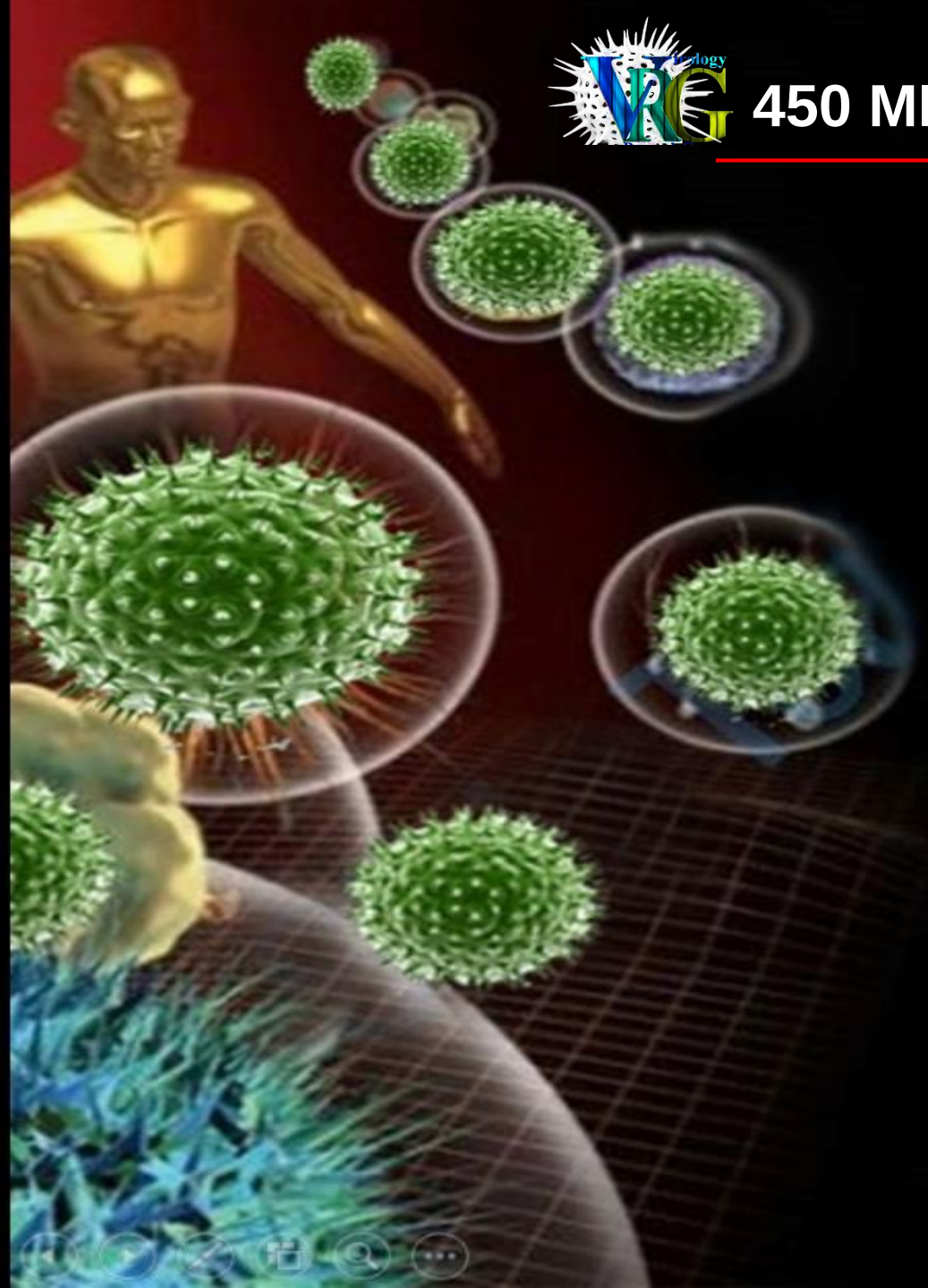


450 MIC Course: Medical Virology

Lecture Four

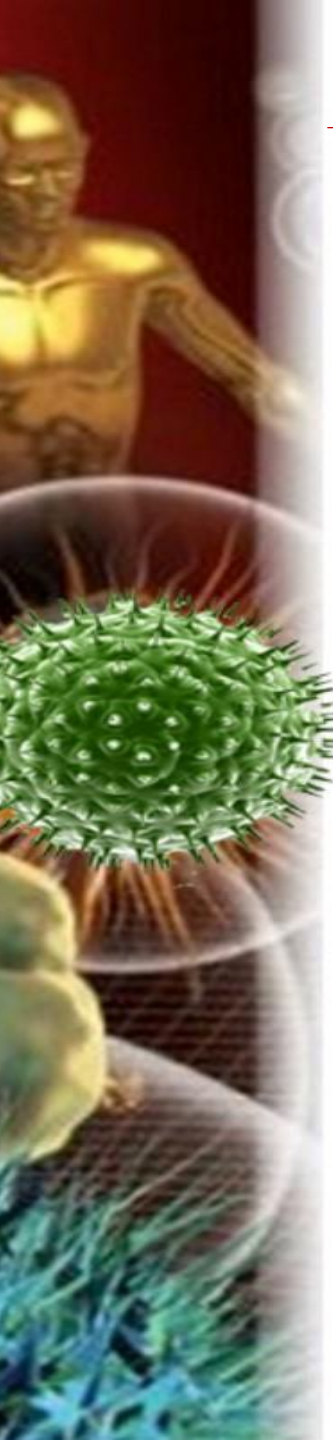
Virus-Cell Interactions

By

Dr. Mohamed A. Farrag

Assistant professor of Virology

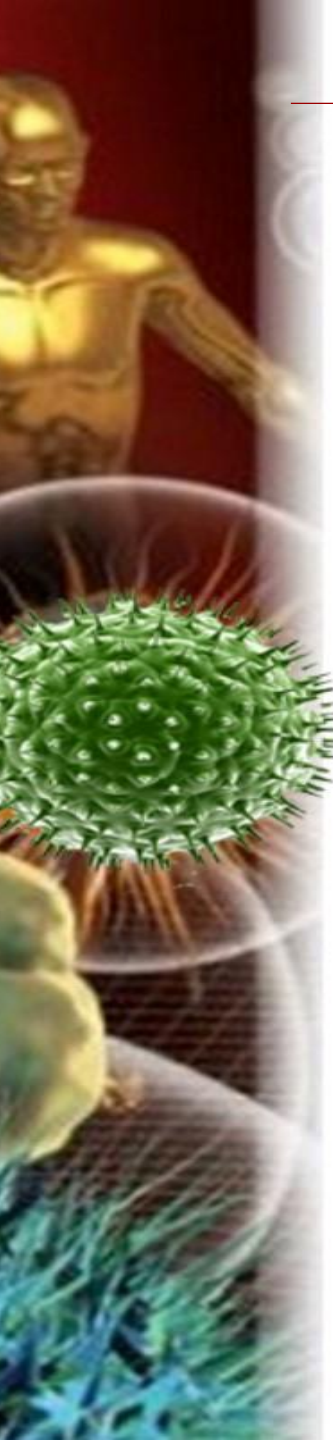
Botany and Microbiology Dept., KSU



Learning outcomes

By the end of this lecture students should

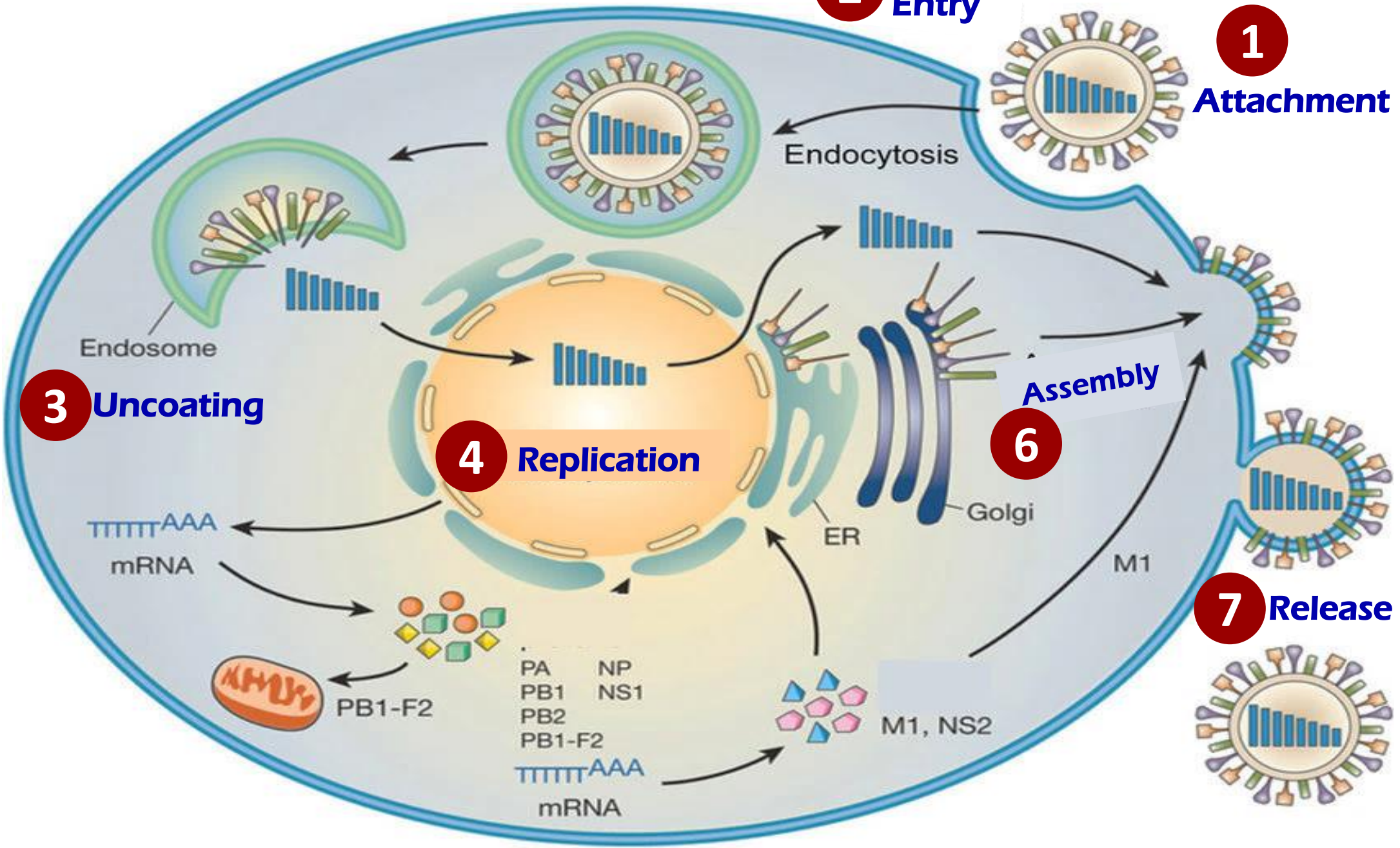
- Know different stages of virus replication cycle.
