Chair of Medical Biology, Microbiology, Virology, and Immunology

STRUCTURE, CLASSIFICATION AND PHYSIOLOGY OF VIRUSES

Viruses are small obligate intracellular parasites, which by definition contain either a RNA or DNA genome surrounded by a protective, virus-coded protein coat. Viruses may be viewed as mobile genetic elements, most probably of cellular origin and characterized by a long co-evolution of virus and host. For propagation viruses depend on specialized host cells supplying the complex metabolic and biosynthetic machinery of eukaryotic or prokaryotic cells. Viruses are unable to generate energy. **As obligate intracellular parasites, during replication, they fully depend on the complicated biochemical machinery of eukaryotic or prokaryotic cells.**

A complete virus particle is called a virion.

The main purpose of a virus is to deliver its genome into the host cell to allow its expression (transcription and translation) by the host cell.

CLASSIFICATION OF VIRUSES

(1) Nucleic acid type: RNA or DNA; single-stranded or double-stranded; strategy of replication.

(2) Size and morphology, including type of symmetry, number of capsomeres, and presence of membranes.

(3) Presence of specific enzymes, particularly RNA and DNA polymerases, and neuraminidase

(4) Susceptibility to physical and chemical agents, especially ether.

(5) Immunologic properties.

(6) Natural methods of transmission.

(7) Host, tissue, and cell tropisms.

(8) Pathology; inclusion body formation.

(9) Symptomatology.

Classification by Biological, Chemical, and Physical Properties

DNA-Containing Viruses

Hepadnaviridae

Parvoviridae

Papovaviridae

Adenoviridae

Herpesviridae

Poxviridae

Iridovoridae

Classification by Biological, Chemical, and Physical Properties

RNA-Containing Viruses

Picornaviridae

Caliciviridae

Togaviruses

Flaviviridae

Coronaviridae

Rhabdoviridae

Filoviridae

Paramyxoviruses

Orthomyxoviruses

Bunyaviridae

Arenaviridae

Reoviridae

Birnaviridae

Retroviridae

Some Useful Definitions in Virology

Capsid: The symmetric protein shell that encloses the nucleic acid genome. Often, empty capsids are by-products of the viral replicative cycle.

Nucleocapsid: The capsid together with the enclosed nucleic acid.

Structural units: The basic protein building blocks of the capsid.

Capsomeres: Morphologic units seen in the electron microscope on the surface of virus particles. Capsomeres represent clusters of polypeptides, which when completely assembled form the capsid.

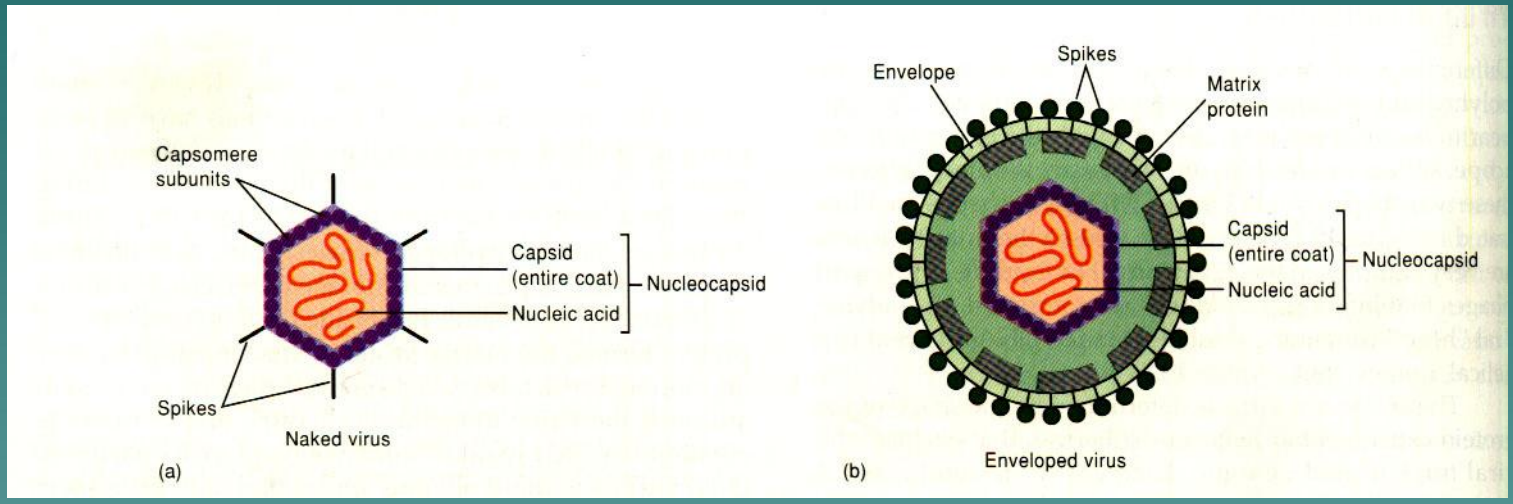
Some Useful Definitions in Virology

Virion: The complete infective virus particle, which in some instances (adenoviruses, papovaviruses, picornaviruses) may be identical with the nlucleocapsid. In more complex virions (herpesviruses, myxoviruses), this includes the nucleocapsid plus a surrounding **envelope**.

Detective virus: A virus particle that is functionally deficient in some aspect of replication. Defective virus may interfere with the replication of normal virus.

Pseudovirus: During viral replication the capsid sometimes encloses host nucleic acid rather than viral nucleic acid. Such particles look like ordinary virus, particles when observed by electron microscopy, but they do not replicate. Pseudovirions contain the “wrong” nucleic acid.

