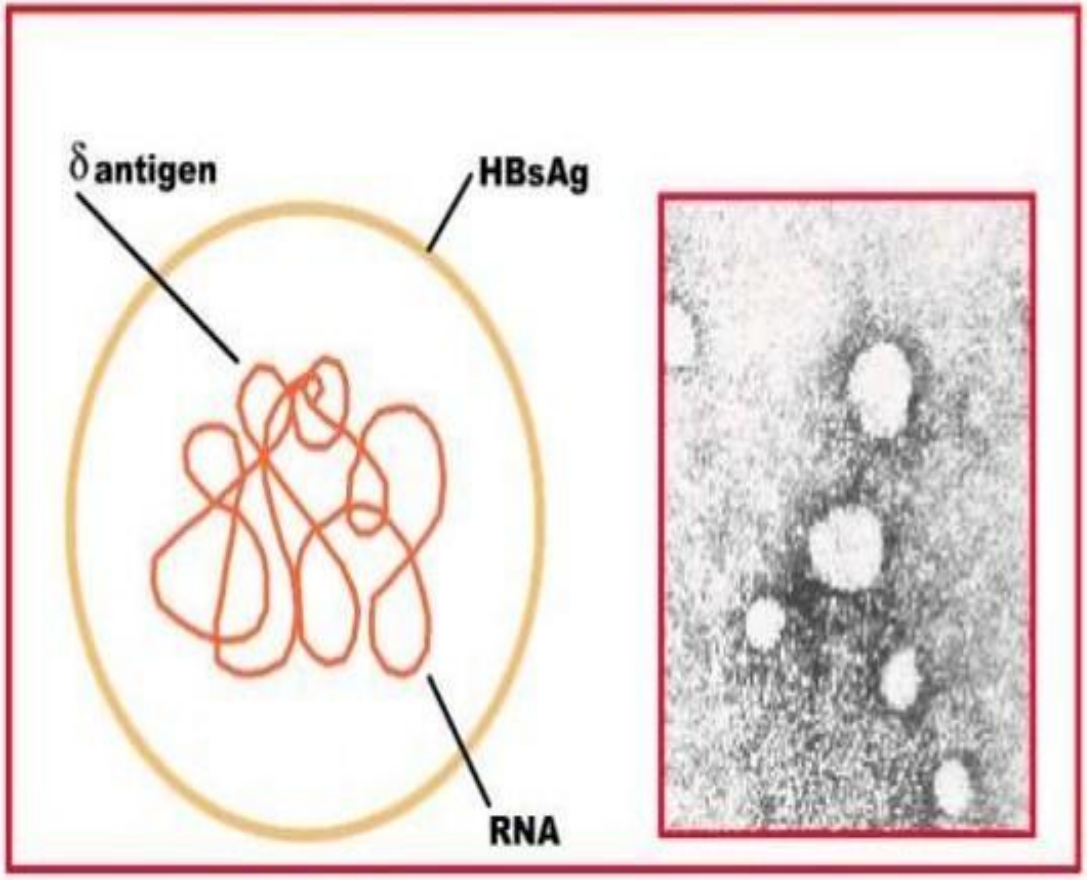
- Combination of HBIG & HB vaccine (24 hrs)

❖ PERINATAL PROPHYLAXIS OF INFANTS

- HBIG 0.5ml IM in thigh immediately after birth
- Full course of HB vaccine started within 12 hrs of birth