- Different ways by which virus interact with host cells.
- Differentiate between apoptosis and necrosis.



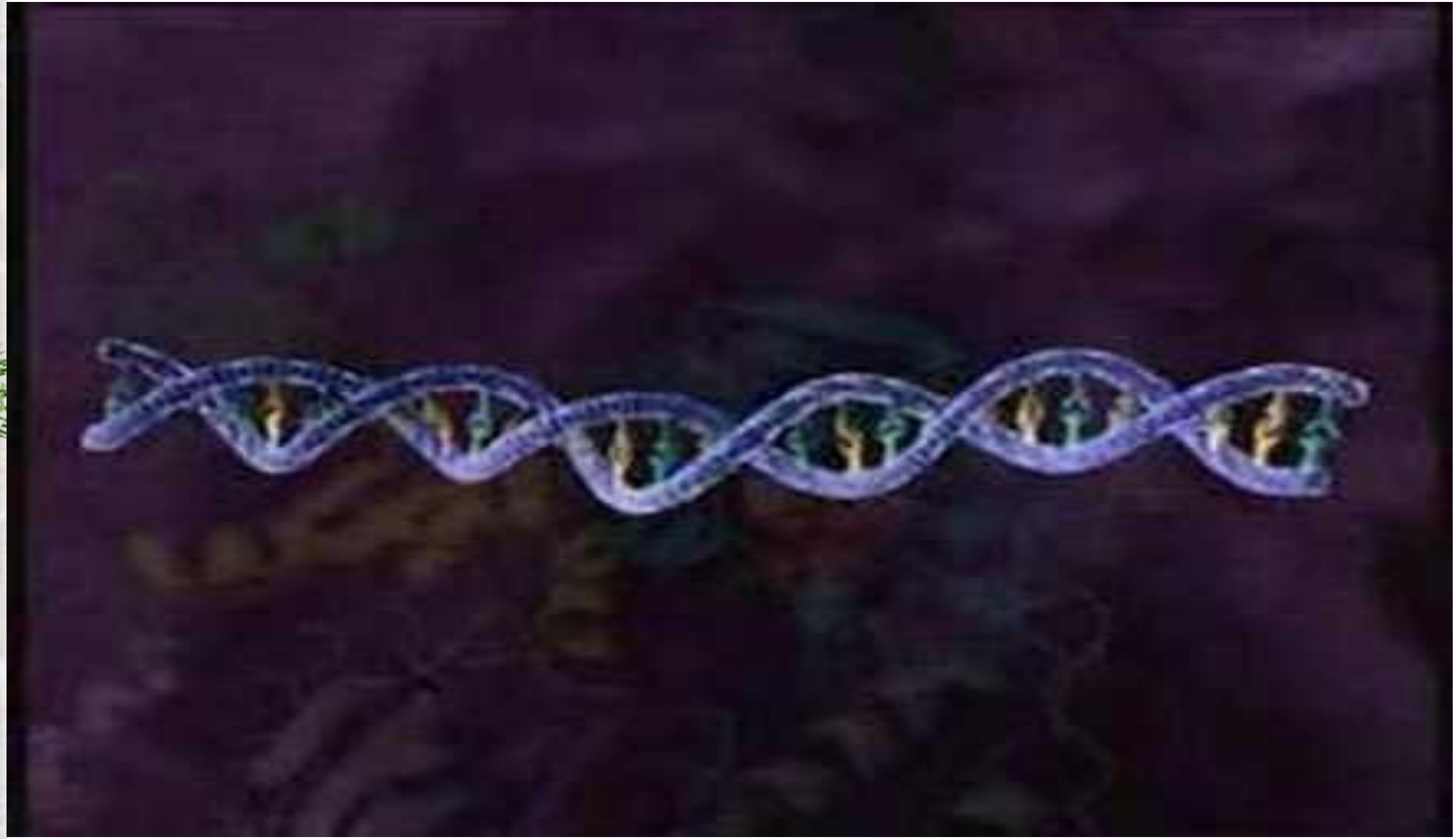
Steps of Virus Replication Cycle

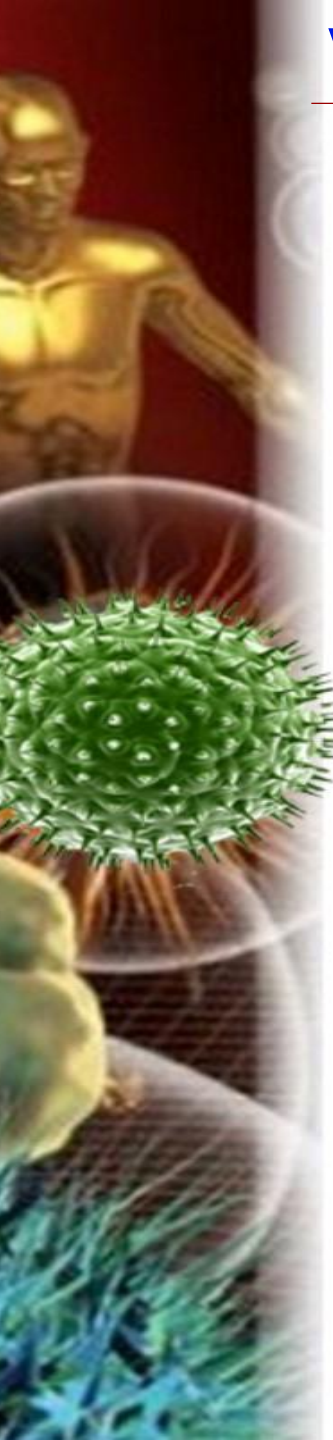
1. Attachment to target cell.
2. Penetration (entry) from cell membrane.
3. Uncoating.
4. Expression (transcription and translation) of viral proteins.
5. Replication of the viral nucleic acid.
6. Virus assembly.
7. Maturation and release from infected cell.