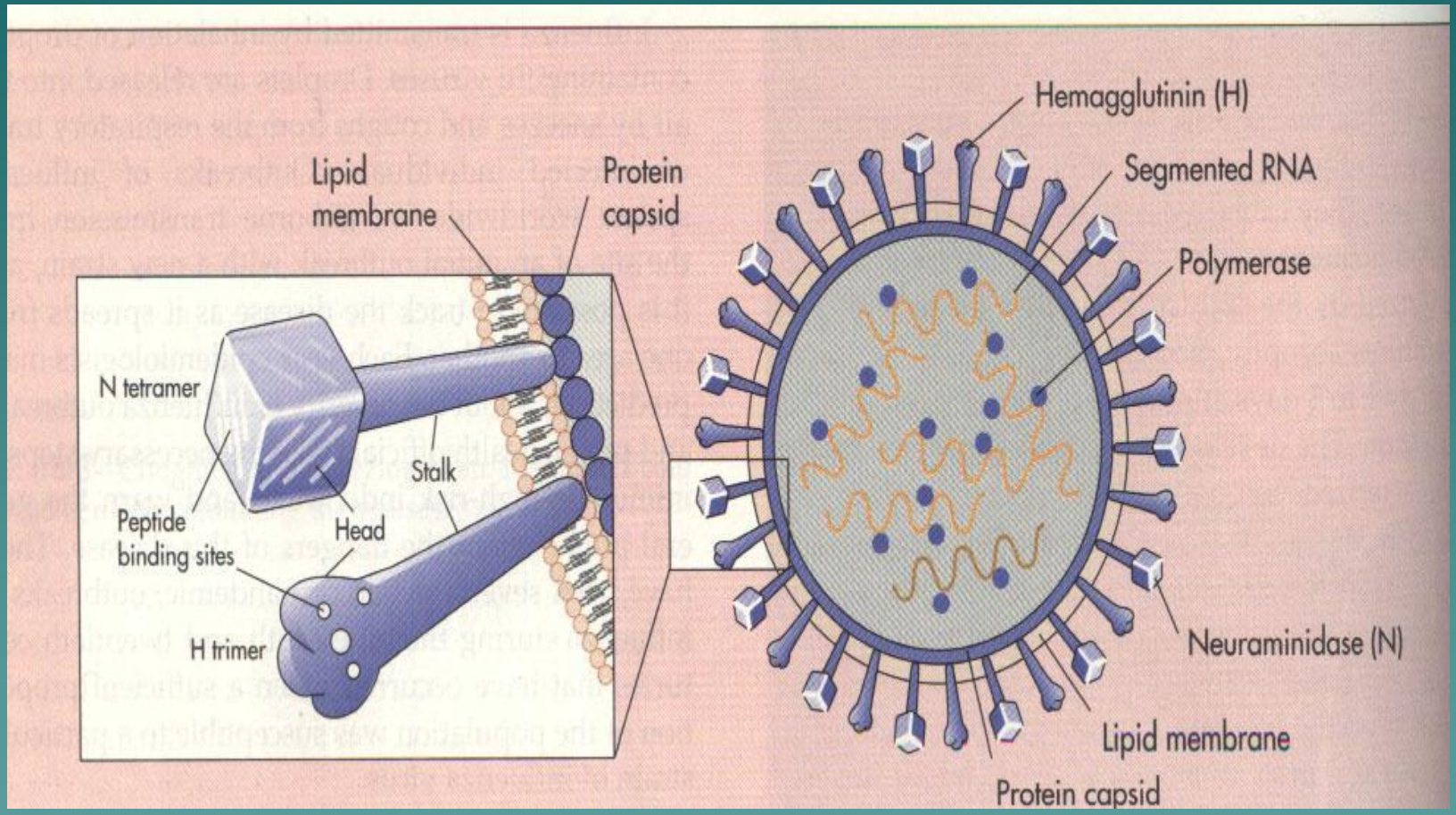
Structure of viruses



A – naked, not containing an envelope aroud capsid

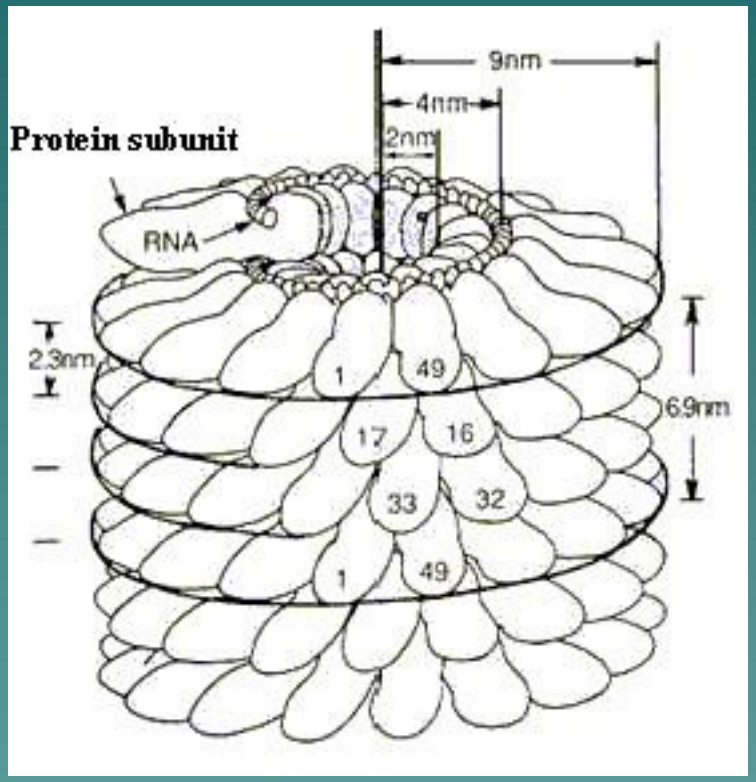
B – enveloped, containing an envelope around the capsid

Structure of viruses



The helical structure of the rigid tobacco mosaic virus rod

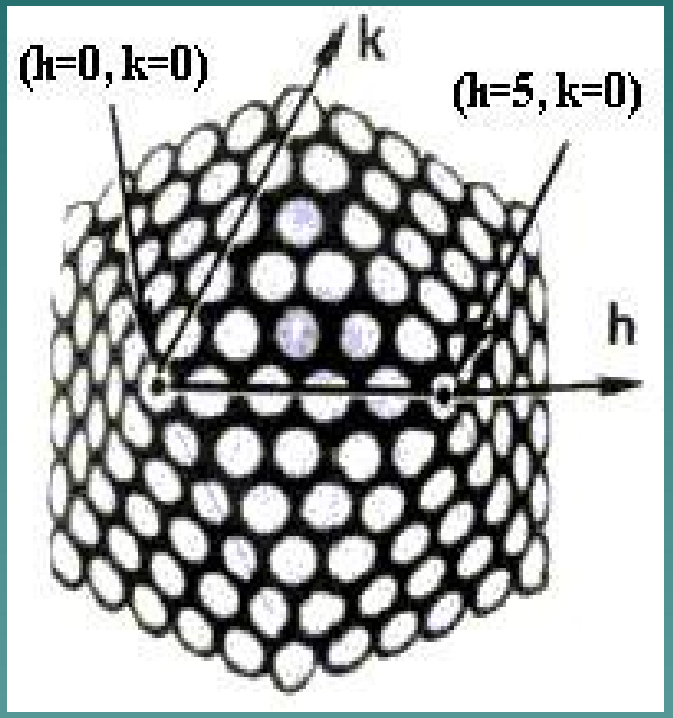
In the replication of viruses with helical symmetry, identical protein subunits (protomers) self-assemble into a helical array surrounding the nucleic acid, which follows a similar spiral path. Such nucleocapsids form rigid, highly elongated rods or flexible filaments;