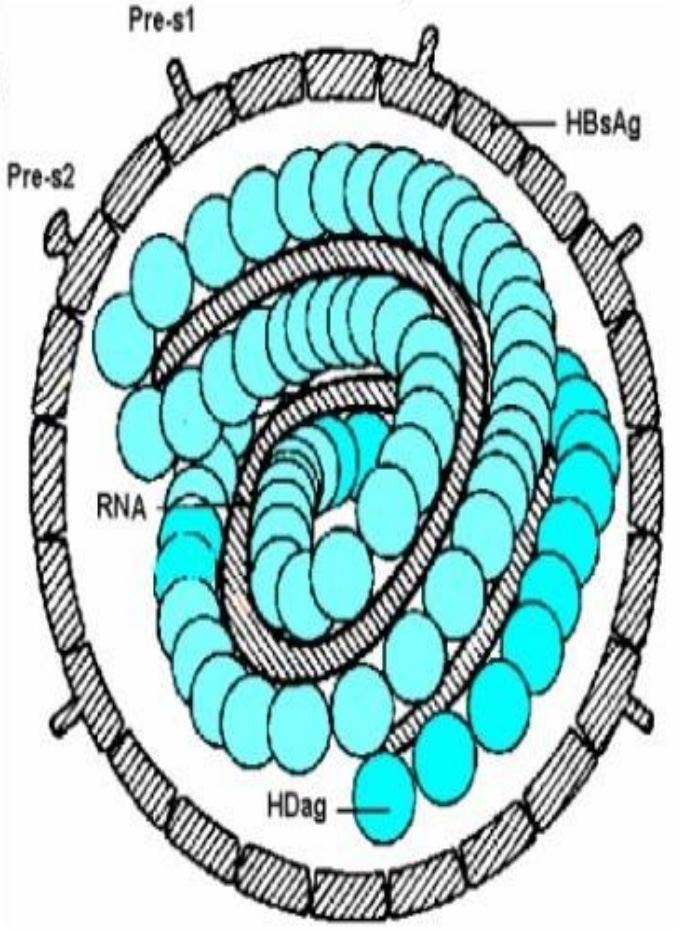
HDV STRUCTURE

Hepatitis D (Delta) Virus



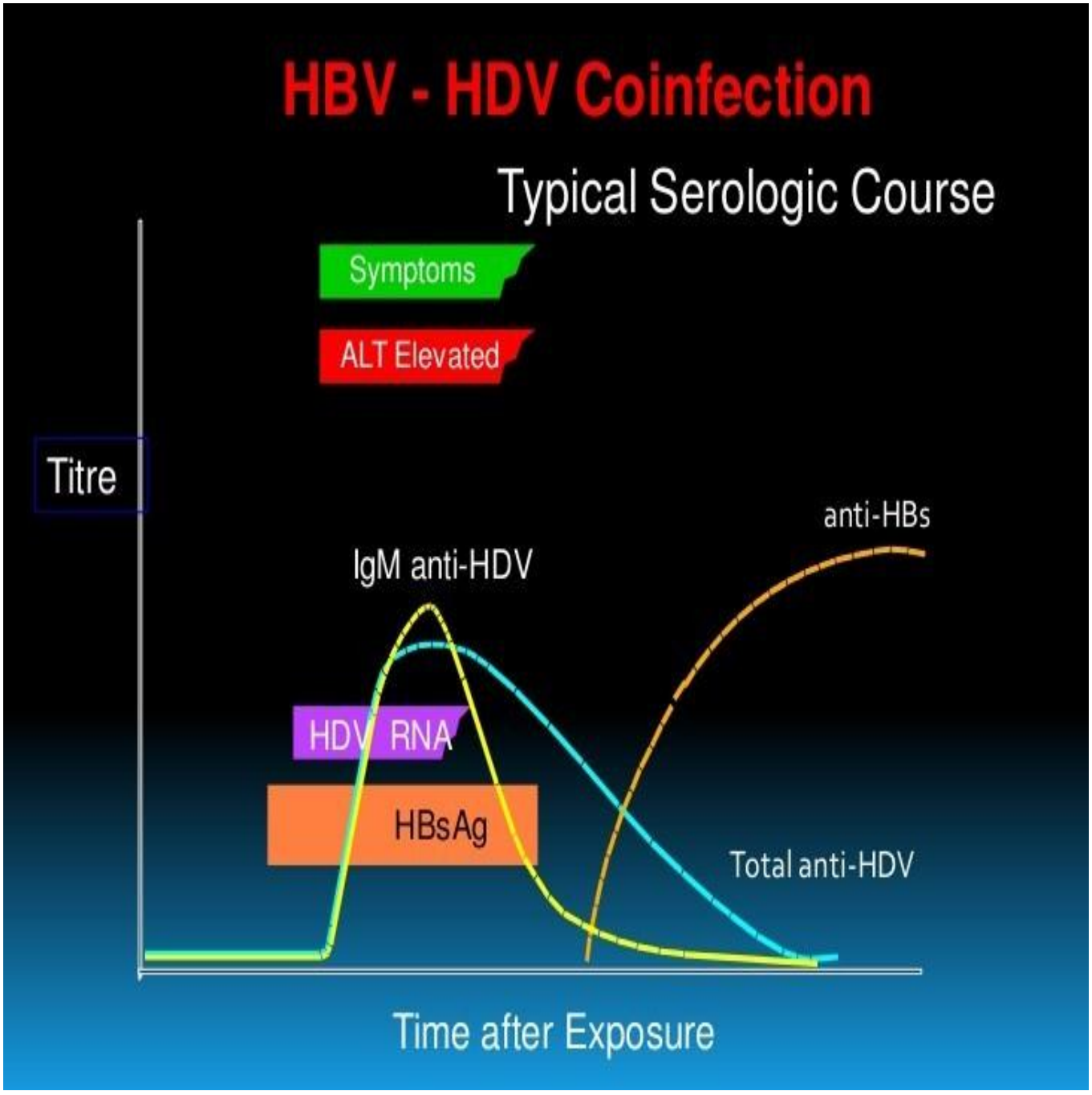
HEPATITIS D VIRUS (HDV, DELTA AGENT)

VIRION: spherical, 36-38 nm,
HBV capsid, HDV nucleoprotein
NUCLEIC ACID: (-) ss RNA, circular
Satellite virus : replicates only
in the presence of HBV

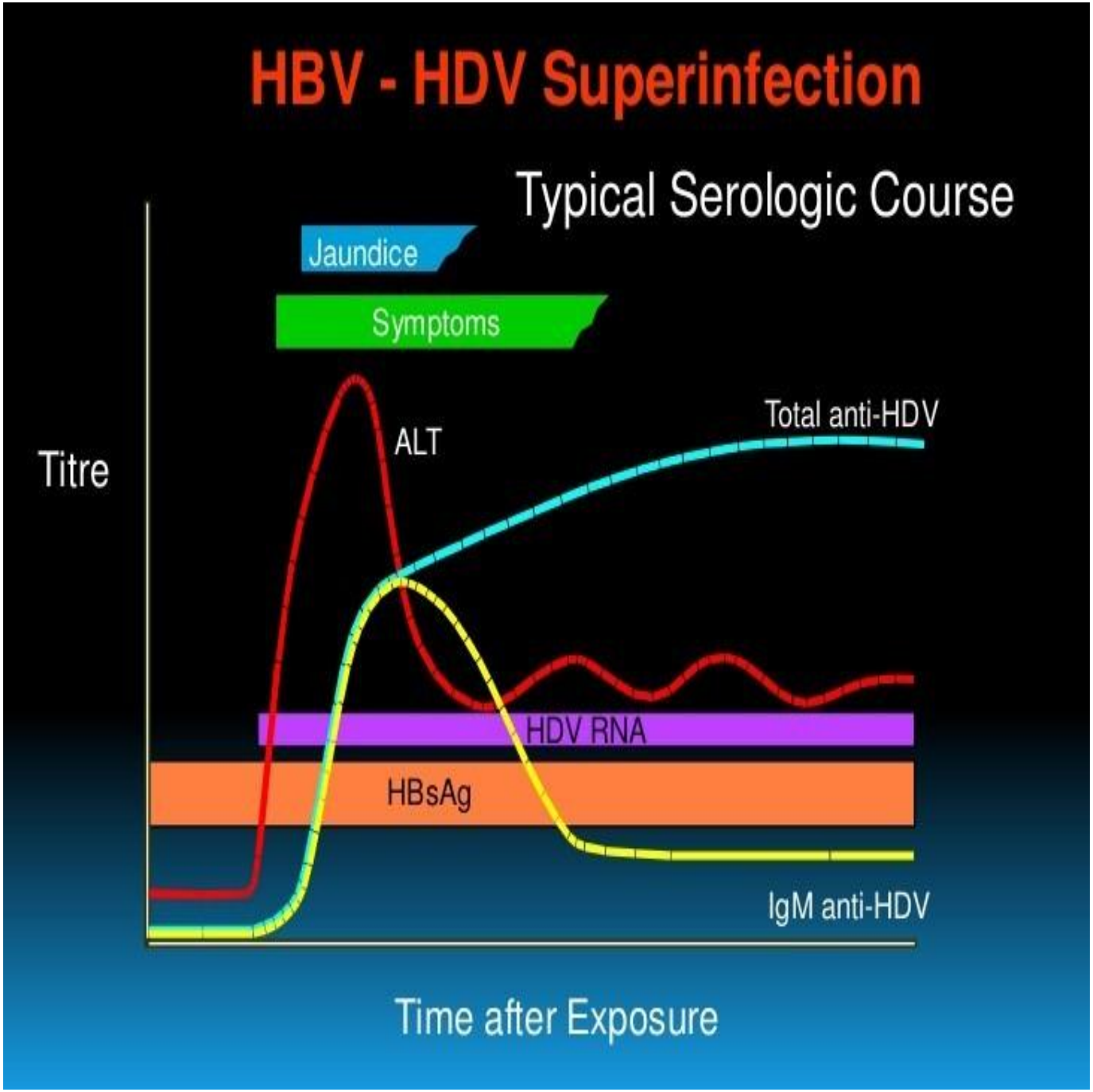


Hepatitis D virus (HDV)