Steps of Virus Replication Cycle



Steps of Virus Replication Cycle – *video*



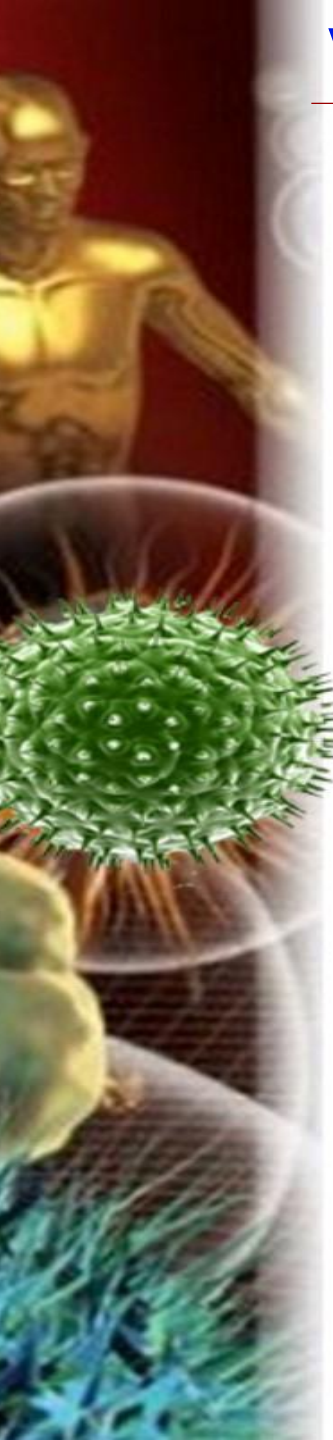


Virus-Cell Interactions

- Viral infection may kill host cells but cytopathic effects are not a necessary consequence of viral replication.

- Conversely, cytopathic effects can be induced by viruses without completing a productive cycle of replication.

- Binding of a viral attachment protein to its cellular receptor can initiate dramatic effects such as cell-to-cell fusion, apoptosis or signaling cascades.



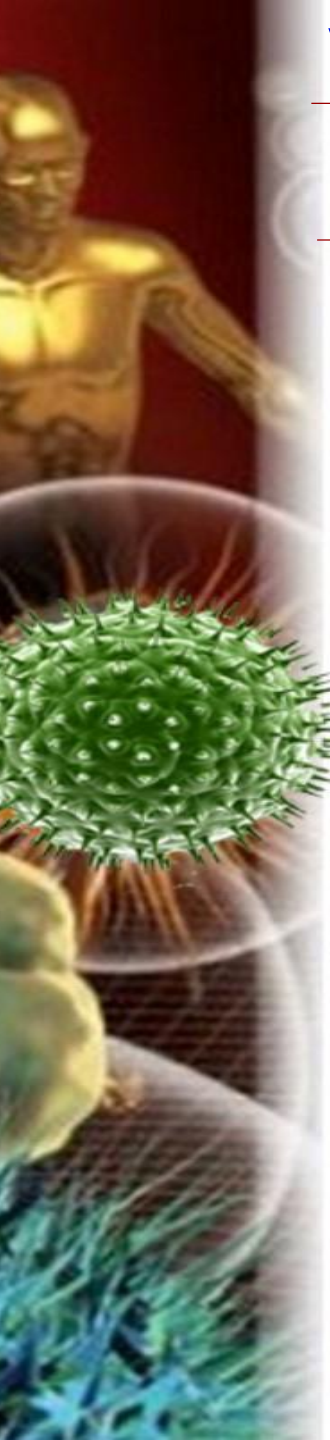
Virus-Cell Interactions

- During infection, some viruses induce a global downregulation of transcription of host genes, while viral genes are actively transcribed.

- Infection with other viruses may have a differential effect upon transcription of genes of the host cell, some of which are upregulated, others downregulated and some unchanged.

- Virus infection can reduce translation of host mRNA while viral messages are translated at a high rate, due to differential mechanisms of translation initiation.

- Viral infection can alter the expression of certain cell surface proteins, such as the cellular receptor for the virus or MHC class I proteins.



Virus-Cell Interactions

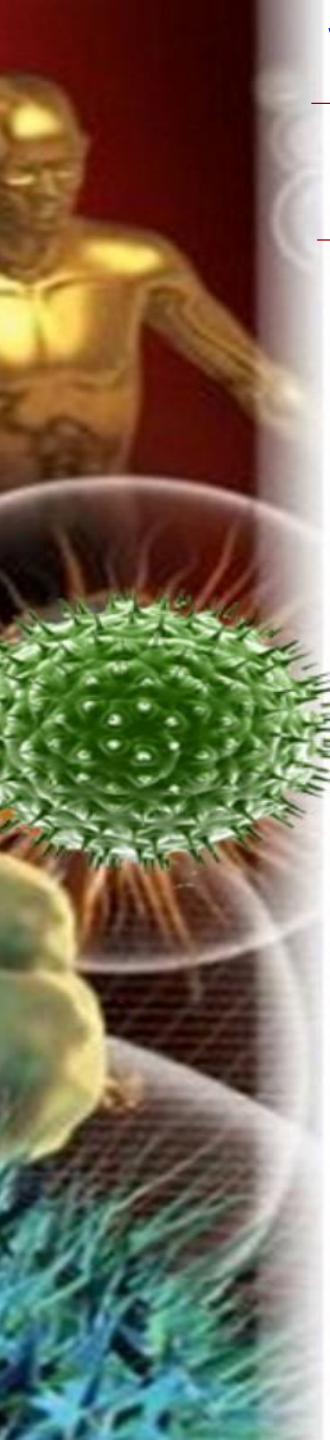
1 – Productive viral replication may not destroy host cells

- During infection, about 1000 virions are produced daily. If each virion contains 5000 molecules of protein, then 5 million molecules of viral proteins will be produced daily.

- One billion protein molecules are produced daily by cellular production. It means that viruses use only 1% of host cellular machinery of protein synthesis.

- **Can nascent virus be released without lysis of the host cell ?**

- Naked viruses assemble intracellularly and efficient release often requires lysis of the host cell to free individual virions.



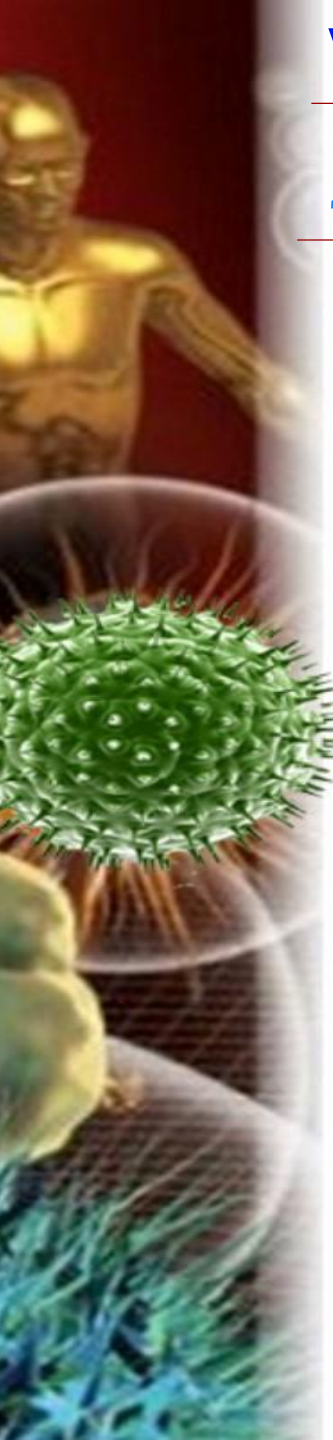
Virus-Cell Interactions

1 – Productive viral replication may not destroy host cells

- **Can nascent virus be released without lysis of the host cell ?**

- Enveloped viruses, particularly enveloped RNA viruses, normally mature by budding across a cellular membrane, either the plasma membrane or an internal membrane, such as the endoplasmic reticulum or Golgi apparatus.

- Thus virus release causes no cytolysis and the infected cell may continue to produce infectious virions indefinitely, unless the immune response intervenes to destroy infected cells or limit virus production.