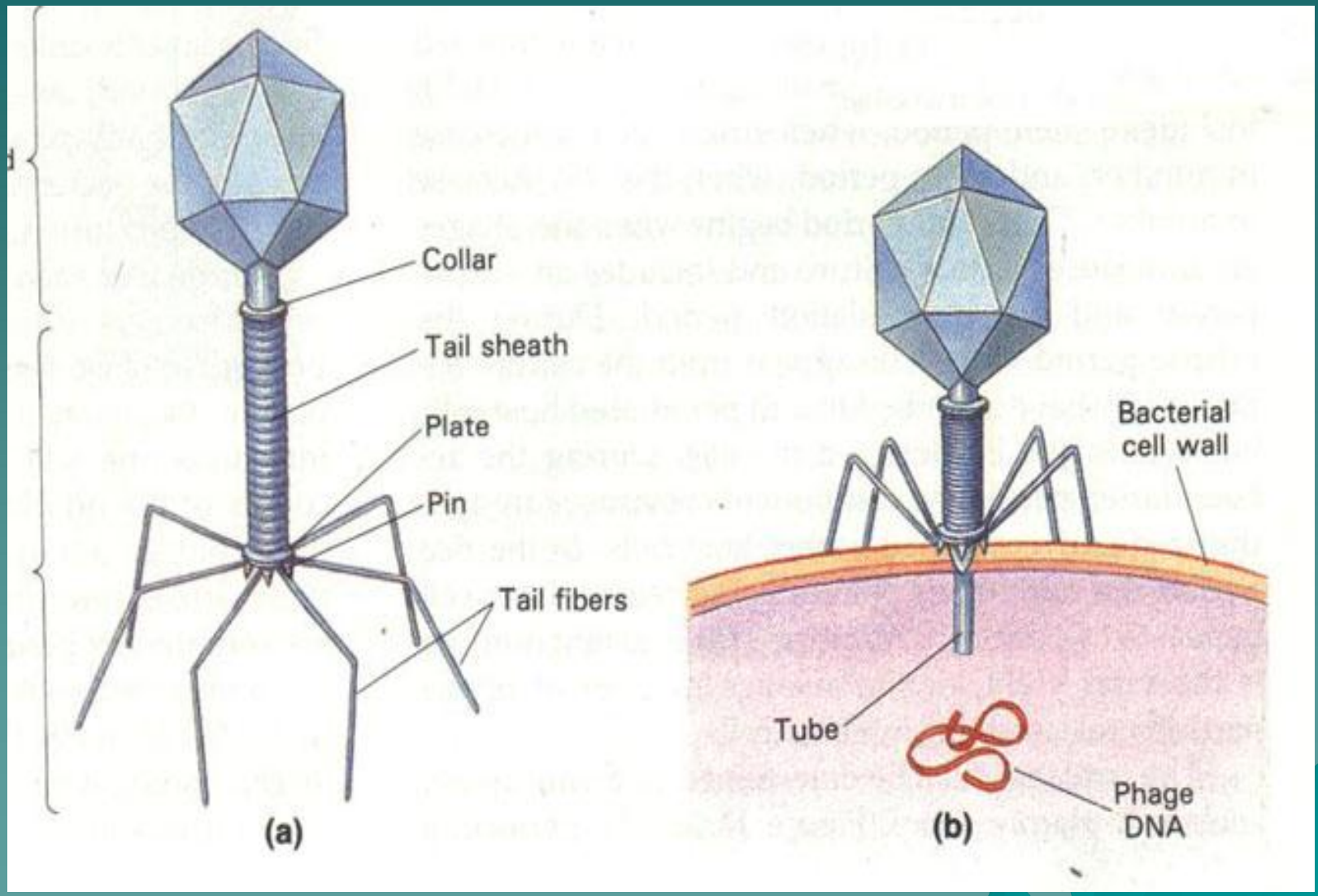
Icosahedral Symmetry

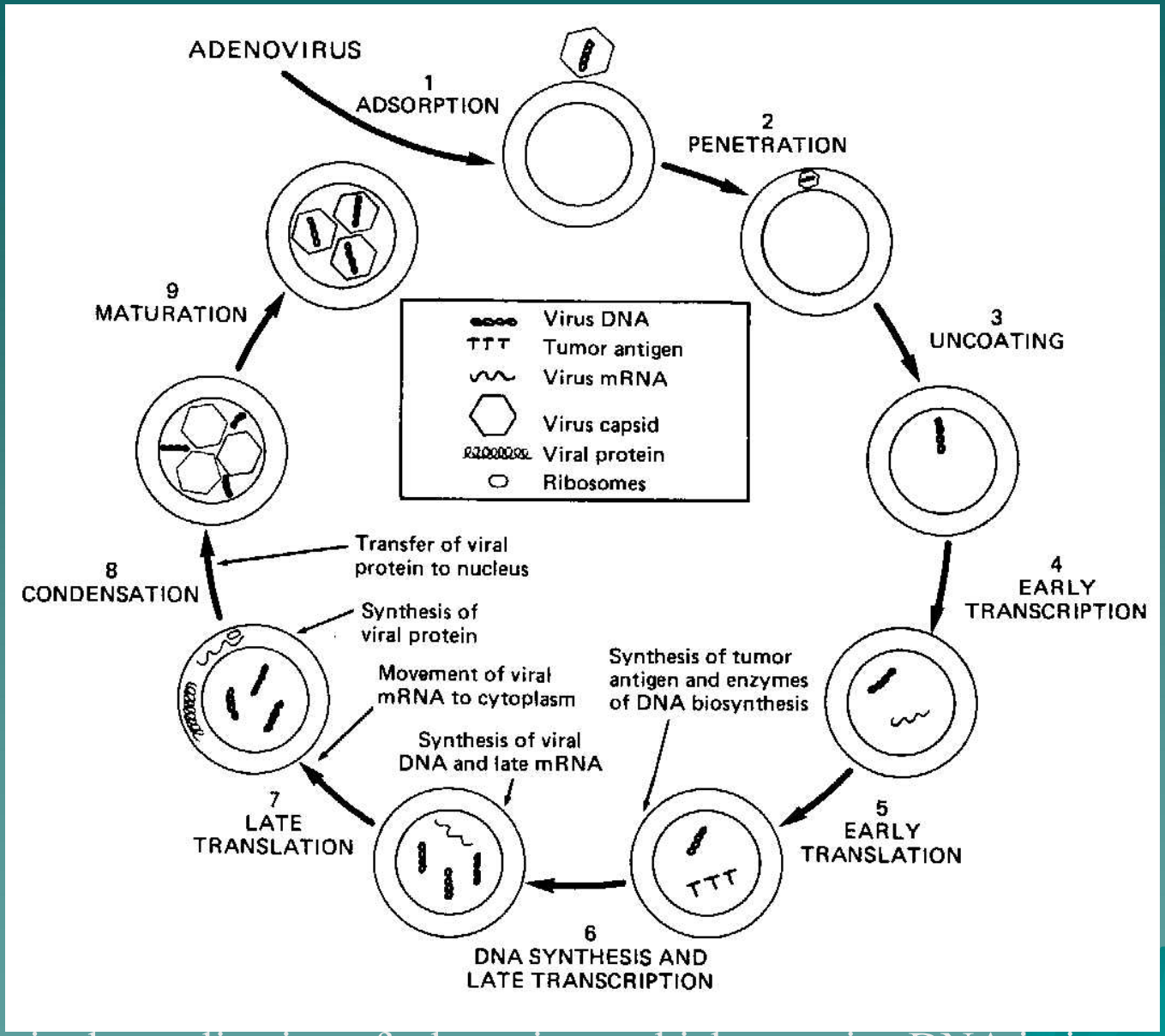
An icosahedron is a polyhedron having 20 equilateral triangular faces and 12 vertices

Lines through opposite vertices define axes of fivefold rotational symmetry: all structural features of the polyhedron repeat five times within each 360° of rotation about any of the fivefold axes.