- Delta virus
- Incomplete defective RNA virus.
- Requires coating of hepatitis B surface antigen (HBsAg) for entry into and exit from the hepatocyte.
- HDV- antigen and Anti-HDV in serum
- Route of transmission: Similar to HBV


HBV - HDV Coinfection
Typical Serologic Course
Symptoms
ALT Elevated
Titre
anti-HBs
IgM anti-HDV
HDV RNA
HBsAg
Total anti-HDV
Time after Exposure

HBV - HDV Superinfection



Hepatitis D Prevention

- Hepatitis D can be prevented by vaccinating susceptible persons with Hepatitis B vaccine

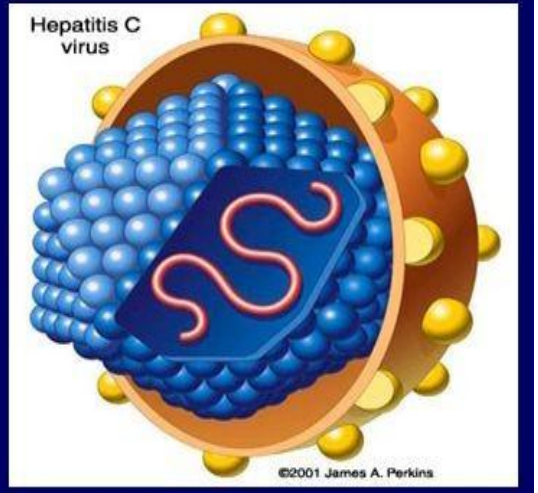
Hepatitis C virus: Classification & structure

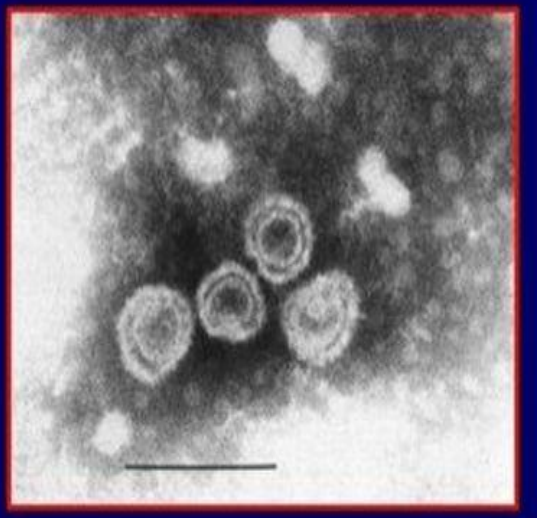
- Family: *Flaviviridae.*
- Genus: *hepacivirus.*

- The virus is small, 60 – 80 nm in diameter.

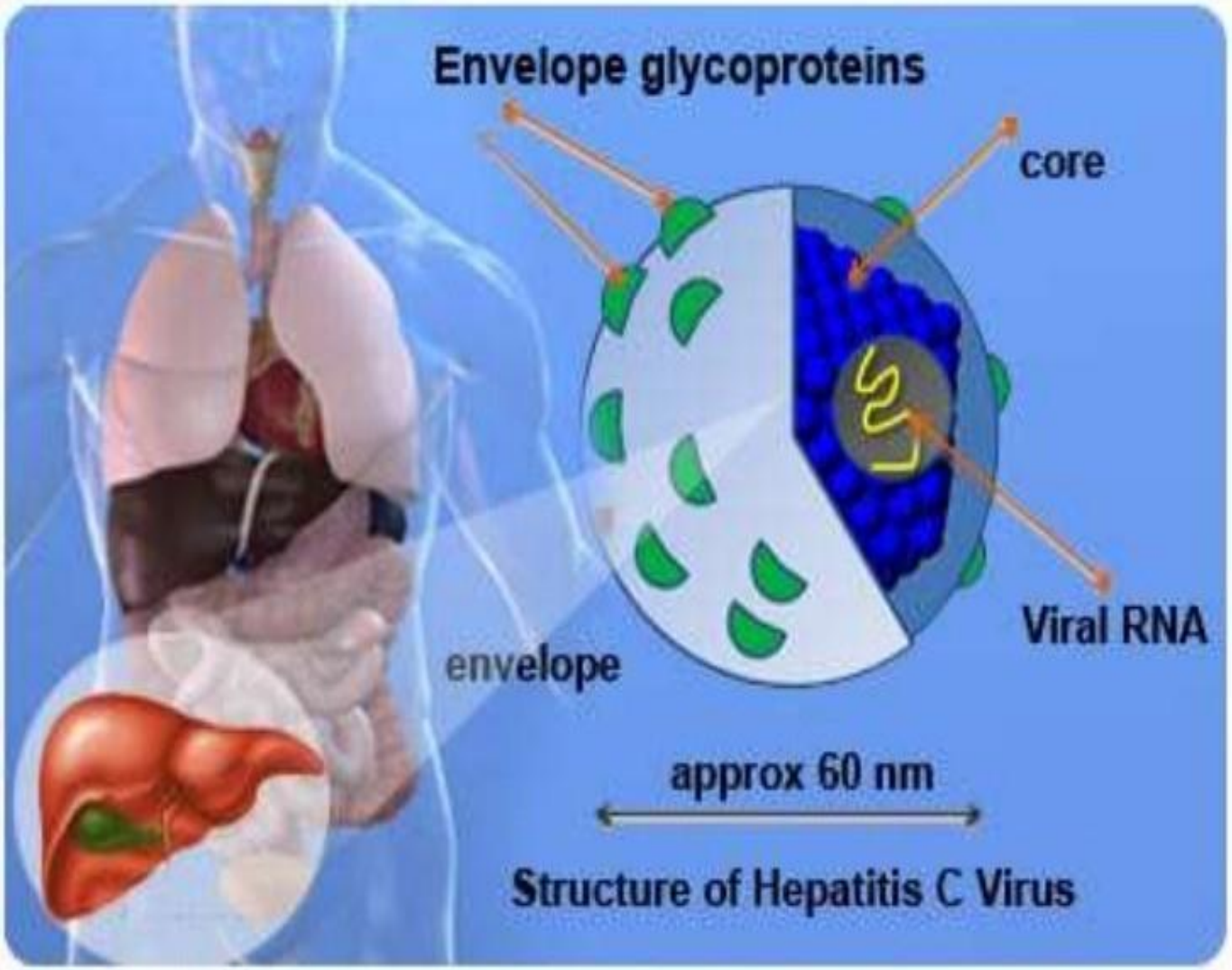
- Consists of an outer envelope, icosahedral core and linear positive polarity ss-RNA gemone.