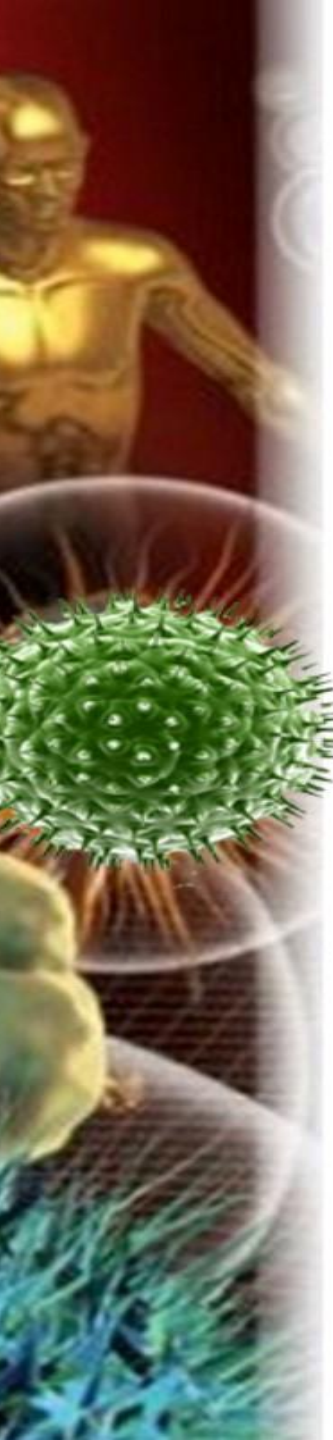


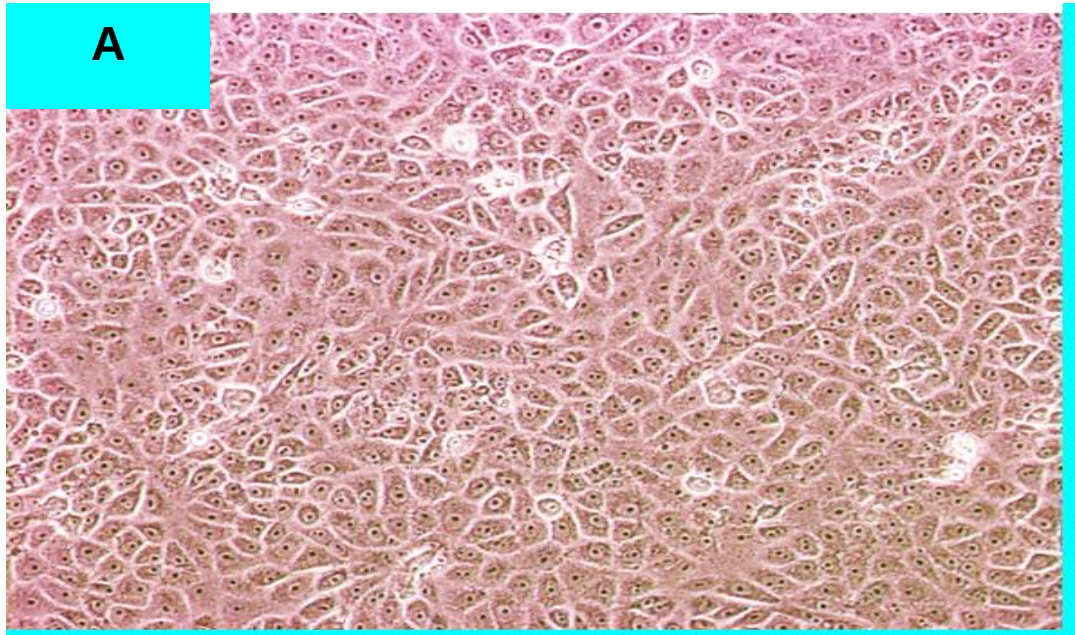
Virus-Cell Interactions

2 – Productive viral replication is not required for cytopathology

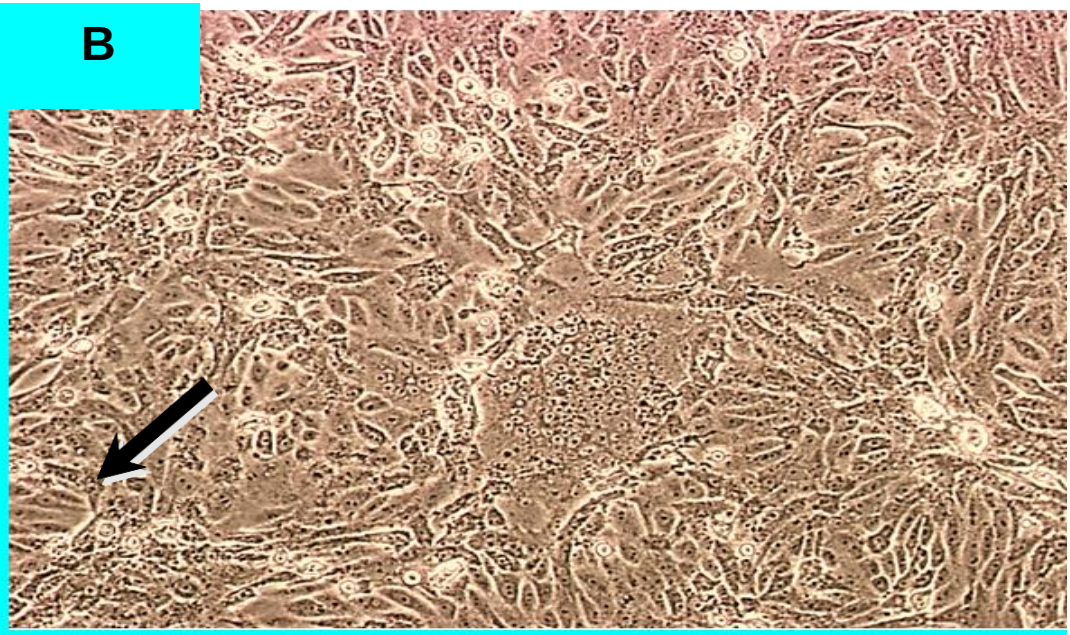
- The virus may initiate pathological processes in potential host cells without completing a productive cycle of infection.

- A viral inoculum may produce massive fusion of host cells that are converted into a multinucleated syncytium within minutes.