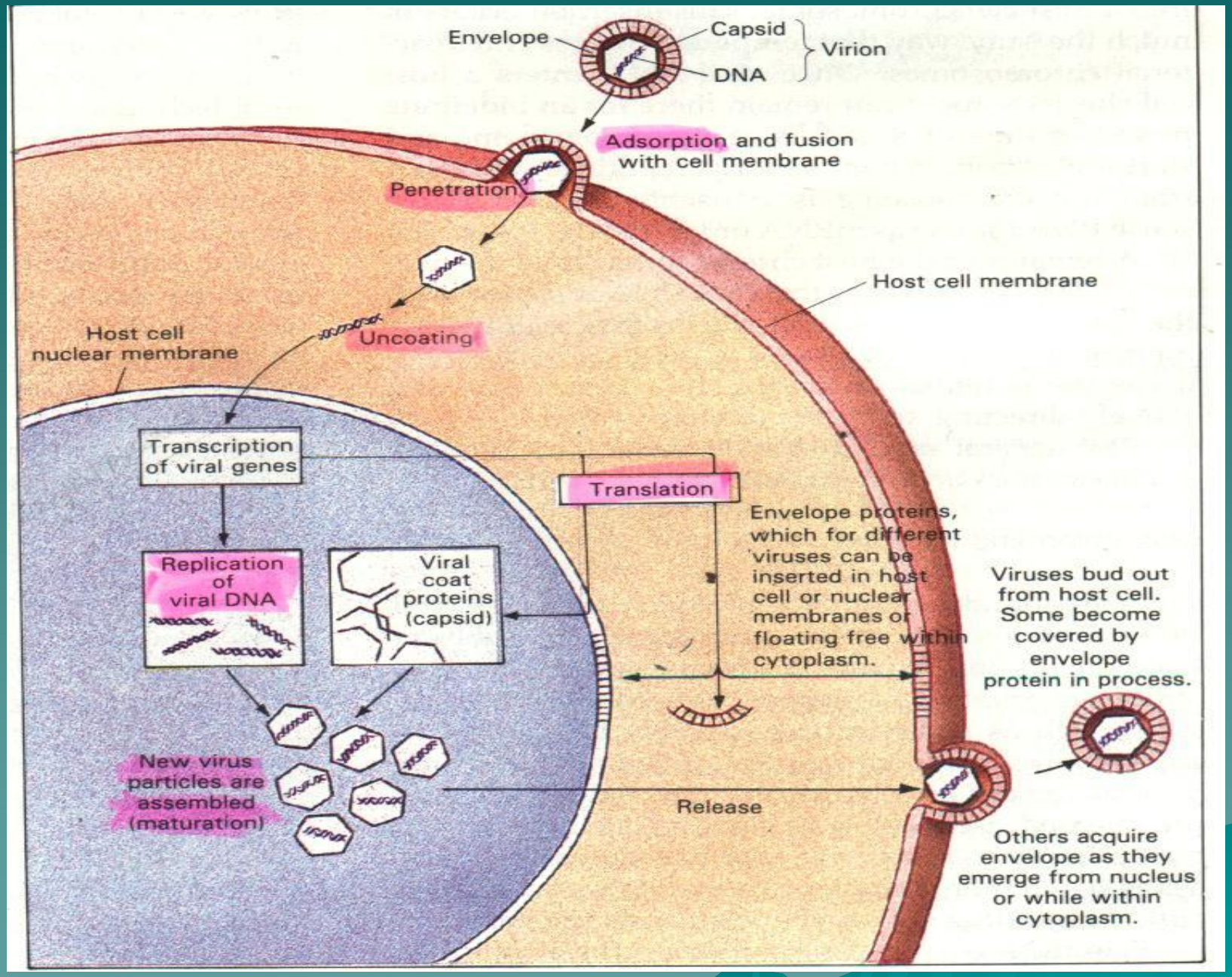


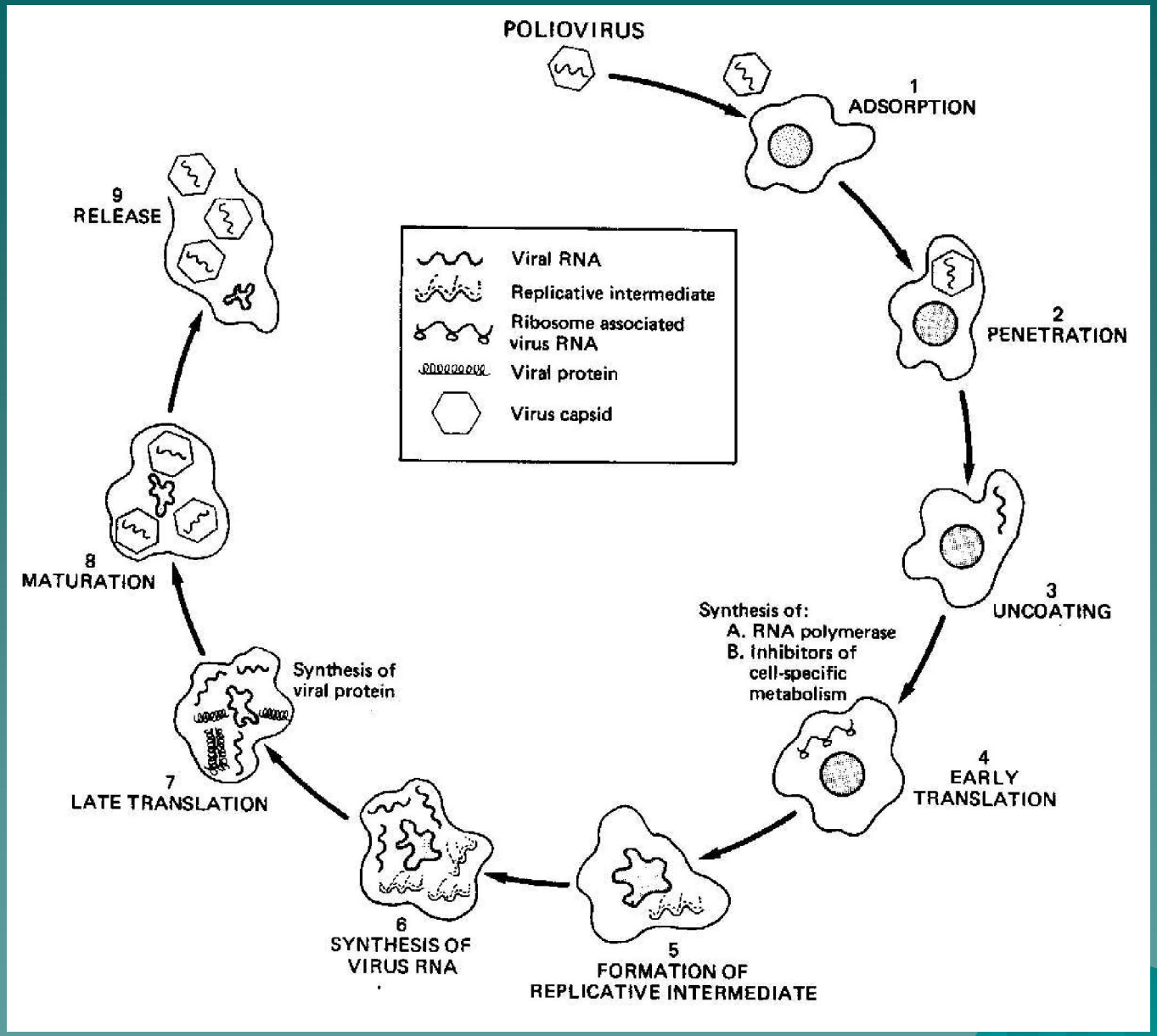
Combined symmetry



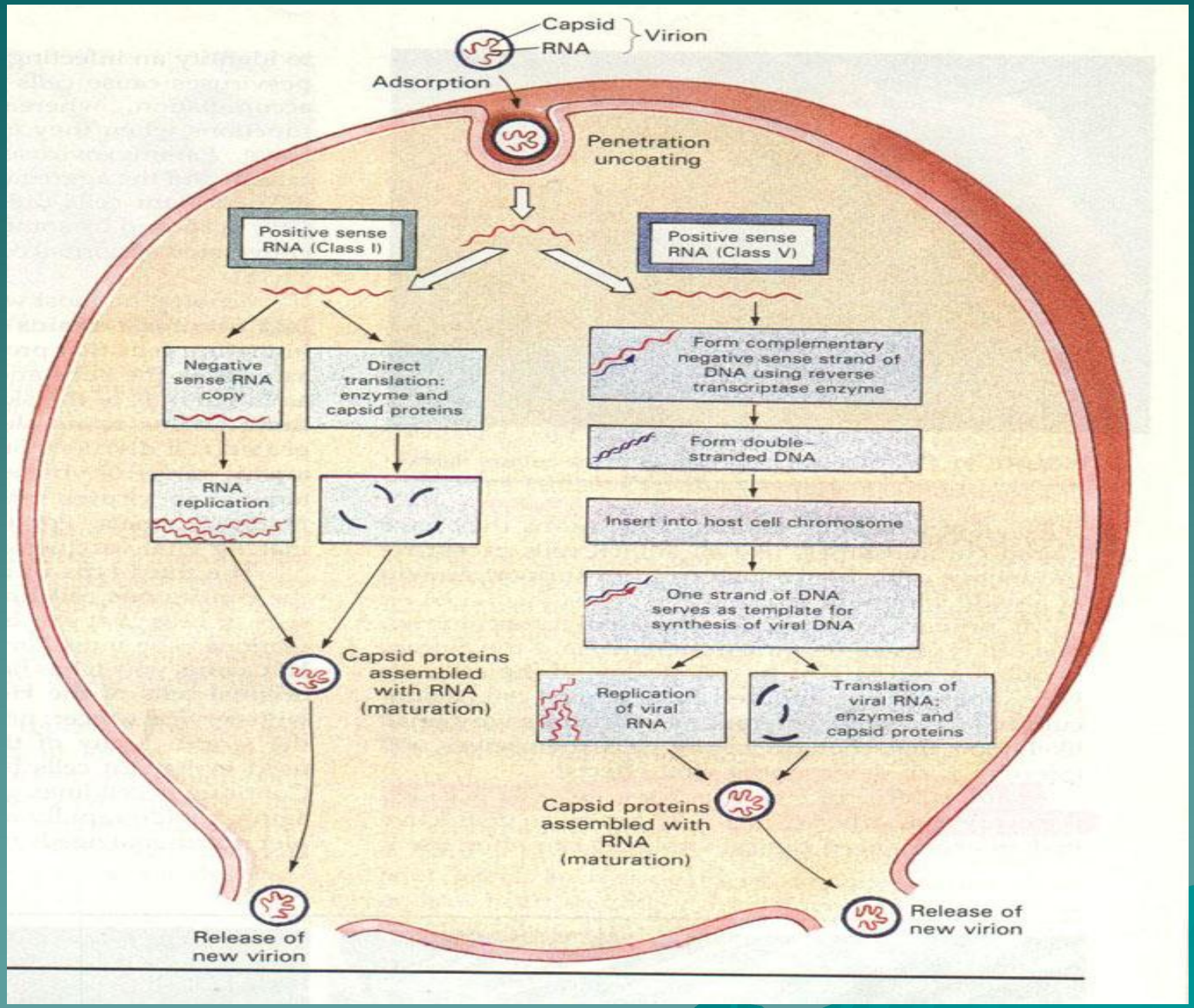


Steps in the replication of adenovirus, which contains DNA in its genome


Envelope
Capsid
DNA
Virion
Adsorption and fusion with cell membrane
Penetration
Host cell membrane
Uncoating
Host cell nuclear membrane
Transcription of viral genes
Translation
Replication of viral DNA
Viral coat proteins (capsid)
Envelope proteins, which for different viruses can be inserted in host cell or nuclear membranes or floating free within cytoplasm.
Viruses bud out from host cell. Some become covered by envelope protein in process.
New virus particles are assembled (maturation)
Release
Others acquire envelope as they emerge from nucleus or while within cytoplasm.