- There are 6 major genotypes (1 – 6), genotype 4 is the dominant in Saudi patients.

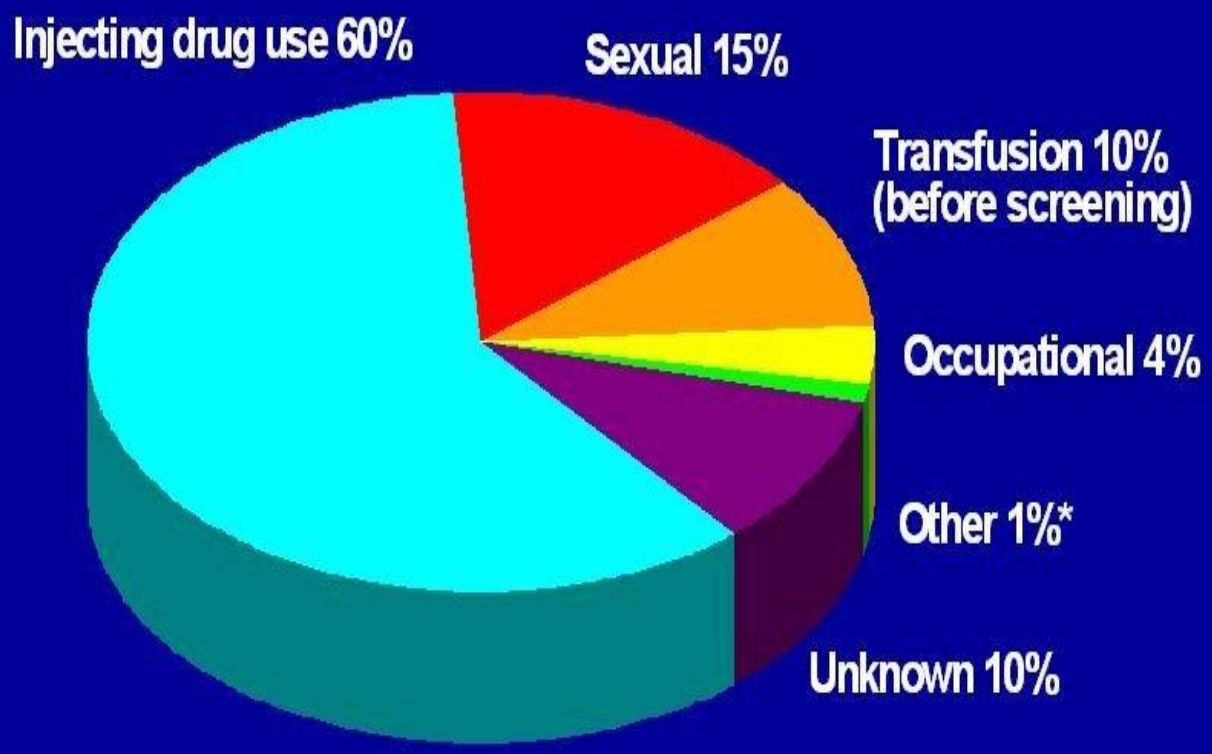




STRUCTURE OF HEPATITIS C



Routes of Transmission



* Nosocomial; iatrogenic; perinatal

CLINICAL FEATURES

- Incubation period: 50 days (15 – 150 days)
- 90% : Asymptomatic
- 10%: Mild flu like illness with jaundice & raised serum amino transferrases
- Extrahepatic Manifestation : Arthritis

  Glomerulonephritis

DIAGNOSIS

- HCV RNA detected in 1 – 2 weeks after infection
- Anti HCV is + ve 6 weeks after infection

Clinical Course

- 85% : Chronic liver disease
- 15 – 20% : Cirrhosis in 10 – 30 yrs
- 7 – 15% of cirrhosis patient: Hepatocellular carcinoma

Treatment for Chronic HC

- For CHC: IFN-α + Ribavirin 6 - 12 months

  Side Effects

  - Ribavirin: Hemolytic anemia
  - Interferon: Flu like symptoms

- Liver Tranplantation in Cirrhosis

Hepatitis A

- CLASSIFICATION:

  Group: Group IV ((+) ssRNA)