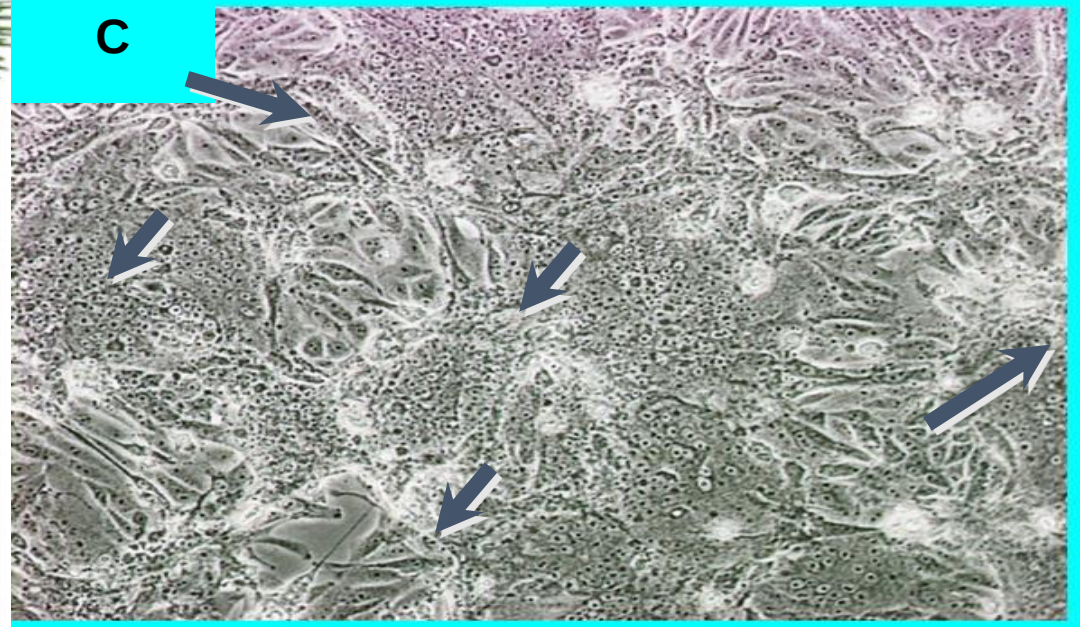




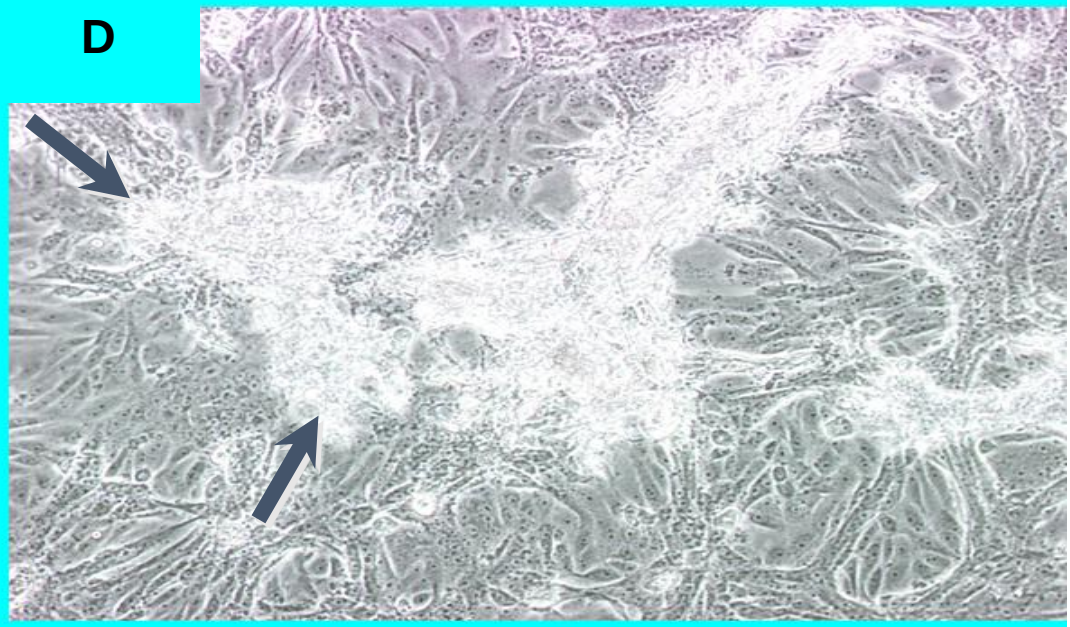
Control



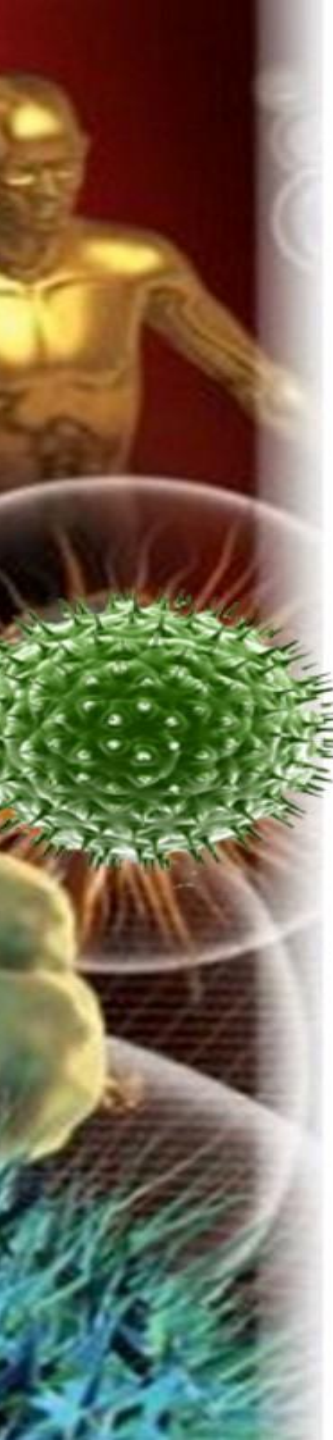
36h post-infection

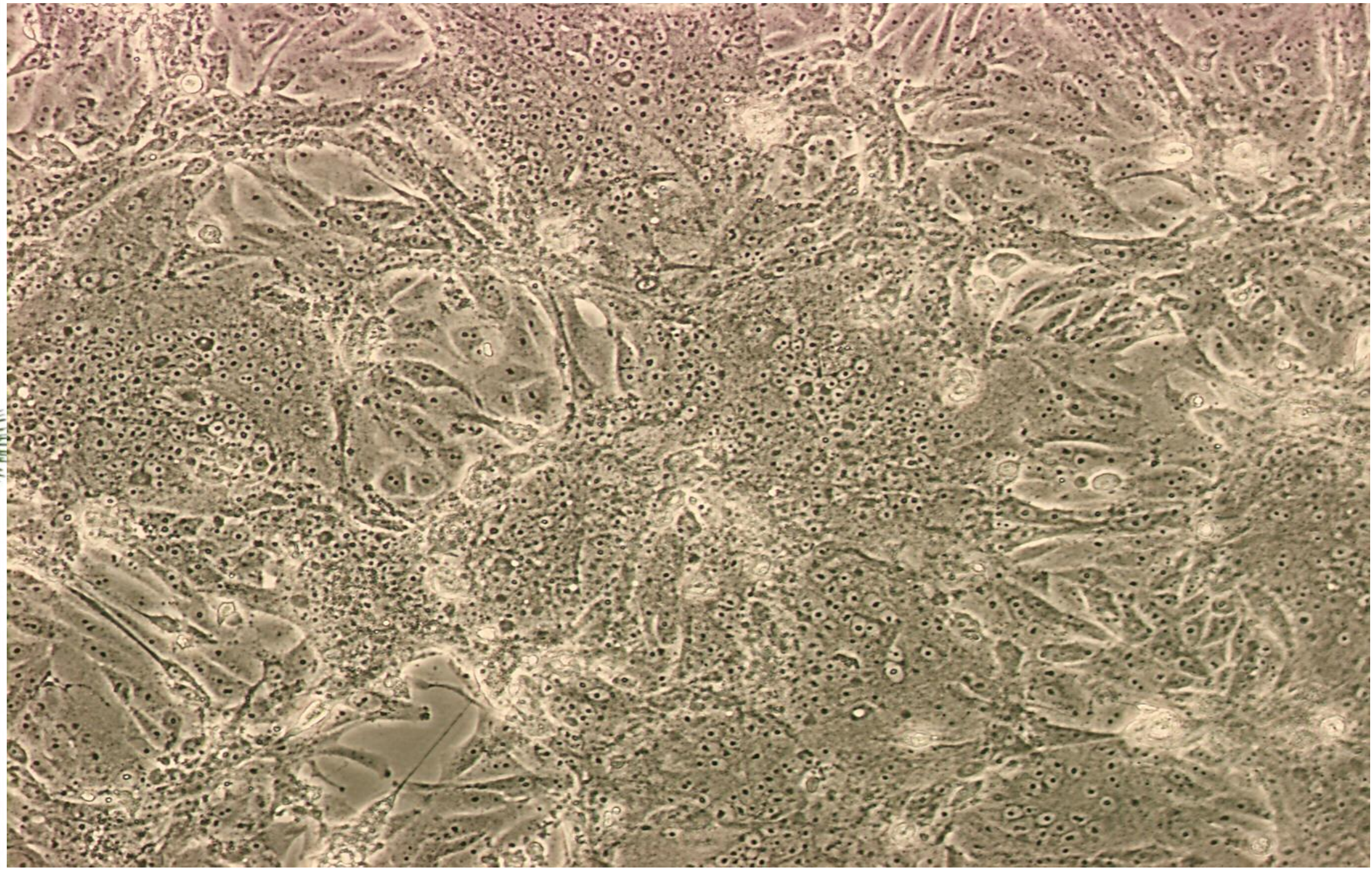


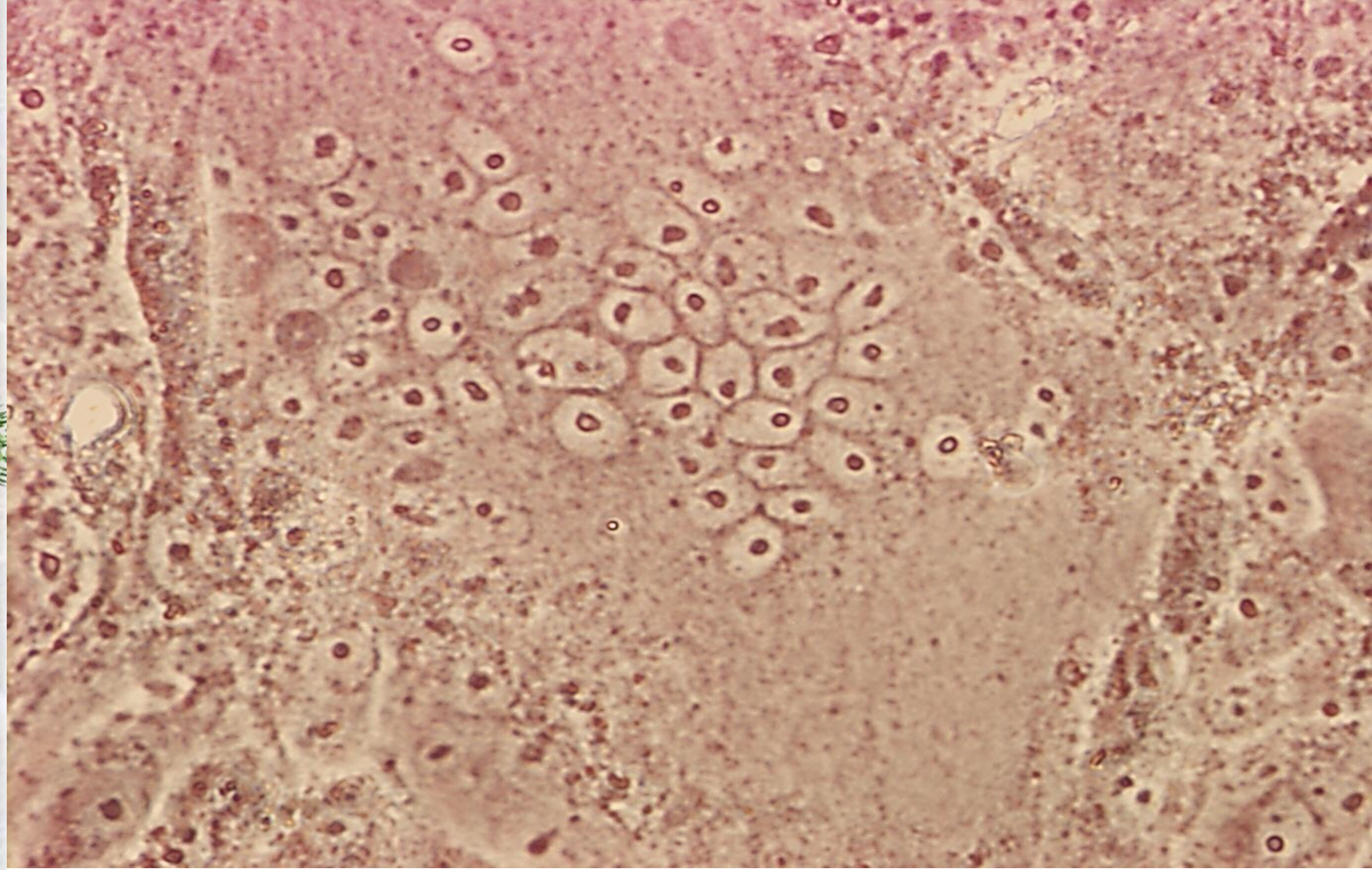
48h post-infection

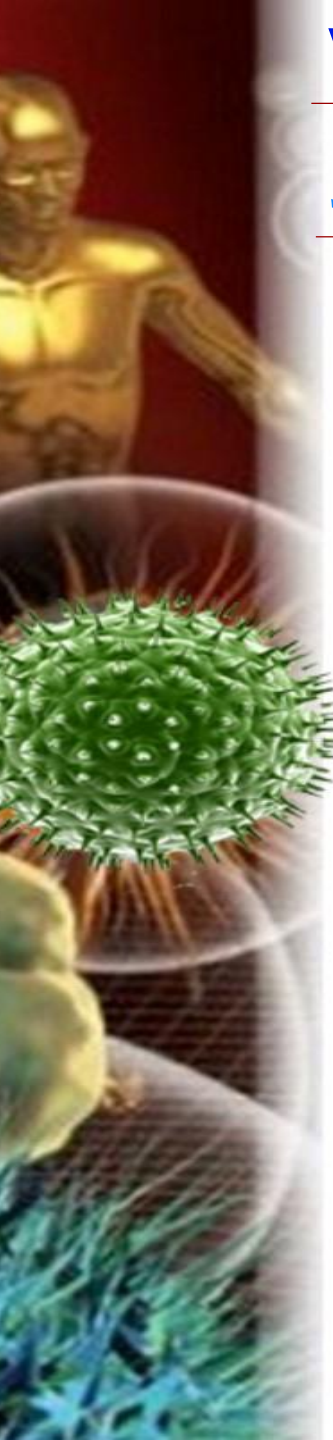


72h post-infection









Virus-Cell Interactions

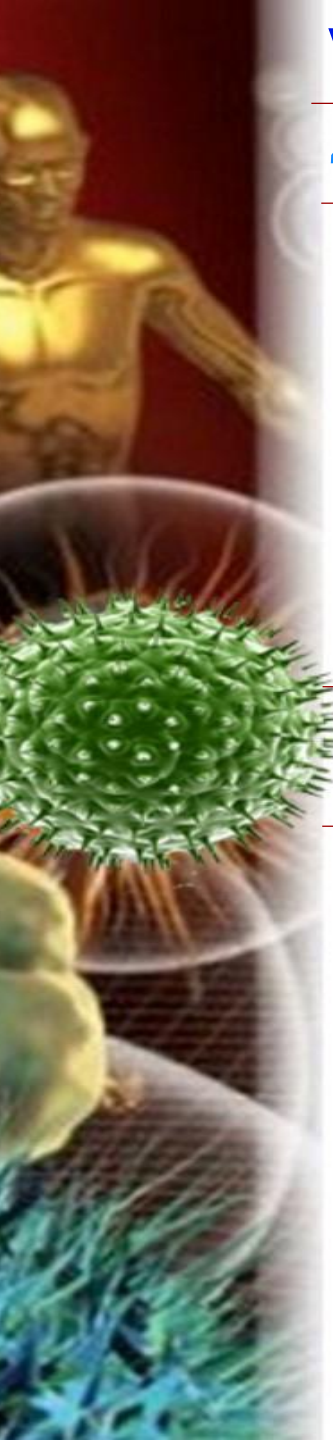
3 – Viral modulation of host cell transcription

- Many viruses initiate a general reduction of host cell transcriptional activity that often begins soon after infection. Ex: Poliovirus

- In some instances, viral infection decreases the transcription of a specific gene in a differential manner. Ex: Lymphocytic Choriomeningitis Virus reduces production of growth hormone.