Replication of poliovirus, which containing an RNA genome


Capsid
RNA
Virion
Adsorption
Penetration
uncoating
Positive sense
RNA (Class I)
Positive sense
RNA (Class V)
Negative
sense RNA
copy
Direct
translation:
enzyme and
capsid proteins
Form complementary
negative sense strand of
DNA using reverse
transcriptase enzyme
Form double-
stranded DNA
RNA
replication
Insert into host cell chromosome
One strand of DNA
serves as template for
synthesis of viral DNA
Capsid proteins
assembled
with RNA
(maturation)
Replication
of viral
RNA
Translation of
viral RNA:
enzymes and
capsid proteins
Capsid proteins
assembled with
RNA
(maturation)
Release of
new virion
Release of
new virion

Measuring the Size of Viruses

A. **Filtration Through Collodion Membranes of Graded Porosity**:

B. **Sedimentation in the Ultracentrifuge**

C. **Direct Observation in the Electron Microscope**:

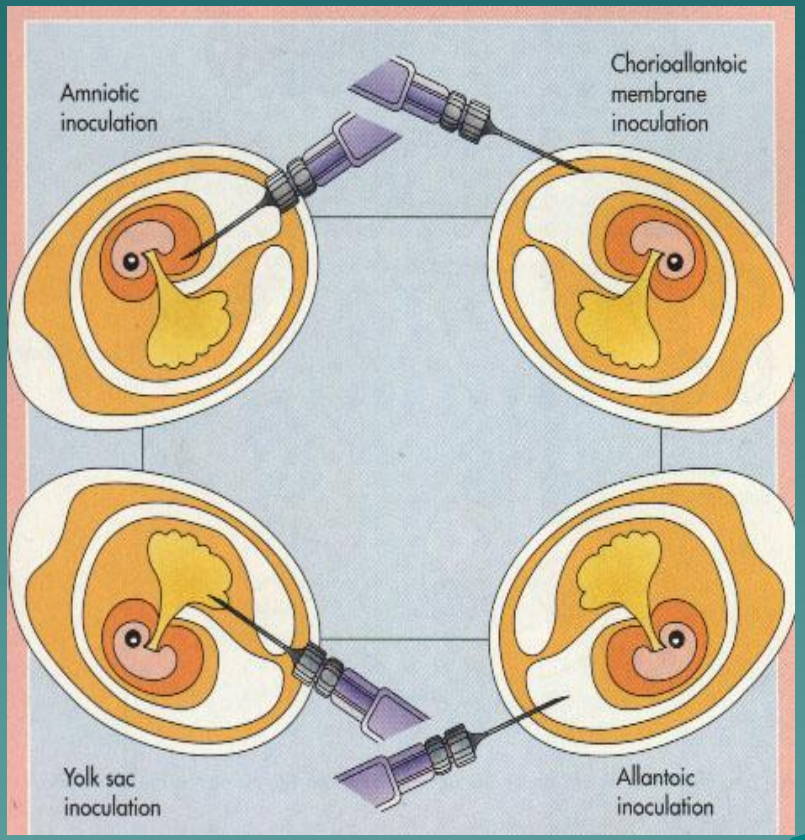
D. **Ionizing Radiation**: When a beam of charged particles such as high-energy electrons, alpha particles, or deuterons passes through a virus, it causes an energy loss in the form of primary ionization. The release of ionization within the virus particle proportionately inactivates certain biologic properties of the virus particle such as infectivity, antigenicity, and hemagglutination. Thus, the size of the biologic unit responsible for a given function in a virus particle can be estimated.

E. **Comparative Measurements:**

(1) *Staphylococcus* has a diameter of about 1000 nm. (2) Bacteriophages vary in size (10-100 nm). (3) Representative protein molecules range in diameter from serum albumin (5 nm) and globulin (7 nm) to certain hemocyanins (23 nm).

Cultivation of Viruses

A. Chick Embryos: Virus growth in an embryonated chick egg may result in the death of the embryo (eg, encephalitis virus), the production of pocks or plaques on the chorioallantoic membrane (eg, herpes, smallpox, vaccinia), the development of hemagglutinins in the embryonic fluids or tissues (eg, influenza), or the development of infective virus (eg, polio virus type 2).



Cultivation of Viruses

B. Tissue Cultures:

Primary cultures are made by dispersing cells (usually with trypsin) from host tissues. In general, they are unable to grow for more than a few passages in culture, as secondary cultures.

- **Diploid cell** strains are secondary cultures which have undergone a change that allows their limited culture (up to 50 passages) but which retain their normal chromosome pattern.

- **Continuous cell lines** are cultures capable of more prolonged (perhaps indefinite) culture which have been derived from cell strains or from malignant tissues They invariably have altered and irregular numbers of chromosomes.

Cell Cultures

HeLA,

Hep-2,

Detroit-6,

KB,

Vero,

Fibroblasts of human embryou,

Kidney of rhesus monkey,

WI-38,

RD,

Primary cultures of chiken fibroblasts

Morphologic and Structural Effects

1 **The cytopathic effect, or necrosis** of cells in the tissue culture (polio-, herpes-, measles-, adenovirus, cytomegalovirus, etc).

2 **The inhibition of cellular metabolism**, or failure of virus-infected cells to produce acid (eg, enteroviruses).

3 **The appearance of a hemagglutinin** (eg, mumps, influenza) or complement-fixing antigen (eg, poliomyelitis, varicella, measles).

4 **The adsorption of erythrocytes** to infected cells, called hemadsorption (paramfluenza, influenza). This reaction becomes positive before cytopathic changes are visible, and in some cases it is the only means of detecting the presence of the virus

5 **Interference by a noncytopathogenic virus** (eg, rubella) with replication and cytopathic effect of a second, indicator virus (eg, echovirus).

6 **Morphologic transformation** by an oncogenic virus (eg, SV40, Rous sarcoma virus), usually accompanied by the loss of contact inhibition and the piling up of cells into discrete foci Such alterations are a heritable property of the transformed cells.