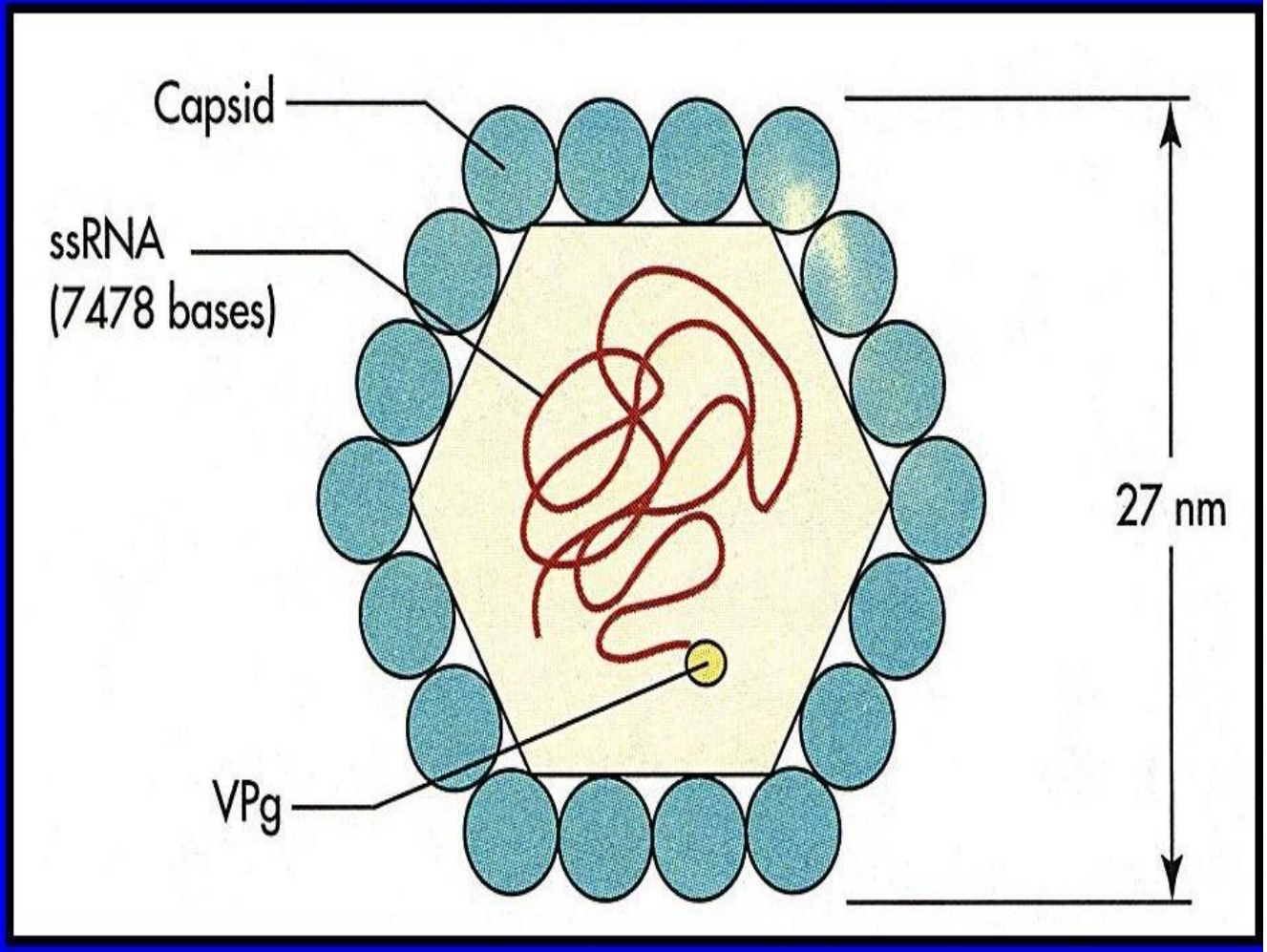
  Family: Picornaviridae

  Genus: Hepatovirus

  Specie: Hepatitis A virus

- Hepatitis A infection does not cause chronic liver disease and is rarely fatal, but it can cause debilitating symptoms.

Hepatitis A Structure



Epidemiology

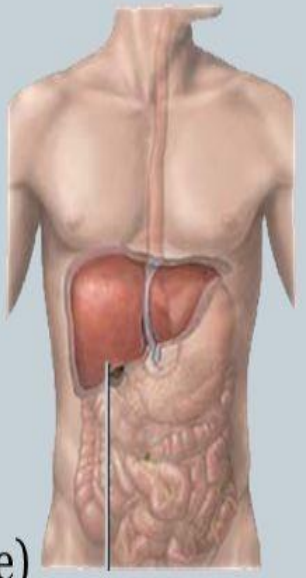
- Most common Viral Hepatitis
- Source of Infection: **patients**.
- Route of spread : Faeco-oral
- Patient remains infectious 2 weeks prior to & for upto 1 week after onset of illness
- Overcrowding & Poor Sanitation
- No carrier state

CLINICAL FEATURES

- Incubation period 15 – 45 days
- Asymtomatic (90%):
  - Clinically silent
  - Nonspecific: Anorexia
    Nausea
    Vomiting
- Symptomatic (10%):
  Jaundice, Dark urine & Pale stools

Symptoms

Hepatitis A signs and symptoms typically don't appear until you've had the virus for a few weeks. Signs and symptoms of hepatitis A include:



- Fatigue
- Nausea and vomiting
- Abdominal pain or discomfort.
- Loss of appetite
- Low-grade fever
- Dark urine
- Muscle pain
- Yellowing of the skin and eyes (jaundice)
- Acute liver failure

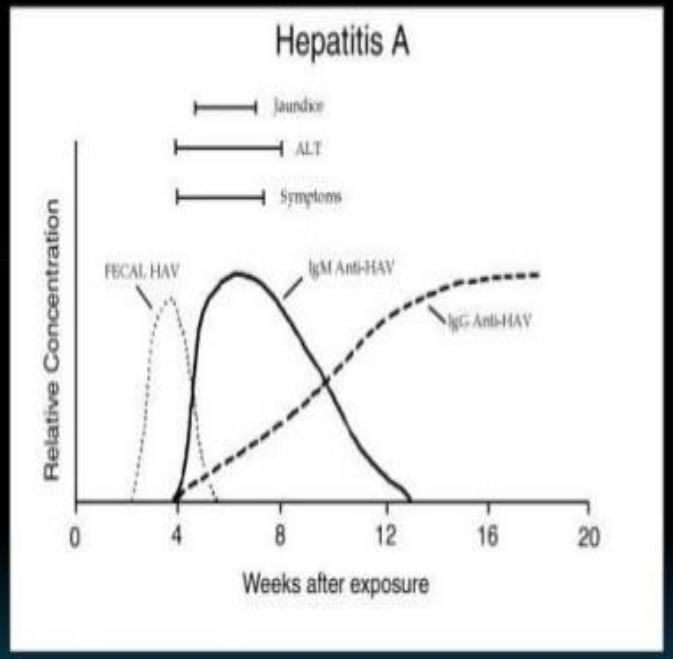
In rare cases, hepatitis A can cause acute liver failure, which is a loss of liver function that occurs suddenly.

DIAGNOSIS

- Anti HAV IgM +ve: Acute infection

  Disappears within

  3 months of recovery.



- Anti HAV IgG is of no diagnostic value

  as it persists years after infection.

TREATMENT

- DIET

- Raw juice diet for 3 to 5 days.
  Oranges, lemons, sugarcane and carrots may be used for juices. During this period, the bowels should be cleaned daily with lukewarm water enema.
- An all-fruit diet for further 3 to 5 days, with three meals a day at five-hourly intervals.