- Some viruses have a differential effect on the expression of selected host genes.

  Ex: Human cytomegalovirus (CMV) infection changes transcription of 5% of cellular genes and approximately an equal number of genes exhibited enhanced or reduced transcription.



Virus-Cell Interactions

4 – Viral modification of host cell protein synthesis

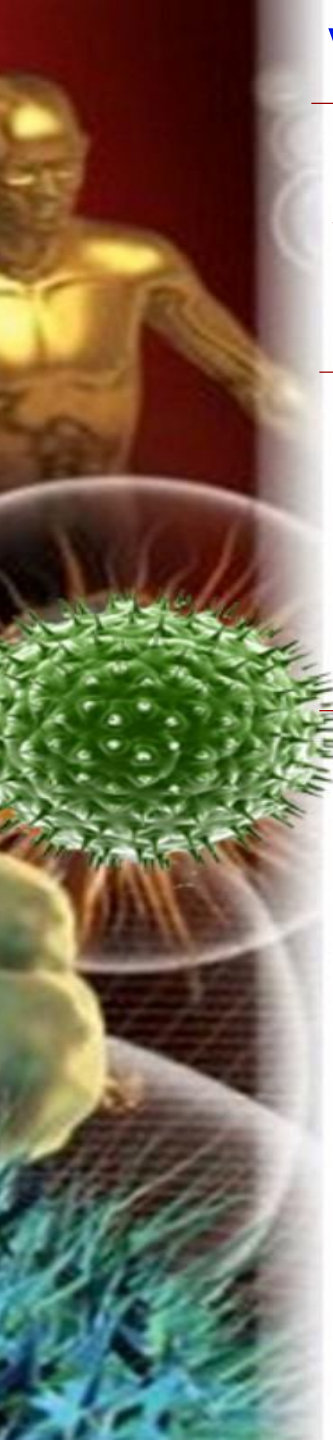
- **Poliovirus and many other picornaviruses contain a viral protease that markedly reduces synthesis of host proteins. The protease cleaves a cellular protein essential for the binding of the ribosome to mRNA.**