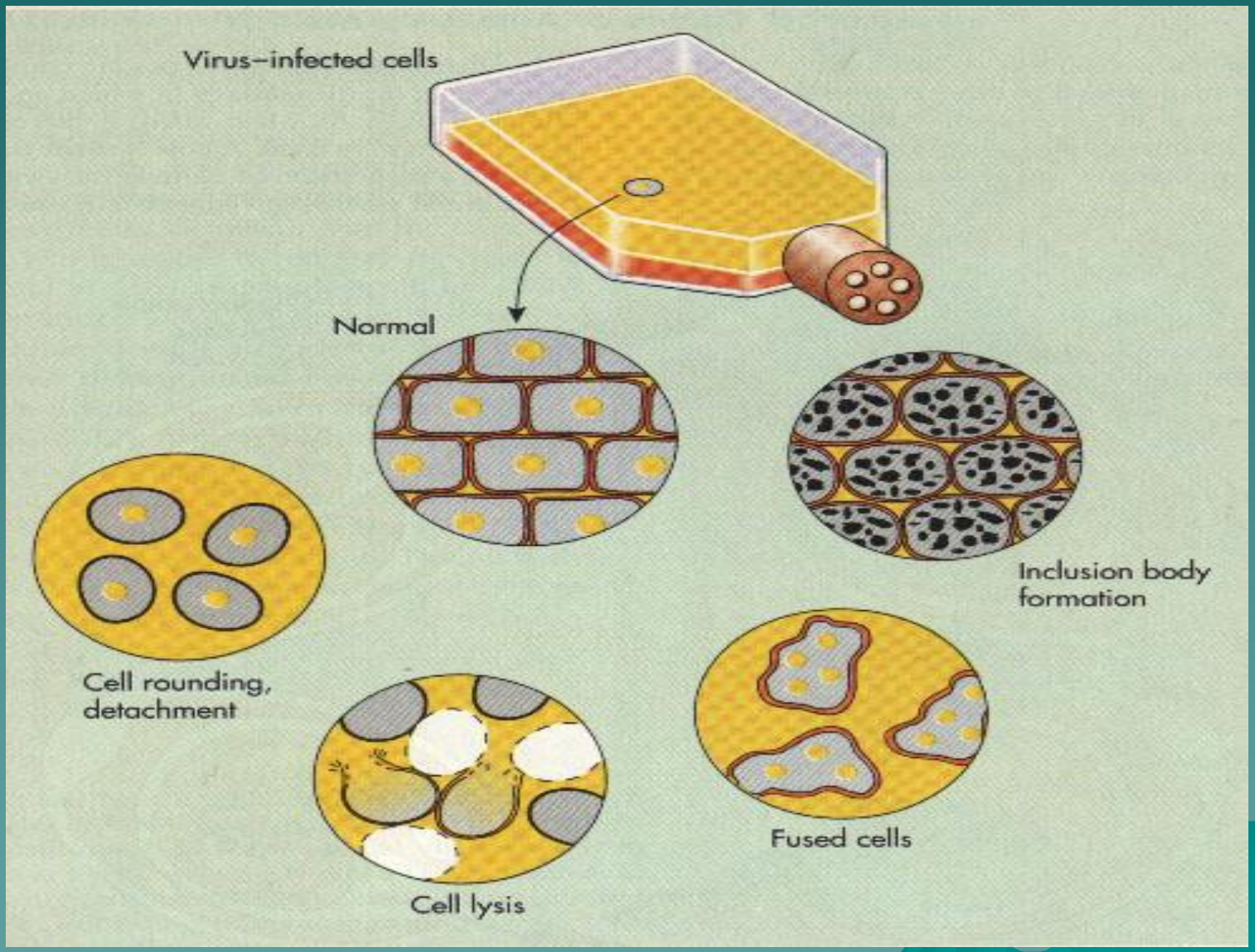
Morphologic and Structural Effects

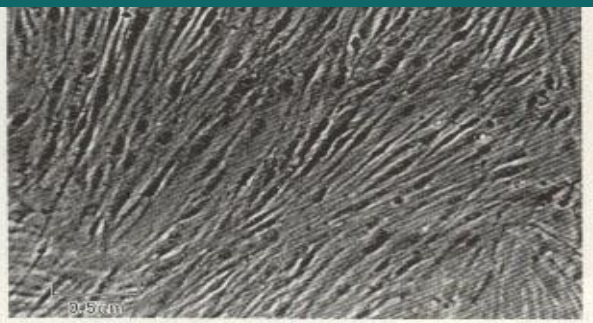
7 **Formation of syncytia, or polykaryocytes**, which are large cytoplasmic masses that contain many nuclei (*poly,* many; *karyon*, nucleus).

8 **Alteration of cytoskeleton** organization by virus infection.

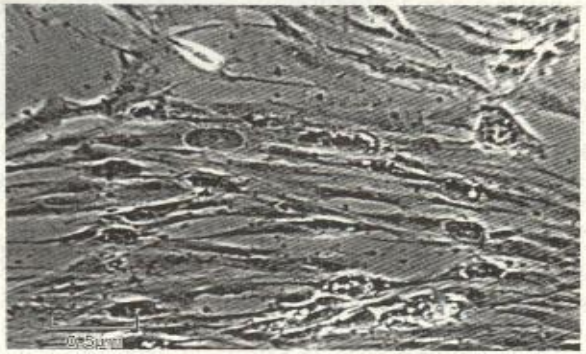
9 **Genotoxic Effects** (Chromosome damage may be caused directly by the virus particle or indirectly by events occurring during synthesis of new viral macromolecules (RNA, DNA, protein).

10 **Inclusion Body Formation** (They may be situated in the nucleus (herpesvirus), in the cytoplasm (pox virus), or in both (measles virus)

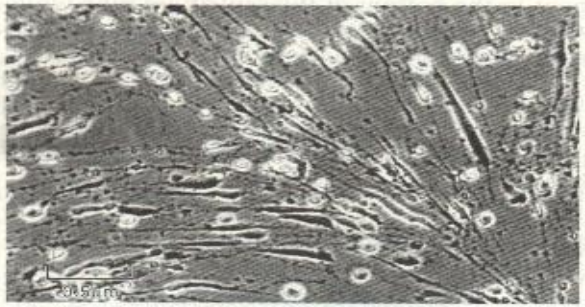

Virus–infected cells
Normal
Inclusion body formation
Cell rounding, detachment
Fused cells
Cell lysis



(a)



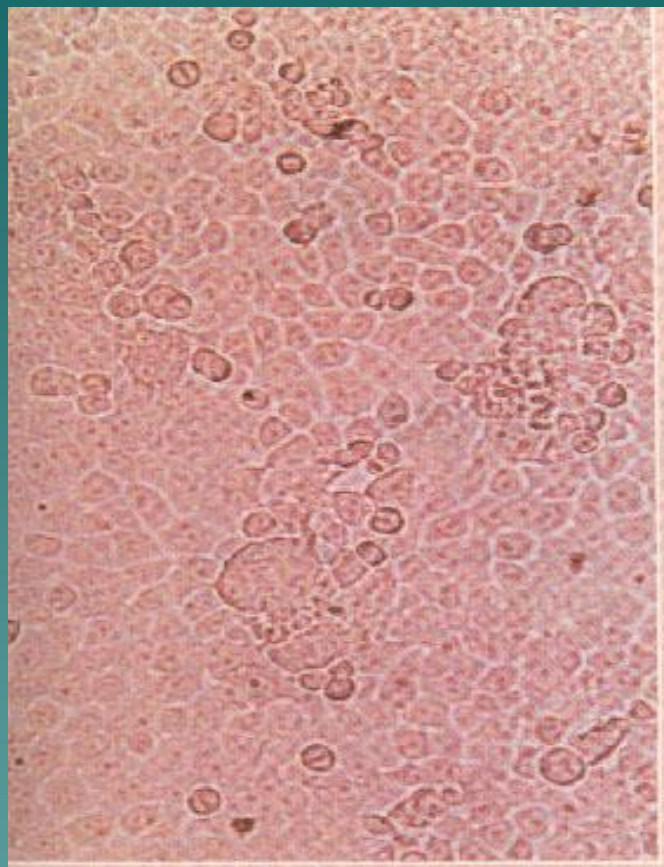
(b)



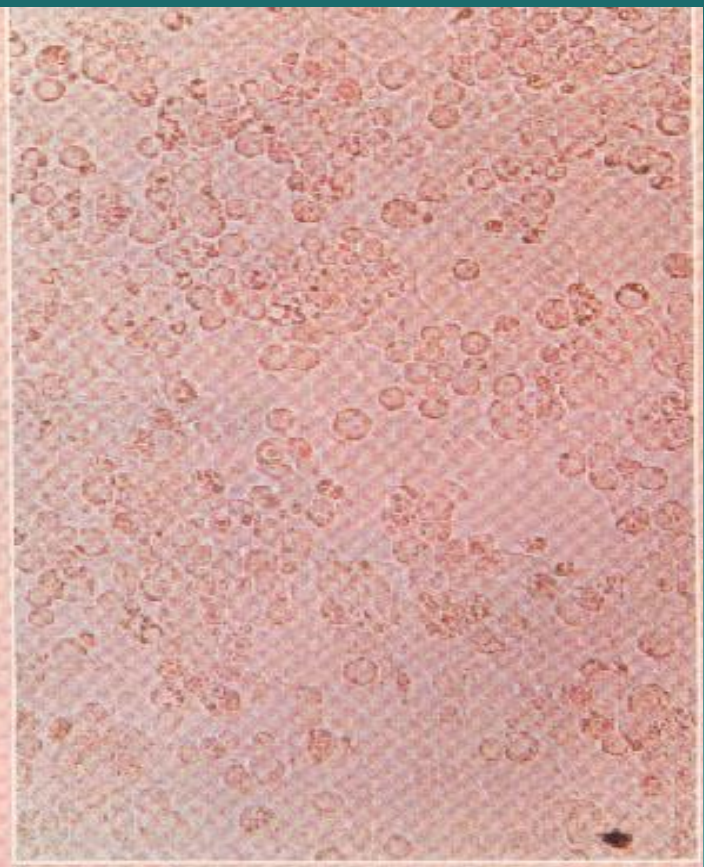
(c)