- Food especially beneficial: Limejuice, Pear, Barley water. Coconut water, sugarcane juice and radish leaves Juice.
- Avoid: Alcohol, Fried and fatty foods, too much butter and clarified

  butter, meats, tea, coffee, pickles, condiments and pulses.

- OTHER MEASURES

- 1. Drink plenty of water with lemon juice.

  2. Adequate rest.

Prevention

- Vaccine - Formalin inactivated
- 2 doses 0, 6 -12 months
- IM deltoid or gluteal
- Protection period 25 yrs in adult &

  15 – 20 yrs in children

Hepatitis E virus (HEV)

- Single-stranded RNA,
- At least four Genotypes.
- Enterically trasmitted by contaminated water
- "Enterically Transmitted Non A Non B Hepatitis"
- Symptoms similar to Hepatitis A
- Self Limiting & no progression to chronic liver disease
- Incubation period: 40 days (15 – 60 days)

DIAGNOSIS

- ELISA for IgM & IgG anti HEV
- HEV RNA in serum or stools

PREVENTION

No vaccine available

HIV AIDS

S.Nandhini

Introduction

- HIV was first Identified in 1981 in USA among homosexuals
- In 1983, French investigator named Lymphadenopathy associated virus (LAV).
- In 1984 virus was isolated by Gallo and co-workers from national institute of health in United States.

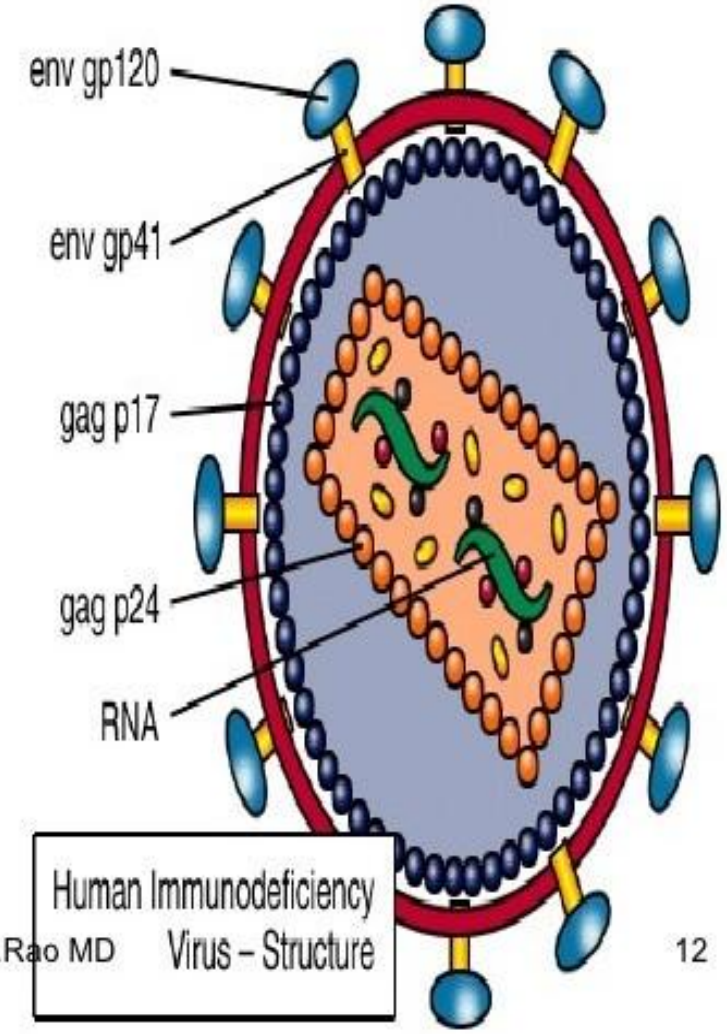
They named Human T-cell Lymphotropic virus III (HTLV-III).

Contd.

- Thailand was the first country in the SEAR to report a case of AIDS, in 1984.
- In 1986, a new strain of HIV was isolated in West African patient with AIDS which is called HIV-2.
- In May 1986, international committee on taxonomy gave a new name called Human immune deficiency virus.
- Since its identification, HIV/AIDS is devastating disease of mankind

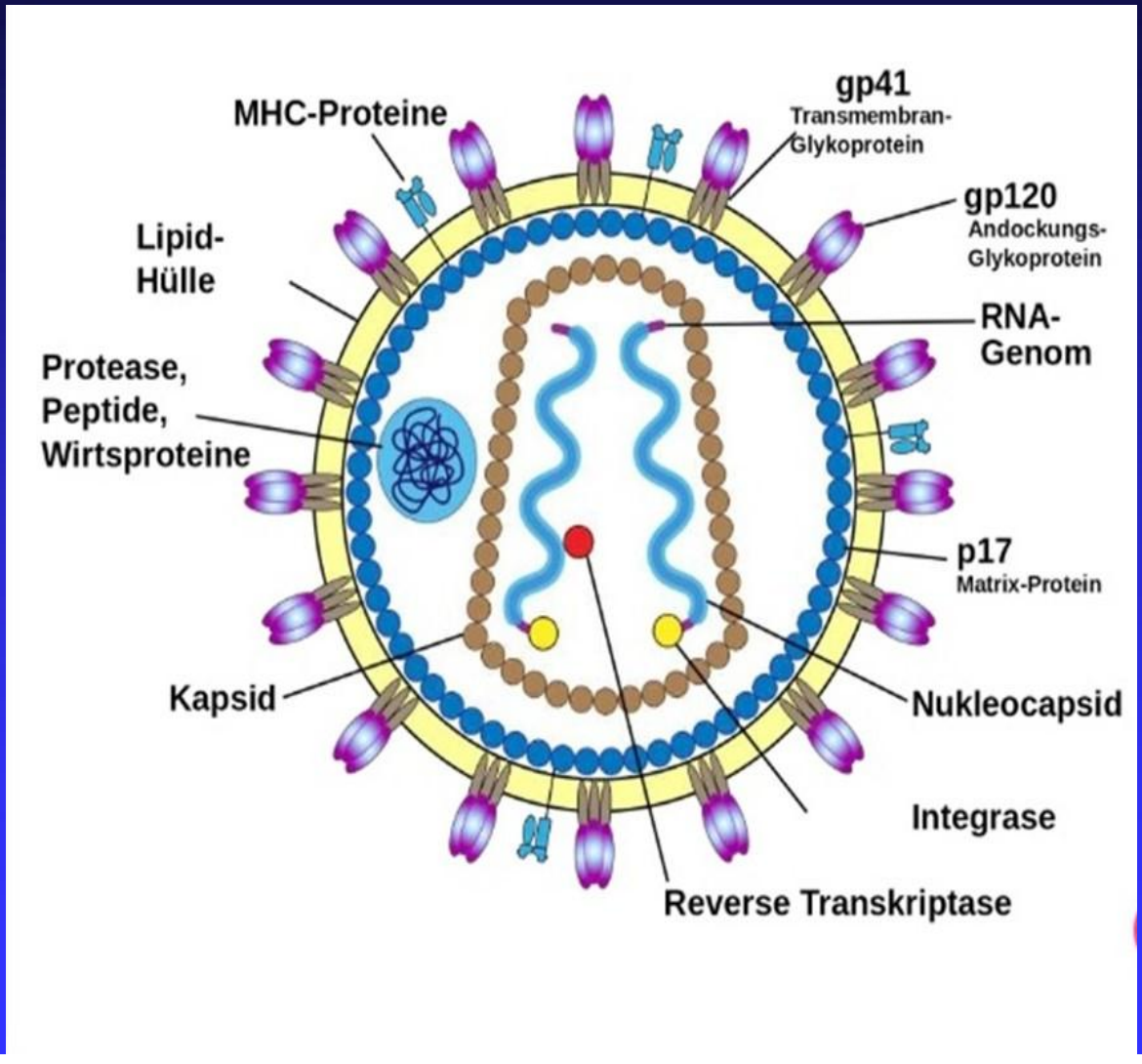
Family : Retroviridae
Subfamily : Lentivirus