5 – Virus-induced alterations in cellular membranes

A – Blocking or downregulation of the cellular receptor for virus

- **Blocking of cellular receptors: Cells infected with avian sarcoma leucosis viruses are known to resist superinfection by other closely related strains of retroviruses (reciprocal resistance).** Shedding of virus protein that occupy the cellular receptors**.**

- **Downregulation of cellular receptors: expression CD4 on the surface of HIV-infected cells is reduced by at least 10-fold in comparison with uninfected cells.**



Virus-Cell Interactions

Virus-induced alterations in cellular membranes

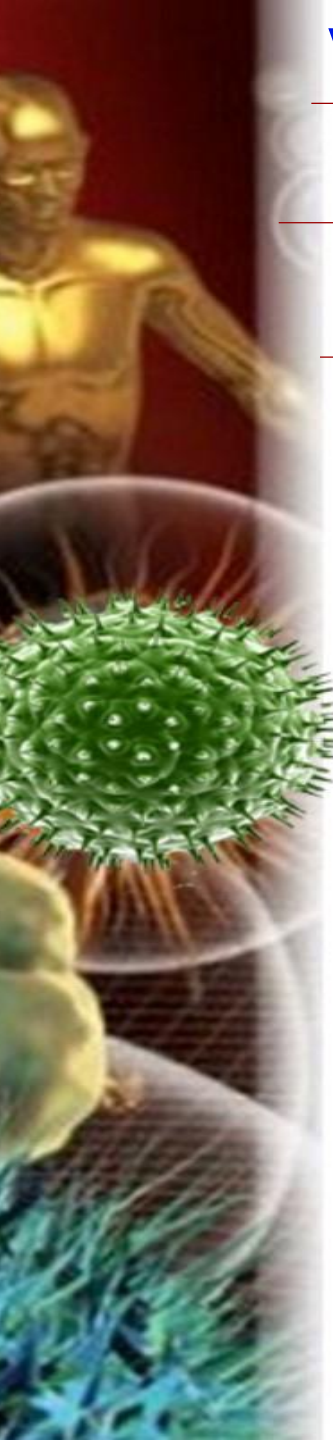
B – Modulation of major histocompatibility complex (MHC) expression

- HIV downregulates MHCI.

C – Viral proteins that serve as ion channels

- Alteration of membrane permeability by the introduction of viral proteins that serve as ion channels.

- When influenza virus is endocytosed during the process of viral entry, the drop in pH leads to the formation of M2 ion channel. This process mediates uncoating and release of RNA.

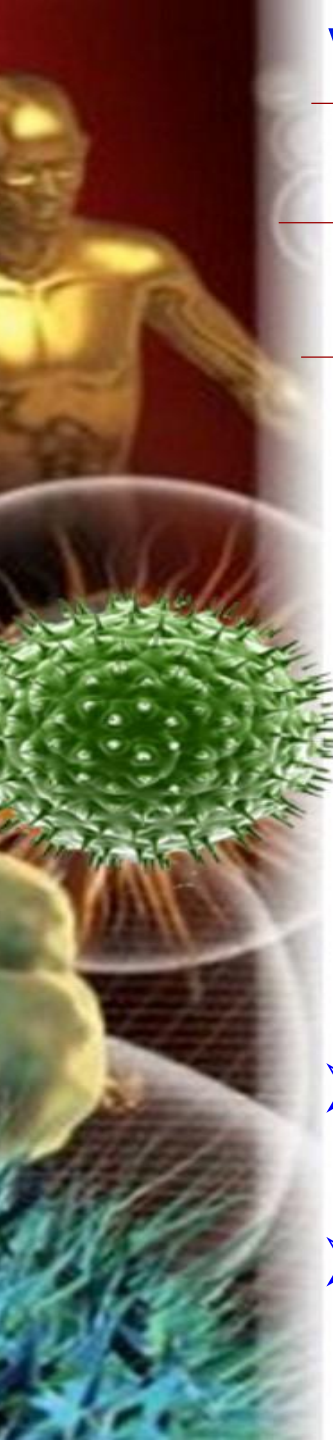


Virus-Cell Interactions

VIRUS-INDUCED CELL DEATH: APOPTOSIS AND NECROSIS

A – Necrosis

- Induced by any severe insult to cells such as heating, cooling, unphysiological pH, other physical or chemical trauma, as well by the action of specific viral proteins.
- Necrotic cells can be identified by loss of membrane integrity with spilling of cellular contents and random degradation of DNA. The residual cellular debris is then engulfed by local phagocytes.
- Ex: Ebola virus