Figure 13.17

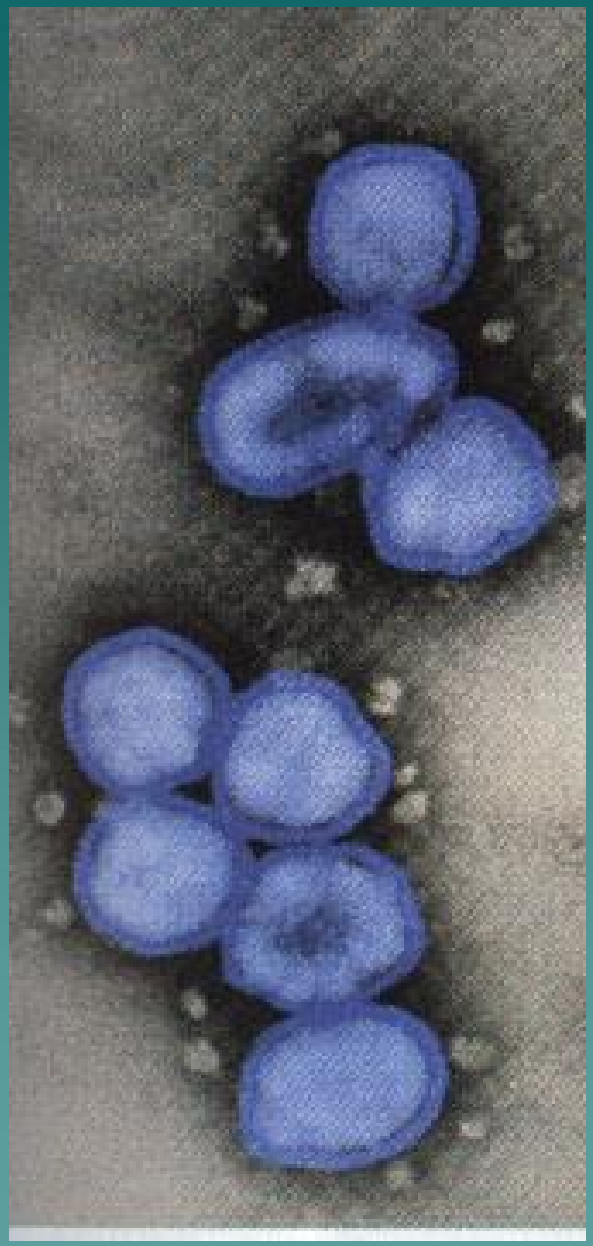
Cytopathic effects of virus infection on tissue culture. (*a*) Fetal tonsil diploid fibroblasts, uninfected. (*b*) Same cells infected with adenovirus. (*c*) Same cells infected with herpes simplex virus. Note that the monolayer is totally destroyed.

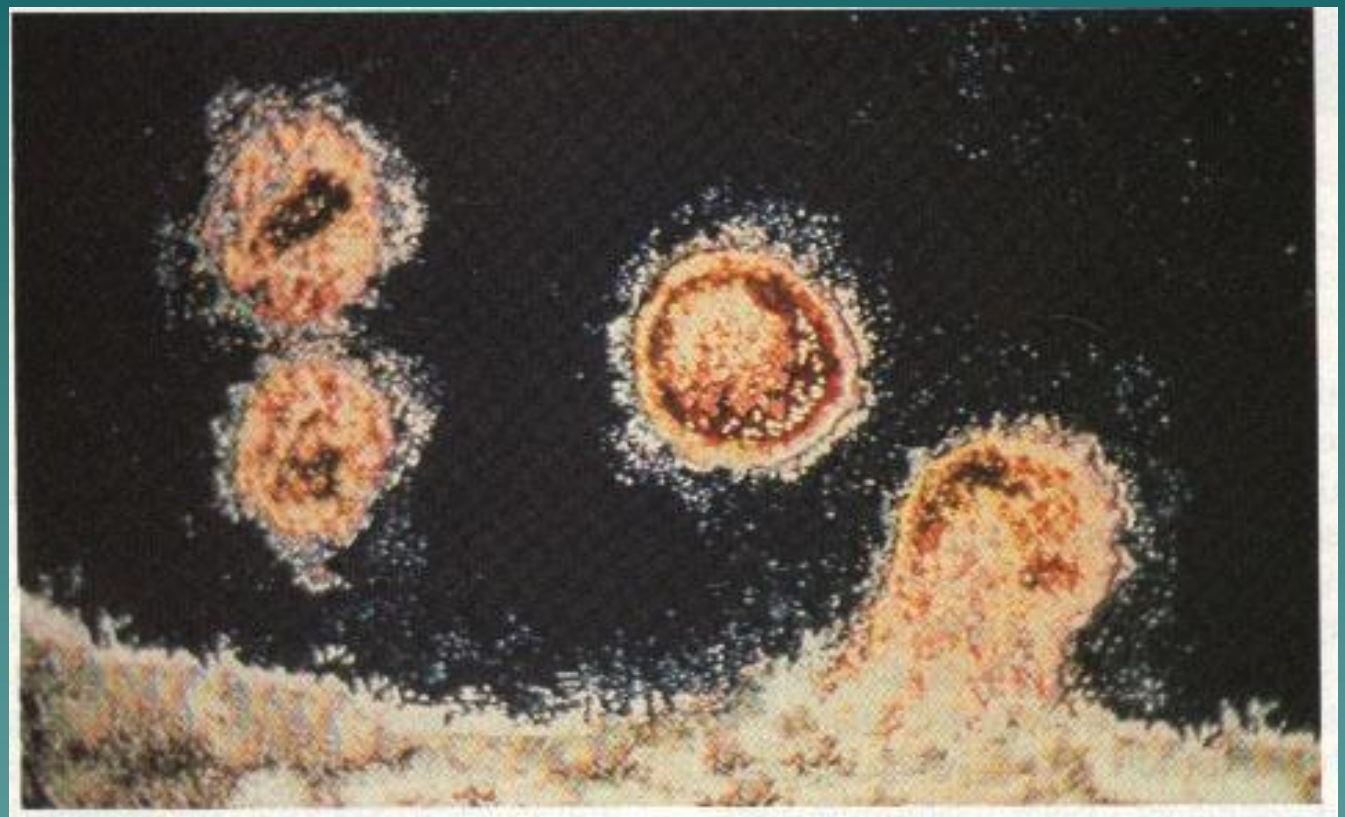


3, Light micrograph showing the cytopathic effect on Ep-2 cells grown in tissue culture by an infection with lenovirus.