- RNA virus, 120nm in diameter
- Envelope gp160; gp120 & gp41
- Icosahedral symmetry
- Nucelocapsid
  - Outer matrix protein (p17)
  - Major capsid protein (p24)
  - Nuclear protein (p7)
- Diploid RNA with several copies of reverse transcriptase



Human Immunodeficiency Virus – Structure

Structure of the Human Immunodeficiency Virus
HIV is a Retrovirus



WHAT IS HIV ?

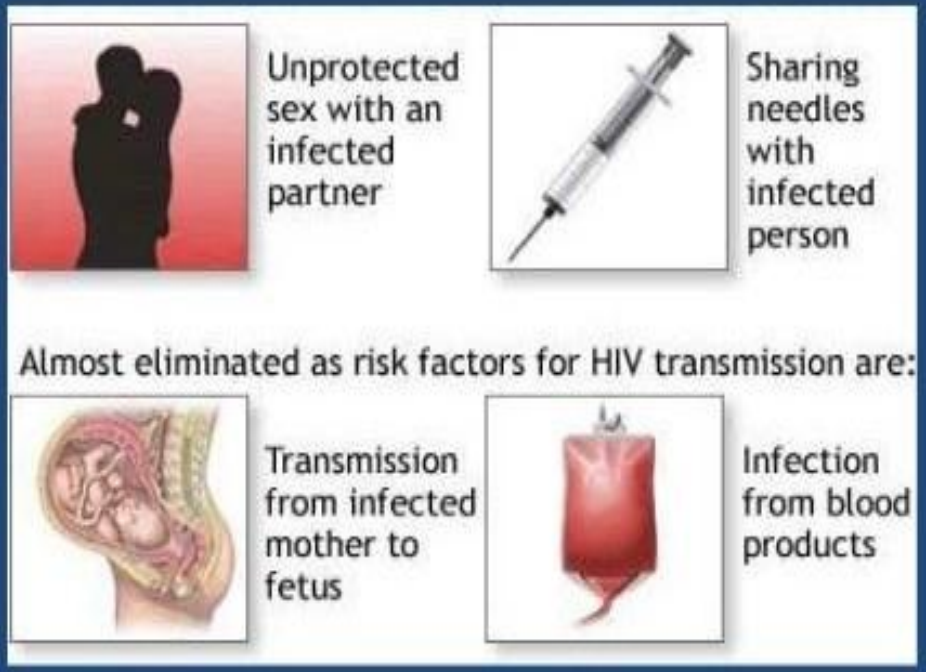
Human **I**mmunodeficiency **V**irus

H *= Infects only* ***H****uman beings*

I *= Immunodeficiency virus weakens the immune system and increases the risk of infection*

V *=* ***V****irus that attacks the body and eventually overcomes the body's immune system*