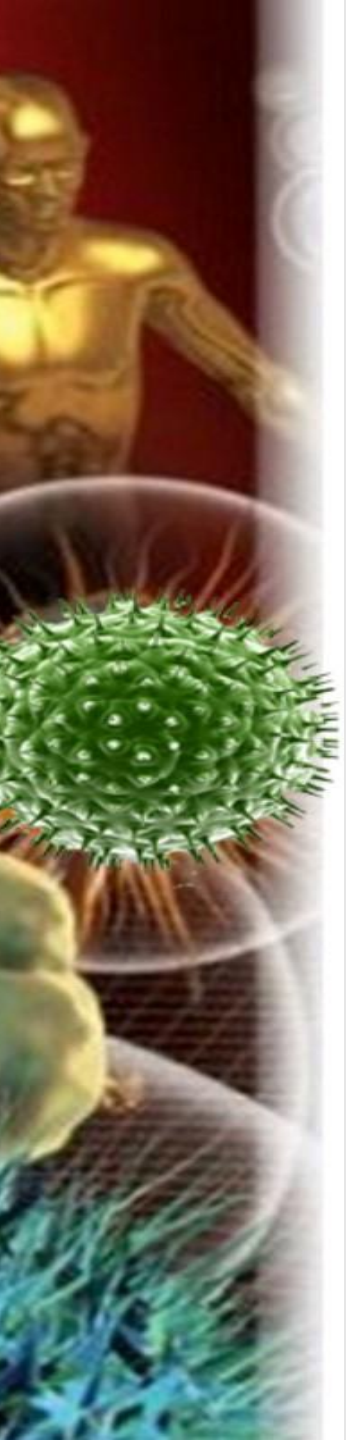


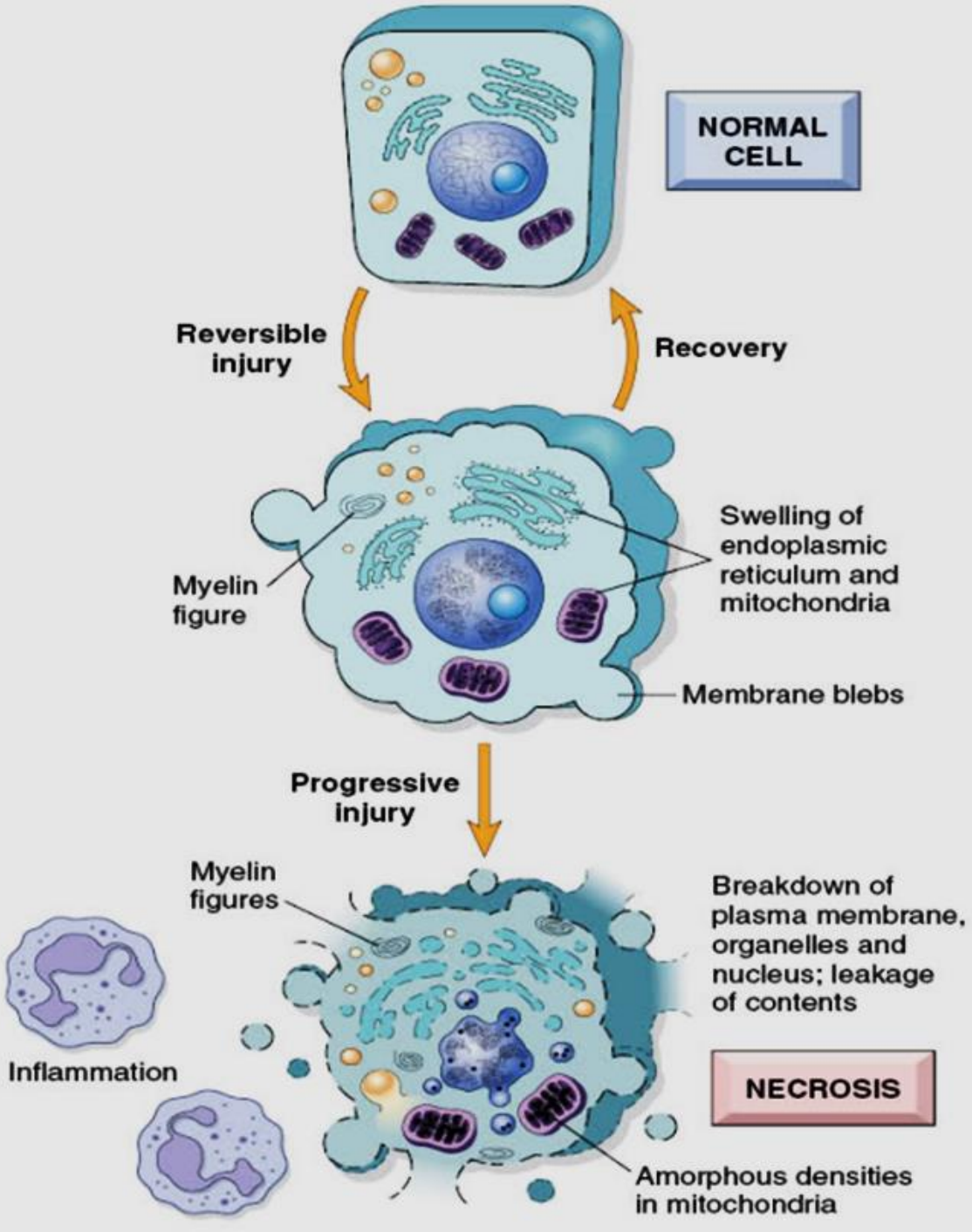
Virus-Cell Interactions

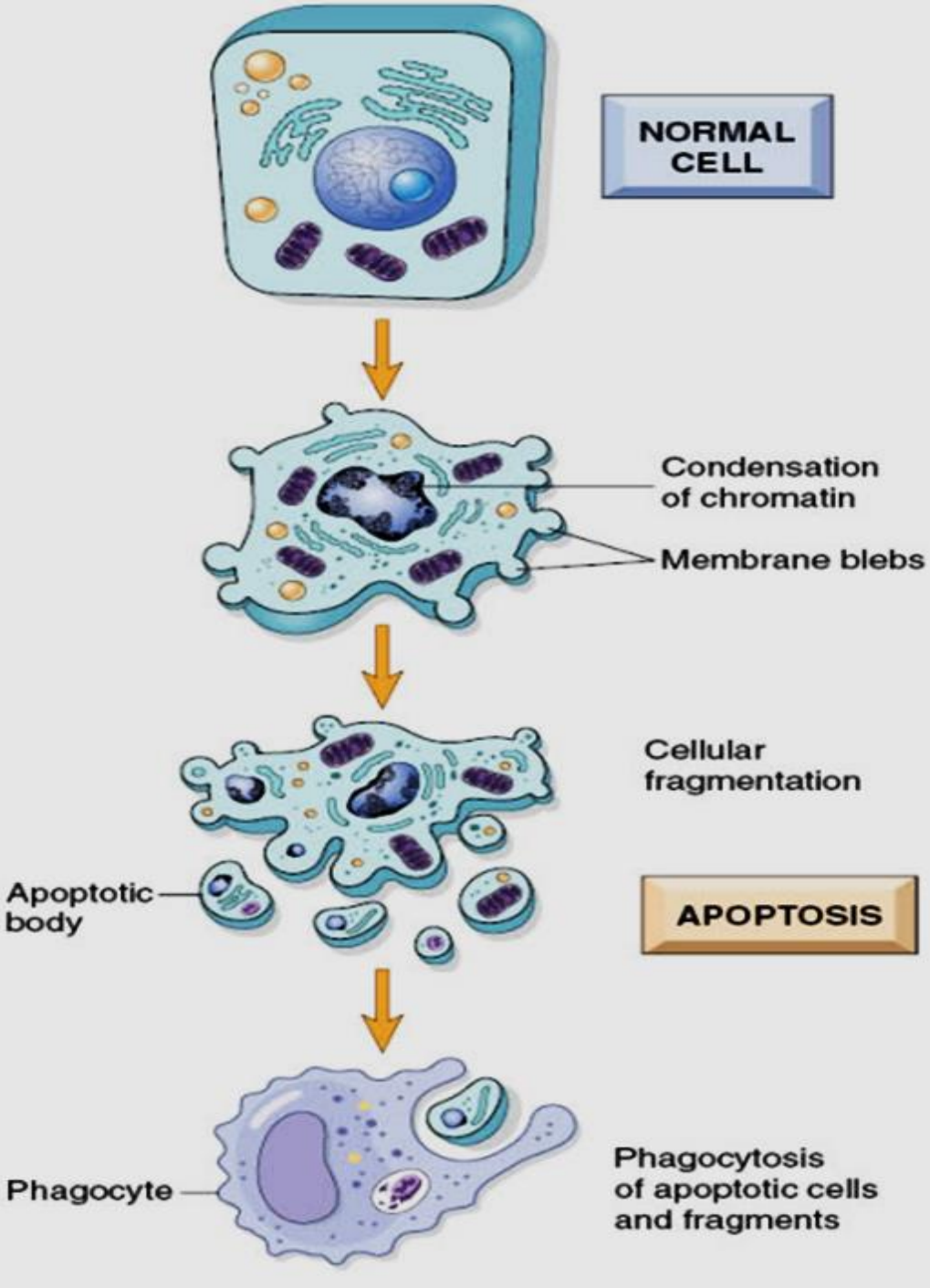
VIRUS-INDUCED CELL DEATH: APOPTOSIS AND NECROSIS

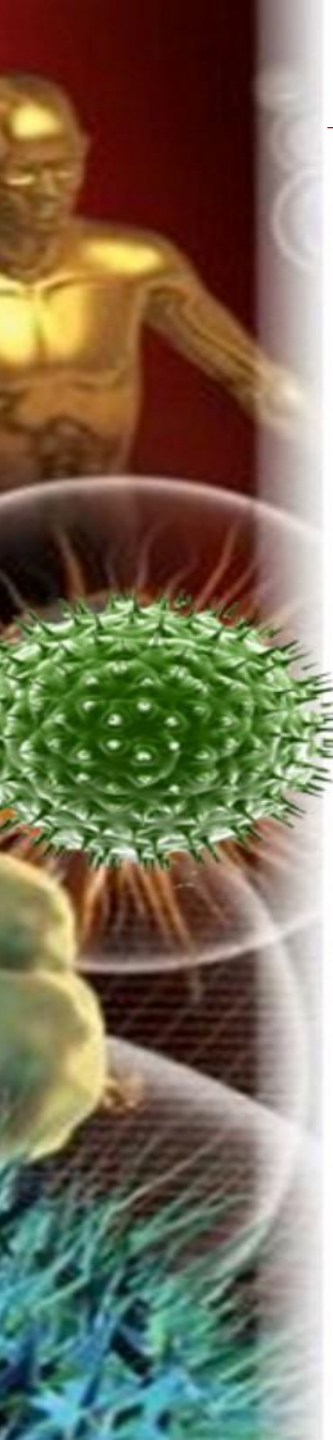
B – *Apoptosis* (programmed cell death)

- Apoptosis is accomplished by a cascade of biochemical steps that produce several morphological stigmata, including blebbing of the plasma membrane (which remains intact in contrast to the membranes of necrotic cells) and condensation of chromatin around the periphery of the nuclear membrane.
- Terminally, the cell shrinks, condenses and breaks up into membrane-bound apoptotic bodies that contain cytoplasm, nucleoplasm or both.
- Ex: Reovirus, HIV, and Adenovirus
- Some viral proteins may induce apoptosis indirectly, by inactivating a host protein that blocks a constitutive cellular apoptosis pathway.




NORMAL CELL
Reversible injury
Recovery
Swelling of endoplasmic reticulum and mitochondria
Myelin figure
Membrane blebs
Progressive injury
Myelin figures
Breakdown of plasma membrane, organelles and nucleus; leakage of contents
Inflammation
NECROSIS
Amorphous densities in mitochondria


NORMAL CELL
Condensation of chromatin
Membrane blebs
Cellular fragmentation
Apoptotic body
APOPTOSIS
Phagocyte
Phagocytosis of apoptotic cells and fragments



Learning outcomes – Reviewing

- Know different stages of virus replication cycle.
- Different ways by which virus interact with host cells.
- Differentiate between apoptosis and necrosis.


Thank
You