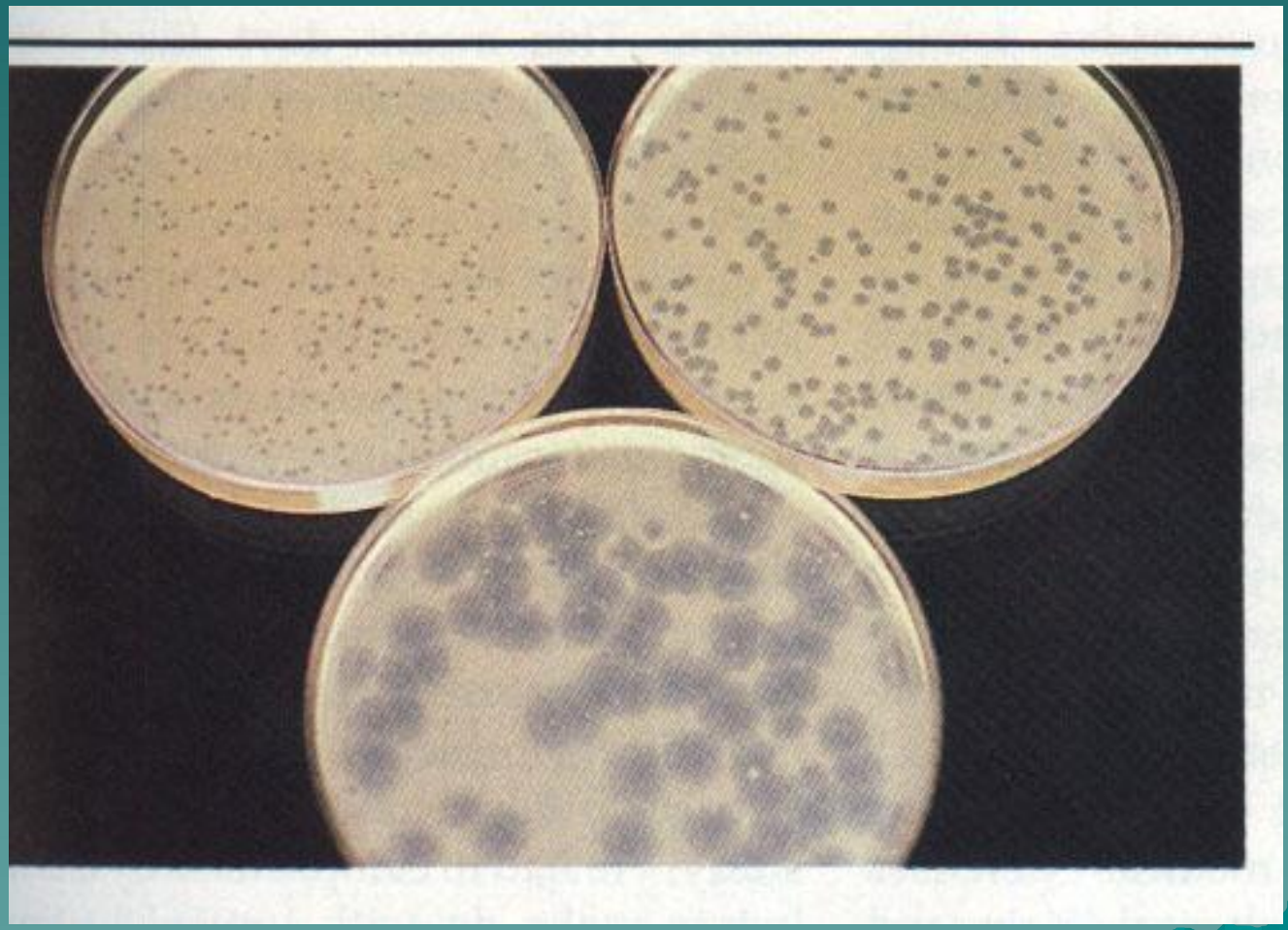


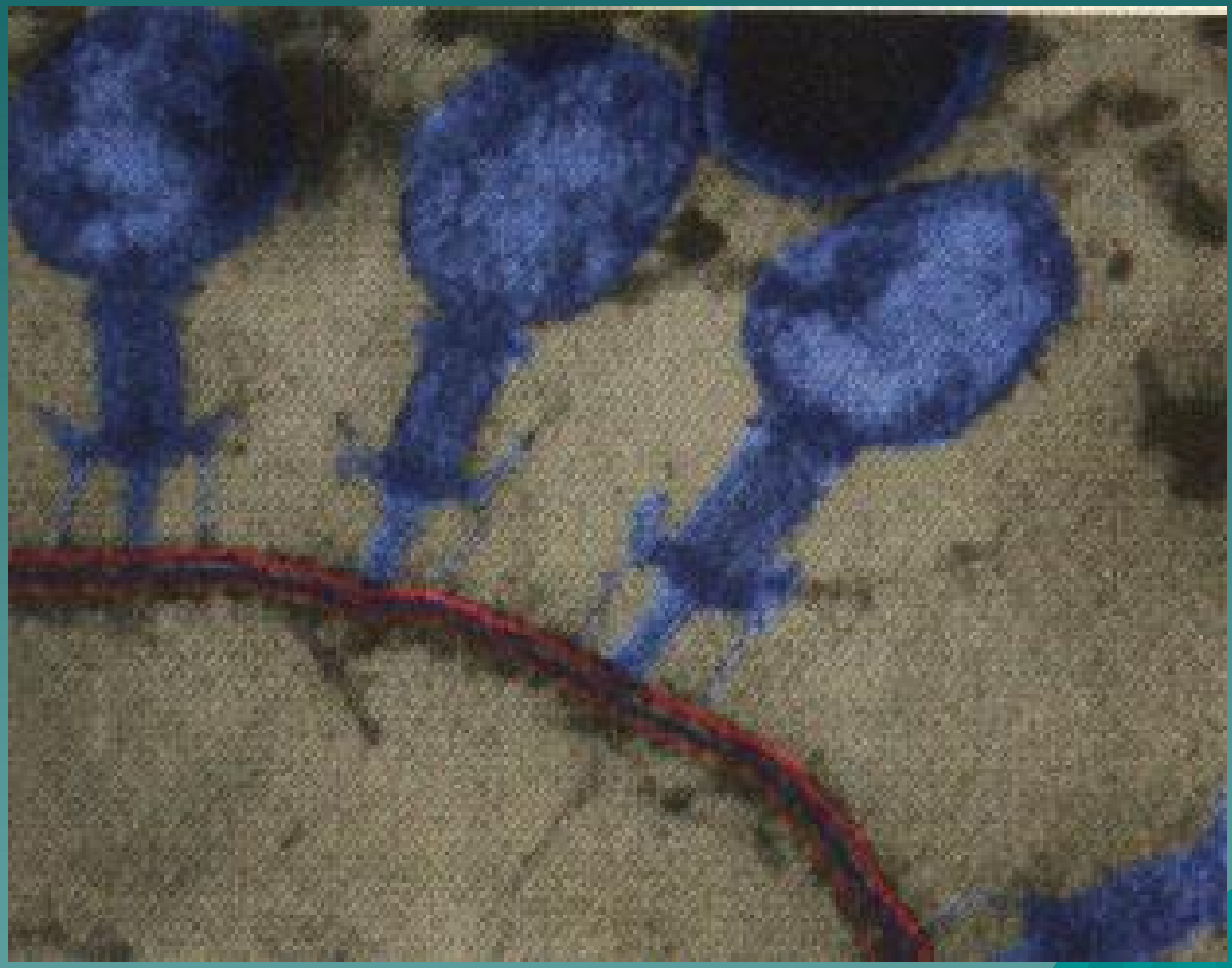
B4, Light micrograph showing the cytopathic effect on HEp-2 cells grown in tissue culture by an infection with respiratory syncytial virus.

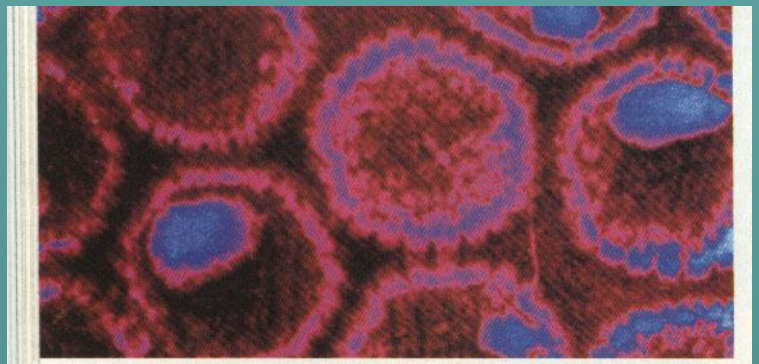




G. 9-22 Colorized electron micrograph of the human immunodeficiency virus (HIV
at causes AIDS budding from the host cell that produced it.







(a)

(b)