HIV Modes of Transmission



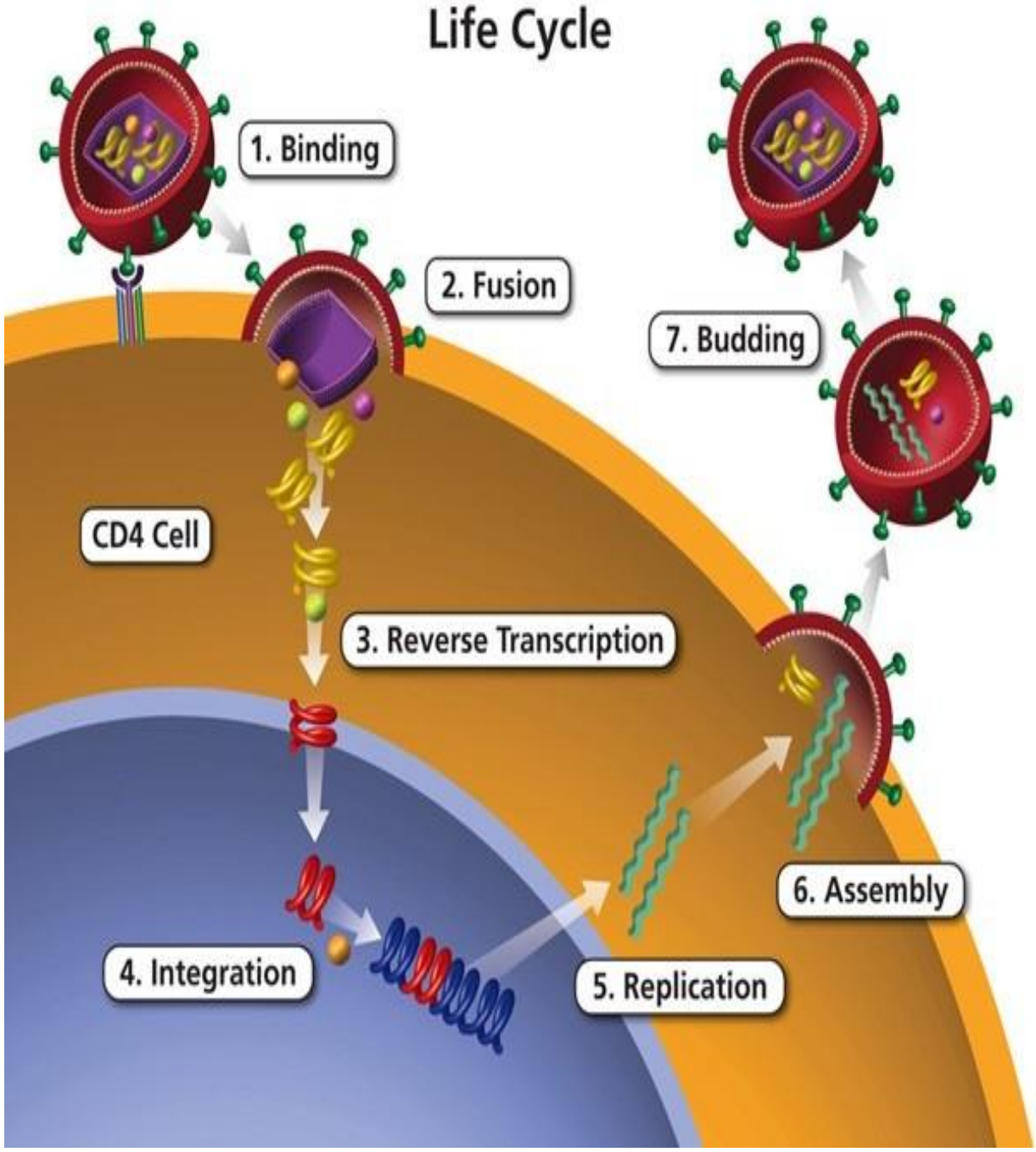
- vertical transmission of HIV from mother to child is the main route by which childhood HIV infection is acquired
- the risk of perinatal acquisition is 25-40% without intervention

- *The body fluids have been proven to spread HIV:*

- *blood*
- *semen*
- *vaginal fluid*
- *breast milk*
- *other body fluids containing blood*
- *cerebrospinal fluid surrounding the brain and the spinal cord*
- *synovial fluid surrounding bone joints*

PATHOGENESIS :

- *Attachment of virus at the CD4 receptor and chemokine co-receptors .*
- *viral fusion and uncoating*
- *Reverse transcriptase .*
- *Migration to nucleus*
- *Integration of the viral DNA into cellular DNA by the enzyme integrase*
- *Transcription and RNA processing*
- *Protein synthesis.*
- *protease cleaves polypeptides into functional HIV proteins and the virion assembles*
- *virion budding*
- *Virion maturation*


Life Cycle
1. Binding
2. Fusion
CD4 Cell
3. Reverse Transcription
4. Integration
5. Replication
6. Assembly
7. Budding

FOUR STAGES OF HIV

STAGE 1 – PRIMARY :

- *flu like illness - occurs two to six weeks after infection or there may be*
- *no symptoms at all*
- *Infected person can infect other people*

Stage 2 - Asymptomatic

- *This stage is free from symptoms*
- *There may be swollen glands.*
- *HIV antibodies are detectable in the blood*
- *This stage is last for about ten years*

STAGE 3 – SYMPTOMATIC :

The person starts showing symptoms like fever, skin disease.

The immune system deteriorates emergence of opportunistic infections and cancers

STAGE 4 - HIV ⇨ AIDS :

- *The immune system weakens*
- *The illnesses become more severe leading to AIDS*
- *The illnesses become more severe leading to emergence of opportunistic infections and cancers*

SYMPTOMS :

The symptoms of this :

- *diarrhea*
- *fatigue or weakness*
- *fever*
- *headache*
- *joint pain*
- *night sweats*
- *rash*
- *swollen glands*
- *weight loss*
- *yeast infections (of the mouth or vagina) that last a long time or occur frequently*

Diagnostic Tests for HIV Infection

- Serological methods for detection of antibody
  - Rapid tests
  - ELISA
  - Western blot
- Antigen detection methods
  - P24 antigen capture test
  - Polymerase Chain Reaction (also known as PCR or viral load)

Laboratory Diagnosis of HIV infection

1) **Non Specific Tests-** The following tests help to establish the immunodeficiency in HIV infection.

a) **Total Leukocyte and lymphocyte count-** to demonstrate leucopenia and lymphopenia. The lymphocytic count is usually below 2000/mm^3

b) **T cell subset Assays**- Absolute CD4+ cell count is less than 200 /L.T4 T8 ratio is reversed.. The decrease in CD4 is the hall mark for AIDS.

c) **Platelet count** shows Thrombocytopenia.

d) **IgA and Ig G levels** are raised

e) **Diminished cell mediated Immunity** as indicated by skin tests

f) **Lymph node biopsy** shows profound abnormalities.

Laboratory diagnosis

Laboratory procedures for the diagnosis of HIV infection include tests for immunodificiency as well as specific tests for HIV.

A. **Immunological** tests. The following parameters help to establish the immunodeficiency in HIV infection:

l . Total leucocyte and lymphocyte count to demonstrate leucopenia and a lymphocyte count usually below 2,000 /c.mm.

2. T cell subset assays. Absolute T4 cell count will be usually less than 200/c.mm. T4: T8 cell ratio is reversed.

3. Platelet count will show thrombocytopenia.

4. Raised IgG and IgA levels.

5. Diminished CMI as indicated by skin tests.

6. Lymph node biopsy showing profound abnormalities.

HIGHLY ACTIVE ANTIRETROVIRAL DRUGS

- NUCLEOSIDE REVERSE TRANSCRIPTASE
  - *Zidovudine*
  - *Stavudine*
- NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR
  - *Efavirenz*
  - *Nevirapine*
- PROTEASE INHIBITOR
  - *Atazanavir*
  - *Darunavir*

PREVENTION

There's no vaccine to prevent HIV infection and no cure for AIDS. But it's possible to protect yourself and others from infection. That means educating yourself about HIV and avoiding any behavior that allows HIV-infected fluids — blood, semen, vaginal secretions and breast milk — into your body.